Lesson S30: PreAnesthetic Assessment of the Pediatric Patient with Osteopetrosis and Lung Mass

Authored by: Megha Patel, MD, Fellow in Pediatric Anesthesia, Lurie Children’s Hospital, Chicago, IL; Cheryl Gooden, MD, Associate Professor of Anesthesiology, Icahn School of Medicine at Mount Sinai New York, NY

Reviewed by: Elizabeth A.M. Frost MD, Clinical Professor of Anesthesia, Icahn School of Medicine at Mount Sinai, New York, NY

REVIEW DATE: April, 2013

Practice Gaps

Osteopetrosis is a rare, inherited disease that poses several important considerations for anesthetic care, particularly issues surrounding airway management. Anesthesiologists may encounter patients with this pathology and may not be aware of the potential complications.

Objectives

At the end of the lesson, the participant will be able to:

1. Define osteopetrosis
2. Describe the three primary types of osteopetrosis
3. Identify clinical manifestations of osteopetrosis
4. List the physiologic implications of lateral positioning for thoracic surgery
5. Name the techniques for achieving single lung ventilation in the pediatric patient
6. Describe how to use single lung ventilation techniques
7. Recognize the pros and cons of each technique for single lung ventilation
8. Explain the challenges specific to endobronchial blocker placement for surgery involving the right upper lobe
9. Anticipate a situation in which one of the techniques for single lung ventilation might be preferred
10. Recognize methods to adapt currently available techniques/devices to accommodate neonates and infants for thoracic surgery
Case Presentation

A 4-month-old female with a past medical history of malignant infantile osteopetrosis (MIOP) presented with right upper lobe aspergilloma and was scheduled for right thoracotomy with wedge resection. She had persistent parainfluenza infections, pancytopenia and a seizure disorder controlled with dilantin. Her hemoglobin was 9.8 gm. The patient had no allergies and previous general anesthesia for venous access was uneventful. She weighed 5 kg. Physical examination revealed failure to thrive, macrocephaly and hepatosplenomegaly. Findings on bone survey were consistent with osteopetrosis.

Introduction

The term “osteopetrosis” - also known as Albers-Schonberg disease - means “bone of stone,” named because it describes a group of disorders in which abnormal bone growth leads to bones of increased density.¹

Fig. 1: Osteopetrosis of the pelvis

Normal bone growth depends on a balance between osteoblasts, which make bone, and osteoclasts, which resorb bone. Osteopetrosis is an osteoclast disorder with abnormal bone resorption leading to unopposed osteoblast function and bone formation. The exact mechanism is unknown. Evidence indicates that a carbonic anhydrase enzyme deficiency causes defective hydrogen ion pumping by the osteoclasts. Bone resorption is affected because an acidic medium is needed for dissociation of calcium hydroxyapatite from bone matrix. Thus, bone formation persists while resorption decreases.² Despite increased density, bones are fragile. Symptoms correlate with the degree of osteoclast dysfunction. Patients can be asymptomatic or possess extreme deformity and multiple systemic ramifications, including stunted growth, physical deformities, scoliosis, anemia, recurrent infections
and hepatosplenomegaly. Bone expansion causes marrow narrowing and the overgrowth of sites of extramedullary hematopoiesis. Deafness, blindness and facial paralysis may be caused by pressure of bone on cranial nerves. A “space alien” face has also been described along with hypocalcemia. Diagnosis is made through skeletal X-rays showing increased density and a chalky white bone appearance and is confirmed with bone density tests or bone biopsy. The only reported cure for this disease, with variable success, is bone marrow transplant.

Classification

Disorders of osteopetrosis can be further classified into various types based on mode of inheritance. There are 3 main types of osteopetrosis.

1. **Malignant infantile osteopetrosis (MIOP)** is an autosomal recessive condition diagnosed soon after birth. The incidence is thought to be about 1 in 200,000 with mortality rates reported to be 70% by age 6 and 100% by age 10. Unopposed osteoblasts invade the bone marrow, leading to pancytopenia. Patients are immunocompromised, coagulopathic, and anemic, making surgical procedures especially risky. Abnormal bony formation can lead to unusual anatomy, and difficult airway management. Malformation of the paranasal and mastoid sinuses can cause nasal stuffiness, which is frequently the presenting symptom. Patients with MIOP present with failure to thrive and growth retardation. Pancytopenia leads to anemia, bleeding, and opportunistic infections from a poorly formed immune system. Extramedullary hematopoiesis causes hepatosplenomegaly and potential hemolysis. Hypoplastic dentition, blindness, hearing loss, or airway obstruction are other manifestations. Bone marrow transplant is thought to be the only therapy for MIOP.

2. **Benign osteopetrosis, or Albers-Schönberg disease** (a German radiologist and gynecologist), is an autosomal dominant condition which usually manifests in early adulthood. This form is more common than MIOP, with an incidence of about 1 in 20,000. The site for classical Albers-Schönberg disease has been identified on chromosome 1 (1p21). Patients suffer from frequent fractures with poor healing, scoliosis or other spine abnormalities. Life expectancy is not usually affected by this condition, but quality of life can be complicated by osteomyelitis, pain, arthritis, or headache. Some patients are asymptomatic.

3. **Intermediate osteopetrosis** refers to patients with symptoms that cannot be categorized as autosomal dominant or recessive. Diagnosis is usually made in the first decade of life, and patients tend to have more severe symptoms than occur with the benign version. Symptoms may include blindness or hearing loss, due to cranial nerve impingement by abnormal skull formation; or hematological abnormalities due to poorly formed bone marrow. An inheritance pattern or chance is not clearly delineated.

Differential diagnosis

The differential diagnoses of osteopetrosis include several disorders that may result in diffuse osteosclerosis, such as hypervitaminosis D, and hypoparathyroidism, Paget’s disease, diffuse bone metastasis of breast or prostate cancer (although these lesions are usually osteolytic rather osteoblastic), intoxication with fluoride, lead or beryllium, and hematological disorders such as myelofibrosis, sickle cell disease and leukemia. Tuberculosis has also been considered as part of the differential diagnosis.
Anesthetic considerations

The patient’s airway may be anatomically altered by bony masses and abnormalities. Multiple intubation tools should be readily available in the operating room in case of a difficult intubation.

Dentition is typically distorted and compromised. Anemia may require preoperative transfusion. Infection should be ruled out and treated as appropriate. Scoliosis may make positioning difficult and a fragile skeleton can cause increased compression of the dependent lung when placed in the lateral position. In older patients, poor hearing or sight may affect the process of obtaining informed consent. Hepatosplenomegaly can interfere with lung volume and limit the patient’s ability to tolerate single lung ventilation.

The degree of pancytopenia determines the precautions required in the operating room. For example, thrombocytopenia can lead to increased surgical blood loss, and a baseline anemia may lower the threshold at which blood transfusion may be necessary. Sterility is paramount, given the compromised immunity, and perioperative antibiotics or antifungals should be used as necessary.

Single lung ventilation

In the case presented, the principal problems were low weight, failure to thrive and the presence of a lung mass. The surgeon indicated that lung isolation was required. To adequately access the lung mass and excise it, the diseased lung was collapsed and single lung ventilation initiated. This maneuver, especially in very young children, poses several problems for the anesthesiologist.12

Indications and contraindications

There are two major indications for lung isolation and single lung ventilation. The first is the inability to ventilate an abnormal lung because of the presence of large lung cysts, bullae, bronchopleural cutaneous fistulas, or major disruption of the bronchial anatomy, as in trauma. The second indication is the need to avoid contamination of a normal lung in the case of infection/empyema, hemorrhage, or bronchopulmonary lavage. Single lung ventilation may also be used for improved surgical access or exposure for specific types of surgeries (i.e. pneumonectomy, thoracoscopy, upper lobectomy, or thoracic aortic aneurysm repair).

Contraindications include severe respiratory impairment limiting adequate oxygenation, such as severe bronchopulmonary dysplasia (BPD) or technical barriers to safe placement.

Physiologic implications and positioning during thoracic surgery

Children, especially newborns, experience changes during lateral positioning.13

Ventilation/perfusion (V/Q) mismatch during thoracic surgery can occur as a result of general anesthesia, muscle relaxants, or supine and lateral positioning. All of these factors can lead to atelectasis and decreased functional residual capacity (FRC), contributing to increase in alveolar dead space. Volatile anesthetics interfere with hypoxic pulmonary vasoconstriction, limiting the body’s physiologic mechanism of diverting perfusion away from poorly ventilated lungs. When adult patients are placed in the lateral position, gravity and hydrostatic pressure gradients cause perfusion toward
the dependent (healthy) lung and away from the nondependent (diseased) lung. As such, V/Q mismatch is minimized. In contrast, for infants, oxygenation is improved with the healthy lung up – which is opposite the normal positioning for thoracic surgery. Infants have a soft and compressible ribcage that cannot withstand body weight. Incorrect positioning can lead to atelectasis in the dependent lung. In addition, their smaller body size creates less of a hydrostatic pressure gradient, so this mechanism, while useful in adults, contributes far less to V/Q matching in infants.

Right- versus left-sided thoracic surgery can pose particular difficulty in pediatric patients, especially neonates and infants. The distance between the carina and the bronchial branch to the right upper lobe is far shorter than that found on the left side. In neonate and infant patients, this distance is extraordinarily short, leaving little to no room for error. Whichever modality is used to separate the lungs, the patient must be placed in an exactly proper position to ensure that the right upper lobe is not inadvertently insufflated, thus not permitting collapse of that lung.

**Techniques for single lung ventilation**

Several techniques have been described for single lung ventilation in pediatric patients, each with its own unique benefits and drawbacks. The patient’s size, anatomy, co-morbidities, and surgical plan must all be taken into consideration before choosing the best modality. The following are current techniques.

**Deliberate mainstem intubation**

The simplest method to ventilate a single lung is by deliberate mainstem intubation. For right mainstem intubations (that is, to collapse the left lung), the endotracheal tube (ETT) is advanced while auscultating the left lung until the breath sounds can no longer be heard. The steep angle of the left bronchus promotes the advancement of the ETT towards the right side, if a blind technique is used. Left mainstem intubations are slightly more difficult. The patient’s head may have to be turned to the right with the bevel of the tube facing the right side while it is advanced, again listening for cessation of breath sounds on the opposite side. In order to fit within the mainstem bronchus, the chosen ETT must be at least a 0.5-1.0 mm internal diameter which is smaller than the endotracheal tube size that would normally be used for tracheal intubation. Fiberoptic bronchoscopy can and should be used to confirm or assist with placement. The distance from the cuff to the tip of the tube must be shorter than that of the bronchus to avoid obstruction of the upper lobe orifice by the cuff. Uncuffed tubes may fail to completely isolate the lung and prevent healthy lung from becoming contaminated. The advantages of this technique are that it can be used at any age and done in emergency situations. The disadvantages are that there is no port through which the operative lung may be suctioned; also, there is slow collapse of the operative and diseased lung. The ETT can be withdrawn into the trachea at the end of the case to reinsufflate the surgical lung, which is useful if the patient requires mechanical ventilation postoperatively. Because minimal airway manipulation is required, deliberate mainstem intubation is the most straightforward approach to one lung anesthesia.

**Endobronchial blockers**

Endobronchial blockers are increasingly favored in the pediatric population and include a Fogarty® embolectomy catheter (Edwards Lifesciences) and the Arndt® endobronchial blocker (Cook Medical). See Figure 2. The Fogarty® embolectomy catheter can either be placed through or alongside the ETT.
It has a wire stylette that can be bent prior to placement to aid in directing its tip. Because these instruments come in small sizes, they can be used successfully in neonates and infants.

**Fig. 2: The Arndt® endobronchial blocker**

There are two popular techniques for placement. The first technique involves intubating the operative bronchus with an ETT and passing a guide wire. The ETT is removed, and the blocker is advanced over the guide wire. An ETT is then reinserted into the trachea, next to the blocker. With the second technique, the blocker is advanced under direct laryngoscopy (DL), and once past the cords, it is turned 90 degrees towards the operative lung. An ETT is then placed alongside the blocker. In both scenarios, a fiberoptic scope is used to confirm blocker placement.

The Arndt® blocker is available in 5, 7, and 9 Fr sizes and has a multiport adaptor. The smallest size - the 5 Fr - has a 2.5 mm diameter, and determining the appropriate size of the ETT depends on the size of the fiberoptic scope. The three port adapter allows for fiberoptic scope, blocker, and circuit to be attached at the same time. Traditionally, it can only be used with ETT 4.5 mm or greater. With the multiport adaptor in position, the patient can continue to be ventilated while the blocker is placed. The fiberoptic scope is placed into the lumen of the blocker and held in place with a nylon loop that extends from its distal end. This loop is used to guide the blocker during placement. Once the blocker is in place, the loop is then released and the scope removed. The adapter lumen used to pass the scope can then serve intraoperatively for suctioning or oxygen delivery. The multiport adaptor gives the Arndt blocker greater utility than the Fogarty® embolectomy catheter, but the ability to adequately ventilate the patient when the fiberoptic scope and blocker are in place can significantly increase airway resistance by taking up space within the tube, limiting its utility in very small children. In the case presented, the Arndt® endobronchial blocker was used in a patient who would otherwise not have been able to accommodate its size simply by placing the blocker outside the tube. Unlike the Fogarty® catheter, the Arndt has a low pressure-high volume balloon, lending itself to less airway trauma.

The advantages of endobronchial blockers are that they are more predictable and provide better operating conditions. The inflated balloon prevents contamination, and one can avoid tube exchange postoperatively in patients who require continued mechanical ventilation. A disadvantage is the possibility of balloon dislodgement into the trachea, obstructing both lumens and preventing ventilation altogether. Precise blocker position is necessary in order to prevent ventilation of the right upper lobe, and care must be taken to avoid over distention of the balloon, as this can cause mucosal edema. If closed-tip blockers are used, intraoperative suction or continuous positive airway pressure (CPAP) is not possible.

**Univent tubes**

A Univent® tube (Fuji Systems) is an ETT with a second lumen containing a blocker with a distal balloon that can be advanced into a bronchus. (See Figure 3.) The tube was designed as an alternative to double lumen ETT. A conventional single lumen tube is designed with an integrated small channel in the concave anterior wall that contains a movable bronchial blocker used for lung isolation. A thin lumen in the blocker itself allows lung deflation and permits various ventilatory patterns in the blocked lung (oxygen inflow, CPAP, jet-ventilation). The primary indications for the Univent® tube include...
difficult intubation, risk of aspiration and planned postoperative ventilation. The smallest size available has a 3.5 mm internal diameter, but the dual tube design creates a larger diameter in total, making it most appropriate for patients age 6 or older. The advantage of this tube is that displacement is less likely since the blocker tube is attached, and it can be used to apply CPAP or suction to the operative lung. Disadvantages are that the low volume/high pressure balloon can cause mucosal damage, the blocker minimizes the diameter of the ETT creating increased resistance to flow, and the smaller sized Univent® tube blocker is usually not large enough for the egress of air and insufflation with oxygen.

**Double Lumen Tubes**

A double lumen tube (DLT), as the name implies, is a single tube with two lumens of unequal length. The shorter, large tube is placed in the trachea, while the longer, small tube ends in the bronchus. The smallest size available is 26 Fr, appropriate for age 8 or older. For placement, the tube is advanced under direct laryngoscopy until the bronchial cuff is just past the vocal cords. It is then turned 90 degrees, depending on whether a left or right-sided DLT is to be used, and advanced until the tracheal cuff passes the cords. Both cuffs are inflated, and either the bronchial or tracheal lumen is clamped, depending on which side is to be operated. Left DLTs are preferred to right due to the shorter right mainstem and potential for right upper lobe obstruction. Advantages are the ability to suction and apply CPAP, as well as the fact that the high volume low pressure cuffs cause less airway damage. Lung isolation is thought to be more reliably obtained with this technique. The primary disadvantage is the lack of size availability for small children and limitations in placement in patients with difficult airways.

**Clinical application**

Generally, technique choices are largely related to patient age and size. For patients up to 2 years of age, endobronchial intubation with a conventional single lumen tube or endobronchial blocker (Fogarty® embolectomy catheter) is preferred. For those that are 2 through 6 years of age, endobronchial blockers (Arndt®) work well. For ages 6 through 8 years, endobronchial blockers or Univent® tubes are good options. For those that are 8 years of age or older, a double lumen tube may be considered.

Intraoperative strategies to optimize oxygenation during single lung ventilation include ensuring placement post-positioning, use of a high FiO2, and maintenance of volatile MAC < 1 to avoid inhibition of hypoxic pulmonary vasoconstriction. Tidal volume should be kept around 5 - 10cc/kg, titrated to keep peak pressures < 30 mmHg. Continuous positive airway pressure (CPAP) to the nondependent lung or positive end expiratory pressure (PEEP) to the dependent lung is often helpful. Nitrous oxide can increase cuff volume/pressure and decrease oxygen availability and is better avoided. The cuff/balloon should only be inflated to the minimum volume necessary to allow a leak free system but while avoiding excessive pressure on the airway mucosa.
Management of the case presented

Following placement of standard ASA monitors, anesthesia was induced via an in-situ peripheral 24g IV with propofol 10mg and vecuronium 0.5mg. An infant Glide Scope® (Verathon Medical) blade was used to assess the difficulty of the airway, and no gross abnormalities were seen. A #3.5 cuffed endotracheal tube was placed without difficulty. Confident that visualization would be straightforward with direct laryngoscopy, a Miller #1 blade was then used to place a 5 Fr Arndt® bronchial blocker alongside the ETT. A fiberoptic bronchoscope was passed through the ETT to appropriately position the endobronchial blocker. This maneuver was repeated after placing the patient in the left lateral decubitus position. Single lung ventilation was then initiated. During the course of the surgery, return to two lung ventilation was intermittently necessary to maintain oxygenation, but the case proceeded without complication.

Conclusion

Rare diseases can often create challenges in the operating room, primarily due to the clinician’s unfamiliarity with the symptomatology. Osteopetrosis is one such disease, as the extent of bone abnormalities can affect airway management in particular. Other associated complications of this bone disease can be compounded by thoracic surgery in a pediatric patient, as single lung ventilation may be poorly tolerated. Awareness of disease manifestations in osteopetrosis as well as multiple techniques available for single lung ventilation in thoracic surgery will allow the anesthesiologist to be fully prepared when presented with a similar situation in the operating room.
References

POST-TEST

1. **The differential diagnosis of osteopetrosis is least likely to include:**
   a. Paget’s disease
   b. Tuberculosis
   c. Diseases with osteolytic lesions
   d. Hypoparathyroidism

2. **With regard to Double Lumen Tubes:**
   a. The smallest size is 18 French
   b. The smallest size is 26 French
   c. Size always changes with heat
   d. The smallest size is most appropriate for neonates

3. **Benign osteopetrosis or Albers-Schonberg disease:**
   a. Manifests at birth
   b. Occurs with an incidence of approximately 1:20,000 live births
   c. Causes a major reduction in life expectancy
   d. Is always symptomatic in all patients

4. **The incidence of MIOP is:**
   a. Unknown
   b. Approximately 1 in 2,000 live births
   c. Variable according to geographic location
   d. About 1 in 200,000 live births

5. **To minimize V/Q mismatch during thoracic surgery:**
   a. Infants should be positioned with the healthy lung up
   b. Adults should be positioned with the healthy lung up
   c. Infants should be positioned with the healthy lung down
   d. Positioning is not a major consideration
6. Osteopetrosis is characterized by:
   a. Abnormal bone resorption and unopposed bone formation
   b. Excessive production of carbonic anhydrase
   c. Decreased bone formation
   d. All of the above

7. With osteopetrosis, bones are likely to have:
   a. Increased density
   b. Increased fragility
   c. Decreased marrow
   d. All of the above

8. Which of the following is a disadvantage of Univent tubes?
   a. Frequent blocker displacement
   b. Cannot be used to apply CPAP to the operative lung
   c. Low volume/high pressure balloon cuff
   d. Frequent failures in placement

9. Indications for lung isolation and single lung ventilation do NOT include:
   a. Inability to ventilate an abnormal lung
   b. Need to avoid contamination of a normal lung
   c. Improved surgical access
   d. Severe respiratory impairment limiting adequate oxygenation

10. Anesthetic considerations in osteopetrosis include:
    a. Anemia
    b. Airway abnormalities
    c. Risk of infection
    d. All of the above