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Case Report

Midodrine: A Golden Therapeutic Sword for High-Output Chylothorax

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ABSTRACT

Chylothorax, a significant complication after congenital heart surgery, adversely impacts children's health and can lead to various morbidities, including nutritional deficiencies, prolonged ICU stays, extended hospitalizations, and an increased risk of mortality. Initial management of this condition involves nutritional strategies, such as providing gut rest and implementing a diet based on medium-chain triglycerides and low fat. Pharmacological options and surgical interventions are subsequently considered for refractory cases. This report describes a child who developed high-output chylous effusion following open-heart surgery for the correction of congenital heart disease. This effusion was successfully managed using chest drainage, nutritional intervention, and pharmacotherapy with midodrine. We hope the observations from this case report will help interventionists optimize chylothorax management and consider midodrine as a therapeutic option and a potential area of research for managing high-output chylothorax, before resorting to surgical intervention. ***(Iranian Heart Journal 2025; 26(3): 92-98)***

KEYWORDS: Chylothorax, Midodrine, High-output chylous effusion

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Chylothorax stands as a rare yet serious early postoperative complication following pediatric cardiothoracic surgery. Its overall reported incidence in pediatric patients ranges from 2.8% to 3.8%, with higher rates observed in neonates. [1, 2, 3] Postoperative lymphatic failure has been attributed to 3 primary mechanisms: traumatic leakage from the thoracic duct or its branches, pulmonary lymphatic perfusion syndrome, and reduced central lymphatic flow. [4, 5, 6] Pulmonary lymphatic perfusion syndrome is characterized by impaired lymphatic drainage resulting from increased central venous pressure associated with right heart dysfunction. [7] The gold standard for diagnosing chylothorax is the detection of chylomicrons in pleural fluid via lipoprotein electrophoresis. [1, 8] Nonetheless, diagnosis can also be established if either: (a) milky or whitish pleural fluid is present, accompanied by a white blood cell (WBC) count > 1000 cells/μL, a lymphocyte percentage > 70–80%, and a triglyceride level > 110 mg/dL in a non-fasted child; or (b) the pleural fluid triglyceride level is higher than the serum triglyceride level. [1, 8]

High-volume chylous losses result in severe nutritional, metabolic, and immunologic abnormalities and are associated with very high morbidity and mortality if chylothorax is not promptly addressed. [2, 9] While definitive

evidence-based guidelines for managing postoperative chylothorax in children are yet to be established, nutritional management remains the cornerstone of treatment. [10, 11] Management protocols often involve strategies such as complete gut rest with total parenteral nutrition (TPN), a diet rich in medium-chain triglycerides (MCTs) and low in fat, or defatted breast milk for neonates, frequently accompanied by adjunctive octreotide infusion. [9, 11] If a child fails to respond to conservative measures or develops refractory or persistent chylothorax, interventional or surgical treatments may be required. These options include thoracic duct repair, muscle flap coverage, right thoracotomy or video-assisted thoracoscopic surgery (VATS), talc pleurodesis, or chest exploration. [12-14] Recent research indicates that midodrine, an α1-adrenergic agonist, is also effective in managing refractory chylothorax before surgical interventions are considered. [15, 16] This report details a case of high-output chylothorax that developed following congenital cardiac surgery and was successfully managed with midodrine, in conjunction with nutritional intervention and water seal drainage.

CASE PRESENTATION

A 3-year, 9-month-old immunized boy weighing 8.5 kg, born to non-consanguineous parents, presented to the outpatient department with recurrent respiratory tract infections, respiratory distress, and cyanosis (SpO_2 76% on room air). Echocardiography and cardiac catheterization revealed a diagnosis of type-I truncus arteriosus with a large subtruncal ventricular septal defect, bilateral superior vena cava, and a bridging innominate vein. The patient also exhibited severe pulmonary hypertension, with a mean pulmonary artery pressure of 55 mm Hg and elevated pulmonary vascular resistance (5.49 Wood units), which was reversible.

The child underwent truncus arteriosus repair via the Rastelli procedure. The postoperative course was uneventful, managed with diuretics (furosemide and spironolactone), aspirin, inotropes, and supportive care. He was discharged seven days post-surgery. However, during a follow-up visit 1.5 months after discharge, the child developed severe respiratory distress, facial swelling, and abdominal distension.

On clinical examination, the child presented with facial puffiness, a temperature of 37.2 °C, and tachypnea (respiratory rate: 38/min). His oxygen saturation (SpO_2) was 94% while receiving 1 liter per minute of supplemental oxygen. He appeared anicteric, wasted, and non-edematous, with a visible BCG scar.

Chest findings included a bulge on the left side, restricted chest movement, and reduced expansibility. The trachea was deviated to the right, with stony dullness on percussion and absent breath sounds below the 4th intercostal space, accompanied by coarse crepitations.

Chest X-ray (Figure 1) revealed a homogeneous opacity in the middle and lower zones of the left hemithorax. Bedside ultrasonography (Figure 2) confirmed a large pleural effusion, prompting urgent left-sided intercostal chest drainage (ICD) with a water seal.

During the procedure, 470 mL of turbid, milky-white pleural fluid (Figure 3) was drained, after which the child showed significant clinical and radiological improvement post-drainage (Figure 4). Pleural fluid analysis demonstrated markedly elevated triglycerides (576 mg/dL) with normal glucose (81.8 mg/dL), elevated protein (4 g/dL), and chloride levels (111 mmol/L), along with lymphocyte-predominant pleocytosis (1100 WBCs/μL; 85% lymphocytes). Microbiological studies were negative for acid-fast bacilli and adenosine deaminase, with sterile cultures. Hematologic evaluation revealed hemoglobin 11.6 g/dL, leukocytosis (8000 WBCs/μL;

58% neutrophils, 37% lymphocytes), thrombocytosis (350,000 platelets/μL), and hypoalbuminemia (2.0 g/dL). Hepatic and renal profiles were within normal limits, including alanine aminotransferase (32 U/L), aspartate aminotransferase (36 U/L), serum creatinine (0.7 mg/dL), and blood urea nitrogen (35 mg/dL). The child was maintained nil per os (NPO) while continuing diuretics and supportive management. Immediate postprocedural ultrasonography and chest radiography revealed decreased pleural fluid, right ventricular dysfunction, and radiological improvement.

The patient received a 20% human albumin transfusion on days 1 and 2 following intercostal drainage. MCT-based low-fat diet was initiated on postprocedural day 1; nevertheless, despite decreased output volume, the milky character of pleural fluid persisted. Serial imaging demonstrated ongoing pleural effusion with inadequate volume reduction (output remained > 20 mL/kg/day, measuring 410 mL on postprocedural day 5). Given the patient's stable condition, TPN was not initiated. As the pleural fluid output and characteristics remained unchanged (persistent high-volume chylous drainage), we reviewed the literature for alternative management options. Two case reports (1 pediatric and 1 adult) described the successful management of refractory chylothorax using midodrine without adverse effects. [15, 16] Based on this evidence, we initiated off-label midodrine therapy, an α-1 adrenergic agonist, at an initial dose of 0.5 mg/kg/day divided into 3 doses for postcardiac surgery chylothorax. The dose was subsequently titrated upward to 1 mg/kg/day. By day 3 of midodrine therapy, we observed a marked reduction in pleural fluid output (145 mL) with improved fluid characteristics (Figure 5).

Serial radiographic monitoring demonstrated resolution of the chylothorax, with pleural drainage decreasing to < 2 mL/kg/day by day 10 of midodrine therapy (Figure 5). Complete resolution occurred by day 12, permitting chest tube removal on postprocedural day 14. No midodrine-related adverse effects were observed during hospitalization. Following comprehensive parental education regarding follow-up care, MCT diet duration, and transition to regular diet, the patient was discharged.

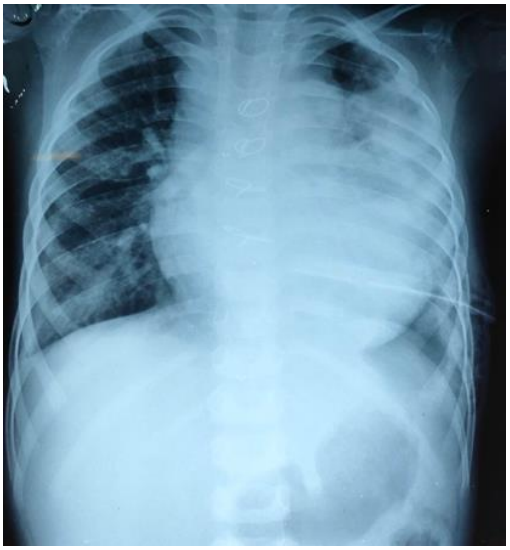

Figure 1. Chest X-ray (anteroposterior view) demonstrates homogeneous opacity involving the upper, middle, and lower zones of the left hemithorax.

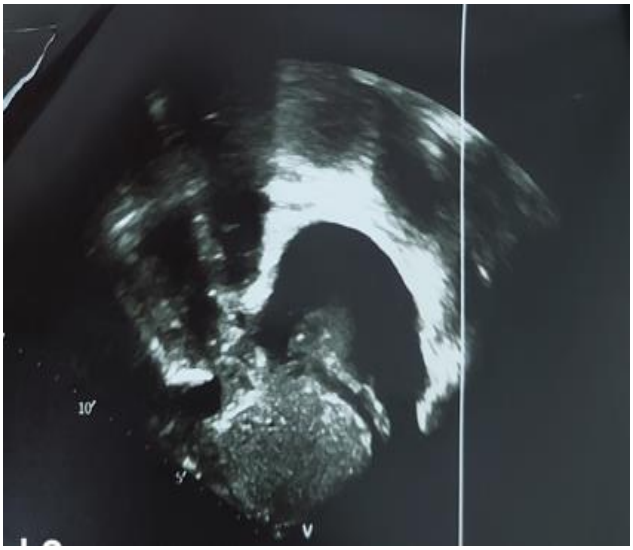

Figure 2. The patient's echocardiogram demonstrates significant left-sided pleural effusion.

Figure 3. The image shows chylous pleural fluid collected in a water-seal drainage system following intercostal catheter placement.

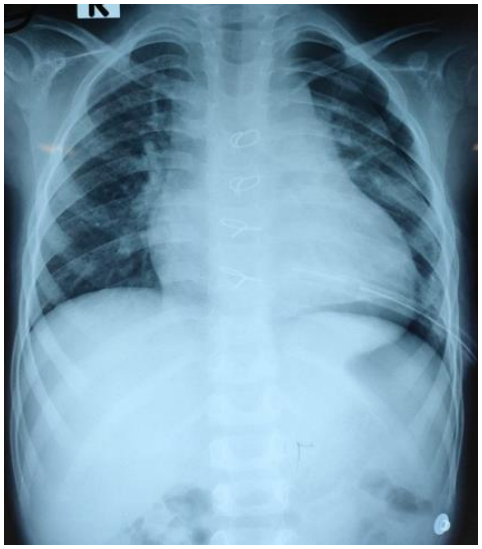

Figure 4. The patient's chest X-ray shows improvement after intercostal catheter placement.

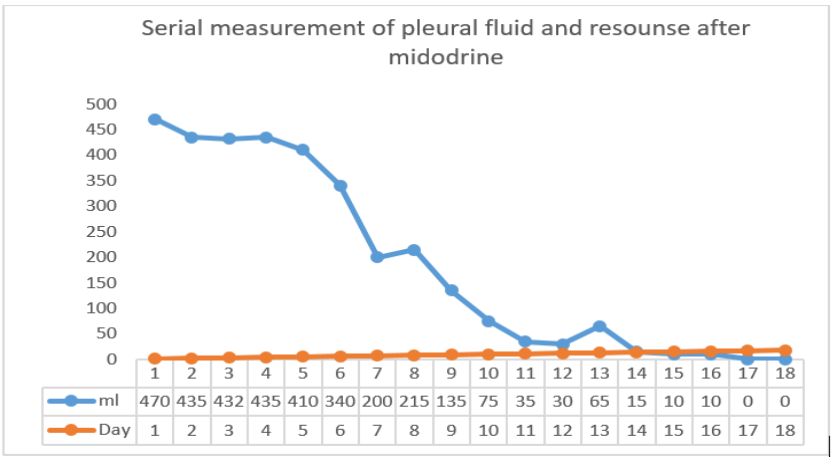

Figure 5. The image showcases the serial quantification of pleural fluid output demonstrating therapeutic response to midodrine administration.

DISCUSSION

Outcomes following complex cardiac surgery in the pediatric population have improved due to recent advancements in the medical and surgical care of congenital heart disease; still, the burden of postoperative morbidity remains significant. Chylothorax, a relatively rare complication after cardiothoracic surgery, can lead to nutritional, metabolic, and immune deficiencies in affected children if not addressed promptly in the early postoperative period. Several theories have been proposed regarding the development of chylous fluid accumulation in the chest cavity, primarily attributing it to lymphatic system injury, systemic venous hypertension, and right ventricular dysfunction after surgical correction. [7] While no consensus diagnostic criteria exist for chylothorax, our patient met several

established supportive indicators: (1) milky-white pleural fluid appearance; (2) elevated pleural fluid triglycerides (576 mg/dL); and (3) lymphocyte-predominant pleocytosis (1100/μL WBC with 85% lymphocytes), findings consistent with multiple published studies. [1,8] Chylothorax may be classified as high-output (≥ 20 mL/kg/day) or low-output (< 20 mL/kg/day). Based on daily drainage volume, this case qualified as high-output chylothorax. [17]

Conservative management to promote lymphatic healing typically includes gut rest through NPO status with TPN, followed by gradual advancement to either MCT-based enteral nutrition or a low-fat diet. Current guidelines suggest initiating either an MCT-based diet or a low-fat regimen for all chylothorax cases at diagnosis. [15] For high-output chylothorax (≥ 20 mL/kg/day), current recommendations advocate an initial NPO status with TPN, with daily monitoring of output volume. When chylous output decreases to < 10 mL/kg/day, management may transition to low-output protocols, though optimal treatment duration remains undefined in the literature. [10]

Initial management included tube thoracostomy and NPO status. After 48 hours of observation, considering the child's nutritional requirements, we initiated MCT-based enteral nutrition. Nonetheless, chylous output remained unchanged (persistent high-volume drainage). Given the patient's ability to tolerate oral intake and the known risks of TPN, including infection risk and cost burden, we opted for an oral MCT diet rather than TPN. [18] When conservative measures failed to reduce output, we reviewed the literature for alternative interventions before considering surgery. Limited evidence exists for octreotide infusion as a preoperative intervention, while case reports describe successful use of oral midodrine for refractory chylothorax in adults, neonates, and infants. [15, 16, 19] One study in adults showed that midodrine is effective against post-surgical chylothorax at a dose of 20 mg 3 times per day, and a neonate having chylothorax successfully resolved at a dose of 1 mg/day without any adverse effect. [16-18] We started midodrine initially at a dose of 0.5 mg/kg/day. The condition slightly improved after 3 days of initiation, and we increased the dose to 1 mg/kg/day, and after that, the output significantly decreased. Midodrine, a selective α-agonist, causes systemic vasoconstriction and may reduce the chyle flow by increasing the contraction of smooth muscle of the lymphatic vessel. [15, 16-18]

Consistent with the proposed mechanism and published reports, our patient demonstrated an excellent clinical response to oral midodrine therapy, achieving complete resolution of chylous drainage. Chest tube removal was performed on posttreatment day 12 (for the initial drainage catheter) and day 14 (for subsequent monitoring), corresponding with full resolution of the chylothorax.

CONCLUSIONS

Midodrine, an oral selective α-agonist, causes systemic lymphatic constriction. Consequently, it may be used as an adjunctive therapeutic medication for chylothorax, potentially by decreasing chyle leakage from the lymphatic system. This case report may encourage researchers to further investigate the therapeutic use of midodrine, aiming to determine an appropriate dosage regimen and evaluate its safety profile in the management of high-output chylothorax.

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Conflict of Interest
The authors declare no conflicts of interest.

Ethical Considerations

Informed written consent for publication was obtained from the child's legal guardian.

Authors' Contributions

- Conception of the study and data gathering: AT
- Study design, data collection, and analysis: AT
- Management of chest drainage: MIH
- Manuscript writing and submission: AT, NAH
- Manuscript editing and final approval: AT, NAH

REFERENCES

1. Samanidis G, Kourelis G, Bounta S, Kanakis M. Postoperative Chylothorax in Neonates and Infants after Congenital Heart Disease Surgery—Current Aspects in Diagnosis and Treatment. Nutrients 2022:14:1803.

2. Mery CM, Moffett BS, Khan MS, Zhang W, Guzmán-Pruneda FA, Fraser CD, et al. Incidence and treatment of chylothorax after cardiac surgery in children: Analysis of a large multi-institution database. J Thorac Cardiovasc Surg 2014; 147: 678–86.

3. Buckley JR, Graham EM, Gaies M, Alten JA, Cooper D, Costello JM, Domnina Y, Klugman D, Pasquali SK, Donohue JE, et al. Clinical epidemiology and centre variation in chylothorax rates after cardiac surgery in children: A report from the Pediatric Cardiac Critical Care Consortium. Cardiol Young 2017; 27:1678–85.

4. Savla JJ, Itkin M, Rossano JW, Dori Y. Postoperative chylothorax in patients with congenital heart disease. J Am Coll Cardiol 2017; 69: 2410–22.

5. Dori Y, Keller MS, Fogel MA, et al. MRI of lymphatic abnormalities after functional single-ventricle palliation surgery. Am J Roentgenol 2014; 203:426–31.

6. Dori Y, Keller MS, Rome JJ, et al. Percutaneous lymphatic embolization of abnormal pulmonary lymphatic flow as treatment of plastic bronchitis in patients with congenital heart disease. Circulation 2016; 22:1160–70.

7. Kreutzer J, Kreutzer C. Lymphodynamics in Congenital Heart Disease: The Forgotten Circulation. JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY 2017; 69(19):2423-7.

8. Maldonado F, Hawkins FJ, Daniels CE, Doerr CH, Decker PA, Ryu JH. Pleural fluid characteristics of chylothorax. Mayo Clin Proc. 2009; 84:129–33.

9. Rocha G, Arnet V, Soares P, Gomes AC, Costa S, Guerra P, Casanova J, Azevedo I. Chylothorax in the neonate-A stepwise approach algorithm. Pediatr Pulmonol 2021;56: 3093–105.

10. Justice L, Buckley J R, Floh A, Horsley M, Alten, J, Anand V, Schwartz S M. Nutrition Considerations in the Pediatric Cardiac Intensive Care Unit Patient. World J Pediatr Congenit Heart Surg. 2018; 9:333–43.

11. Chan EH, Russell JL, William WG, Van Arsdell GS, Coles JG, McCrindle BW. Postoperative Chylothorax After Cardiothoracic Surgery in Children. Ann Thorac Surg 2005; 80 (5): 1864-70.

12. Takahashi Y, Kinoshita Y, Kobayashi T, Arai Y, Ohyama T, Yokota N, Saito K, Sugai Y, Takano S. Management of refractory chylothorax in the neonatal intensive care unit: A 22-year experience. Pediatr Int 2021; 64: e15043.

13. Clark M E, Woo R K, Johnson S M. Thoracoscopic pleural clipping for the management of congenital chylothorax. Pediatr Surg Int 2015; 31: 1133–37.

14. Ahmed M A. Post-Operative Chylothorax in Children Undergoing Congenital Heart Surgery. Cureus 2021;13: e13811.

15. Roca CM, García M J, Pedro V, Gómez Y, Herranz I M. Midodrine in refractory chylothorax after pediatric cardiac surgery: A case report. European journal of clinical pharmacy 2016; 18: 414-41.

16. Patel D, Rahmanian M, Iqbal J, Scheinin S, Lee J, Seethamraju H. Midodrine: Breaking The New Ground In The Treatment Of Chylothorax. J chest 2019; 08:257.

17. Shin YR, Lee H, Park YH, Park H.K. Chylothorax after Surgery for Congenital Cardiac Disease: A Prevention and Management Protocol. Korean J Thorac Cardiovasc Surg 2020; 53: 41–48.

18. Lawati T T, Jamie A A, Mufarraji N A. Central line associated sepsis in children receiving parenteral nutrition in Oman. Journal of Infection and Public Health 2017; 10(6): 829-32.

19. Tamaoka S, Osada A, Kin T, Arimitsu T, Hida M. Midodrine, an Oral Alpha-1 Adrenoreceptor Agonist, Successfully Treated Refractory Congenital Chylous Pleural Effusion and Ascites in a Neonate. Chest 2021; 159 (4):e189-e191.