Case Report: Smith-Lemli-Opitz Syndrome and the intraoperative use of fresh frozen plasma

Author(s): DA Young (1), FD Porter (2)
Affiliation(s): (1) Baylor College of Medicine/Texas Children's Hospital; Houston, Texas (2) Heritable Disorders Branch, National Institute of Child Health and Human Development, National Institutes of Health; Bethesda, Maryland

Introduction: Smith-Lemli-Opitz Syndrome (SLOS) is an autosomal recessive disorder of cholesterol synthesis with an estimated incidence of 1:50,000. SLOS is associated with a broad clinical presentation and several anesthetic implications including increased risk of difficult intubation and aspiration pneumonia. SLOS results from a mutation on chromosome 11 in the gene encoding 7-dehydrocholesterol reductase (DHCR7). DHCR7 is responsible for the reduction of 7-dehydrocholesterol (7-DHC) to cholesterol in the final step of cholesterol synthesis. As a result of this mutation, elevated levels of 7-DHC have been associated with toxic effects and lack of cholesterol production has been implicated in the development of neurologic manifestations and adrenal insufficiency. Adrenal insufficiency has been reported in SLOS due to a lack of endogenous steroid production. Treatment of SLOS is supportive using cholesterol supplementation and management of associated conditions. Fresh frozen plasma (FFP) is a good source for cholesterol supplementation and we will describe the intraoperative use of FFP in a patient with SLOS.

Case Report: Our patient is a 7-year-old boy, 17 kg, with a history of SLOS, scheduled for tibial osteotomy and dental restoration. He has no drug allergies; preoperative medication consists of enteric cholesterol supplementation. Past medical history is significant for gastroesophageal reflux, developmental delay, and failure to thrive. Past surgical history is significant for repair of undescended testes, hypospadias, syndactyly, and ptosis. Vital signs were within normal limits, physical exam was significant for microcephaly, and airway examination was judged to be adequate. A previous echocardiogram was significant for a patent foramen ovale. Laboratory studies including cell blood count and electrolytes were within normal limits. Intraoperative management consisted of inhalation induction with sevoflurane followed by iv placement. Our patient then received 10 cc/kg of FFP. Mask ventilation and intubation were both easy and uneventful. Maintenance of anesthesia was with sevoflurane, fentanyl, and rocuronium. The intraoperative course was uncomplicated and the patient was extubated awake at the conclusion of the procedures. No evidence of adrenal insufficiency occurred. His perioperative course was uneventful.

Table 1: Common clinical features of Smith-Lemli-Opitz Syndrome.

<table>
<thead>
<tr>
<th>microcephaly</th>
<th>hypotonia</th>
<th>growth retardation</th>
<th>ptosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>micrognathia</td>
<td>pulmonary hypoplasia</td>
<td>failure to thrive</td>
<td>cryorchidism</td>
</tr>
<tr>
<td>antverted nares</td>
<td>congenital heart disease</td>
<td>gastroesophageal reflux</td>
<td>hypospadias</td>
</tr>
<tr>
<td>cleft palate</td>
<td>syndactyly</td>
<td>developmental delay</td>
<td>ambiguous genitalia</td>
</tr>
</tbody>
</table>

Discussion: SLOS was first described in 1964 and is a relatively common genetic disorder with an incidence only behind cystic fibrosis and phenylketonuria. Diagnosis of SLOS is by detection of an elevated 7-DHC level. Since identification and treatment of SLOS is now possible, the likelihood of patients requiring anesthesia services in the future is likely to be higher. Anesthesia considerations are based on associated conditions but typically involve an increased risk of difficult intubation, aspiration of gastric contents, and adrenal insufficiency. Other manifestations of SLOS such as congenital heart disease and neurologic disorders must also be considered. The incidence of malignant hyperthermia has not been shown to be increased for patients with SLOS. Adrenal insufficiency can occur in patients with SLOS.
during stressful conditions including the perioperative period. The etiology of adrenal insufficiency in SLOS is postulated to occur from lack of endogenous adrenal steroid production due to the lack of cholesterol. Cholesterol supplementation is preferred to chronic corticosteroid administration since long-term administration of corticosteroids can result in significant morbidity including hypertension, gastrointestinal bleeding, and diabetes. Corticosteroids only focus on the prevention of adrenal insufficiency while cholesterol supplementation prevents the accumulation of toxic 7-DHC while also supplying a precursor to produce endogenous steroids. The use of FFP in SLOS patients has been anecdotally reported to improve the overall condition of medical patients with acute infections and poor wound healing. During the perioperative period, anecdotal evidence suggests that patients with SLOS who receive FFP also have improved outcomes and are less likely to develop acute adrenal insufficiency. Simvastatin, an HMG-CoA reductase inhibitor, is currently under investigation in the treatment of SLOS. Simvastatin is hypothesized to block the cholesterol synthesis pathway to avoid the formation of toxic compounds such as 7-DHC. We have presented the use of intraoperative FFP in a patient with SLOS. Anesthesiologists should anticipate requests in the future for the use of intraoperative FFP in patients with SLOS and understand the rationale for its use.

References: