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Case Report

Esophageal Perforation in a Patient with Smith-Lemli-Opitz Syndrome

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ABSTRACT

Smith-Lemli-Opitz syndrome (SLOS) is a rare syndrome caused by an inborn error of cholesterol metabolism secondary to a deficiency in the 7-dehydrocholesterol (7-DHC) reductase enzyme leading to hypocholesterolemia. A broad spectrum of clinical manifestations can have significant surgical and anaesthetic implications. Patients exhibit growth retardation, microcephaly, congenital heart disease and moderate to severe intellectual disability. Distinctive facial features including micrognathia, cleft palate and prominent incisors can lead to difficult airway management [1]. We present the case of a 16-year-old female with SLOS who developed an esophageal perforation following esophageal foreign body retrieval. Anaesthetic and surgical considerations in a patient with SLOS are discussed.

Introduction

Smith-Lemli-Opitz syndrome (SLOS) is an autosomal recessive syndrome characterized by multisystemic abnormalities affecting the cardiorespiratory, genitourinary, gastrointestinal and central nervous systems. Prevalence of SLOS is estimated to be 1:20,000 to 1:40,000 live births, more commonly in individuals of northern or central European ancestry [1]. Characteristic features include narrow forehead, cleft palate, epicanthal folds, ptosis, micrognathia, anteverted nares and low-set ears. Patients exhibit postaxial polydactyly, 2-3 toe syndactyly, hypotonia, short stature and ambiguous genitalia [1]. There is a wide spectrum of disease severity, with mild forms exhibiting only subtle facial characteristics and little to no intellectual disability. DHCR7 is the only gene in which pathologic variants are known to cause SLOS. Most studies have identified an inverse correlation between serum cholesterol concentration and clinical severity of disease [1]. Patients with the lowest concentration of cholesterol (~ 10 mg/dL) exhibit the highest levels of mortality.

Case Description

In infancy, the patient was diagnosed with SLOS, due to positive genetic testing for the DHCR7 gene mapped to chromosome 11q12-13. The patient exhibited a constellation of findings including micrognathia, mental retardation, microcephaly, seizure disorder, Tetraolgy of Fallot (TOF) corrected in infancy, and a failure to thrive that prompted placement of a gastrostomy tube. Medical records indicated that the patient had a history of difficult intubation in the past, requiring fiberoptic intubation through a laryngeal mask airway (LMA) for prior surgical procedures. Now at 16 years of age, this 46 kg female presented with dysphagia, increased drooling, and regurgitation. Chest x-ray confirmed an esophageal foreign body and an upper endoscopy was planned for retrieval.

The patient arrived at the endoscopy suite, agitated, with a 22G IV in place. Standard ASA monitors were placed and the patient with bolused with midazolam and 0.5 mcg/kg dexmedetomidine. At this time, nitrous oxide and sevoflurane were utilized for inhalational induction to

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maintain spontaneous ventilation. Direct laryngoscopy failed to visualize the vocal cords by an experienced anaesthesiologist. Dexmedetomidine infusion was started at 0.5 mcg/kg/hr and 1-2 mg/kg propofol was bolused and the patient was successfully intubated orally using a fiberoptic bronchoscope. The endoscopist discovered the esophageal foreign body to be a marble, which was removed following repeated attempts. Upon examination of the esophagus following foreign body removal, a small tear was noted in the posterior wall of the cervical esophagus. A general surgery consult was called immediately, with the recommendation that no operative intervention was appropriate at this time. Upon emergence, the patient was extubated and managed postoperatively with cessation of oral intake, maintenance of oral hygiene, broad spectrum antibiotics and parenteral nutritional support in the intensive care unit. The patient was discharged home within 21 days in stable condition.

Discussion

SLOS syndrome raises several perioperative concerns. Patients with SLOS may present features associated with Pierre Robin sequence, including micrognathia, cleft palate and pseudomacroglossia, with an abnormally hard tongue [2]. The anaesthesiologist must be prepared for difficult ventilation and or intubation in patients with SLOS, utilizing fiberoptic bronchoscopy, video laryngoscopy, emergency airway devices and accessory anaesthesia providers as necessary. In addition to the potential for a difficult airway, cardiorespiratory complications can lead to further complications. An increased frequency of upper respiratory tract infections is seen in infancy and early childhood. Patients may chronically aspirate secondary to gastroesophageal reflux, pyloric stenosis or Hirschsprung disease [2]. Gastrostomy tube placement is common due to feeding intolerance, esophageal dysmotility, hypomotility and oral-motor incoordination, as evidenced in our patient.

Congenital pulmonary anomalies including hypoplastic or incomplete lobulation of the lungs can lead to reduced lung volumes and functional residual capacity, leading to a predilection for desaturation during anaesthetic induction. Congenital heart disease can affect 37-84% of patients, commonly including atrioventricular canal defects and anomalous pulmonary venous return [3]. Behavioural symptoms in patients with SLOS include hyperreactivity, irritability, sleep cycle disturbances, self-injurious behaviour, autism spectrum disorders, and deficiencies in social interactions. Developmental abnormalities of the central nervous system include abnormalities of myelination, cerebral ventricular dilatation, holoprosencephaly, Dandy-Walker malformation and structural malformations of the corpus callosum and cerebellum [4].

Adrenal insufficiency and electrolyte abnormalities including hypoglycemia can be seen in patients with SLOS, as cholesterol is a precursor to steroid hormones. Low serum testosterone concentrations can be seen in severely affected males. Although case reports have described the incidence of muscular rigidity and malignant hyperthermia (MH) in SLOS patients, there is insufficient evidence to support an association between SLOS and MH [2]. It is probably unnecessary to utilize a non-triggering anaesthetic in these patients, as the risk for MH is minimal, and there are numerous other anaesthetic implications to consider. Children with SLOS exhibit severe UVA mediated photosensitivity [3]. Differential diagnosis includes Trisomy 13 syndrome, Trisomy 18 syndrome, Dubowitz syndrome, Meckel-Gruber syndrome, Noonan syndrome, Simpson-Golabi-Behmel syndrome, Pseudotrisomy 13 syndrome, Pallister-Hall syndrome, and Nguyen syndrome [5].

Cholesterol supplementation can result in clinical improvement in patients with SLOS; exogenous supplementation with egg yolks or crystalline cholesterol can raise cholesterol levels and decrease the levels of precursors 7-DHC and 8-DHC. Management of the disease is facilitated by a nutrition consultation, physical, speech and occupational therapies; gastrostomy tube placement for feeding, and surgical correction of congenital heart disease and musculoskeletal abnormalities. Psychotropic drugs including haloperidol, trazadone and aripiprazole should be strictly avoided in these patients as they can cause elevated levels of 7-DHC [6]. Iatrogenic esophageal perforation can occur during endoscopic removal of a foreign body. The size of the defect, its edges, and the presence of bleeding must be investigated prior to attempting endoscopic closure. Tissue sealants such as fibrin glue and cyanoacrylate can be utilized in addition to clip applicators if the defect is smaller than 10 mm [7]. If the size of the defect is between 30-70% of the esophageal lumen, endoscopic stent placement has been advised.

In the case of esophageal stenosis or a perforation larger than 2 cm, a self-expandable metallic stent has been advocated to prevent leak and stricture formation as well as to facilitate mucosal healing. Stenting is not recommended when perforation is in the cervical esophagus, gastroesophageal junction or when the defect is greater than 6 cm, as the stent can easily migrate [7]. Surgical repair of esophageal perforation is recommended in the presence of a tracheoesophageal fistula, or when perforation involves the thoracic cavity with evidence of sepsis. Immediate surgical intervention is not advised secondary to esophageal friability and the risk of anastomotic disruption. Infection usually resolves 4-6 weeks following initial injury, at which time surgical repair is deemed appropriate. Pediatric esophageal perforation is usually managed conservatively, as long as there is no downstream obstruction, contamination is well addressed, and nutrition is optimized [7]. Although the combination of esophageal perforation in a patient with SLOS provides numerous anaesthetic challenges, it can be managed appropriately with careful perioperative planning.

Consent

The patient's family provided informed consent to publish this manuscript.

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