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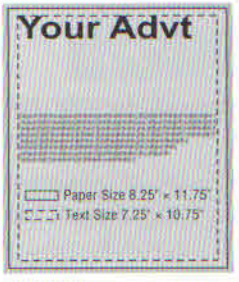

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ORIGINAL ARTICLE

A Simple Biogenic Method for the Synthesis of Silver Nanoparticles using *Syngonium podophyllum*, an Ornamental Plant

[1]Nilesh S Paul, [2]Raman P Yadav

ABSTRACT

The potential of ornamental plant *Syngonium podophyllum* leaf extract has been explored for the synthesis of silver nanoparticles, which was confirmed by appearance of absorption peak at 420 nm in ultraviolet–visible (UV–Vis) spectrum. Silver nanoparticles were predominantly spherical in shape and size observed under scanning electron microscopy (SEM) was in the range of 11 to 26 nm. A sharp signal recorded at 3 keV under energy-dispersive X-ray (EDX) spectrum indicated the presence of elemental silver nanoparticles. Zeta potential was measured as –26.77 mV, which indicated the presence of moderately stable silver nanoparticles in the solution. Under Fourier transform infrared (FTIR), two prominent bands were assigned, i.e., 3,454.89 cm^{-1} represents the O–H stretching vibration and 1,637.46 cm^{-1} represents the –NH stretching vibration of the amide group. It indicates that protein might be responsible for the synthesis.

Keywords: Characterization, Green synthesis, Silver nanoparticles, *Syngonium podophyllum.*

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INTRODUCTION

Silver nanoparticles are one of the most promising products in the nanotechnology industry. Silver nanoparticles are particularly in high demand due to their widespread use. They are also more increasingly known for their healing properties, offering treatment options for various illnesses that cannot be treated with traditional methods. The development of nanotechnology has given new possibilities of using the silver nanoparticles as an active biomedical factor. Therefore, the silver nanoparticle is one of the most used nanoparticles that have gained importance.[1] The most important application of silver nanoparticles is their antimicrobial activities.[2,3] Silver nanoparticles have long been recognized in biomedical applications mainly due to potent antimicrobial activity.[4,5] Advancements in nanotechnology display arena of methods for the synthesis of nanoparticles of various shapes and sizes depending on their specific requirements.[6,7] Presently, physical and chemical methods have their own limitations.[8] Biogenic processes have evolved as a simple and viable option for the synthesis of nanoparticles and have several advantages over the chemical and physical methods.[9,10] Biogenic synthesis of nanoparticles using microorganisms has many drawbacks associated with microbial culture and their maintenance.[11,12] To overcome these limitations, plant systems are potentially advantageous for the synthesis of nanoparticles.[13,14] The present study highlights the new source of plant material, i.e., aqueous extract of *Syngonium podophyllum* leaf, for biogenic synthesis of novel silver nanoparticles. To the best of our knowledge, this is the first report where ornamental plant *S. podophyllum* has been explored for the synthesis of silver nanoparticles.

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MATERIALS AND METHODS

Preparation of Extract

Syngonium podophyllum leaves were obtained from the MGM Institute of Health Sciences, Navi Mumbai. Leaves were washed in running water and twice with sterile distilled water and allowed to dry in air for 2 weeks, to remove the moisture completely. The dried leaves were pulverized well with mortar and pestle to make powder. Leaf extract was prepared by taking 5 gm of powder in 100 mL of deionized water and the mixture was boiled for 10 minutes. The leaf broth was then cooled and filtered with Whatman filter paper No-1. Filtrate was stored in a refrigerator for further use.

Synthesis of Silver Nanoparticles

Silver nitrate ($AgNO_3$) was obtained from Sigma-Aldrich; 3 mM aqueous solution of $AgNO_3$ was prepared; 5 mL of extract was added to 15 mL of 3 mM $AgNO_3$ and allowed to react at 90°C for 25 minutes. A visual color change of the mixture was observed after 20 minutes. The synthesis of the silver nanoparticles in the solution was confirmed by the results obtained from ultraviolet–visible (UV–Vis) spectral analysis.

Ultraviolet–visible Spectroscopic Analysis

The bioreduction of silver ions in aqueous solution was monitored by measuring UV–Vis spectra of the solution. The UV–Vis spectra of these aliquots were monitored as a function of time of reaction on Shimadzu UV–Vis spectrophotometer operated at a resolution of 1 nm. The periodic scan of the absorbance was performed between 200 and 1,100 nm wavelength by using UV–Vis spectrophotometer (Shimadzu).

Scanning Electron Microscopy Analysis

The scanning electron microscope (SEM) analysis was performed with field emission gun (FEG)-SEM, model JSM 7600F, instrument at the Sophisticated Analytical Instrument Facility, Indian Institute of Technology-Bombay, Mumbai.

Energy-dispersive X-ray Spectroscopy

Energy-dispersive X-ray (EDX) spectroscopic study was performed with nanoparticles containing system to determine the elemental composition of silver in the suspension.

Zeta Potential Measurement

To understand the possible charge present on the nanoparticle surface, zeta potential was measured on Zetasizer (Zeta meter Delsa NanoC, Beckman Coulter, Japan).

Fourier Transform Infrared Spectroscopy Measurement

Fourier Transform infrared (FTIR) spectroscopy measurement of sample was performed using Bruker, Germany, Model-3000 Hyperion Microscope with Vertex 80 FTIR System, range: 7,500–450 cm^{-1}. Sample was prepared on KBr pellet and it was allowed to dry. This was then used for characterization.

RESULTS AND DISCUSSION

Visual Observation

Change in color on mixing of plant extract with $AgNO_3$ solution is generally observed by that system which is able to synthesize nanoparticles.[15] The ornamental plant *S. podophyllum* (Fig. 1) is established for the silver nanoparticle synthesis by using a simple process. A distinct change from light turbid yellow color to a brownish color was observed by mixing of aqueous leaf extract of *S. podophyllum* with 3 mM $AgNO_3$ solution at 90°C (Figs 2A and B). The change in color of reaction mixture was very fast and it was recorded within 25 minutes, which indicates the formation of silver nanoparticles. This might be a result of $AgNO_3$ reduction and stimulation of surface plasmon resonance. No precipitation was observed and color change was stable even after completion of the reaction. Dubey et al[16] also demonstrated the use of leaf extract of ornamental plant *Rosa rugosa* for the synthesis of silver nanoparticles.

Fig. 1: Picture of *S podophyllum* plant

Figs 2A and B: Visual observation: (A) Leaf extract of *S. podophyllum;* (B) reaction mixture of $AgNO_3$ solution and leaf extract with silver nanoparticles

Ultraviolet–visible Spectroscopic Analysis

The color change exhibited by the reaction sample during synthesis of silver nanoparticles is due to the excitation of electrons of the transition metal, which affects the absorbance in the UV region. Therefore, the silver nanoparticles synthesized by aqueous leaf extract of *S. podophyllum* were characterized by UV–Vis spectrophotometer. Optical properties of nanoparticles are sensitive to size, shape, concentration, agglomeration state, and refractive index, thus making UV–Vis spectroscopy a valuable tool for nanoparticle identification and characterization.[17] The peak was observed at 420 nm, which corresponds to the absorbance of silver nanoparticles (Fig. 3). Silver nanoparticles generally display unique optical properties in relation to their surface plasmon resonance.

Scanning Electron Microscopy

The morphology and size of the generated silver nanoparticles were analyzed by SEM (FEG-SEM, Model- JSM 7600F). Silver nanoparticles were observed with varied size ranging from 11 to 26 nm (Fig. 4). A number of researchers have analyzed biologically synthesized silver nanoparticles with the help of SEM. Geethalakshmi and Sarada[18] have also used SEM for the characterization of silver nanoparticles synthesized from *Trianthema decandra* extract. The analysis showed that the particles were cubic shaped and the size existed in the range from 25 to 50 nm. Kumar et al[19] have synthesized nanoparticles from silver using *Morus nigra* leaf extract. Scanning electron microscope analysis has indicated that size of generated silver nanoparticles was of 200 nm and appears to be spherical in morphology. Jancy and Inbathamizh[20] have also analyzed $AgNO_3$ solution in its reduced form by using SEM where they have clearly indicated the distinguishable $AgNO_3$ particles (1000 nm size) and silver particles in the bioreduced colloidal suspensions (15–20 nm in size) owing to their size difference.

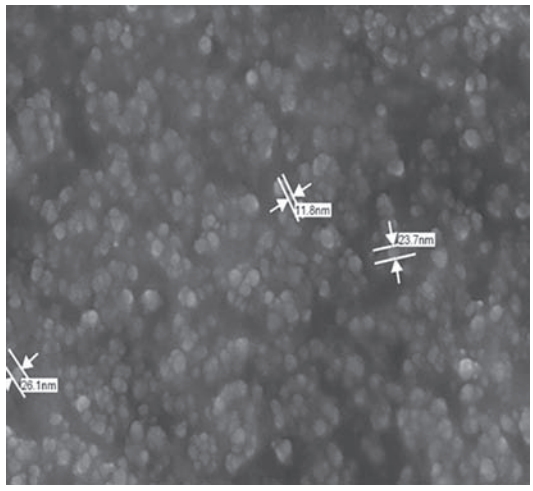

Fig. 4: Scanning electron microscope image of generated silver nanoparticles (scale – 100 nm magnification) by aqueous leaf extract of *S. podophyllum*

Scanning electron microscopic image of silver nanoparticles synthesized by aqueous leaf extract of *S. podophyllum* revealed that these silver nanoparticles are predominantly spherical in shape embedded in matrix.

Energy-dispersive X-ray Spectroscopy

Silver nanoparticles synthesized by aqueous leaf extract of *S. podophyllum* were further characterized by EDX for confirmation of elemental silver nanoparticles in the suspension. A sharp signal was observed at 3 keV of silver nanoparticles along with other peaks in EDX spectrum of 0–10 keV, which indicates the presence of elemental silver nanoparticles in the suspension (Fig. 5). Gajbhiye et al[21] have also used EDX spectroscopy to confirm the presence of elemental silver extracellularly in biologically synthesized silver nanoparticles by common fungus, *Alternaria alternata.* It was confirmed that the presence of elemental silver by the sharp signals with optical absorption band peak in the range of 3 to 4 keV is typical for the absorption

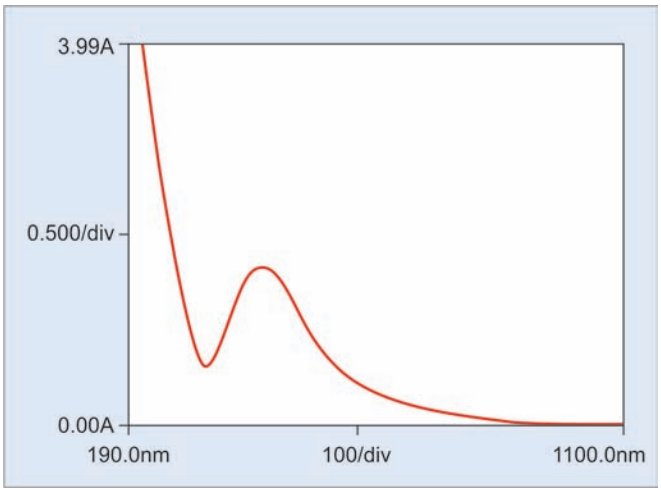

Fig. 3: Ultraviolet–visible absorption spectra of silver nanoparticles synthesized by aqueous leaf extract of *S. podophyllum*

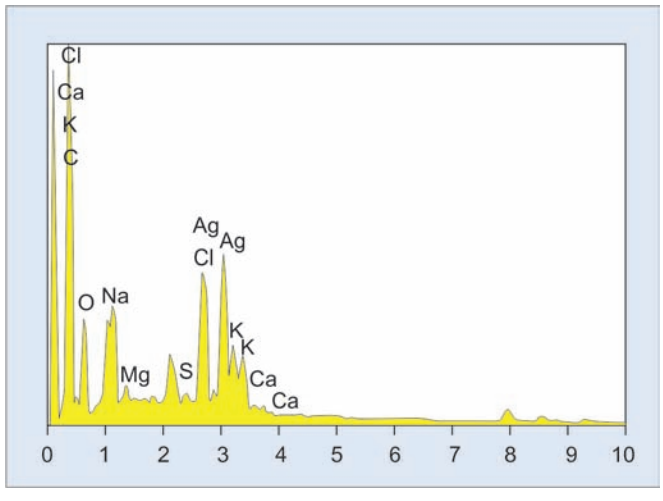

Fig. 5: Energy-dispersive X-ray curve with Ag peak in silver nanoparticle containing system

of metallic silver nanocrystallites. Foroughi and Khalil[22] investigated the synthesis of stable silver nanoparticles by bioreduction method using aqueous extracts of the manna of hedysarum plant and the soaproot (*Acanthe phylum bracteatum*). They have also confirmed the existence of an elemental silver signal in the solution containing silver nanoparticles in EDX spectrum.

Zeta Potential Measurement

In view to know the surface charge of nanoparticles synthesized by aqueous leaf extract of *S. podophyllum* for understanding the parameter, i.e., related to nanoparticle aggregation in dispersion, zeta potential was measured. Electrophoretic mobility of generated silver nanoparticles in the sample was measured as a value of –26.77 mV (Fig. 6). The result clearly showed that silver nanoparticles generated by leaf extract of *S. podophyllum* are moderately stable in the reaction system due to electrostatic repulsion. Plant-based generation of nanoparticles is generally advantageous over others where stable silver nanoparticles can be achieved without adding a different physical or chemical capping agent. Heydari and Rashidipour[23] have also demonstrated a green synthetic approach for the synthesis of silver nanoparticles by utilizing extract of oak fruit hull (Jaft) and characterized the generated nanoparticles using zeta potential for understanding the surface of synthesized nanoparticles and predicting the long-term stability of dispersion. In the absence of any electrolyte in deionized water, the zeta potential value of dispersed synthesized Ag nanoparticles was –25.3 mV.

Fourier Transform Infrared Spectroscopy Analysis

Fourier transform infrared has been widely used to know the nature of surface adsorbents in nanoparticles. Fourier transform infrared spectroscopic studies were carried out to identify possible groups/molecules responsible for the reduction of $AgNO_3$ to silver nanoparticles by aqueous leaf extract of *S. podophyllum*. Representative spectra of generated nanoparticles manifest the various absorption peaks (Fig. 7). The two prominent bands seen at 3454.89 and 1637.46 cm–1 were assigned to the stretching vibrations. The band at 3454 cm–1 represents the O–H stretching vibration. The band at 1637.46 cm–1 represents the –NH stretching vibration of the amide group. The short stretch peaks were also observed at 1458.84, 1383.59 and 1231.43 cm^{-1}. The FTIR results indicate that the protein might be responsible for the formation, capping, and stabilization of silver nanoparticles. Sathyavathi et al[24] also demonstrated FTIR spectra of aqueous silver nanoparticle preparation synthesized from *Coriandrum sativum* leaf extract. It has been confirmed by infrared spectroscopic study that the carbonyl group has the ability to form amino acid residues and proteins that strongly binds to metals, which suggests that proteins prevent agglomeration of metallic nanoparticles possibly by forming an outer layer of covering (i.e., capping of silver nanoparticles). Kalishwaralala et al[25] have demonstrated biosynthetic approach of silver and gold nanoparticle synthesis using *Brevibacterium casei* and characterized using FTIR analysis to identify the possible (protein) biomolecule responsible for capping and efficient stabilization of the synthesized metallic nanoparticles from *B. casei.*

CONCLUSION

Although number of plant-based biological processes have already been established for the synthesis of silver nanoparticles, still a search for new source for the synthesis of silver nanoparticles is fascinating aspect of research. We have reported the synthesis of silver nanoparticles using new source of plant material, i.e., aqueous leaf

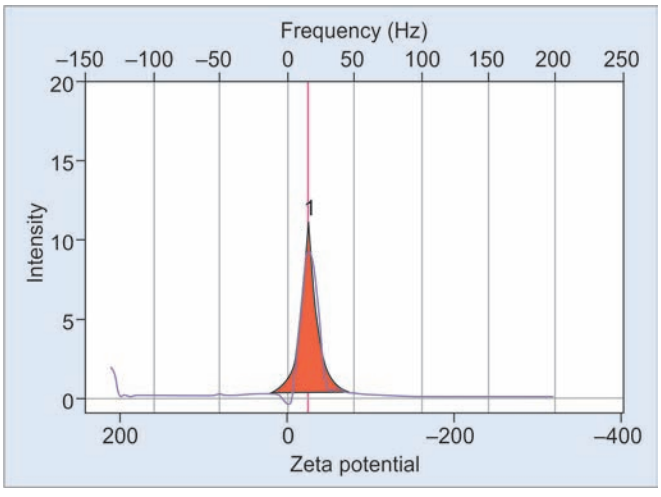

Fig. 6: Zeta potential of silver nanoparticles generated by leaf extract of *S. podophyllum*

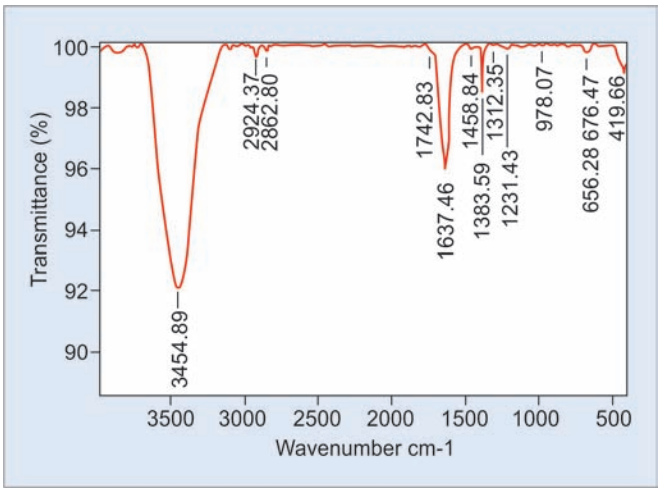

Fig. 7: Fourier transform infrared spectra of silver nanoparticles generated by aqueous leaf extract of *S. podophyllum*

extracts of ornamental plant *S. podophyllum.* This biogenic process provides a simple, fast, and efficient way for the generation of silver nanoparticles. These silver nanoparticles are moderately stable at room temperature. The FTIR study suggests that the protein might play an important role in the synthesis and stabilization of silver nanoparticles. The work carried out in the current article can pave the way toward the new prospective acceleration to fulfill demands of newer ecological, green chemistry-based method for the synthesis of silver nanoparticles.

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ORIGINAL ARTICLE

Red Blood Cell Count: Brief History and New Method

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ABSTRACT

Introduction: Red blood cells (RBCs) were observed under microscope by Jan Swammerdam in 1658. The RBC count was done in 1852 by Professor Karl Vierordt from Germany for the first time almost after 192 years. After this, the other scientists have also done RBC count with different methods. Hayem used a new diluting fluid (Hayem's diluting fluid) for RBC count which is used even today. The present methods have many errors mainly due to sampling, diluting, and pipetting.

Materials and methods: In this study, the modified method of RBC counting has been shown. The RBC counting was done using hemoglobinometer pipette and modified diluting fluid – Hayem's fluid mixed with Leishman's stain (HFLS) RBC diluting fluid – in the ratio of 97.5 mL of Hayem's RBC diluting fluid and 2.5 mL of Leishman's stain to make 100 mL. Amber colored glass bottle top dispenser was used to dispense 2 and 4 mL of diluting fluid into the glass test tubes .With aseptic precautions, 10 and 20 µL of blood samples were collected by using the hemoglobinometer pipette (marked with black marker pen to get accurate measurement for 10 µL) from finger prick with sterile needle. The blood samples were added to the glass test tubes containing HFLS RBC diluting fluid and mixing was done with a glass stirrer. With the help of glass capillary tube, Neubauer chambers were charged and observed under microscope.

Results: Red blood cells were seen better. The RBCs retained their shape and size even after 96 hours when the blood samples mixed with HFLS RBC diluting fluid were kept at room temperature.

Conclusion: Red blood cells were seen better with this method and diluting and charging errors were minimized.

Keywords: Glass bottle top dispenser, Hayem's red blood cell diluting fluid, Hemoglobinometer pipette, Leishman's stain, Red blood cell count.

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INTRODUCTION

Red blood cell (RBC) count is done as a part of complete blood examination for diagnostic and prognostic purposes. The RBC count is also one of the hematological experiments in physiology performed by students. Presently, the students are using hemocytometer for doing total RBC count, which contains Neubauer's chamber and the RBC pipette. The dilution fluid used is Hayem's fluid, which is colorless. The principal of this method is based on diluting the blood with Hayem's fluid and then counting the RBCs.

Historical Background

Jan Swammerdam, a Dutch naturalist, was the first person to see RBCs under the microscope in 1658, followed by Antoni van Leeuwenhoek in 1695. In next 150 years, in medical history, despite the availability of stains like iodine, suffron, and ammonia carmine for staining tissues and cells, there was no advances made in knowledge of morphology of blood cells or counting of blood cells.[1,2]

Professor Karl Vierordt from University of Tubingen performed the first blood counts in 1852 and laid the foundation of laboratory study of hematology as an aid to clinical diagnosis.[3] He used a glass capillary of known diameter whose capacity could be measured and the blood was blown on a slide covered with a thin smear of albumen. Micrometer was used to do the RBC count under microscope. Later, he improved the method by diluting the blood with a solution of gum arabic and his methods were fairly accurate. In 1855, Cramer made an improvement by pipetting diluting fluid and blood separately into a mixing vessel. He used the principle of capillary space using a glass slide and two strips of glass of equal and known thickness to count the RBCs. Pierre-Carl Joseph Potain invented the diluting pipette, similar to the RBC pipette used at present.[3] Louis-Charles Malassez devised a method of RBC counting in a length of capillary tube (elliptical in cross section).[3,4] Dreyfuss gave Georges Hayem the title, Father of Hematology.[4] At present, Hayem's RBC diluting fluid is still the most commonly used fluid to do RBC count.[5]

Sir William Richard Gowers modified the counting chamber with the principle of ruling the floor of the counting chamber.[6,7] Richard Thoma made an important improvement in the counting chamber. Thoma pipette is the common diluting pipette used today. Later, Thoma devised a separate leukocyte pipette.[8] Alferow devised

a counting chamber with a detachable coverslip and this was filled by capillary action.[9] McMunn[3] in 1903 used photography as an aid to accurate counting. Burker modified the counting chamber. Max Levy Company from Philadelphia modified the hemocytometer by making it from a single block of glass.

In 1921, Dreyer[10] described a modified method to do blood count and he diluted 0.1 mL blood in 19.9 mL diluting fluid to do RBC counting. Many errors in blood cell counting have been described by Abbe, Lyon and Thoma, Berkson, Nouvel, Lavergne, Biggs and McMillan, Lancaster and White.[3,11-14] The above methods are having error due to sampling, diluting, and pipetting. The error in RBC counting is 15 to 30%.[11-15] In recent years, unopette system has been used to do RBC count.[16]

Students often face difficulty in counting the RBCs as they could not see properly because they are not stained. In an earlier study, we have shown that RBCs are better visualized using Hayem's fluid mixed with Leishman's stain (HFLS) as a diluting fluid.[17] In the present modified method, students will find it easy to perform the procedure because of easy dilution method and identification of stained RBCs. A bottle top dispenser is used to deliver each time an accurate predetermined volume of the HFLS diluting fluid into a glass test tube.[18]

MATERIALS AND METHODS

Materials

(1) Hemocytometer (Fig. 1); (2) Hayem's fluid with composition of sodium chloride – 2 gm, sodium sulfate – 4.4 gm, mercuric chloride – 1 gm, distilled water – 400 cc (1 and 2 purchased from Fisher Scientific Qualigens Company); (3) Leishman's stain that contains methylene blue and eosin – 0.15 gm of dry stain slowly made up to 100 mL with acetone-free methyl alcohol (from Ranbaxy Fine Chemicals Limited); (4) Modified diluting fluid (HFLS RBC diluting fluid/Hayem's fluid mixed with Leishman): 390 mL of Hayem's fluid mixed with 10 mL of Leishman's stain, so total volume is 400 mL (in the ratio of 97.5 mL of Hayem's RBC diluting fluid and 2.5 mL of Leishman stain to make 100 mL); (5) Hemoglobinometer pipette (Hb pipette) has a mark for 20 µL. This pipette has been marked with a marker pen for 10 µL; (6) Amber colored glass bottle top dispenser (Fig. 2) with graduations for different volumes; (7) Sterile needle; (8) 5 mL glass test tubes; (9) Glass capillary tubes; and (10) Microscope.

Methods

Modified Method of Total RBC count

- In this method Hb pipette is used instead of RBC pipette to take an accurate volume of blood (10 and 20 µL).
- Hayem's fluid mixed with Leishman's stain RBC diluting fluid is used instead of Hayem's fluid.
- Specific amount of HFLS RBC diluting fluid of 2 and 4 mL is delivered into glass tubes using an amber colored glass top bottle dispenser which has graduations for different volumes. This will reduce the errors in dilution. It will also reduce pipetting and mixing errors which occur with the use of RBC pipette.
- Mixing of the blood with the HFLS RBC fluid can be done with glass stirrer and also by tilting the test tube upside down 4 to 5 times.
- The glass capillary tube is used for charging the Neubauer chamber which reduces the charging error.

The HFLS RBC diluting fluid was mixed well and stored in the amber colored glass dispensing bottle. This mixture is used as diluting fluid. 2 and 4 mL of this diluting fluid were taken in two different glass test tubes and these were kept in a rack. With aseptic precautions finger prick was done and blood was collected with the Hb pipette. 10 µL (with Hb pipette marked for 10 µL) and 20 µL of blood was collected and this blood was transferred to the glass test tubes containing 2 and 4 mL of HFLS RBC diluting fluid respectively. The dilution of blood in both

Fig. 1: Materials in conventional method

Fig. 2: Materials in new method

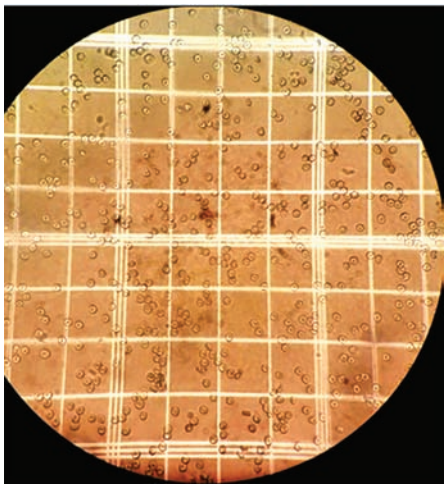

Fig. 3: Magnification 40× for 10 µL

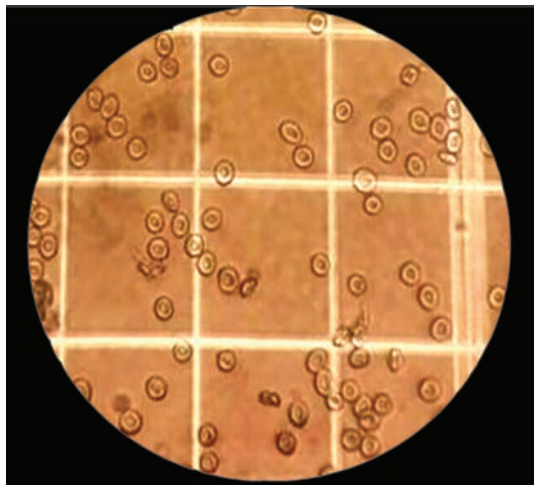

Fig. 4: Enlarged view

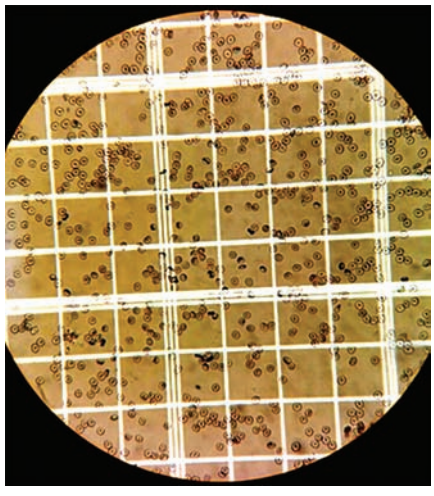

Fig. 5: Magnification 40× for 20 µL

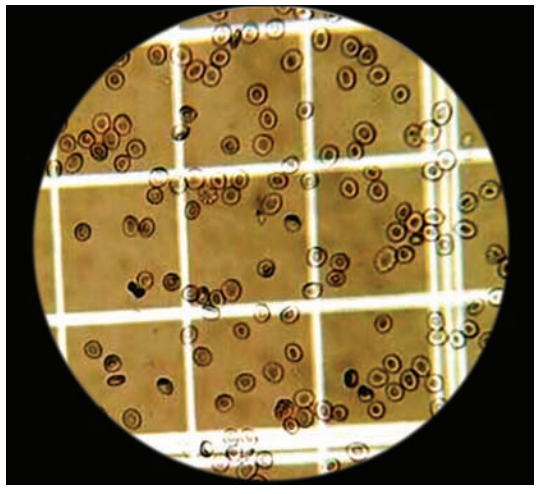

Fig. 6: Enlarged view

the glass test tubes was 1:201. With the help of capillary tube the fluid containing blood sample mixed with HFLS RBC diluting fluid was taken and the charging of the Neubauers chamber was done. Under 10× and 40× magnification RBCs were observed.

RESULTS

The RBCs were seen under 10× and 40× magnification and were seen clearly. Their shape and size were normal. The RBC count was done under 40× magnification. They were seen after taking sample (blood mixed in the HFLS RBC diluting fluid) and charging Neubauer's chamber at 24, 48, 72, and 96 hours. The RBCs retained their shape and size throughout the study period (even after 96 hours). There was no clumping of RBCs (Figs 3 to 6).

DISCUSSION

In this modified method, HFLS RBC diluting fluid is used for better visualization of RBCs. Sodium chloride maintains isotonicity. Sodium sulfate maintains the size and shape of the RBCs. The eosin present in the diluting fluid stains the RBCs which helps in their easy identification. Mercury chloride acts as a preservative. For easy and accurate delivery of diluting fluid into the glass test tubes, a dispenser bottle is used. For obtaining an accurate volume of blood, hemoglobinometer pipette is used instead of RBC pipette. Also smaller volume of blood sample (10 µL) can be obtained with hemoglobinometer pipette. There is better mixing of the blood with the diluting fluid in the glass test tube than in the RBC pipette. With the use of glass capillary tube, charging the Neubauer chamber is easy and overflow is avoided.

CONCLUSION

The application of modified method with HFLS RBC diluting fluid is useful. It can be used for optimum visualization and counting of RBCs.

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ORIGINAL ARTICLE

Seroprevalence of *Mycoplasma pneumoniae* among Patients with Community Acquired Pneumonia in a Tertiary Care Hospital at Navi Mumbai

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ABSTRACT

Community-acquired pneumonia (CAP) is often clinically classified as typical or atypical. *Mycoplasma pneumoniae* is the primary causative organism responsible for atypical pneumonia, which constitutes 10 to 20% of all pneumonia cases. Although prevalence studies have been performed extensively abroad, in India, such work has been seldom carried out. The present seroprevalence study carried out with this fact has shown 12.6% IgM and 16.0% IgG prevalence of the mycoplasma antibodies in the locality. These findings will encourage in undertaking further extensive study on this self-replicating unique bacterium.

Keywords: Antibodies, *Mycoplasma pneumoniae*, Prevalence.

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INTRODUCTION

Mycoplasma pneumoniae is a unique bacterium that did not always receive attention considering the difficulties in cultivation, though it causes number of diseases and high degree of morbidity and mortality associated with it, both in children and adults.[1] *Mycoplasma pneumoniae* represent the smallest self-replicating bacterium. Since its initial description in 1940s, an eventual elucidation as a highly evolved pathogenic bacterium, it is now recognized as an exclusively human pathogen, existing in close association with the epithelial cells of the host respiratory tract.[1] It is known to be causing infections in humans for many decades now. Eventually, it has come up to become the second most common etiological agent of community-acquired pneumonia (CAP) after *Streptococcus pneumoniae*.[2] Reports of disease burden from United States mention average incidence of *M. pneumoniae* as 30.6% of CAP and is responsible for more than one lac hospitalizations each year, thus, stating it as a well-recognized pulmonary pathogen in the West.[3] Studies from India (Delhi and Chennai) mention average disease burden of 28.6% pneumonia cases.[4] Search of published literature did not reveal any similar studies having been carried out in Navi Mumbai. The current study is undertaken to find out the seroprevalence of this bacterium in a Tertiary Care Center of Navi Mumbai.

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MATERIALS AND METHODS

The study was conducted in a Tertiary Care Center of Navi Mumbai, Maharashtra, India. A total of 150 patients with CAP diagnosed on clinical, radiological basis, and blood counts were included.

Sample Collection

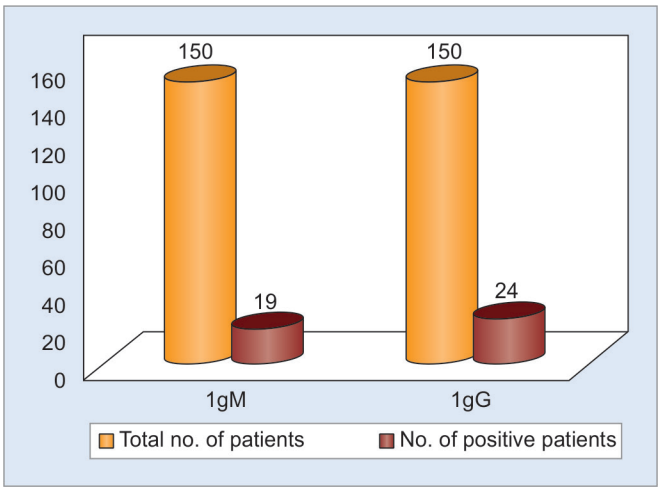
Using all the sterile precautions, 2 to 3 mL of venous blood sample was collected by venepuncture. Plain tubes were used to collect blood. After collection, serum was separated and transferred into sterile Eppendorf tubes. These were then stored at –80°C till further processing.

Sample Processing

ERION enzyme-linked immunosorbent assay (ELISA) *classic Mycoplasma pneumoniae* IgM/IgG (VIRION/SERION, Germany), a commercial qualitative and quantitative assay for detection of *M. pneumoniae* antibodies in human serum or plasma, was used. The procedure was adopted as per manufacturer's instructions.

In Case of IgM Detection

Serum samples were pretreated with rheumatoid factor absorbents prior to IgM detection. For this rheumatoid factor absorbent was diluted 1:4 by adding 200 µL of Rf-absorbent to 800 µL of dilution buffer. Patient serum was then diluted 1:101 by distributing 10 µL of serum into 1 mL of the above diluted Rf-absorbent. It was then mixed well by vortexing and incubated for 15 minutes at room temperature.



Graph 1: Presence of IgM and IgG antibodies to *M. pneumoniae* among patients

In Case of IgG Detection

Serum samples were diluted 1:101 by distributing 10 µL of serum into 1 mL of dilution buffer. It was then mixed well by vortexing.

Brief procedure: Pipette diluted samples and control/standard sera into designated microtest wells (100 µL) and incubate for 60 minutes at 37°C in moist chamber. This was followed by four washes with 300 µL of Wash buffer each time. Pipette conjugate solution alkaline phosphatase conjugate (APC) (100 µL) and incubate for 30 minutes/37°C in moist chamber. Repeat washing step. Pipette substrate solution pNPP (100 µL) and incubate for 30 minutes at 37°C in moist chamber. Pipette stopping solution STOP (100 µL) and read absorption at 405 nm.

RESULTS

The patients included in the study (n = 150) were screened for the presence of IgM and IgG antibodies to *M. pneumoniae*. IgM antibodies to *M. pneumoniae* were found positive in 19 out of 150 cases (12.66%), p-value 5.976E-20, i.e., <0.05 (significant). IgG antibodies to *M. pneumoniae* were found positive in 24 out of 150 cases (16%), p-value 8.204E-17, i.e., <0.05 (significant) (Graph 1).

DISCUSSION

The observations made in the study show that *M. pneumoniae* infections are present in this part of the country as well. The prevalence percentage found for IgM was 12.66% (19 cases) and IgG was 16% (24 cases). Thus, there is possibility of pneumonia caused by *M. pneumoniae* alone and are in combination with other pathogens. Routine screening of the organism by adopting the simple methods will help monitoring the presence of this bacterium.

The current study is in concordance with Basil et al,[5] who found the seroprevalence of *M. pneumoniae* in 16 out of 100 cases (16%) in their study in Delhi, India. Chaudhry et al,[6] from Delhi, India studied 134 patients, of these 26 (19%) were positive for antibodies against *M. pneumoniae* by ELISA test. This is in accordance with the present findings. Kashyap et al[7] in Delhi, India found the prevalence of *M. pneumoniae* by ELISA to be 21.3% (16 out of 75 cases) whereas Sahoo et al,[8] in Mangaluru, India found a 37% prevalence by ELISA. This difference in the prevalence of *M. pneumoniae* infections among various workers could be due to various reasons like patient study group, age and sex distribution, and the predisposing factors. The spread of *M. pneumoniae* infections in the community is by means of droplet infections and fomites. Viability and spread of *M. pneumoniae* from one patient to another may depend on environmental and climatic conditions like temperature, humidity, and season. Lastly, the health education of the patients regarding prevention of the disease and implementation of aseptic procedures by the health care workers and doctors may be responsible for variation in the prevalence.

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ORIGINAL ARTICLE

A Prospective Comparative Study of Post Total Knee Arthroplasty Pain Management by Epidural *vs* Local Infiltration

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ABSTRACT

In a randomized controlled trial, we compared whether local infiltration analgesia would result in better pain management after total knee arthroplasty (TKA) than epidural analgesia (EA). Two groups were made with 30 patients each. Group local infiltration analgesia (LIA) with a total of 30 patients (mean age of 65 years) received LIA with a periarticular injection of a mixture of ropivacaine, adrenaline, and ketorolac that was prepared under strict sterile conditions. In group EA, 30 patients (mean age of 67 years) were given EA. There was no statistically significant difference of pain at rest. The mean opioid consumption was higher in those receiving local infiltration. Most secondary outcomes were similar, but EA patients had lower pain scores when walking and during continuous passive movement. If EA is not readily available, local infiltration provides similar length of stay and similar pain scores at rest following TKA.

Keywords: Epidural analgesia, Local infiltration analgesia, Pain management, Total knee replacement, Visual analog scale.

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Conflict of Interest: None

INTRODUCTION

Total knee arthroplasty (TKA) is a common surgical procedure but is painful and requires careful management in order to balance patient comfort and early postoperative function. Traditional methods of pain management, such as the use of parenteral opioids provide inadequate pain relief and are limited by excessive adverse effects. Epidural analgesia (EA) is used in many institutions and can provide good pain control. However, the failure rate with EA approaches 20% and is commonly associated with adverse effects, such as excessive motor block.[1]

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The more recent use of peripheral nerve blocks, such as continuous femoral block, has been shown to provide pain control equivalent to epidural techniques, and with fewer adverse effects, especially when used as part of a multimodal analgesic regimen.[2] Consequently, the use of continuous femoral block in this context has come to be regarded by many to be the gold standard for pain relief after TKA.[3] An initial bolus of ropivacaine 2 mg/mL and subsequent infusion[4,5] of ropivacaine 1 to 2 mg/mL injected around the femoral nerve provides not only very good postoperative pain relief but also ready mobilization on the evening of and days after surgery.

Local infiltration analgesia (LIA) at the surgical site has become relatively common for a number of surgical procedures and can produce effective analgesia and has the advantage of relative simplicity compared with other regional anesthesia techniques.[6] Subsequently, an effective protocol for LIA was developed and then shown to provide effective pain control and ability to ambulate in a series of 86 patients having TKA.[7] Since then, there have been 20 further studies in which several studies demonstrated improved pain control and reduced adverse effects with the LIA technique compared with placebo. Currently, a few studies have been compared LIA with other regional anesthesia techniques; two studies with EA and two with continuous femoral nerve block (FNB).

A recent observational study[8] quantified the incidence of persistent pain as 36% after primary knee arthroplasty, and showed that the most important independent predictor of persistent pain was the degree of pain relief in the first week after operation.

MATERIALS AND METHODS

A total of 60 patients were consecutively assigned alternately. All patients were operated with regional anesthesia: The local infiltration anesthesia group with spinal anesthesia and the epidural anesthesia group with spinal or epidural anesthesia. Thirty patients were assigned to the epidural anesthesia group with postoperative pain relief by infusion of local anesthetics (ropivacaine 2 mg/mL) through a lumbar epidural catheter introduced preoperatively. Another 30 patients were assigned to the local infiltration anesthesia group for postoperative

pain relief with a mixture of ropivacaine 2 mg/mL, 150 mL; adrenaline 0.1 mg/mL, 5 mL; and ketorolac 30 mg/mL, 1 mL (a total of 156 mL) that was prepared under strict sterile conditions. The mixture was distributed into three 50 mL syringes. The patients were operated under spinal anesthesia (bupivacaine 5 mg/mL, 3–4 mL). Ropivacaine is new local anesthetic drug i.e., considered less toxic and has replaced bupivacaine as the local anesthetic of choice.[8] We added adrenaline to ropivacaine for infiltration in the knee intraoperatively, as described by Kerr and Kohan.[7] Ketorolac was added to supplement analgesia.

A visual analog scale (VAS) (Fig. 1) is a pain measurement instrument i.e., used to measure the intensity of pain. Using a ruler, the score is determined by measuring the distance (mm) on the 10-cm line between the "no pain" anchor and the patient's mark, providing a range of scores from 0 to 10. A higher score indicates greater pain intensity. Based on the distribution of pain VAS scores in postsurgical patients who described their postoperative pain intensity as none, mild, moderate, or severe, the following cut points on the pain VAS have been recommended: No pain (0–4 mm), mild pain (5–44 mm), moderate pain (45–74 mm), and severe pain (75–100 mm).[9]

Surgical Technique

Surgery in both groups was performed using a tourniquet with pressure between 250 and 300 mm Hg. Average surgical time was 71 minutes. All patients had intravenous (IV) antibiotic prophylaxis given approximately 30 minutes preoperatively. A straight anterior skin incision and a medial parapatellar arthrotomy were used. The femoral bone cuts were made with the help of an intramedullary guide, and the tibial cuts with an extramedullary guide. Bone resections were cleaned with pulsative lavage. We used the PFC prosthesis (DePuy) with an all-poly tibial plateau, and all parts were fixed with cement with gentamicin (Palacos R+G; Heraeus Medical, Hanau, Germany).

Local infiltration anesthesia was performed in the following order:

- After preparation of the bone and before cementing the components, the posterior aspect of the capsule was infiltrated with 52 mL of the mixture.
- After cementing the components, the second syringe containing 52 mL was infiltrated in the structures medially and laterally and in the capsules.
- The capsule was closed and the last 52 mL was infiltrated in the front of the capsule, subcutaneously and in the skin after closure. Every patient had a drain. The same regime for postoperative oral analgesia was used in both groups. Low-molecular-weight heparin (0.6 mg) was given subcutaneously for 3 days, starting 1 day preoperatively.

Evaluation

Both groups were followed according to the same protocol. Pain was assessed using the VAS once an hour for 4 hours postoperatively, and then every fourth hour until 8 am on postoperative day 2. Intravenous analgesia, if used, was also registered with details of dosage and time given.

Patient Satisfaction

When pain registration was discontinued at 8 am on postoperative day 2, patients were asked to give their opinion regarding the postoperative pain control method. The options were "very satisfied," "satisfied," "acceptable," and "not satisfied."

Functional Recovery

Patient progress was documented daily by the patient's physiotherapist regarding active range of motion, what postoperative day the patient independently moved in and out of bed, and what postoperative day the patient walked independently with crutches or walking frame. The number of patients with an extension defect of >5° on postoperative day 1 and at discharge was recorded. Range of motion was measured with a short-arm goniometer. Time spent in the recovery room (minutes) was recorded, as were number of days until discharge.

Acceptability

Visual analog scale for measuring pain was found to be quite acceptable to patients. Some older patients with cognitive impairment had difficulty in understanding and therefore completing the scale needed supervision to measure the score.

Reliability

Test–retest reliability has been shown to be good, but higher among literate ($r = 0.94$, $p = 0.001$) than illiterate patients ($r = 0.71$, $p = 0.001$) before and after attending a rheumatology outpatient clinic.

Ability to detect Change

In patients with chronic inflammatory or degenerative joint pain, the pain VAS has demonstrated sensitivity to changes in pain assessed hourly for a maximum of 4 hours and weekly for up to 4 weeks following analgesic therapy ($p = 0.001$).

RESULTS

There was no difference between groups in terms of pain. The mean pain score was 5.5 (local infiltration) and 4.2 (EA) (Table 1). Among 30 patients receiving local infiltration,

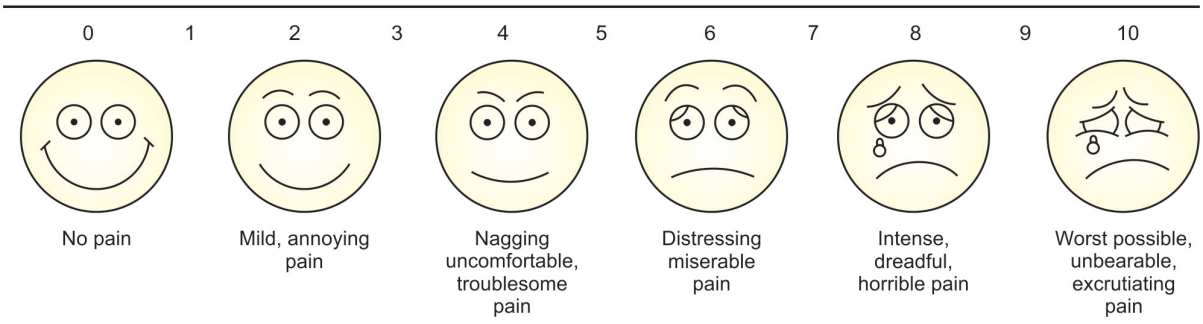

Fig. 1: Visual analog scale

3 also received IV analgesia and 1 received EA because of high pain scores. Among 30 EA patients, none received any extra analgesia for pain relief.

A difference in pain during walking between the groups was detected in the model. The β estimate for the treatment effect implies that the local infiltration group had a mean pain during walking of 0.81 points higher than did the EA group (p = 0.0084).

A borderline difference between the groups in pain during physiotherapy was detected. The β estimate for the treatment effect implies that the local infiltration group had a mean pain score during physiotherapy of 0.55 points higher than did the EA (p = 0.0951).

A difference in pain while using continuous passive movement (CPM) between the treatment groups was detected. The β estimate for the treatment effect showed that the local infiltration group had a mean pain score during CPM of 0.88 points higher than did the EA group (p = 0.0132) Table 1.

One adverse event was reported to our Institutional Review Board. This patient had received local infiltration and developed infection and had to be taken for wound wash. This was judged not to be related to participation in the study because it occurred on the 5th postoperative day.

Table 1: Pain score

Groups	*Mean age*	*Mean pain score (VAS)*	*Pain score with physiotherapy*	*Pain score with CPM*
EA	67	4.2	5.6	6.5
LIA	65	5.5	6.1	7.4

DISCUSSION

Although the primary outcome was similar in both groups, some secondary outcomes favored EA. Epidural analgesia patients had statistically significantly better pain control while walking and during CPM, although the difference was <1 on a scale of 0 to 10. A recent study reported similar pain scores with local infiltration compared with continuous FNB[10] and recommended the former as a cheaper and easier alternative. Dalury et al[11] reported that local infiltration following total knee replacement (TKR) provided better analgesia than conventional pain management. Busch et al[12] found that local infiltration reduced patient-controlled epidural anesthesia (PCEA) use and improved patient satisfaction. Kehlet and Andersen[13] reviewed 14 studies and found support for local infiltration with a single injection, but not via a wound catheter. Limitations noted for many of the studies included the inadequate assessment of pain and unsatisfactory quality comparators, such as inadequate analgesic regimens for the controls or the use of nonsteroidal anti-inflammatory drugs (NSAIDs) in patients receiving local infiltration but not among controls. The effect of local infiltration on length of stay was unclear in these studies. McCartney and McLeod[14] emphasized that only 4 of 21 studies of local infiltration after TKR compared it with other regional analgesic techniques, either PCEA or continuous FNB. Local infiltration provided better analgesia than either FNB or PCEA, but criticisms included the administration of NSAIDs to the local infiltration groups and complications associated with local infiltration. Raeder[15] commented on a study that found that local infiltration provided better analgesia than intrathecal morphine along with IV PCEA,[16] but this comparator was considered suboptimal. Local infiltration was deemed promising, but research was advocated both to identify the roles of each individual component of local infiltration and to compare it with the best potential alternatives. Our study addresses many of these criticisms by comparing local infiltration with an excellent alternative (PCEA) using NSAIDs in both groups, and using many detailed and validated outcome measures, analyzed at many time points.

Local infiltration might be better suited for patients for whom EA is contraindicated. Further research is also needed to determine whether the addition of a nerve block to local infiltration would improve postoperative analgesia. For institutions in which EA is not readily available, local infiltration provides similar length of stay and similar pain scores at rest following TKR.

CONCLUSION

Local infiltration analgesia is a simple technique and shows promise of early postoperative pain relief after TKA. However, in the present study, EA showed a significant edge in the intensity of pain relief after TKA.

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ORIGINAL ARTICLE

Effect of Sahaja Yoga Meditation on Heart Rate Variability

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ABSTRACT

Introduction: Nowadays, people are showing a keen interest in yoga and meditation as an alternative therapy to manage psychological stress and stress-related diseases. Yoga is a spiritual discipline with many proven health benefits. There are different types of yoga techniques practiced worldwide for their known health enhancement effects and for reduction of stress and its related disorders. One of the meditation techniques is Sahaja Yoga. It is a unique technique of meditation that involves mental state of internalized attention characterized by mental silence and emotionally positive experience of bliss. The present study has been undertaken to find out the heart rate variability (HRV) in Sahaja Yoga meditators during rest and meditation.

Objectives: To study the HRV in Sahaja Yoga meditators during rest and meditation.

Materials and methods: A total of 20 volunteers aged 25 to 40 years were considered for the study. The volunteers were practicing Sahaja Yoga meditation (SYM) regularly for 5 years or more. The HRV was recorded during rest with eyes closed and 15 minutes of SYM in a quiet room.

Results: Statistical analysis was done using student paired t test. Results are given as mean ± standard deviation (SD). The mean R–R interval, total power (TP), low frequency (LF), high frequency (HF), and LF/HF ratio were studied during rest and during meditation. The HF (during rest 16.2383 ± 11.1896 and during meditation 28.4875 ± 14.5112) was high and LF/HF ratio (during rest 2.262211 ± 1.346382 and during meditation 1.30545 ± 1.200041) was low during meditation compared with that during rest, which was statistically significant.

Conclusion: Increase in HF and decrease in LF/HF ratio during meditation signifies that meditation shifts sympathovagal balance toward the parasympathetic side, hence signifying a relaxed state of body and mind in Sahaja Yoga meditators.

Keywords: Heart rate variability, Meditation, Sahaja Yoga meditators, Stress, Sympathovagal balance.

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INTRODUCTION

The World Health Organization (WHO) has defined health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity."[1] According to the WHO Global status report 2010, noncommunicable diseases (NCDs) are the leading cause of death globally, killing more people each year than all other causes combined.[2] In India, NCDs account for 60% of all deaths, making them the leading cause of death.[3] It is now believed that one of the root causes of most of these NCDs is stress. Stress is defined as "any stimulus that disturbs or interferes with the normal physiologic equilibrium of an organism." Every human being experiences some sort of stress in their day-to-day life. The negative effects of stress on human body described in the literature are numerous and involve almost all organ systems. Recent studies have now shown that stress impairs immune functioning of an individual and hence fails to protect the optimal functioning of many vital organ systems.[4]

Yoga and Meditation

Yoga is considered by many as one of the best tools to manage stress. Yoga is said to originate from India in 5000 BC. Around 900 BC, the ancient sage Patanjali evolved the eight stages of yoga, which is called as Ashtanga Yoga. Yoga combines specific postures (asanas), breathing techniques (pranayama), meditative techniques (dhyana), chants (mantras), and wisdom teachings (sutras) to encourage union of body and mind. Yoga is a psychosomatic-spiritual discipline for achieving union and harmony between mind, body, and soul and the ultimate union of our individual consciousness with the universal consciousness or divine.

In India, many types of yoga techniques are practiced, such as Hatha Yoga, Sahaja Yoga, Raja Yoga, Jnana Yoga, Integral Yoga, Karma Yoga, Bhakti Yoga, Mantra Yoga, Kundalini Yoga, Laya Yoga, and many more.[5] In recent years, yoga has gained worldwide attention for

the treatment of various diseases and maintaining good health. It is estimated that more than 30 million people in the world today are practicing yoga for its health benefits.[6,7] Meditation is an integral part of yoga. Meditation practice helps in reducing stress to a great extent.[8] When practiced regularly, meditation is believed to assist in the build-up of consistent insensible behaviors of microdimensions with constructive effects on physiological and psychological performance of human beings. Meditation reduces the activity of the sympathetic component of the autonomic nervous system while at the same time enhancing the activity of the parasympathetic component. This process results in relaxation response of the body, manifesting as slowing down the heart rate and increase in the blood flow to the viscera.[9]

According to some recent studies, the vagal nerve complex plays a crucial role in modulating the body's inflammatory response to infectious disease, other forms of physical injuries, and psychosocial stress.[10-13] The body's inflammatory response plays a major role in the pathogenesis of many acute and chronic diseases. Studies have shown that meditation and yoga practices modulate the activity of vagal nerves.[14]

Heart Rate Variability

The heart rate is controlled by the autonomic nervous system. This system has two parts, the sympathetic and the parasympathetic. The sympathetic branch increases heart rate and the parasympathetic branch decreases heart rate. Heart rate variability (HRV) is an indicator of the dynamic interaction and balance between these two branches of the system. Heart rate variability is the amount of heart rate fluctuation around the mean heart rate, which can be used as a mirror of the cardiovascular health. It is valuable noninvasive tool to investigate the sympathetic and parasympathetic function of autonomic nervous system and is used to study various human physiological responses to different stimuli like exercise, stress, and meditation.[15-17]

Sahaja Yoga Meditation

Sahaja Yoga meditation (SYM) employs simple applications of silent affirmations. It assists an individual to achieve a state of mental silence in which the entire attention is focused on the present moment and one is free from unnecessary mental activity. Target experience of SYM is a state of thoughtless awareness characterized by the mental silence and emotionally positive experience of bliss.[18] This internal silence turns out to be a source of personal peace that counteracts the complexities of day-to-day existence including psychological stress while improving creativity, efficiency, and self-confidence.[19] Numerous studies have shown that the autonomic nervous system activity is affected by meditation.

This study was undertaken to observe the effect of SYM on HRV.

MATERIALS AND METHODS

The study was conducted in the clinical laboratory of the Department of Physiology, Mahatma Gandhi Mission Medical College, Navi Mumbai, India, in association with International Sahajayoga Research and Health Centre, Navi Mumbai, India. A total of 20 volunteers aged 25 to 40 years participated.

Inclusion Criteria

- Men and nonpregnant women in the age group of 25 to 40 years.
- Subjects regularly practicing SYM and attending nearest Sahaja Yoga center located in Mumbai and Navi Mumbai for the last 5 years or more.
- Those subjects who were willing to give consent and comply with the study protocol.
- All subjects were screened by a senior physician by taking detailed history and examination for general physical health. Healthy persons and those who were not on medications were considered for the study.

Informed consent was taken from all subjects. The ethical committee approved the study.

Exclusion Criteria

- Those subjects who smoked cigarettes and consumed tobacco and alcohol or had any major physical illnesses.
- Those subjects taking medications that are known to alter the HRV.
- Subjects who were on any prophylactic medications, multivitamins, health supplements, Ayurvedic or homeopathic medicines for health promotion.

Recording of HRV

The HRV was recorded during rest with eye closed and 15 minutes of SYM in a quiet room. The probe of pulse oxymeter was clipped to the subjects' left index finger; care was taken that the subject did not move their hand. The probe was connected to the annuphotorheograph that was in turn connected to a personal computer applying software (Variability Analyzer 2008). The recorded HRV raw data were analyzed to get HRV graph and Fast Fourier transform power spectrum. For computing HRV indices, a recommendation of task force was followed.[16] Very low frequency (VLF), low frequency (LF), and high frequency (HF) spectral powers were determined by integrating power spectrum between 0.00 and 0.04, 0.04 and 0.15, and 0.04 and 0.5 Hz respectively, and expressed

in normalized units. Total power (TP) was calculated between 0.00 and 0.5 Hz and illustrated in absolute unit of millisecond squared.

STATISTICAL ANALYSIS

The data were analyzed by applying paired t test. Results are given as mean ± standard deviation (SD); p-value <0.05 was considered as significant.

RESULTS

The mean R–R interval, TP, LF nu, HF nu, and LF/HF ratio were studied during rest and during meditation. The mean R–R interval of the subjects increased from 0.7070 ± 0.707 during rest to 0.7080 ± 7.675 during meditation (Table 1 and Fig. 1). The frequency domain parameters, the TP, increased from a mean of 898.15 ± 731.1756 ms^2 during rest to 967.745 ± 1597.5783 ms^2 during meditation (Table 1 and Fig. 2). Very low frequency decreased from the mean of 22.8591 ± 9.4900 during rest to 15.2207 ± 6.7726 during meditation significantly (Table 1 and Fig. 3). Low frequency also decreased from the mean of 27.0565 ± 11.2199 during rest to 26.4967 ± 13.8779 during meditation, but not significantly (Table 1 and Fig. 4). Increase in the HF was highly significant from the mean of

Table 1: Heart rate variability parameters in rest and meditation

HRV parameter	*Rest (mean ± SD)*	*Meditation (mean ± SD)*	*t-value*	*p-value**
Mean R–R interval	0.7070 ± 0.707E-02	0.7080 ± 7.675E-02	–0.114	0.910
TP $(ms)^2$	898.15 ± 731.1756	967.745 ± 1597.5783	–0.270	0.790
VLF (nu)	22.8591 ± 9.4900	15.2207 ± 6.7726	3.354*	0.003
LF (nu)	27.0565 ± 11.2199	26.4967 ± 13.8779	0.171	0.866
HF (nu)	16.2383 ± 11.1896	28.4875 ± 14.5112	–4.454*	0.000
LF/HF ratio	2.308001 ± 1.346381	1.310721 ± 1.20004	4.485*	0.000

*p-value <0.05 is significant

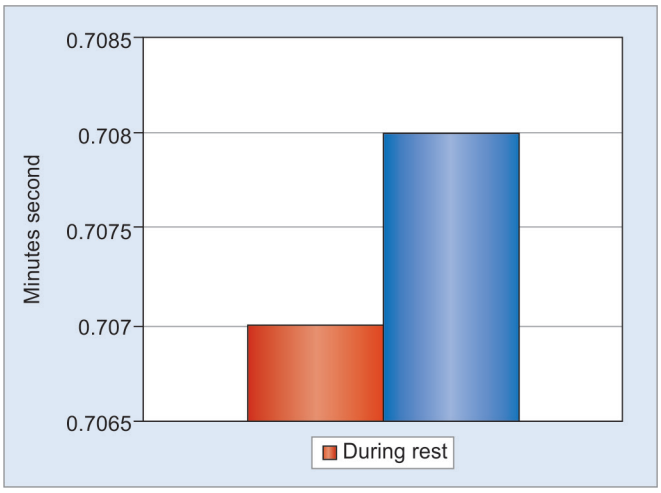

Fig. 1: Mean R–R interval during rest and meditation

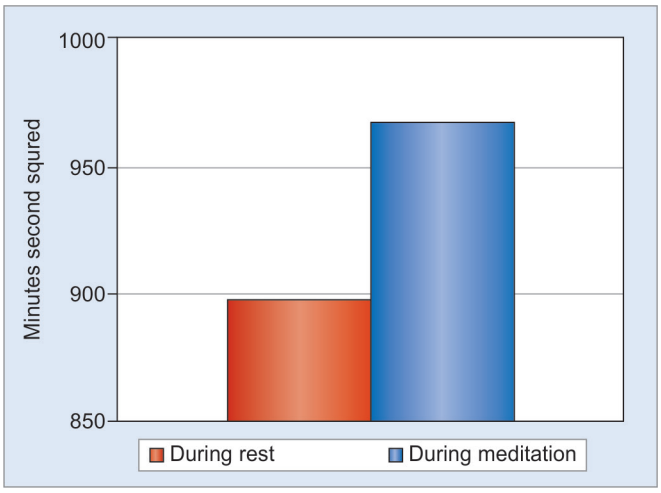

Fig. 2: Total power during rest and meditation

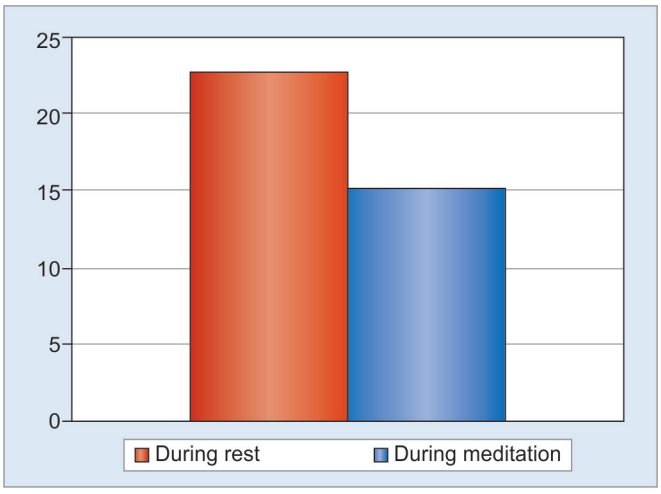

Fig. 3: Very low frequency during rest and meditation

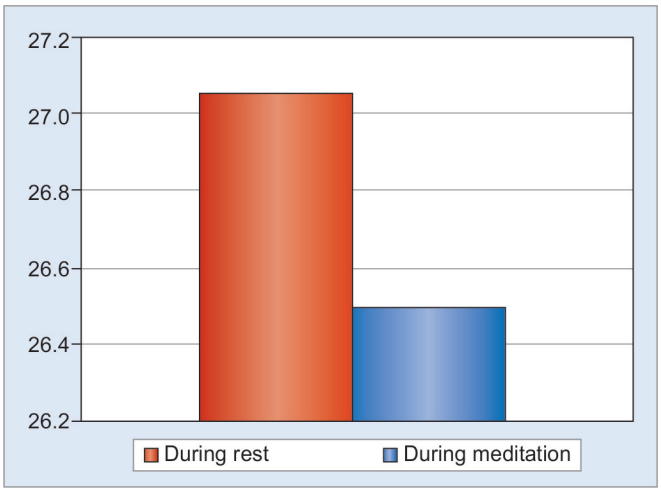

Fig. 4: Low frequency during rest and meditation

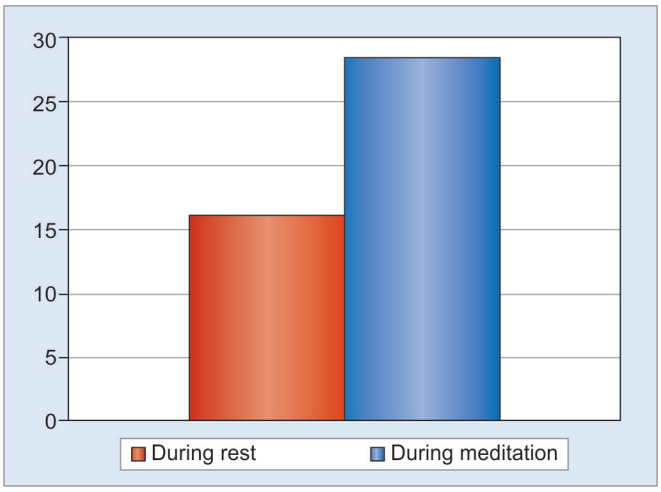

Fig. 5: High frequency during rest and meditation

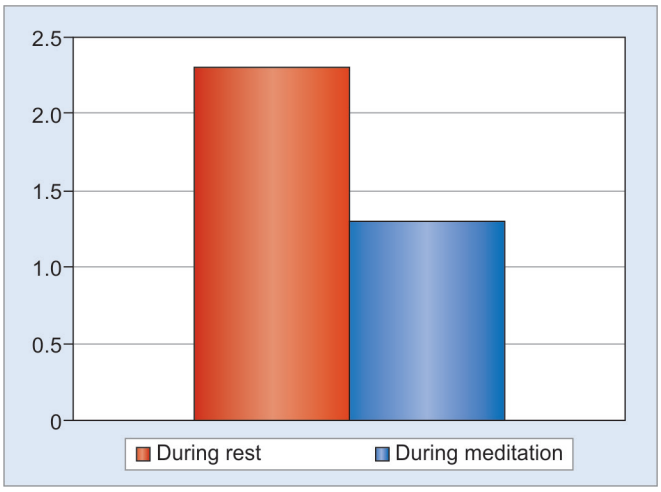

Fig. 6: Low frequency/high frequenc ratio during rest and meditation

16.2383 ± 11.1896 to 28.4875 ± 14.51128779 during meditation, with p-value <0.01 (Table 1 and Fig. 5). The LF/HF ratio decreased significantly from 2.308001 ± 1.346381 during rest to 1.310721 ± 1.20004 during meditation, with p-value <0.01 (Table 1 and Fig. 6).

DISCUSSION

The study shows increase in the mean R–R interval after practice of SYM consistent with the findings of Nesvold et al[20] who studied HRV during nondirective meditation.

The outcome of the study has been found to be similar to various studies undertaken during meditation.[21-23] It suggests that decrease in the LF component and increase in HF component of HRV during meditation shifts the sympathovagal balance toward a reduction in sympathetic tone and enhanced parasympathetic tone. Thus, lower LF/HF ratio during meditation indicates enhanced parasympathetic modulation of HRV and better sympathovagal balance. Many studies with SYM in the treatment of anxiety, depression,[24] work stress,[25] hypertension and heart diseases,[26] asthma,[27] and seizure control and EEG changes in patients of epilepsy[28] have shown positive results.

Sahaja Yoga is a simple noncommercial meditative technique practiced for spiritual and mental well-being. The technique is simple and does not involve adoption of any complicated postures. It can be easily practiced by any person. The yogic tradition encourages aspirants to pursue the awakening of energy, traditionally known as "kundalini," that facilitates the achievement of the Sahaja state. The meditative experience is characterized by a sensation of normal, or even heightened, alertness in conjunction with a state of complete mental silence.[18] This is associated with a sense of relaxation and positive mood and a feeling of benevolence toward oneself and others. Meditation by the Sahaja Yoga technique is, according to tradition, an innately therapeutic process that is beneficial for a number of chronic diseases, mental and physical.

The exact mechanism by which Sahaja Yoga benefits HRV cannot be deciphered from the present study. Although classical yoga books attribute the positive effects of Sahaja Yoga to activation of "Kundalini," a hypothetical center of energy at the base of the spine, it is postulated that somehow the Sahaja state does modulate our autonomic nervous system, and through the connections of the latter with the hypothalamus, it may also regulate our neuroendocrine systems. As hypothalamus is also connected to reticular formation, Sahaja Yoga practice may inhibit reticular activating system by modulating inflow of sensory stimuli to it. This promotes alpha wave activity in the cerebral cortex that is conducive of a relaxed state of mind. Further research is required about the physiological basis of positive effect of SYM on our autonomic system.

CONCLUSION

The study indicates that the increase in HF component and decrease in LF/HF ratio during meditation significantly shifts sympathetic and parasympathetic balance toward parasympathetic side, and overall increase in HRV indicates better autonomic status. The lower LF/HF ratio in Sahaja Yoga group indicated a robust sympathovagal balance in yoga subjects. Also, higher levels of HF recorded in the yoga group indicated a parasympathetic dominant (relaxed) state of mind and body in Sahaja Yoga practitioners.

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The authors are extremely grateful to HH Shri Mataji Nirmala Devi, the founder of Sahaja Yoga, for developing the unique technique of SYM for benefit of mankind and for tirelessly traveling around the globe for more than

40 years to give *en masse* self-realization to thousands of people, in more than 120 countries of the world, free of cost. We are thankful to all the Sahaja Yoga meditators for their active participation in the study on a voluntary basis.

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REVIEW ARTICLE

Pigmented Purpuric Dermatoses

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ABSTRACT

Pigmented purpuric dermatoses (PPD) are a group of histopathologically similar conditions that are primarily differentiated based on morphology. The basic pathological finding is a lymphocytic perivascular infiltrate with hemorrhage limited to the papillary dermis without fibrinoid necrosis of the vessels. The etiology is unknown; they run a chronic course and are fairly resistant to treatment. We present this review for the physicians to kindle interest in this not-so-uncommon entity.

Keywords: Pigmented purpuric dermatoses, Purpura, Schamberg's disease.

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INTRODUCTION

Pigmented purpuric dermatoses (PPD) are a group of histopathologically similar conditions that are primarily differentiated based on morphology. They are generally categorized into five groups: Progressive PPD (i.e., Schamberg's disease), purpura annularis telangiectodes (i.e., Majocchi's disease), lichen aureus, PPD of Gougerot–Blum, and eczematid-like purpura of Doucas–Kapetanakis.[1,2] A few other rarer variants have also been described in the literature (Table 1).[3-12] However, this classification does not change the management or prognosis.[1,2]

Epidemiology

It is difficult to quantify the epidemiology of PPD as it is an uncommon diagnosis in India and elsewhere. Nevertheless, Sharma and Gupta found the prevalence to be 0.18% of the total patient input over a period of 1.5 years.[13] Pigmented purpuric dermatoses appear to be four times more frequent in males than in females.[13] They may occur at any age,[1,2] but most commonly in the 3rd or 4th decade.[13] They are infrequently reported in preadolescent children and adolescents,[2] the commonest type being Schamberg's,[14] although the pigmented purpuric lichenoid dermatoses variant is not reported in this age group.[10] Lichen aureus and Majocchi disease predominantly occur children and young adults.[1,2,10]

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Etiology (Secondary PPD)

Idiopathic cases are the most common (70%) and mostly resemble Schamberg's disease. Although multiple underlying causes have been outlined (Table 2)[1,15-22], most of them lack specificity.[23] Drugs are responsible for 14% of the cases and comprise the most frequent among the provocative factors.[23,24] Multiple reports citing PPD as a manifestation of mycosis fungoides occur in the literature,[25-27] and few have even preceded typical mycosis fungoides. Interestingly, recent reports have also suggested the role of contact allergens as possible etiological agents in PPD. Engin et al[28] showed 54% of the PPD patients were positive to one or more allergens following patch test.

Pathogenesis

The pathogenesis of PPDs is not well understood. The most widely accepted mechanism is increased capillary dilation and fragility, with resultant rupture of the papillary dermis capillaries and possible aneurismal dilation of the end capillaries.[13,29] Venous hypertension, exercise, or gravitational dependency are commonly associated findings.[1] Also, some of the previously mentioned etiologies may be the precipitating factors.

In addition, recent data suggests the role of cell-mediated immune responses.[13] Perivascular infiltrate in Schamberg's disease consists primarily of CD3+, CD4+, and CD1a+ dendritic cells (DCs) (i.e., Langerhans cells) in a well-defined pattern, with close spatial contact between the lymphocytes and DCs.[30] Conditions like contact dermatitis and graft-*vs*-host disease, which are thought to have an immune/cell-mediated mechanism, share a similar pattern of inflammatory cells. The modulation of cellular adhesion molecules in dermal endothelial cells (ICAM-1, ELAM-1) and in lymphocytes (LFA-1) suggests a mechanism for lymphocyte trafficking into affected area

Table 1: Classification of pigmented purpuric dermatoses

Sl. no.	*Types*	*Synonyms*	*First description*
1	Purpura annularis telangiectodes	Majocchi's disease	Majocchi[3]
2	Progressive PPD	Schamberg's disease	Schamberg[4]
3	Itching purpura	Eczematoid purpura of Doucas and Kapetanakis; disseminated pruriginous angiodermatitis	Doucas and Kapetanakis[5]; Lowenthal[6]
4	Pigmented purpuric lichenoid dermatosis	Gougerot–Blum syndrome	Gougerot and Blum[7]
5	Lichen purpuricus	Lichen aureus	Martin[8]; Calnan[9]
6	Granulomatous PPD		Saito and Matsuoka[10]
7	Linear PPD		Hersh and Shwayder[11]
8	Transitory PPD		Osment et al[12]

PPD: Pigmented purpuric dermatoses

Table 2: Etiological factors for secondary pigmented purpuric dermatoses

Etiological factors	*Associations*
Drugs[15-19]	Antihypertensives (CCBs, beta-blockers, ACE inhibitors, nitrites, furosemide, and other diuretics), analgesics (aspirin, paracetamol, NSAIDs), antihistamines, antidepressants, chlordiazepoxide, carbamazepine, glipizide, bezafibrate, medroxyprogesterone acetate, raloxifene, pseudoephedrine, vitamin B1 derivatives, interferon-alpha (in hepatitis C infection), antibiotics (ampicillin and cotrimoxazole), polyvinyl pyrrolidone, topical 5-fluorouracil
Food additives	Tartrazine, creatine supplements
Contact irritants and allergens[20]	Metals, dyes, clothing, alcohol ingestion
Infections[1,21,22]	Beta-hemolytic streptococci, toxoplasma, rickettsiae, hepatitis virus B and C, dental infections
Vascular diseases	Stasis dermatitis
Neoplasia	Mycosis fungoides
Collagen vascular disorders.	Lupus erythematosus, rheumatoid disease

CCBs: Calcium channel blockers; ACE: Angiotensin-converting enzyme; NSAIDs: Non-steroidal anti-inflammatory agents

of inflammation and their interaction with endothelial cells and DCs.[13] Disappearance of the inflammatory infiltrate from affected areas following treatment with topical steroids and daily psoralen plus ultraviolet A (PUVA) further consolidates the immune theory.[30] C3 and C1q deposits on the wall of lesional blood vessels from patients with pigmented purpuras suggest that immune complexes may also play a role in the pathogenesis of these diseases.[15]

Clinical Features

Progressive Pigmented Purpuric Dermatosis[1,4,31]

Patients are mostly young adult males, but PPDs may occur at any age including childhood. The lesions are most frequent on the legs but may occur anywhere on the body and may be few in number or very extensive. They consist of pinhead-sized reddish puncta resembling grains of cayenne-pepper that further form irregular plaques of orange or brown pigmentation (owing to hemosiderin) (Figs 1A and B). It is usually asymptomatic, although there may be some slight itching. The eruption is characteristically very chronic and may persist for many

Figs 1A and B: Patient of progressive pigmented purpuric dermatosis: (A) Multiple purpuric macules and papules interspersed among hyperpigmented macules giving the classical cayenne-pepper appearance; (B) few of them coalescing to form orange plaques

years. The pattern of the eruption changes, with slow extension and often some clearing of the original lesions. Spontaneous cure may occur eventually.

Purpura Annularis Telangiectodes

It may occur at any age, but patients are more likely to be adolescents or young adults. Lesions occur at any site, often in the absence of venous stasis, and may be few in number or very numerous. Early lesions are bluish-red annular macules in which dark-red telangiectatic puncta appear. The central part of the lesion fades, with peripheral extension giving it the annular configuration, and sometimes, slight atrophy is noticed in the center.[1,31]

Pigmented Purpuric Lichenoid Dermatosis of Gougerot and Blum

This eruption occurs especially in men aged between 40 and 60 years. It is characterized by minute, lichenoid papules that tend to fuse into plaques of various hues, in association with purpuric lesions similar to those of Schamberg's disease. Lesions are usually seen on the legs and rarely on the trunk and thighs.[1,31]

Lichen Aureus

This is a more localized, more intensely purpuric but often asymptomatic eruption that may have rather lichenoid morphology. It presents as sudden-onset lichenoid papules in association with purpuric lesions, seen commonly on the lower limbs and occasionally on the trunk and the face. The lesions are often solitary and may be yellowish, golden, rust-colored, or purple.[1,31]

Itching Purpura

Except for being extensive, rapid in onset, and associated with persistent, severe pruritus, it is more or less similar to Schamberg's disease. The lesions consist of erythematous and purpuric macules that may become confluent starting at the ankles and may spread to involve the entire lower limbs. Spontaneous improvement after a few months is usual, but recurrences may occur and a fluctuating but chronic course is frequent. The itching may respond to topical corticosteroids and oral antihistamines.[1,5,6]

Miscellaneous

Granulomatous variant consisting of a PPD-like eruption on the dorsum of the feet, with the biopsy revealing a superimposed granulomatous infiltrate, has been reported. Linear[11] and quadrantic[32] or zosteriform[33] morphology of PPD has also been described. Isolated reports of familial occurrence,[34,35] autosomal dominant[36] in nature, have been seen in patients with Schamberg's disease. Transitory PPD was described by Osment et al, includes entities like angioma serpiginosum, and is different from other PPDs, though the clinical differences between them are minor. Itching purpura of Lowenthal is considered to be a more symptomatic variant of Schamberg's disease.[31]

Dermoscopy

A dermatoscope is a noninvasive, diagnostic tool that magnifies subtle clinical surface features of skin lesions as well as unveils some subsurface skin structures not normally visible even with a magnifying lens. Dermoscopic findings in progressive PPD change according to the evolution of the lesions (Table 3, Fig. 2).[37]

Table 3: Dermoscopic findings in progressive pigmented purpuric dermatoses[37]

Stage	*Description*
Early	Red brownish or red coppery background, brighter or comparatively clearer with a few red dots, and globules.
Established	Red brownish or red coppery background, red dots, globules and patches are seen prominently. Some gray dots and a network of brownish to gray interconnected lines, which are less prominent.
Resolving	Background becomes more brownish coppery and reddish tinge reduces. Central red globules and dark brown pigment deposit indicate hemosiderin deposits in periphery. Gray dots and a network of brownish to gray interconnected lines are seen
Old or completely resolved	Pigment deposits appear blackish brown. There are no red globules and dots.

Fig. 2: Dermoscopic appearance of established lesions of progressive pigmented purpuric dermatosis: Multiple red dots and globules, majority of which are intermixed and surrounded by dark brown dots and interconnected lines

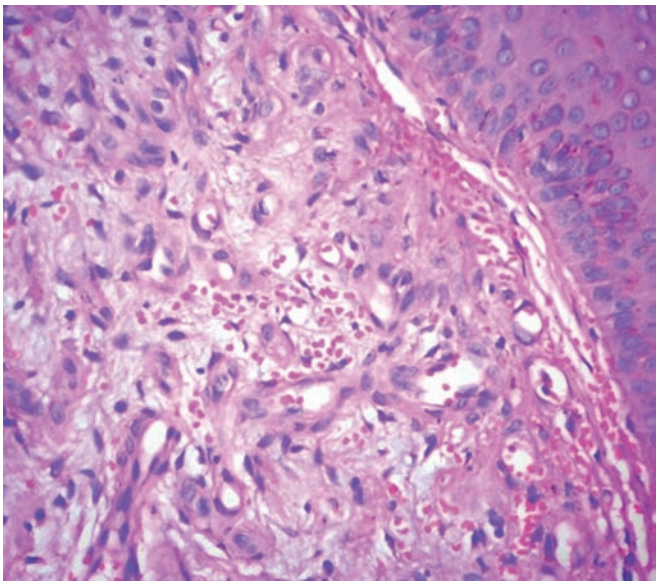

Fig. 3: High-power view of the dermis showing multiple extravasated red blood cells and few perivascular lymphocytes; no signs of leukocytoclastic vasculitis (H&E, 400 ×)

Table 4: Newer therapeutic options

Therapeutic option	*Proposed mechanism of action in PPD*
Bioflavonoids (rutoside) and ascorbic acid[43]	Increases capillary resistance; inhibits specific enzymes that are activated in inflammation; potent antioxidative radical scavenging activities
Pentoxifylline[44]	Reduces expression of adhesion molecules (ICAM-1 expression on keratinocytes and E-selectin expression on endothelium in upper dermis); interferes with the T-cell/keratinocyte adherence resulting in inhibition of exocytosis of lymphocytes to the epidermis
Griseofulvin[45]	Immunomodulatory effect
PUVA[46,47]	Immunomodulation with alteration in the activity of the T lymphocyte and the concomitant suppression of Il-2 production
Cyclosporine A[48]	Inhibitor of CD4+ T cells, which predominate in the inflammatory infiltrate in PPD

PPD: Pigmented purpuric dermatoses; PUVA: Psoralen plus ultraviolet A

Histopathology[23,31,38]

Despite morphological variations giving rise to a clinical classification, the basic histopathology is more or less similar. There is a perivascular infiltrate of lymphocytes and macrophages centered on the superficial small blood vessels of the skin with endothelial cell swelling and narrowing of the lumina. However, overt vasculitis is not usually observed. Extravasation of red blood cells (Fig. 3) with marked hemosiderin deposition in macrophages is typically seen, though the degree of hemosiderin deposition may be variable. Special stains, such as Perls stain and Fontana-Masson may be used to demonstrate hemosiderin, which also helps to differentiate PPD from stasis dermatitis, where a deeper deposition is seen. When lymphocytic infiltrate is lichenoid, it is diagnosed as lichenoid dermatosis of Gougerot and Blum;[39] when spongiosis/neutrophils are marked, the diagnosis is itching purpura;[40] and a rare variant has been described with superimposed granulomatous infiltrate.[10]

The cellular infiltrate in all types contains CD4+ T cells in close contact with CD1a+ Langerhans cells.[30,41] IgA-associated lymphocytic vasculopathy has been described,[42] but its relevance is vague, and because direct immunofluorescence is often negative, it is not recommended.

Differential Diagnoses

The most important differential diagnosis is leukocytoclastic vasculitis, but differentiation based on palpable purpura, associated pain, and features of vasculitis on histopathology is not difficult. Other conditions that present with purpuric lesions, such as purpuric clothing dermatitis, hyperglobulinemic purpura, early mycosis fungoides, purpuric clothing dermatitis, stasis pigmentation, scurvy, and drug hypersensitivity reactions need to be considered and ruled out.[31]

Treatment

No therapy has proven benefit as PPD tends to persist for years and is very resistant to treatment. Nevertheless, reassurance, avoidance of leg dependency, and support hosiery seem the most appropriate approach. Topical corticosteroids and antihistamines may take care of associated pruritus.[1,2]

Some evidence supports the use of topical steroids to control and/or improve PPD. A therapeutic trial may be given for 4 to 6 weeks, although their prolonged use is best avoided. Few newer therapeutic options have been suggested in some reports, but the level of evidence is poor (Table 4)[45-48]. More studies to outline effective treatment strategies need to be carried out.

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REVIEW ARTICLE

An Excellent Teacher

Ronald M Harden

ABSTRACT

A teacher plays a key role in medical training programs and is responsible for the success or failure of many education developments. This article examines the attributes of an excellent medical teacher using a three-circle model. In the inner circle are the technical skills required by the teacher as an information provider, a facilitator of learning, a curriculum developer, and an assessor. In the middle circle is how the teacher approaches their teaching—with an understanding of basic education principles, with appropriate attitudes and ethics, with an evidence-informed strategy, and working as a team member. In the outer circle is the professionalism of the teacher, evaluating their own competence and keeping up-to-date with their subject and education practice.

Keywords: Curriculum, Medical education, Student engagement, Teaching skills.

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INTRODUCTION

In medical education, much attention has focused on the curriculum including the subjects to be addressed and the approaches to teaching and learning and assessment. In the past decade, there has been an emphasis on the expected learning outcomes, on the use of new learning technologies including e-learning and simulation, on performance assessment, on curriculum strategies including integration and interprofessional education, and on approaches to the selection of students.

Key to all these developments and their success in practice is the teacher. In the absence of a "good" teacher, such developments are likely to fail. In the traditional curriculum too, the quality of the teacher is important as noted more than 50 years ago by Sir Derrick Dunlop, an eminent Scottish physician and teacher: "It is important to remember that the actual details of the curriculum matter little in comparison to the selection of students and teachers. If these are good any system will work pretty well; if they are indifferent the most perfect curriculum will fail to produce results."[1]

Teaching, however, is not easy. Teaching, suggested Brookfield,[2] is "the educational equivalent of white water rafting." Teaching skills, however, can be developed.[3] Faculty development programs, however, have tended to concentrate on the technical aspect of teaching, such as giving a lecture, facilitating a group, or setting a multiple choice question paper. These represent, however, only part of a set of attributes required of the "excellent teacher."

EXCELLENT TEACHER

An excellent teacher can be defined using the three-circle learning outcomes model.[4] In the inner circle are the technical skills expected of a teacher (doing the right thing), in the middle circle is how the teacher approaches their teaching (doing the thing right), and in the outer circle is the professional development of the teacher (the right person doing the job). Based on this model, an excellent teacher can be defined in terms of the following equation:

$$ET = (I + R + F + A + C + L) \times (S \times E \times D \times T) \times (P)$$

where ET is the Excellent Teacher, I is the Information provider, R is the Role model, F is the Facilitator, A is the Assessor, C is the Curriculum planner, L is the Learning resource developer, S is the Scientific education principles, E is the Ethics and attitudes, D is the Decision making, T is the Team working, and P is the Professionalism. The addition symbol has been used in relation to the technical skills in the first part of the equation as an excellent teacher may not be expected to be excellent in all of the areas. A multiplication symbol has been used in terms of approaches to practice and professionalism in the later parts of the equation as these are essential and a "zero" would be incompatible with excellence in a teacher.

TECHNICAL SKILLS

The first set of attributes relates to the teacher's technical competencies. These are based on the different roles expected of the teacher as described by Harden and Crosby[5] in the Association for Medical Education in Europe (AMEE) Guide no. 20, The Good Teacher Is More Than a Lecturer: The Twelve Roles of the Teacher. As each role requires special expertise, it would be unusual for

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a teacher to be excellent in all of the six roles described (each role has two elements). However, an awareness and understanding of the different roles is essential.

Information Provider in the Classroom and Clinical Context

We are probably most familiar with the teacher as an information provider, providing the student with the knowledge required through lectures and other means. Despite criticism, the lecture has remained a widely used method of instruction, and it has been estimated that the average student may attend as many as 1,800 lectures in the course of their studies. As Brown and Manogue[6] have argued the problem is not that lectures are bad but that the lecturer is bad. The excellent lecturer motivates the student and provides the required key information clearly along with practical examples. The excellent teacher not only provides the student with relevant information but also serves as a doorkeeper, educating the student in an era of "ubiquitous information" to ask the right question, to know where they can obtain information, and to understand how they can evaluate it.[7]

Role Model

The teacher not only provides the student with appropriate information but also serves as a role model in the classroom and in the clinical setting. The importance of the teacher as a role model has been well documented.[8,9] Students are more likely to model their behavior and ethical decisions on those demonstrated by teachers rather than those advocated in lectures or textbooks. "Do as I do, not as I say" is the message students recognize.

Facilitator of Learning and a Mentor

There has been a significant shift of emphasis from the role of the teacher as information provider to the teacher as a facilitator of learning. This has been described as a move from "the sage on the stage" to "the guide on the side." Student engagement in their learning and in the curriculum has been emphasized as highlighted in the ASPIRE-to-excellence initiative (www.ASPIRE-to-excellence.org). Approaches, such as problem-based or team-based learning focus attention on this changing role for the teacher.

Not all teachers find this change in their role easy as found in problem-based learning where some sessions develop, inappropriately, as mini-tutorials rather than facilitated discussion and opportunities for students to engage in their own learning. Teachers, as noted by Schmidt and Moust,[10] if they are to be an effective teacher in a problem-based curriculum, need to have the ability to communicate with students in an informal way in the small group sessions and to encourage student learning by creating an atmosphere in which open exchange of ideas is facilitated.

A teacher may also be expected to serve as a mentor. Megginson et al[11] have defined mentoring as "offline help by one person to another in making significant transition in knowledge, work or thinking." The mentor is usually not the member of staff who is responsible for the teaching or assessment of the student and is therefore,"offline" in terms of relationship with the student. Mentorship is less about reviewing the students' performance in a subject or an examination and more about a wider view of issues relating to the student.

Teacher as an Assessor

Perhaps one of the most challenging roles for the teacher and one where there is most disagreement is that of assessor of students' performance. Best practice for assessment was described in the Ottawa Consensus statements.[12-17] The excellent teacher not only assesses whether the student has achieved the required learning outcomes at the end of the course or phase of a course but also assesses the student's progress during the course, providing feedback as necessary. Where problems are identified, additional assistance may be necessary to support the student in achieving the expected learning outcomes. It is important that the excellent student is also recognized and appropriate challenging learning opportunities provided. Medical schools can be judged not just by how they manage the average student but how they deal with the student in difficulty and the student who is excelling. There is also a move to thinking of not just "assessment-of-learning" but "assessment-for-learning" where assessment is more closely integrated with the education program.

In thinking about assessment, there are six questions that the teacher should ask:[3]

1. Why is the student assessed? For example, is it as an end-of-course examination or to assess progress and provide feedback?
2. What should be assessed? The assessment should reflect and match the expected learning outcomes for the course.
3. How should the student be assessed? A range of methods should be adopted including a written examination, with multiple choice or constructed response questions, a performance examination, such as an Objective Structured Clinical Examination, and a portfolio as a record of a student's learning over time. A grid should be used to relate the assessment approach to the learning outcomes for the course.
4. When should the student be assessed? This can be at the end of the course, during the course, and for selection of students on entry to the course.

5. Who should be responsible for the assessment? Some countries have a national licensing examination, but there are advantages if responsibility is left with the medical school, provided that standards are monitored. In the assessment of competence, there is an important role for peer-assessment and self-assessment.
6. Where should assessment be conducted? Assessment in the workplace can make a contribution.

Curriculum Planner

Most medical schools and postgraduate bodies have curriculum committees, and an important role for the teacher is the contribution they can make to curriculum planning. Ten questions should be addressed:[3]

1. What is the medical school or training program's vision or mission?
2. What are the expected learning outcomes?
3. What content should be included?
4. How should the content be organized?
5. What educational strategies should be adopted?
6. What teaching methods should be used?
7. How should assessment be carried out?
8. How should details of the curriculum be communicated?
9. What educational environment or climate should be fostered?
10. How should the process be managed?

Learning Resource Developer

With the increased emphasis on independent learning and learning personalized to each student and with the availability of e-learning tools including virtual patients, teachers can contribute by developing learning resources for use by students. Not all teachers have the necessary technical or instructional design skills but they can contribute their content expertise as a member of a team and to facilitate the students' learning they can identify and annotate in a study guide available resources.[18]

HOW THE TEACHER APPROACHES TEACHING

The first part of the equation, as we have described, addresses the technical skills expected of a teacher. An excellent teacher, however, is more than just a technician. The excellent teacher approaches teaching with an understanding of basic educational principles, has an appropriate attitude, adopts an evidence-informed approach, and works as a member of a team.

Understanding of Basic Educational Principles

Teaching is both an art and a craft with underpinning principles that inform good teaching practice. There is extensive literature on educational psychology, but an in-depth understanding is not required for the teacher. Harden and Laidlaw[19] described the four FAIR important principles covering feedback, activity, individualization, and relevance.

Feedback

The excellent teacher gives the student timely feedback about their performance in relation to the expected learning outcomes.

Activity

Learning should be active rather than passive. This applies to all learning situations including the lecture where students may be engaged through the use of an audience response system or by inviting students to discuss an issue with those seated next to them.

Individualization

Each student has different needs and aspirations, and learning should be personalized taking these into account. Of the four principles referred to, this is the most difficult to achieve. With consideration, it is possible to move in this direction even within a relatively traditional curriculum. The use of electives or options in the curriculum is one example.

Relevance

This is an essential feature of any educational program. It is reflected in the move to greater authenticity in the curriculum when the expected learning outcomes, the assessment, and the learning opportunities provided match the capabilities expected of the doctor on graduation.[20]

Attitude of Teachers toward Teaching

The excellent teacher does not see teaching as a chore. He or she brings to it a passion for their subject and a passion for student learning. A master lecturer, for example, does not simply bring to the lecture the necessary technical skills to deliver a lecture. Lowman[21] reported that students described clarity of presentation as a feature of the "master lecturer," but this was not enough. The "master lecturer" also needed to provide emotional stimulation, inspiring and exciting the students and conveying an enthusiasm for the subject and for students' learning.

Informed Decisions

The excellent teacher does not base their teaching practice on prejudices, hunches, opinions, and guesses (the PHOG approach).[22] Just as in medicine, there is a need for clinical judgment, so also in teaching there is a need

for educational judgment. Where evidence is available, however, this should be used to inform teaching practice. The Best Evidence Medical Education (BEME) Collaboration has led this move.[23]

Member of Team

The excellent teacher works as a member of a team alongside other teachers and educationalists. This collaboration reflects the move to integrated curricula and the need to help ensure a smoother transition across the different phases of education. It may also involve students as partners in the learning process rather than as simply consumers.

PROFESSIONALISM IN TEACHING

The last part of the equation reflects the excellent teacher as a professional. This involves:

- The teachers conducting themselves with responsibility and according to recognized standards of behavior. This is addressed in AMEE's "Teacher's Charter" (www.amee.org).
- The teacher evaluating their personal performance as a teacher. This can be a self-assessment, but is usually informed by student surveys or peer assessment.
- The teacher keeping themselves up-to-date in their own subject and also with current educational practice.

EXCELLENCE ON AGENDA

Excellence is very much on today's agenda. Tom Peters examined excellence in business, the Olympics rewards excellence in athletics, the Nobel Prize recognizes excellence in academia, the Man Booker Prize for Fiction represents excellence in literature, and the Turner Prize, more controversially, recognizes excellence in art. In medical schools, the ASPIRE-to-excellence initiative recognizes excellence in education in the areas of social accountability, student engagement, assessment, faculty development, and simulation (www.ASPIRE-to-excellence.org).[23] The achievement of individual teachers has also been recognized with teaching awards locally in schools around the world and internationally with the Karolinska Prize for research in medical education. The question that arises, however, is how does one assess excellence in a medical teacher? In this article, a series of criteria are proposed that relate to the technical skills of the teacher, how they approach their work as a teacher, and their professionalism as a teacher.

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REVIEW ARTICLE

Uterine Transplantation: An Option beyond Surrogacy

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ABSTRACT

Over the years, a lot has developed in the field of infertility and artificial reproductive techniques worldwide, but the uterine factor infertility still remains an unresolved issue in reproductive medicine. Absolute uterine factor infertility is synonymous with congenital absence of uterus or a physiologically nonfunctioning uterus. Very few options including surrogacy and adoption are available for these patients. Both surrogacy and adoption are associated with legal, ethical, financial, religious, and psychological issues. For some of these patients, uterine transplant could be a viable option in future. However, the ability of uterus to carry the pregnancy to the period of viability and the effect of immunosuppressant on the fetus make the uterine transplant a more complex operation than any other transplants. From the earliest uterine transplant tried in 1931 in Germany to the first successful child birth following transplant in Sweden in 2014, uterine transplantation has come a long way. Among the countries that have tried this till now, Sweden has reported five cases of successful births posttransplant. Behind these successful cases, there is dedication and perseverance of few individuals who continued their efforts in spite of repeated failures. At the moment, the uterine transplant can be considered experimental at the best. However, considering the large number of hysterectomies done all over the world and uteruses available for transplantation, uterine transplant has potential to surpass, in numbers, the other transplant in near future.

Keywords: Artificial reproduction techniques, Reproductive medicine, Uterine factor infertility, Uterine transplant.

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INTRODUCTION

Organ transplantation has been popular in many fields as a lifesaving procedure. Considering the higher rate of hysterectomy in our country for both gynecological and obstetric causes, uterine transplant would have been an expectedly popular surgery. However, unlike the other organ transplants uterine transplantation is rather a life-enhancing but not a lifesaving procedure, done only for absolute uterine factor infertility. Uterine factor infertility is the most unresolved issue in reproductive medicine. It includes congenital absence or a physiologically nonfunctioning uterus. Surrogacy and adoption are the options for these patients, but both are associated with moral and ethical difficulties. For some of these patients, who have been born without uterus or who have lost their uterus through illness, uterine transplant is a viable option.

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History

Trials on Animals

In 1964 and 1966, at the University of Mississippi Medical Center the first autotransplantation of the uterus was performed on animal (dog) and subsequently delivered a pregnancy from that uterus.[1] In 2010 Diaz-Garcia and coworkers, at the University of Gothenburg in Sweden, did the world's first successful allogenic uterus transplantation, in a rat, with healthy offspring.[2]

Trials on Humans

In 1931 in Germany, a Danish transgender woman, died from organ rejection 3 months after receiving one of the world's earliest uterine transplants.[3] With the availability of *in vitro* fertilization in 1978, uterine transplantation research was deferred.[4] In Saudi Arabia in 2000, a uterine transplant was performed, from a 46-year-old hysterectomy patient into a 26-year-old recipient[5] whose own uterus was removed due to postpartum hemorrhage. The transplanted uterus functioned for 99 days, but ultimately needed to be removed due to thrombosis. In Turkey, in 2011, the world's first uterus transplant from a deceased donor was conducted by a team of doctors at Akdeniz University Hospital.[6] The patient was a 21-year-old Turkish woman, Derya Sert, who was born without a uterus. She had menses for 6 cycles posttransplant and also got pregnant, however, abortion took place at 8 weeks of gestation. In Sweden in 2012, the first mother-to-daughter womb transplant was done by Swedish doctors at Sahlgrenska University Hospital at Gothenburg University led by Mats Brannstrom.[7-9]

First Successful Pregnancy

A Swedish woman of 36 years of age had received a uterus in 2013, from a live 61-year-old donor. In October 2014,

it was announced that, for the first time, a healthy baby had been born to a uterine transplant recipient. First menstruation occurred 43 days after transplantation and she continued to menstruate at regular intervals. After 1 year of transplantation, first single embryo was transferred, which resulted in pregnancy. She was then given triple immunosuppression with tacrolimus, azathioprine, and corticosteroids, which was continued throughout pregnancy. She had three episodes of mild rejection, one of which occurred during pregnancy which were all reversed by corticosteroid treatment. Fetal growth was monitored by ultrasound and color Doppler all throughout the pregnancy. The patient was admitted with preeclampsia at 31 full weeks and 5 days, and a cesarean section was done because of abnormal cardiotocography. A male baby with a normal birth weight for gestational age (1775 gm) was born.[10] In Sweden, totally nine uterine transplantations have been done till today, out of which five resulted in successful pregnancies. The first uterine transplant performed in the United States took place on 24 February 2016 at the Cleveland Clinic but failed due to infection by *Candida albicans*, which caused damage to the local artery compromising the blood support of the uterus and necessitating its removal.[11]

Need for Uterine Transplant

Absolute uterine factor infertility is the indication for uterine transplant. That includes congenital absence (Mayer Rokitensky Kuster Hauser syndrome) and acquired due to Asherman syndrome or hysterectomy performed due to obstetric cause in the treatment of postpartum hemorrhage or gynecological cause, such as malignancy. Surrogacy and adoption are options for these patients but both approaches, unfortunately, deprive them of the maternal experience of pregnancy and birth. There are some psychological, ethical, religious, legal, and financial issues also associated with it. In fact, surrogacy is prohibited in some countries.

DONORS

Donor selection is done by two approaches. In Sweden, they used live-donor approach whereas in Cleveland clinic trial they used deceased-donor approach. Each approach has pros and cons. The live-donor approach gives control over the timing of the transplant and allows a far more thorough assessment of the donor's medical profile and suitability. But, it also puts a healthy individual at risk, particularly, since pelvic surgeries are performed near so many vital organs. The deceased-donor approach dramatically reduces the pool of available organs. It also offers technical advantages because we are able to recover the uterus with larger vessels.

PROCEDURE

Candidates for transplant are generally chosen from age 18 to 36 years with absolute uterine factor infertility. Counseling regarding procedure and risks is essential. *In vitro* fertilization procedure starts before transplantation. Patients ovaries are stimulated, eggs are retrieved and fertilized *in vitro* with partner's sperms. Six to ten embryos are selected and frozen. Patient is started on immunosuppressant therapy before surgery. The procedure involves suturing the uterine vessels – a pair on each side of the organ – to the recipient's vessels, after which the vaginal tissues are connected to the recipient's gynecological anatomy. The graft is then securely sewn into the pelvis to stabilize the uterus for future pregnancies.

Originally, it was believed that four of the following six blood vessels (two uterine, two ovarian and also a collateral supply from two vaginal vessels) were necessary to maintain a viable uterus. But subsequent studies showed that the uterus remains viable when supplied by ovarian vessels alone and is capable of pregnancy and delivery. A "microvascular technique" for uterine auto transplantation was developed and used in eight pigs. This technique proved unsuccessful as the subjects failed to achieve a normal menstrual cycle. Postmortem examinations revealed thrombosis of the small uterine blood vessels. To overcome this, a large vessel patch technique or "macrovascular" technique was utilized with limited success. The study involved taking part of the aorta, inferior vena cava, common and internal iliac vessels coupled with the uterine arteriovenous tree, together with the uterus en bloc as a large vessel patch. This "method" was supported by evidence demonstrating that the uterus resected en bloc is probably less likely to undergo blood vessel thrombosis.

After 6 to 8 weeks of transplantation, the patients attain menstrual function. Around 1 year after transplantation the uterus fully heals and frozen embryos can be transferred one at a time. Immunosuppressant drugs are continued throughout pregnancy and monthly biopsies are done to rule out rejection. Delivery is done by cesarean section. Women in the trial who achieve a successful delivery can keep the uterus for further pregnancy – number of pregnancies can be limited up to two, for safety reasons – or the uterus can be surgically removed after the delivery to avoid continued immunosuppression. We can also offer to stop immunosuppressant drugs and let the immune system reject the uterus, which in many cases is absorbed by the body without need for intervention.

Shortcomings of Uterine Transplants

Uterine transplant carries some legal and ethical issues. The patient is kept on immunosuppressant therapy for very

long time which is harmful. And in live-donor approach, a total of four major surgeries are required. First surgery is done on the donor to remove the uterus. Second surgery is transplantation of the uterus. When the patient becomes pregnant, cesarean section (3rd surgery) is done and when childbearing is over then hysterectomy (4th surgery).

CONCLUSION

The uterus is the newest organ to be transplanted. Considering millions of hysterectomies being performed worldwide and enormous number of uteruses are available for transplant, it is surprising that the story of successful uterine transplant has just begun. With the availability of artificial reproductive techniques and surrogacy, the indications for uterine transplant will remain very few. However, when we look at it as a scientific breakthrough, it is a pioneering work by some of the dedicated professionals.

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CASE REPORT

Asymptomatic Patient with Unrecordable Blood Pressure: Could It be Takayasu?

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ABSTRACT

Takayasu's arteritis is a rare, systemic inflammatory vasculitis of large vessels that usually affects women of childbearing age. Also known as pulseless disease or occlusive thromboaortopathy, the disease is named after the Japanese ophthalmologist who in 1905 described a form of retinal arteriovenous anastomoses due to retinal ischemia caused by large vessel vasculitis. We present here a case of a young female who presented with stroke. The patient had stroke which eventually recovered but now was referred for evaluation of her unrecordable blood pressure.

Keywords: Blood pressure, Stroke, Takayasu's arteritis.

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CASE PRESENTATION

A 24-year-old Hindu female patient was referred to our department for low blood pressure (BP). She was asymptomatic at present. She gave history of a left-sided hemiparesis with slurred speech 2 years earlier for which she was hospitalized under care of a neurophysician in a charitable hospital. Computed tomography (CT) brain was carried out, she was treated with aspirin and clopidogrel. She recovered in 3 weeks period except slight blurring of vision. She was following up with neuro outpatient department for past 2 years. A house physician referred her to a medicine outpatient with a note of low BP. Her discharge summary did not mention her pulse or BP during her hospital stay or subsequent follow-up. It only mentioned left-sided hemiparesis with left upper motor neuron facial paralysis, with noncontrast CT scan of brain suggestive of acute infarct in right parietal lobe. A residual neurodeficit in the form of minimal weakness of left hand persisted.

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She is not a known hypertensive or diabetic. There is no history of sensory complaints or any arm or leg claudication. The family history is not suggestive of early-onset cerebrovascular or connective tissue disorder, hypothyroidism, or any other illness. Presently, she complained of minimal blurring of vision for which the resident doctor in neuro outpatient department checked her BP and then referred the case to us. In our outpatient clinic it was found that her bilateral radial, brachial, carotid pulsations were absent. Right femoral pulse was weakly palpable and both dorsalis pedis pulsations could be felt. The BP obviously could not be measured. No bruit was heard over any peripheral artery. The systemic examination was within normal limits except slightly weak grip of the left hand. A case of young hemiplegic female with absent peripheral pulsations was thought to be a case of pulseless or Takayasu's disease and investigated further.

Investigations revealed normocytic normochromic anemia with hemoglobin of 9.6 mg/dL. Erythrocyte sedimentation rate (ESR) was 86 mm at the end of 1 hour by Westergren's method and C-reactive protein (CRP) was 54.7 mg/dL (raised). Renal and liver function tests were normal. Serum thyroid-stimulating hormone was normal. Fasting lipid profile was normal. Venereal disease research laboratory test was negative. Antinuclear antibody titers by immunofluorescence assay were negative and so were anticardiolipin antibodies. Chest radiograph was normal as well. Echocardiography was normal without evidence of valvular abnormalities. Fundoscopy showed a healthy retina and disk.

Computed tomography angiography (Aortography) (Fig. 1) revealed the following:

- Circumferential thickening of the brachiocephalic trunk with near total occlusion of the right common carotid artery up to a length of 3.5 cm.
- Proximal 5 mm of right subclavian artery at its origin is opacified by contrast. Circumferential wall thickening with complete luminal wall stenosis is noted in its mid-portion (21 mm) with distal part well formed by the collaterals.
- Near-total complete occlusion of the left subclavian artery from its origin is seen with circumferential wall thickening with complete luminal wall stenosis in its proximal and middle parts.

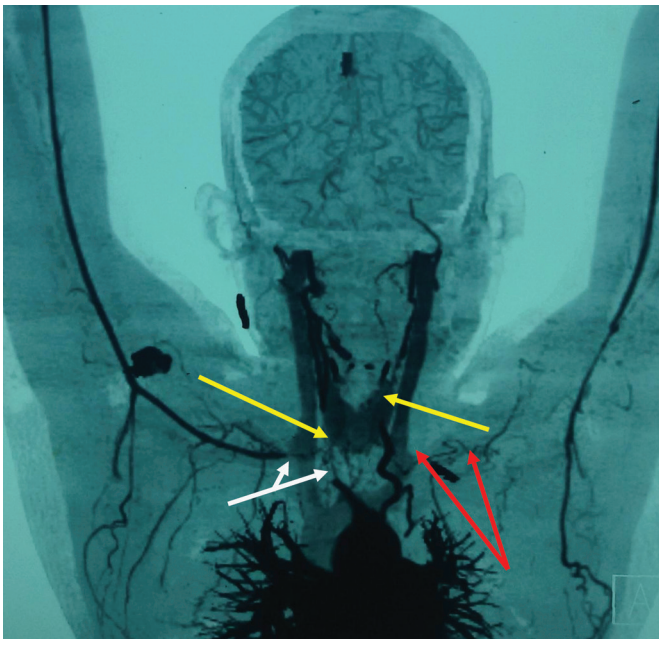

Fig. 1: Computed tomography angiography of the patient showing narrowed vessels. Yellow arrows show narrowed common carotids; white arrows show narrowed brachiocephalic trunk and consequent right subclavian artery; red arrows show narrowed left subclavian artery (when compared with the right side)

- Right vertebral artery is completely opacified.
- Renal and aorta in abdomen are normal without evidence of aneurysm.
- Circumferential wall thickening with a maximum wall thickness of 3.7 mm was noted in the distal aortic arch without significant luminal narrowing.

The arteriography confirmed our clinical diagnosis of pulseless disease as per the American College of Rheumatology (ACR) criteria. She is being treated with weight-based prednisone at a dose of 1 mg/kg. As the disease is in active phase, surgical intervention was deferred. Patient was reassessed after a month. Her acute inflammatory markers were decreased but were still raised, steroids were continued. She did not develop any new symptoms, is asked to follow-up regularly every 2 months.

The present case also raises some pertinent questions about today's clinical practices in the city. Clinical examination starts with checking of vital parameters like temperature, pulse, respiration, and BP, which appears to be missing when the patient was first hospitalized. It may be because of non-MBBS doctors working in charitable hospitals as resident doctors. Secondly, the dependency on investigations is increasing. A case of hemiplegia is first subjected to neuroimaging before clinical diagnosis, otherwise the absent pulsations cannot be missed.

DISCUSSION

Takayasu's arteritis (TA), also known as "pulseless disease," "thromboaortopathy," and "Martorell syndrome," is defined by the Chapel Hill Consensus conference on the Nomenclature of systemic vasculitis as "granulomatous inflammation of the aorta and its major branches."[1] The disease is more common in Asian population with numbers as high as 150 per million in Japan.[2] Incidence is also high in India but exact numbers are not known. An association with the tubercle bacillus was postulated as this disease was commonly seen where tuberculosis is most prevalent. However, the association is not very strong.[3] The median age of presentation is 25 years; however, approximately 25% of cases begin before 20 years of age and 10 to 20% present after 40 years of age.[4] It is characterized by chronic inflammation of arteries leading to wall thickening, fibrosis, stenosis, and thrombosis. It affects predominantly aorta and its branches. The pathogenesis of TA starts in a genetically predisposed individual with perhaps a specific hormonal milieu, followed by an exposure to unidentified antigen leading to mounting of an immunological response that targets large vessels.[3]

The patient may be completely asymptomatic at presentation and the disease may be discovered on routine check-ups when the BP is recorded or may present with devastating complications like stroke. Panja's series of 650 cases of TA, the largest series in India, reported an incidence of stroke to be 22%. Nonspecific features include fever, weight loss, arthralgia, myalgia, malaise, and anemia. As inflammation progresses, stenotic lesions develop and patient develops associated symptoms. Diminished or absent pulses, vascular bruits, hypertension, retinopathy, aortic regurgitation, congestive cardiac failure, neurological manifestation, and pulmonary artery involvement are some of the common manifestation of these patients.[5]

Infiltration with gamma delta T-cells in aortic tissues results in damage of the layers of the vessel wall by perforin. Recognition of heat shock protein 65 may result in recognition and adhesion of these cells. They have previously found restricted VαVβ gene usage of the αβT cell receptor, suggesting that a specific antigen was being targeted. More recently, restricted usage of the VγVδ genes in the infiltrating γδT cells has been reported, supporting their hypothesis, along with the expression of various costimulatory molecules necessary for T-cell activation.[6]

Some patients also had titers of antiendothelial antibodies which, in one study, was found in 18 out of 19 patients with titers 20 times greater than the normal levels.[7] Antinuclear antibodies, antineutrophilic antibodies, or antiphospholipid antibodies were all negative in all patients with TA. Tuberculosis has been particularly implicated in view of the high prevalence of infection, past or present, in affected patients,[8] largely from endemic areas. More recently, viral infection is being investigated as a trigger of vasculitis.[9]

The criteria laid down by the ACR for classification of TA has a sensitivity of 91% and specificity of 98% for the diagnosis. Three or more criteria out of six should be fulfilled for it. The criteria are:

1. Onset before 40 years of age
2. Limb claudication
3. Decreased brachial arterial pulse
4. Unequal arm BP (>10 mm Hg)
5. Subclavian or aortic root bruit
6. Arteriogram abnormality.

There is angiographic evidence of narrowing or occlusion of aorta or its primary branches, or large limb arteries.[10] Ultrasound, CT, and magnetic resonance angiography (MRA) have shown to be as good as conventional angiography for the visualization of vessels affected in TA. Magnetic resonance angiography provides high-resolution detail of vessel wall thickness and luminal calcification; also used to determine the vessel wall thickness and lumen configuration. It allows the measurement of wall enhancement as a reflection of edema and inflammation. Compared with the gold standard of angiography, 2% of stenosed vessel are overestimated as occluded in MRA.[5] Erythrocyte sedimentation rate and CRP are elevated in active disease but not in all patients, ESR being more sensitive than CRP in detecting active disease.[11] Prednisone at a dose of 0.5 to 1 mg/kg is the cornerstone of the disease in its active form. The full dose of steroids is to be taken for at least 8 to 12 weeks and followed by a gradual taper, no more than 10% of the original dose per week when remission occurs. Methotrexate, leflunomide, and azathioprine have all been used in various small-scale trials as steroid sparing agents and in patients with steroid-resistant cases, with methotrexate having an edge above the others. Small trials have shown good efficacy of anti-tumor necrosis factor agents, infliximab and etanercept, in treating patients with refractory TA.[12] Relapses occur when treatment is stopped though.

Tocilizumab is an interleukin-6 antagonist that has been found to be effective in refractory TA.[13]

Cyclophosphamide, in doses of 2 mg/kg, though toxic, is employed when other therapies fail. Evascularization procedures are done when there is:

- Critical renal artery stenosis with hypertension
- Extremity claudication limiting activities of daily living
- Cerebrovascular ischemia or critical stenoses of three or more cerebral vessels
- Moderate aortic regurgitation
- Cardiac ischemia with confirmed coronary artery involvement.[4]

Bypass surgeries have a better rate of revascularization than angioplasty and are used when the involved segment cannot be treated by angioplasty.[14,15] The mere presence of stenosis does not necessitate intervention. The gut, e.g., has such rich collaterals that even critical stenoses of the celiac, superior, or inferior mesenteric arteries usually produce no symptoms and require no surgical intervention. Moreover, many patients with arm claudication will develop collateral circulation and improve substantially over time with medical therapy alone. For upper extremity vascular insufficiency, patiently waiting for a response to medical therapy usually pays higher dividends than undertaking rapid surgical intervention. Surgical intervention should be deferred until it is in remission; procedures done during active disease often produce disappointing results.[16]

This case is reported here to increase the awareness about this pulseless disease in clinical practitioners in our country. Absent pulses and unrecordable BP should not be taken in isolation as indicators of circulatory collapse. Advanced diagnostics with modern tools and machines cannot replace the insight of the clinician. William Osler had said "The good physician treats the disease; the great physician treats the patient who has the disease."

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CASE REPORT

Anesthetic Management of a Patient with Dilated Cardiomyopathy for Inguinal Hernia Repair

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ABSTRACT

Anesthetic management of a patient with dilated cardiomyopathy (DCM) undergoing noncardiac surgery poses a challenge to the anesthesiologist as there is risk of precipitating congestive heart failure or malignant arrhythmias. The anesthesiologist must have the knowledge of its pathophysiology, clinical presentation, diagnostic evaluations, and more so regarding various drugs used during anesthesia. We report a case of DCM with severe left ventricular (LV) dysfunction posted for right inguinal hernia repair managed successfully with epidural anesthesia using ropivacaine.

Keywords: Dilated cardiomyopathy, Epidural anesthesia, Ropivacaine.

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INTRODUCTION

Dilated cardiomyopathy (DCM) is a primary myocardial disease of unknown cause characterized by left ventricular (LV) or biventricular dilation, impaired myocardial contractility, decreased cardiac output, and increased ventricular filling pressures.[1] It may be ischemic or nonischemic. It is defined by the presence of (1) fractional myocardial shortening less than 25% and/or left ventricular ejection fraction (LVEF) less than 45% and (2) LV end-diastolic diameter greater than 117% excluding any known cause of myocardial disease.[2] The prevalence is 0.92%.

The initial manifestation of DCM is usually with signs and symptoms of heart failure. Chest pain on exertion that mimics angina pectoris occurs in some patients. Ventricular dilation may be so marked that functional mitral and/or tricuspid regurgitation occurs. Systemic embolization is also common as a result of the formation of mural thrombi in dilated and hypokinetic cardiac chambers. Supraventricular and ventricular dysrhythmias, conduction system abnormalities, and sudden death are common.[1]

All types of general anesthetics have been successfully used in patients with heart failure. However, drug doses may need to be adjusted. Regional anesthesia is acceptable for suitable operations in DCM patients. However, the pros and cons of regional anesthesia must be carefully weighed.

CASE REPORT

A 45-year-old male, weighing 60 kg, with right inguinal hernia, was scheduled for hernioplasty. The patient had complaints of breathlessness on exertion and occasional palpitations. On general physical examination, he had mild pedal edema, but there were no other signs of heart failure, such as raised jugular venous pressure or hepatomegaly. His blood pressure (BP) was 110/70 mm Hg and pulse rate was 88 per minute. On chest auscultation ejection, systolic murmur was present in the mitral area. There were no rhonchi or rales. Chest X-ray showed cardiomegaly. Electrocardiography showed T-wave inversion in V3 to V6 with occasional ventricular ectopic beats. Echocardiography revealed LVEF 25%, LV hypokinesia with mild-to-moderate mitral regurgitation and right ventricular systolic dysfunction. Therefore, he was diagnosed to be having DCM during preanesthetic checkup. For control of symptoms, he was put on digoxin, diuretics, and beta-blockers, which were continued till the day of surgery. All the biochemical and hematological investigations were within the normal limits.

High-risk consent was taken from the patient in view of poor cardiovascular status (American Society of Anesthesiologists III). On arrival in the operating room, intravenous access was established with 20 G cannula. Electrocardiography, pulse oximetry, noninvasive BP, and SpO_2 were attached for continuous monitoring. Under strict aseptic precautions, epidural catheter was inserted at L3–L4 interspace in sitting position using 18 G Tuohy's needle. Correct placement was confirmed by injecting 3 mL of 1.5% lignocaine with adrenaline as a test dose. Later, 8 mL of 0.5% isobaric ropivacaine with 50 µg of fentanyl was injected epidurally. Adequate sensory block was achieved up to T10 level. Oxygen was supplemented

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via Venturi mask at the rate of 4 L/minute. During the surgery, pulse rate was maintained at 60 to 80 per minute and BP at 100 to 110 mm Hg systolic and 60 to 80 mm Hg diastolic. Surgery lasted for 45 minutes. His postoperative course was uneventful.

DISCUSSION

Dilated cardiomyopathy is the most common type of cardiomyopathy, the third most common cause of heart failure, and the most common indication for cardiac transplantation. It is mostly idiopathic, characterized by LV or biventricular dilation, systolic dysfunction, and normal LV wall thickness. Secondary cardiomyopathies having features of DCM include those associated with alcohol, cocaine, peripartum state, pheochromocytoma, infectious diseases (human immunodeficiency virus), Duchenne's muscular dystrophy, thyroid disease, chemotherapeutic drugs, and radiation therapy.[1] Clinical picture of DCM may vary from only cardiomegaly to severe congestive heart failure, dysarrhythmias, and embolism (systemic or pulmonary). Malignant arrhythmias are the most common cause of death in DCM.[3] Anesthetic management of patients with cardiomyopathy with reduced systolic function is challenging and may be associated with high mortality.[4]

Anesthetic Goals

Key factors in the management of patients with cardiomyopathies are to improve systolic function, maintain normovolemia, avoid sudden hypotension, and prevent sudden death due to ventricular arrhythmias and myocardial depression.[5]

Dilated Cardiomyopathy and General Anesthesia

During general anesthesia, dose-dependent myocardial depression may occur with use of induction agents. Patient may also be vulnerable to drug overdose due to slow circulation time. Moreover, stress response to intubation and extubation may be deleterious to the patient. Propofol in clinically used concentrations decreases sympathetic tone and reduces systemic vascular resistance, which is beneficial. Propofol also has some direct negative inotropic effect on the heart, but studies have shown that the net effect on myocardial contractility is insignificant in clinically used concentrations.[6] All of the potent volatile anesthetic agents are myocardial depressants, and for this reason, high concentration of these agents is best avoided. Among the intravenous induction agents, etomidate is preferred as it causes least cardiovascular depression. Opioids cause little or no cardiovascular depression and decrease the dose of general anesthetics for both induction and maintenance.

Dilated Cardiomyopathy and Regional Anesthesia

During regional anesthesia, modest decrease in systemic vascular resistance secondary to peripheral sympathetic blockade may increase cardiac output. Also, patient remains conscious during surgery, which permits prompt recognition of acute changes in cerebral and cardiovascular function. Therefore, regional technique may be preferred over general anesthesia. However, the decreased systemic vascular resistance produced by spinal anesthesia is not always predictable or easy to control. Precipitous fall in BP may occur after single-shot spinal anesthesia.

Titrated doses of local anesthetics epidurally result in lower risk of hypotension and prolong postoperative analgesia.[7] It also improves myocardial performance by reducing LV afterload without improving contractility, which may be beneficial in a situation of poor ventricular function, where no outflow tract obstruction is present.[8] So epidural was selected over spinal. Injection ropivacaine 0.5% was used as it is less cardiotoxic and produces less motor blockade.[9] Injection fentanyl was preferred as an additive as it has minimal depressing effect on cardiac function and improves quality of analgesia.

Fluid management is also critical and preloading the patient in the preoperative period is not desirable because it may precipitate a congestive heart failure. Central venous pressure-guided fluid should be given in major cases where higher fluid shifts are expected. Vasopressors, such as ephedrine, mephentermine, and phenylephrine, to mitigate against the vasodilating effect of the anesthetics is a rational approach. In our case, 500 mL of Ringer's lactate was given intraoperatively. Injection Xylocard, amiodarone, and defibrillator should be kept ready to treat arrhythmias.

CONCLUSION

Patients with DCM are a challenge to the anesthesiologist. These patients can be well managed by thorough preoperative assessment, medical management, formulating good anesthetic techniques, prompt diagnosis, and management of complications.

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CASE REPORT

Epidermal Cyst of the Breast: A Rare Case Presentation

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ABSTRACT

Epidermal inclusion cyst (EIC) arising from the breast is an interesting, rare, benign, and diagnostically challenging condition, since these may be misdiagnosed as malignant breast neoplasm, both on clinical and radiological examination, thereby creating undue anxiety and apprehension until the definitive diagnosis is formulated. To substantiate it, two cases of epidermal cyst of breast have been described.

Keywords: Benign breast lesions, Breast lump, Epidermal cyst, Epidermal inclusion cyst.

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INTRODUCTION

An epidermoid cyst is a benign cyst usually found on the skin. The cyst has an ectodermal tissue origin. On histopathological examination, the cyst is lined by stratified squamous epithelium underneath of which are found flakes of keratin. Several synonyms exist for epidermoid cysts, including epidermal cyst, epidermal inclusion cyst (EIC), infundibular cyst, and keratin cyst. Epidermal inclusion cyst more specifically refers to implantation of epidermal elements into the dermis.

Epidermal cyst of breast is an uncommon benign condition. It is usually located in the skin layer. It refers to cysts resulting from the proliferation and implantation of epidermal elements within a circumscribed space in the dermis. These cysts are more common on the face, trunk, neck, extremities, and scalp. The occurrence of epidermal cyst in skin of the breast is rare. It presents as a small lump and needs to be differentiated from other non-neoplastic and neoplastic breast lesions. To date, fewer than 30 cases of EICs of the breast have been reported in the English-language literature.[1-6]

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Diagnosis is straightforward for EIC that occur in the breast subcutis as a small nodule, but enlarged cysts in the breast parenchyma require to be differentiated from malignant or benign tumors of the breast. In this study, two cases of epidermoid cyst of breast are presented.

CASE REPORTS

Case 1

A 40-year-old woman came with complaints of a lump in her left breast, since 2 and half months. She noticed the lump during shower. It was initially a size of the pea and gradually increased into the current size. There were no complaints of nipple discharge, and the patient had no history of previous surgery or infection to the breast. No history of hormonal medications or a family history of breast disease.

On examination, the lump was located at the upper inner quadrant of the left breast and measured approximately 3.0 × 1.5 cm. It was firm, immobile, and was fixed to the overlying skin. There was no skin change, nipple retraction, or enlarged axillary lymph nodes.

The mammogram showed a well-circumscribed, high-density oval lesion in the upper inner quadrant of the left breast (Fig. 1). The other breast was normal.

The gross appearance of the specimen was an elliptical cystic lesion measuring 2.8 × 1.2 cm, on cutting open, serous cyst contents oozed out. On histopathological examination, presence of a cyst in the dermis was found, and the cyst was lined by stratified squamous epithelium underneath of which showed flakes of keratin. No malignancy was noted (Figs 2 and 3). The final diagnosis of an epidermal cyst was made.

Case 2

A 48-year-old woman came with the complaint of a mass in her right breast. The mass had been for 2 years. She had history of hysterectomy due to uterine fibroid 2 years ago. Examination revealed a 3.5-cm lesion in the center of the right breast under the nipple region. On examination, the mass was oval, firm, well-circumscribed. After excisional removal of mass, an epidermoid cyst was confirmed on histopathological examination (Fig. 4).

DISCUSSION

A few theories regarding EIC etiology have been postulated, namely congenital development of the cyst

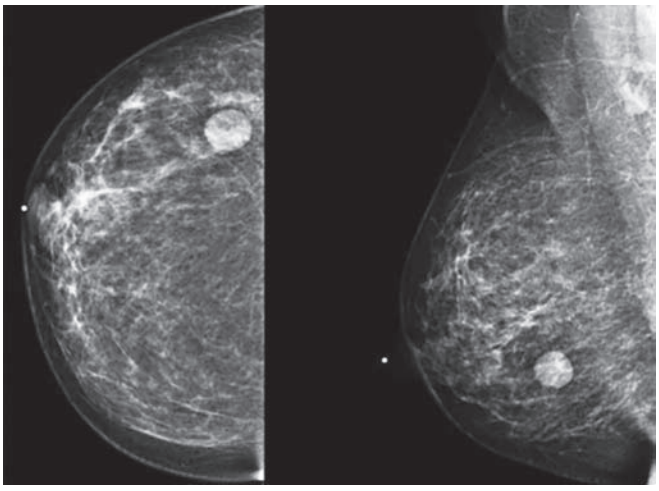

Fig. 1: Mammogram images of the left breast show a well-circumscribed, high-density, oval-shaped lesion in the upper inner quadrant

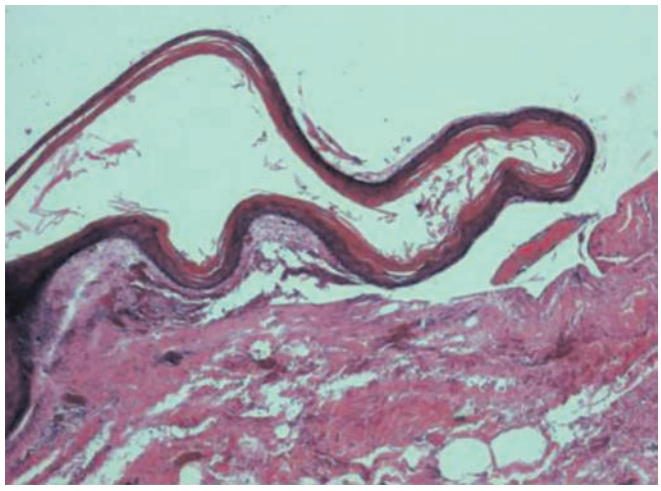

Fig. 2: Cyst lined by stratified squamous epithelium underneath of which seen flakes of keratin (H&E stain, 10×)

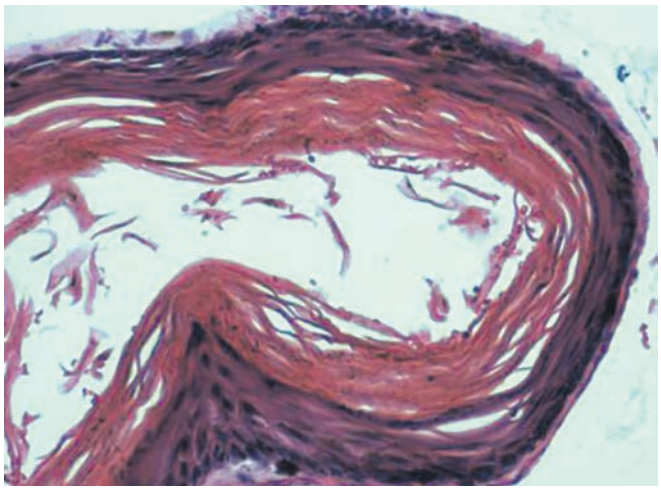

Fig. 3: The cyst wall lined by stratified squamous epithelium and contents of the cyst comprising anucleate squames (H&E stain, 40×)

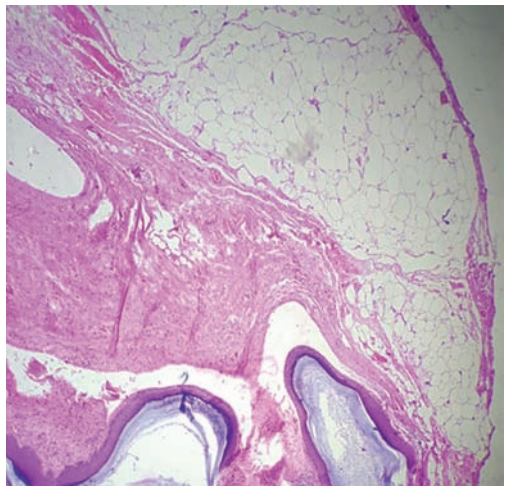

Fig. 4: Cyst lined by stratified squamous epithelium underneath of which seen flakes of keratin (H&E stain, 10×)

secondary to obstructed hair follicles or pores, injury to the epidermis resulting in epidermal fragments being implanted more deeply within the breast tissue, or developed following squamous metaplasia of normal columnar cells within a dilated duct in cases of fibrocystic disease, or within a fibroadenoma or phyllodestumours.[1,2,4,7]

The differential diagnosis of epidermal cyst in breast includes fibroadenoma, breast abscess, breast carcinoma, and this need to be differentiated. Radiologically on mammography, it appears as noncalcified, well-circumscribed homogeneous lesion with increased density. Epidermal cyst can cause severe complications; potential ones include spontaneous rupture leading to inflammation and abscesses and patient present with a discharging sinus in the periareolar region. Although these cysts are benign, they may rarely transform into squamous cell carcinoma.[8,9] Symptomatic cases presenting with an enlarging palpable breast lump, even with typical mammography appearances, excision is usually recommended for definitive histopathological diagnosis so as to exclude a malignant lesion with benign imaging features, and for the prevention of potential risk of malignant transformation.

CONCLUSION

Epidermal cyst is a rare entity in breast. It presents as breast mass with clinical diagnosis of fibroadenoma or breast carcinoma. It should be excised and histologically correlated, to rule out any potential complications that can arise from these cysts. Menville[10] found that 19% of the patients with EIC in his case series showed malignant squamous cell lining on histopathological examination. An EIC of the breast is potentially serious, although such cysts are rare, and differentiation from a malignant or benign breast tumor is required. They may play a role in the origin of the rare squamous carcinoma of the breast, as suggested

by Hasleton et al.[11] Clinically, they can mimic benign as well as malignant tumors.[12,13] Excision is probably the most appropriate treatment, which eliminates the possible risk of malignant transformation as well as undue anxiety.

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CASE REPORT

Pitfalls in the One-stage Management of Rectovestibular Fistula: A Rare Variant of Congenital Pouch Colon

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ABSTRACT

The gold standard for management of rectovestibular fistula is a three-stage procedure in many Western countries. This malformation has been corrected successfully in a single-stage in the Indian subcontinent. This report describes a girl with rectovestibular fistula who was later diagnosed to be a case of congenital pouch colon (CPC).

Keywords: Anorectal malformation, Congenital pouch colon, Rectovestibular fistula.

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INTRODUCTION

Congenital pouch colon (CPC) is an abnormality where a pouch-like dilatation of a shortened colon is associated with an anorectal malformation (ARM). Diagnosis is usually made on an erect abdominal X-ray, which shows a large air–fluid level occupying >50% of the width of the abdomen. This malformation has frequently been reported in northern India. The sporadic cases have been reported from China, Sweden, Japan, and the UK.[1-4] Based on the anatomic morphology of the pouch, the Saxena-Mathur classification differentiates CPC into five types:

Type 1: Ileum opens into the pouch colon (normal colon is absent).

Type 2: Ileum and cecum open into the pouch colon.

Type 3: Ascending and transverse colon open into the pouch colon.

Type 4: Normal colon with a recto-sigmoid pouch.

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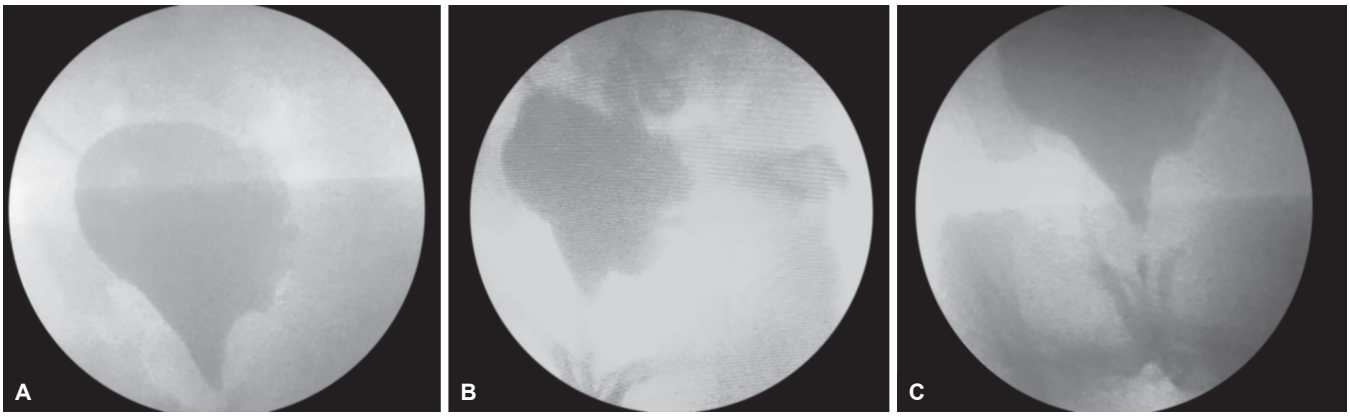
Type 5: Double pouch colon with a short interpositioned normal colonic segment.

CASE REPORT

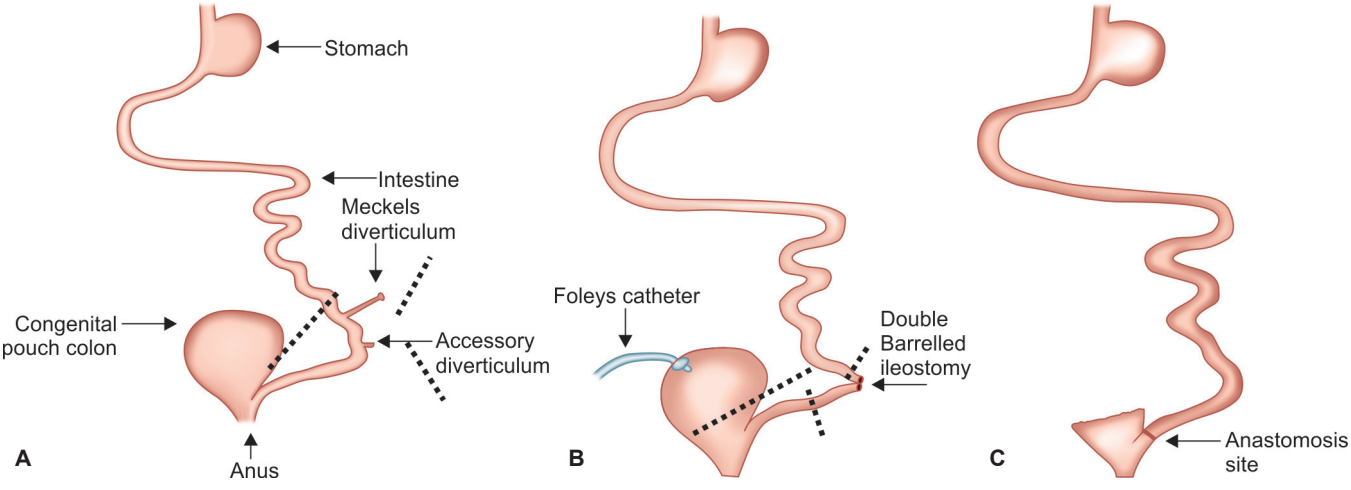
A 2-year-old girl presented with an abnormally sited anal opening since birth. Hemogram, renal and liver function tests, and viral markers were normal. Radiographs of the chest and lumbosacral spine, and abdominal ultrasound were normal. She underwent a posterior sagittal anorectoplasty in January 2013. Following the procedure, she developed wound infection, causing a partial wound disruption. A rescue colostomy was planned in February 2013. However, during surgery the ileocecal junction and cecum were found in the left lower quadrant. The cecum has opening in a huge pouch (about 10 × 10 cm) behind the uterus. The pouch was devoid of colonic haustrations, appendices epiploicae, and had an aberrant blood supply. The ascending, transverse, and descending colon were absent. The uterus was infantile and both the ovaries were normal. There was a long Meckel's diverticulum. A second (accessory) diverticulum is in the terminal ileum 10 cm distal to the Meckel's diverticulum. Meckel's and accessory diverticulum were excised along with a portion of intervening ileum. A double-barreled ileostomy and a tube pouchostomy were fashioned. A staged reconstruction was planned as the patient was weighing only 9 kg. A genitoscopy was done in June 2013. The urethra, bladder, bladder neck, and both the ureteric orifices were normal. A normal vagina and cervix uteri were seen. The neo-anus was dilated daily with #10 Hegar's dilator. Daily pouch irrigations with normal saline were given via three-way Foley's catheter. A contrast enhanced computed tomography of abdomen and pelvis and a fluoroscopy scan (Figs 1A to C) revealed the distal loop of the ileostomy was draining into the pouch, which in turn was opening distally into the anal canal. After initial bowel preparation, the patient underwent pouch excision, ileostomy closure with ileorectal anastomosis in January 2014 (Figs 2A to C). Three months later, the girl has been doing well and found continent.

DISCUSSION

The incidence of CPC, among all the cases of ARM, has been reported to occur from 2 to 18%. High incidence



Figs 1A to C: Fluoroscopy scan: (A) The three-way Foley's draining into the pouch; (B) the distal loop of ileostomy draining into the pouch; and (C) the pouch communicating directly with the neo-anus



Figs 2A to C: Surgical anatomy: (A) Preoperative anatomy, presence of a Meckel's diverticulum with an accessory diverticulum, the ileum communicating directly to the pouch sharing a common wall, which in turn communicates to the anus. Dotted lines show the excised segments during first surgery; (B) a Foley's catheter inserted into the pouch and the formation of a double-barreled ileostomy. Dotted lines show the excised segments during the following surgery; and (C) final postoperative anatomy of the gastrointestinal tract

(55.8%) of CPC with high ARM has been reported from Udaipur, Rajasthan, India.[5,6]

In case a patient presents with constipation after surgical correction of ARM, it is important to differentiate between rectal ectasia, mega rectum, and CPC. In CPC, there is no anal stenosis. The dilated pouch has typical radiological and histopathological features. It is necessary to consider the possibility of CPC preoperatively in a case of ARM posted for surgery. In one stage, the management of rectovestibular fistula in females, especially in Indian context, the authors suggest the routine use of a simple contrast enema as part of a preoperative workup of these patients in order to diagnose this rare variant subtype of CPC associated with rectovestibular fistula. In this case, the condition was not diagnosed on preoperative abdominal ultrasound and plain X-rays. Failure to do so causes undue vexation to the child, parents, and the treating doctors. Psychosocial problems in patients occur due to multiple surgical procedures, and hospitalization.

CONCLUSION

It is advisable to investigate and keep possibility of CPC in a female patient of low ARM.

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CASE REPORT

Vascular Leiomyosarcoma of the Thigh: A Rare Presentation

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ABSTRACT

High-grade mesenchymal soft tissue tumors are rare neoplastic lesions that occur uncommonly in the extremities and in other sites of the body. Herein, we report a case of high-grade vascular leiomyosarcoma of the thigh. The patient was a 72-year-old male with a 4-day history of swelling in his right thigh. Excision biopsy of the tumor showed highly pleomorphic tumor cells arranged typically in perivascular fashion with large areas of hemorrhage and necrosis. Immunohistochemistry was positive for vimentin, smooth muscle actin, and showed a 90% proliferation index on ki-67 labeling. Vascular leiomyosarcomas comprise a group of very infrequent tumors with varied presentation and can occur at unusual sites.

Keywords: Leiomyosarcoma, Malignant, Mesenchymal tumor, Vascular.

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INTRODUCTION

Soft tissue sarcomas are malignant tumors that arise in any of the mesodermal tissues of the extremities (50%), trunk and retroperitoneum (40%), or head and neck (10%).[1] The reported international incidence rates range from 1.8 to 5 per 100,000 per year.[2] Histopathological examination along with ancillary immunohistochemical stains remains a gold standard approach to classify these tumors to determine the cell of origin, and assess their behavior, prognosis, and recurrence. The American Joint Committee on Cancer (AJCC) staging system for soft tissue sarcomas is based on histologic grade, tumor size and depth, and the presence of distant or nodal metastases. Despite improvements in local control rates with wide local resections and radiation therapy, metastasis and death remain a significant problem in 50% of patients who present with high-risk soft tissue sarcomas. Herein, we report an unusual case of a high-grade leiomyosarcoma.

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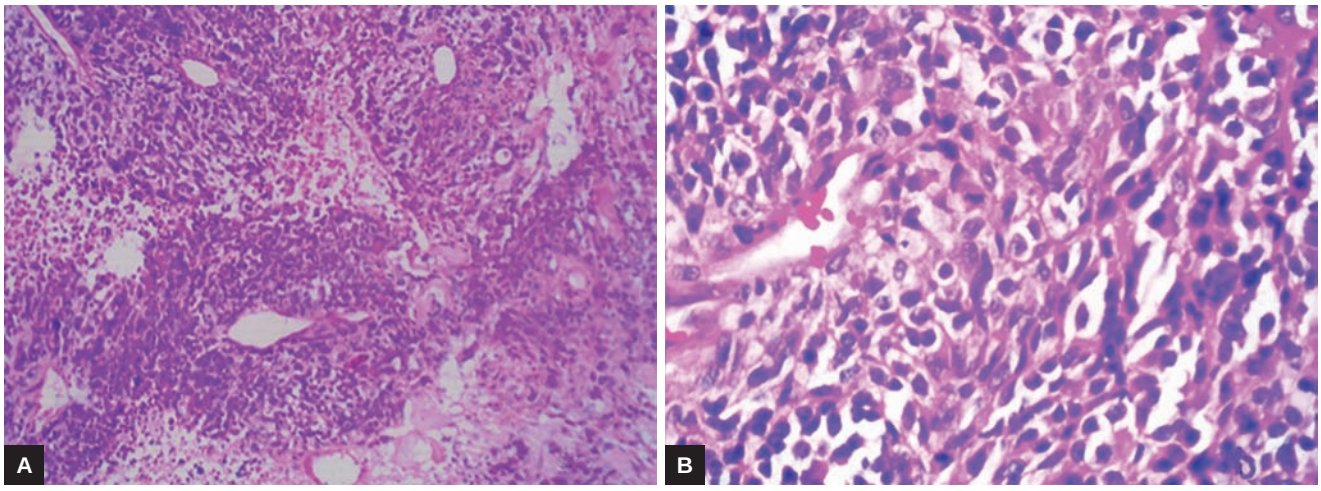
CASE REPORT

A 72-year-old male presented to the surgical outpatient department with a right-sided thigh swelling, which he had noticed only 4 days back. The swelling was painless, nontender, firm to hard in consistency, and occupied the lateral aspect of the thigh. The surgeon carried out wide excision of the swelling. We received several morcellated, grey-white, soft to firm tissue pieces of the tumor, all aggregating 15 × 10 × 4 cm, with areas of hemorrhage and necrosis. Histopathological examination revealed a tumor comprising of tumor cells arranged in predominantly perivascular and alveolar pattern, vague fascicular, and solid sheets separated by confluent areas of necrosis. Individual tumor cells were round to oval, occasionally spindled, showing high N: C ratio, and marked nuclear pleomorphism with hyperchromic nuclei and eosinophilic to vacuolated cytoplasm giving an epithelioid visá-vis rhabdoid morphology. Multiple tumor giant cells, atypical mitoses, and areas of calcification were noted. There was no evidence of myxoid, osseous, cartilaginous areas, or any lipoblasts or pigment in the tumor cells (Figs 1A and B). According to the French Federation of Cancer Centers Sarcoma Group (FNCLCC), a score of 3 + 2 + 2 = 7, inferring grade 3 histologically was reported. A preliminary diagnosis on morphology was that of high-grade malignant neoplasm favoring sarcoma.

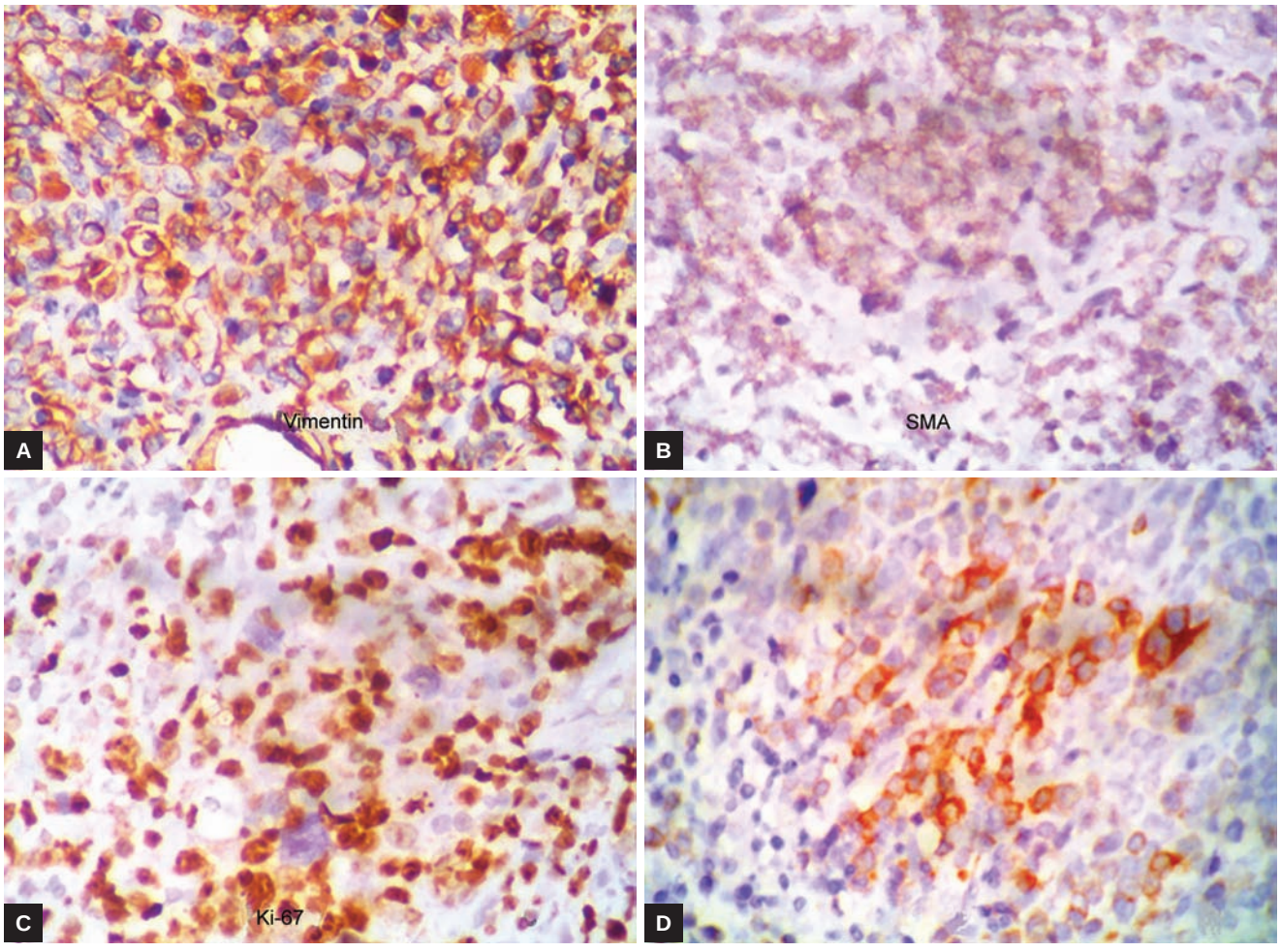
On immunohistochemistry, the tumor cells were strongly positive for vimentin and smooth muscle actin, and negative for pancytokeratin, desmin, CD34, HMB-45, leukocyte common antigen, myogenin, and s100. Ki-67 and Bcl-2 positivity was seen in 90 and 30% of tumor cells respectively (Figs 2A to D). Thus, a diagnosis of leiomyosarcoma was rendered.

DISCUSSION

Leiomyosarcoma is a malignant neoplasm arising from smooth muscle cells which affects individuals of all ages, especially between the 5th and 7th decade of life. Leiomyosarcomas of vascular origin comprise a seemingly rare group of tumors with only a few hundred cases reported in the literature and only isolated instances are recorded in several large autopsy series.[3] The morbidity



Figs 1A and B: Tumor cells with notable perivascular arrangement and vague fascicles with marked nuclear pleomorphism (A: ×10, B: ×40, H&E stain)



Figs 2A to D: (A) Positivity for vimentin; (B) smooth muscle actin; (C) Ki-67 proliferation of 90%; and (D) Bcl-2 index of 30%

and mortality associated with these tumors are primarily a result of direct extension of the tumor along vessels, compromising the circulation. On the contrary, epithelioid leiomyosarcoma in the external deep soft tissue is extremely rare.[4] Site-specific superficial leiomyosarcomas are divided into cutaneous (or dermal) and subcutaneous leiomyosarcomas.[5]

In general, leiomyosarcomas are uncommon tumors and thought to have poor long-term prognosis. Svarvar et al[6] reported on 225 patients with leiomyosarcoma of all types from the Scandinavian Sarcoma Group with a cumulative survival of 49% at 10 years.

Various authors have reported the behavior of vascular leiomyosarcomas. Leu and Makek[7] reported good

prognosis on 5 cases of intramural venous leiomyosarcomas, and Hadju[8] reported low metastatic potential. On the contrary, all the cases reported by Berlin et al[9] had metastases with 5 cases dying from metastatic disease within 5 years. The results of one series showed a very poor outcome in vascular leiomyosarcoma with 75% of patients dying of metastatic disease within the first 3 years of diagnosis, although good local control by surgery and radiotherapy was achieved. This is very similar to the series of Berlin et al.[9] In their experience about half of the patients with leiomyosarcomas of vascular origin had metastatic disease at diagnosis, which indicated either a very aggressive course of the disease or due to delay in diagnosis, as most patients had been misdiagnosed as deep venous thrombosis. Of the 9 patients without metastases at the time of diagnosis, 5 patients developed metastases within 36 months of the disease, indicating that the tumors had an aggressive clinical course.[10]

Our patient died after 5 months of follow-up. Progress in the molecular characteristics of these tumors should in the near future translate into molecular based therapies that can be incorporated into standard treatment strategies.

CONCLUSION

Leiomyosarcomas, being rare, should be kept in the differential diagnosis of high-grade tumors occurring in the extremities. Immunohistochemistry plays an important role in diagnosing such high-grade tumors with an unusual morphology. Thorough sampling, patient history, and clinical correlation with further ancillary testing are mandatory and the need of the hour.

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SHORT COMMUNICATION

Hereditary Elliptocytosis: An Incidental Finding in a 6-year-old Child

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ABSTRACT

A case of hereditary elliptocytosis (HE) in a 6-year-old child diagnosed as an incidental finding has been presented.

Keywords: Hereditary elliptocytosis, Peripheral smear, Sickle cell disease, Thalassemia.

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INTRODUCTION

Hereditary elliptocytosis (HE) is an uncommon disorder often picked up as an incidental finding on routine blood film examination. The estimated frequency of this disorder worldwide is 1 in 2000 to 1 in 4000.[1] Here is a case of HE in a child diagnosed as an incidental finding, which has been discussed.

CASE REPORT

A 6-year-old boy presented with fever and diarrhea for 2 days. A routine complete blood count (CBC) and peripheral smear (PS) for red cell morphology and DC was performed. Hemoglobin (Hb) was 12.7 g/dL, mean corpuscular volume (MCV) = 79.6 fl, mean corpuscular hemoglobin (MCH) = 28.2 pg, mean corpuscular hemoglobin concentration (MCHC) = 35.5 g/dL and red cell distribution width = 14.2%. Peripheral smear showed numerous elliptocytes constituting predominant red blood cell (RBC) population (90%) with very occasional poikilocytes (Fig. 1). No spherocyte was seen. Reticulocyte count was 5%. Possibility of HE was considered. The serum bilirubin performed subsequently was 0.7 mg/dL. The patient gave history of jaundice 2 years ago. However, no documentation was available. The CBC and PS for both the parents were performed which revealed presence of elliptocytes in the father constituting the predominant cell population (90%). The CBC and PS of the mother were within normal limits.

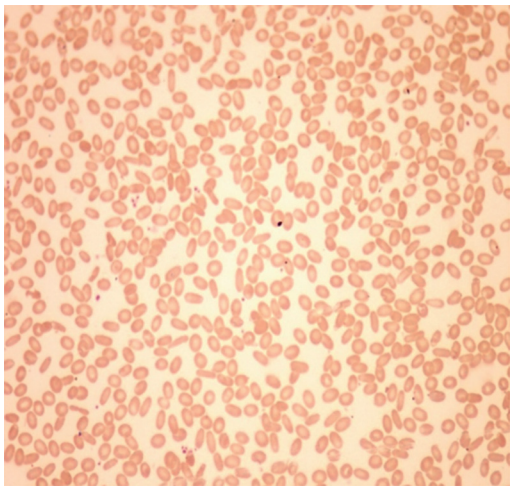

Fig. 1: Peripheral smear showed numerous elliptocytes constituting the predominant RBC population (90%) [Wright stain, 400×]

DISCUSSION

Elliptocytes are RBCs with an oval shape. In HE stained smear, the defect in stability is due to failure of proper spectrin dimer–tetramer association. There are four molecular defects which can cause this: (1) Abnormalities in the alpha-chain of spectrin, (2) abnormalities in the B-chain of spectrin, (3) defective protein 4,[1] and (4) defective protein 3.[2]

Hereditary elliptocyte is more common in African and Mediterranean regions.[3] It is transmitted as an autosomal dominant trait, except for a rare Melanesian variant, which has an autosomal recessive mode of inheritance. *De novo* mutations have been reported in rare cases.[2]

Symptoms of HE vary between members of the same family and in the same individual over time.[4] Most of the patients have a fully compensated hemolytic process with no anemia or splenomegaly. However, the blood film shows 25 to 100% elliptocytes with mild reticulocytosis. 5 to 20% of the patients may present with mild anemia, high reticulocyte count, splenomegaly, gall stones, or chronic leg ulcers. Rarely, crises may occur in these patients secondary to stress or infections.[2] Typically, 50 to 90% (At least 25%) of the RBCs are oval shaped and 10% occur as elongated rod-shaped forms.[2] However, the

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degree of hemolysis does not correlate with the number of elliptocytes present.[4] In the instant case, elliptocytes were seen in the PS.

Both autohemolysis and osmotic fragility are normal in nonhemolytic HE. They are increased in patients with spherocytic elliptocytosis and in patients with HE variants and hemolytic disease. Demonstration of the molecular defect in spectrin molecule confirms the diagnosis, however, the required methods for isolation, enzymatic digestion, and electrophoretic analysis are not routinely available in most laboratories.[2]

In addition to the aforementioned tests, patient's clinical history, characteristics of RBC morphology, and family history are of prime importance in making the diagnosis of HE.[2] In the index case, elliptocytosis was found as an incidental finding in a routine CBC performed for other illness and there was no evidence of hemolysis.

Other causes of elliptocytes in the blood are iron deficiency anemia, macrocytic anemia, sickle cell disease, and thalassemia.[2] The percentage of elliptocytes in these disorders are usually less than 25%, while in HE, they are 90% or more. In the present case, percentage of elliptocytes was found to be 90%.

CONCLUSION

Elliptocytosis was discovered as an incidental finding in the patient on routine CBC sent on hospital admission, which was confirmed on positive family study.

CLINICAL SIGNIFICANCE

Hereditary elliptocytosis is a rare disease, especially in the Indian population. Family study is advised whenever the pathologist comes across elliptocytes as the predominant cell population.

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