Cardiology in the Young

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Successful oral midodrine therapy for treatment of refractory postoperative chylothorax in an infant

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Brief Report

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Abstract

Refractory chylothorax, a postoperative complication of CHD, is difficult to manage and sometimes fatal. Herein, we report the case of a 10-month-old infant with 22-mosaic trisomy and a coarctation complex, who developed refractory chylothorax after cardiac repairs and was successfully treated with midodrine, an oral alpha-1-adrenoreceptor agonist. Midodrine may be used as adjunctive therapy for postoperative refractory chylothorax.

Postoperative chylothorax of CHD surgery is difficult to manage and sometimes fatal.[1] Treatment strategies include parenteral nutrition, octreotide, and surgical approaches; however, some cases are refractory, affecting their morbidity and mortality significantly. Recently, some neural moderators such as alpha-adrenoceptor agonists and beta-adrenoceptor antagonists have been reported as additional treatment for chylothorax. These drugs have been shown to promote lymphatic vasoconstriction, consequently reducing chyle flow.[2] Ethylephrine, an alpha-1-adrenoceptor agonist, is highly effective for adult patients with postoperative chyle leak;[3] however, in Japan, ethylephrine is only available in an injectable form, which can be difficult to administer. Similarly, the efficacy of propranolol, a beta-adrenoceptor antagonist, on chylous effusions in congenital and postoperative infants has been reported.[4] However, its negative inotropy should be considered, especially in the postoperative stage of CHD.

Midodrine, an oral alpha-1-adrenoceptor agonist, has recently been reported as a novel treatment for lymphatic disorders, such as chylothorax[5–7] and Fontan-associated protein-losing enteropathy.[8] We postulated that midodrine may be effective in the postoperative chylothorax of infants with CHD. To our knowledge, this is the first successful case of midodrine therapy for postoperative chylothorax in an infant with CHD.

Case report

The patient was a 10-month-old male, born at 38 weeks' gestation with a birth weight of 1706 g. Due to fetal growth restriction, amniocentesis was performed and 22-mosaic trisomy was identified. After birth, he was diagnosed with ventricular septal defect, coarctation of the aorta, and persistent left superior caval vein by echocardiogram. A two-stage repair was planned, and bilateral pulmonary artery banding was performed on day 8. On day 49, he weighed 2798 g and underwent extended aortic arch anastomosis and ventricular septal defect patch closure.

After the 2nd surgery, the patient developed a high-output chylothorax (>100 mL/day). Although several treatments, such as steroids, factor XIII, octreotide (maximum dose of 10 μg/kg/h), and medium-chain triglyceride milk nutrition, he required prolonged parenteral nutrition. On postoperative day 35, prolonged placement of the central venous catheter resulted in obstructions of both bilateral superior caval vein. Pleural fluid analysis revealed a white blood cell count (1,605 cells/μL, 95% lymphocytes), triglyceride level (56 mg/dL), and cholesterol level (47 mg/dL) consistent with a diagnosis of chylothorax. On postoperative day 62, he developed *Staphylococcus aureus* bacteraemia and sternal osteomyelitis, and open chest drainage was performed on postoperative day 66. Cephazolin was continued for the infection. He had no pleural effusion during total parenteral nutrition; however, the pleural effusion recurred when octreotide was tapered. A pleurodesis was performed on the left side on postoperative day 90 and on the right side on postoperative days 93 and 105. Thereafter, despite increased medium-chain triglyceride milk tolerance, it was insufficient to discontinue central venous nutrition.

Based on previous reports,[5,6] midodrine was administered on postoperative day 140. The dosage of midodrine was started at 0.2 mg/day (0.1 mg/kg/day) every 12 h. No adverse effects, including hypertension or tachycardia, were observed, and pleural effusions subsided, even when enteral nutrition was gradually increased (Fig. 1). Central venous nutrition and octreotide were discontinued on postoperative days 177 and 213, respectively. Medium-chain triglyceride milk was gradually transitioned to regular milk, and he was discharged on postoperative day 340 with a weight of 2594 g.

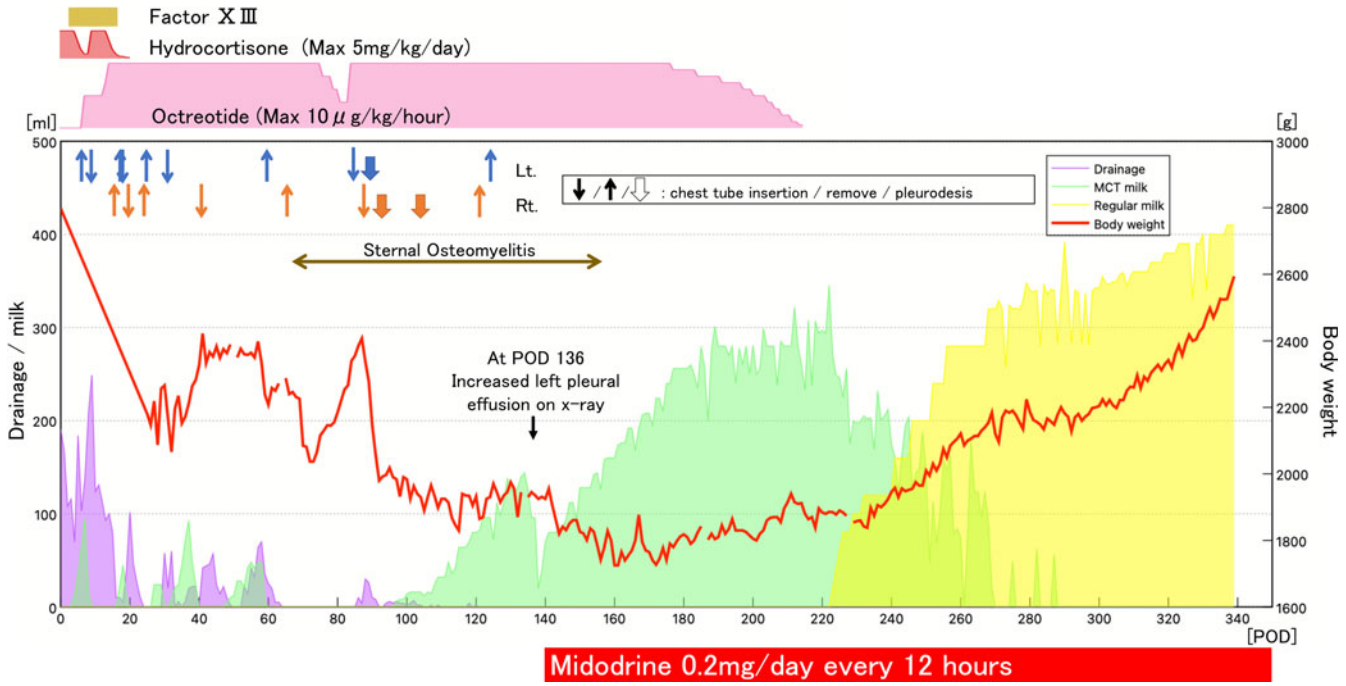

Figure 1. The clinical course of the case. The purple-shaded area indicates the amount of drainage. The green- and yellow-shaded areas indicate the amount of MCT milk and regular milk, respectively. The red line indicates the patient's weight. The horizontal axis indicates the postoperative day. When midodrine administration was started, the decrease in pleural effusion was confirmed by chest radiography, which allowed the progression of nutritional forms, such as increasing the amount of MCT milk and subsequently changing to regular milk. POD = postoperative day; MCT = medium-chain triglyceride.

Although the midodrine was discontinued one year after discharge, there have been no recurrences of chylothorax over the subsequent two years of observation.

Discussion

Our experience with this patient suggested that midodrine was effective for refractory postoperative chylothorax in an infant with CHD and may be an option for such a condition. Refractory chylothorax, one of the postoperative complications of CHD, is difficult to manage and sometimes fatal. While the causes of postoperative pleural effusions vary, congestion of lymphatic flow associated with bilateral superior caval vein obstruction was one of the most important causes in this case. This suggested that midodrine therapy might accelerate lymphatic vasoconstriction and improve chylothorax.

Determining drug dosages for infants is complex. The dosage we determined was based on the standard adult dose, 4–8 mg/day, at one-60th of the adult dose per body weight (0.07–0.13 mg/kg/day).[6,8] Dosages vary in the literature, with 7.5–40 mg/day in adult cases,[6,8] 3.75 mg/day in a 4-year-old girl,[8] and 0.5–1.0 mg/day in a 5-kg neonate.[7] Further studies are needed to determine the appropriate dosage.

Although hypertension is a known side effect of midodrine, the drug is relatively safe and readily available. In infants, treatments such as lymphatic ligation or embolisation of anomalous lymphatic connections are considered to be highly invasive. Furthermore, due to the prolonged requirement for treatment of sternal osteomyelitis following intracardiac repair in this case, midodrine therapy was initiated.

Thus, midodrine may be used as adjunctive therapy for postoperative chylothorax. To validate the efficacy and safety of this drug, further studies are required.

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Competing interests. None.

Ethical standard. The authors assert that this work complies with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. This case was approved by the patient's family.

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