Anesthetic management of an infant with Zellweger syndrome undergoing closure of patent ductus arteriosus and pulmonary artery banding: A case report

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Abstract

Zellweger syndrome (ZS) is a rare autosomal recessive inherited disorder within the spectrum of peroxisome biogenesis disorders. It is a progressive and fatal disorder with multiple congenital anomalies. There may be some challenges for anesthesiologists in patients with ZS. We report the anesthetic management of an infant with ZS undergoing closure of patent ductus arteriosus and pulmonary artery banding.

Introduction

Zellweger syndrome (ZS), reported independently by Bowen et al. in 1964 [1] and Smith et al. in 1965 [2], is an autosomal recessive inherited disorder within the spectrum of peroxisome biogenesis disorders that includes neonatal adrenoleukodystrophy, infantile refsum disease, and rhizomelic chondroplasia punctate. This syndrome also described as “cerebrohepatorenal syndrome” due to multiple congenital anomalies involving brain, liver, and kidneys [1]. Facial dysmorphism, neonatal hypotonia, poor feeding, neurocognitive delay and seizures, hepatomegaly and renal cysts are main characteristics of this disease.

Peroxisomes, an intracellular organelle containing over 50 enzymes for metabolism of fatty acids, are incomplete in peroxisome biogenesis disorders and they fail to perform β-oxidation of fatty acids, the α-oxidation of phytic acid and similar compounds, piperolic acid oxidation, and early plasmalogen synthesis [3]. Due to these defects, very long chain fatty acids accumulate in developing organs such as liver, bone, and kidney and cause intracellular damages. There is also a neuronal migration defect of cortical neurons that can be resulted with cortical gyral abnormalities (lissencephaly, pachygyria, polymicrogyria), generalized or focal leukoencephalopathy, and brain atrophy [4].

We report the anesthetic management of an infant with ZS undergoing closure of patent ductus arteriosus (PDA) and pulmonary artery banding.

Case Report

The patient was a 4.5-month-old girl born at 38 weeks and 1 day of gestation with 2700 g body weight via spontaneous vaginal delivery without the antenatal follow-up. She had one healthy sister and one healthy brother, and there was the consanguinity between her parents. At birth she had dysmorphic face features including hypertelorism, malformed ears, and redundant skin at the neck, and hypotonia. Structural heart defects such as ventricular septal defect (VSD), atrial septal defect (ASD), and PDA, seizures and hydrocephaly was identified after delivery and the baby was transferred to the neonatal intensive care unit (NICU). During the 40 days follow-up in the NICU long chain fatty acids (C24:0/C22:0; C26:0/C22:0; C26:0) were found increased, and ZS was diagnosed. The baby was discharged from hospital after 2 months follow-up. In one of her routine outpatient controls when she was 4.5-month-old, SpO2 was found <90% and acute onset of bronchiolitis was diagnosed. In the physical examination body weight, height and head circumference were 3400 g (<3 percentile), 56 cm (10 percentile), and 35 cm (10 percentile), respectively. Due to the sustained desaturation and poor medical conditions, the baby was transferred to the pediatric ICU. She was intubated, and mechanical ventilation support was initiated. The echocardiography revealed perimembranous VSD, ostium secundum ASD, PDA, bicuspid aortic valve, mild aortic stenosis, mild aortic insufficiency, and moderate pulmonary hypertension. Enteral captopril, intravenous (IV) dobutamine (5 mcg/kg/min), nebulized salbutamol, enteral phenobarbital and IV antibiotic therapy...
were initiated. Due to sustained pulmonary edema, enteral sildenafil citrate was added to the treatment. Tracheostomy was performed due to prolonged mechanical ventilation support. The patient’s pulmonary pressure increased and her general condition gradually worsened. Echocardiography revealed VSD diameter of 6.7 mm, gradient between left-right ventricle was 26 mmHg, ASD diameter of 4.2 mm, and gradient of stenotic aortic was 23 mmHg. Closure of PDA and pulmonary banding were expected to reduce pulmonary blood flow and pulmonary artery pressure.

The baby was accepted for anesthesia as class ASA IV. The parents were informed about the risks and a written informed consent was obtained. Pre-operative laboratory investigations showed abnormalities such as aspartateaminotransferase 152/UL, alanine aminotransferase 77/UL, albumin 2.7 g/dL, and total protein 4.4 g/dL. The baby was transferred to the operating room with O₂ supply through the tracheostomy cannula. After the application of standard noninvasive monitoring including electrocardiogram, SpO₂ and noninvasive intermittent blood pressure, general anesthesia was induced with 4 mg/kg sodium thiopental, fentanyl 2.5 mcg/kg, and rocuronium bromide 0.5 mg/kg. Anesthesia was maintained using controlled ventilation with sevoflurane 2% in 50-50% oxygen in the air through tracheostomy cannula. Central venous and arterial accesses were achieved via the right femoral route with 4 F, double lumen, 5 cm long catheters, respectively. 1 mcg/kg of fentanyl and 0.2 mg/kg of rocuronium were added as needed. Prebanding invasive blood pressure that was 71/34 (47) mmHg increased to 87/48 (61) mmHg following PDA ligation and banding. Furthermore SpO₂ decreased from 99% to 94% after banding (FiO₂ = 0.5). The operation lasted for 75 min without any surgical and/or anesthetic problem. After pulmonary banding 5 mcg/kg/min dopamine infusion was continued for hemodynamic support. After an uneventful closure of PDA and pulmonary artery banding, the baby was transferred to the pediatric ICU intubated. She died in the NICU 9 days later postoperatively.

Discussion

ZS is a progressive and fatal disorder with multiple congenital anomalies. The worldwide estimated prevalence is between 1:50,000 and 1:100,000 [5]. Although classical clinical features are the key factor in the diagnosis of ZS, demonstration of elevated plasma and tissue levels of very long chain fatty acids, phytanic acid, piperolic acid, and bile salt precursors is beneficial in the confirming of the diagnosis [6]. Trisomy 21, Prader–Willi syndrome, and congenital neuromuscular diseases such as spinal muscular atrophy, and congenital myotonic dystrophy are other diseases that should be considered in the differential diagnosis of ZS in hypotonic dysmorphic newborn infants [7]. Although the prognosis is poor and, expected survival is <1 year of age, with attentive care and clinical variability there are reports of children who survive up to 3 years [8]. Death usually occurs due to progressive apnea or respiratory compromise from infection, and liver failure with gastrointestinal bleeding [9].

There may be some challenges for anesthesiologists in patients with ZS. These children often present with respiratory failure due to severe hypotonia, apnea, and recurrent aspiration pneumonia due to gastroesophageal reflux. Careful preoperative pulmonary evaluation is crucial in these children to reveal pulmonary status. In our patient, there was tracheostomy cannula in the airway because of bronchiolitis and prolonged mechanical ventilation support. Although sedative premedication is not advisable because of the risk of respiratory compromise due to preexisting hypotonia, our patient was under sedation to attenuate the anxiety, pain, and agitation associated with mechanical ventilation. Ranitidine was given for aspiration prophylaxis in the perioperative period.

There are some precautions during anesthesia induction and endotracheal intubation. Because of gastroesophageal reflux and possibility of aspiration pneumonia, rapid sequence induction and Sellick maneuver is recommended. During anesthesia induction, depolarizing neuromuscular blockers are not recommended because of the possible risk of hyperkalemia associated with the muscular disease of children with ZS. Besides, non-depolarizing neuromuscular blockers may induce postoperative respiratory depression because of preexisting hypotonia.

Hepatic dysfunction in ZS children can induce several problems such as hypoalbuminemia, coagulopathy, and alteration of the metabolism of the drugs that rely on the liver pathway. In our patient, we used the albumin for hypoalbuminemia, and we preferred anesthetic drugs that were considered as relatively safe with liver dysfunction. In these patients, the chronic use of anticonvulsant medication can additionally alter the hepatic function and anesthetic agents that may decrease the seizure threshold should be avoided. Antibiotic prophylaxis for infective endocarditis is essential in children with congenital cardiac abnormalities.

Conclusion

In conclusion, ZS, although a rare disorder, can pose challenges for anesthesiologists. Detailed preoperative evaluation and readiness for airway problems and multigorgan anomalies can help anesthesiologists to prevent perioperative morbidity and mortality.
References


