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Review Article

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Steroids as a possible effective therapy in the management of large isolated chylopericardium following open heart surgery

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Abstract

Background: Chylopericardium is the collection of lymph fluid inside the pericardial cavity. The incidence of chylopericardium is very low, as this diagnosis is rarely reported following cardiac procedures in children. While some reports were published worldwide on isolated chylopericardium after cardiac surgeries for diverse reasons, it has never been reported after repair for partial anomalous pulmonary venous return. In addition, management of this diagnosis ends up being surgical with minimal concentration on medical treatment which proved unsuccessful. We present a medical approach with corticosteroids as an effective method to treat isolated chylopericardium. *Case presentation:* In this manuscript, we present an approach to treat isolated post-operative chylopericardium in a child following repair of partial anomalous pulmonary venous return. Chylous drainage responded to corticosteroids and completely ceased. There was no need for surgical intervention. *Conclusion:* Until now, isolated chylopericardium has never been reported to occur with partial anomalous pulmonary venous return repair. A review of the literature showed that most patients follow a conservative approach consisting of diuretics and non-steroidal anti-inflammatory agents with some of them undergoing surgical re-intervention. With future research on the topic still needed, we hope that this will encourage physicians worldwide to consider administering a trial of corticosteroids as an option to treat chylopericardium.

Chylopericardium is an effusion of lymph fluid in the pericardial cavity. This fluid has a milky opaque appearance and is commonly rich in triglycerides and chylomicrons. Chylopericardium is a rare complication that occurs following cardiac surgery. It is usually unexpected because the surgical site is anatomically distant from the thoracic duct and cannot be easily damaged during the operation. Certain cardiac procedures may increase the impedance of thoracic duct drainage and elevate venous pressure in the process, but this usually manifests as chylothorax not chylopericardium.[1,2] The incidence of post-operative chylothorax is rare, and it varies from 0.56 to 1.9%, but the incidence of isolated chylopericardium remains lower (0.22%).[3] The diagnosis of chylopericardium is considered debilitating in children as it is associated with high morbidity and mortality from the uncontrolled chyle leaks, which, in turn, leads to hypoproteinemia, immune incompetence, and malnutrition if left untreated.[4,5]

Several reports have been published on the incidence of chylopericardium following cardiac surgeries such as correction of atrial septal defect, ventricular septal defect, transposition of great arteries, tricuspid atresia, and Tetralogy of Fallot. The first report that described chylopericardium was in 1981, and a few subsequent cases were reported thereafter.[1–13] One case in the literature reported isolated chylopericardium following total anomalous pulmonary venous return repair surgery in 1984.[7] In this paper, we report a large isolated chylopericardium treated non-surgically and effectively with steroids in a patient who underwent repair for partial anomalous pulmonary venous return followed by a comprehensive review of the literature and the management.

Methodology

This review was conducted and finalised in March 2019. The literature review is up to date, and articles were critically appraised for validity and relevance. A comprehensive search was conducted in PubMed, Medline (1946–2018), and Google Scholar for the presence of grey literature. Articles were included if they were published in the English language and reported on the incidence or prevalence of chylopericardium in children. The search was limited to

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Table 1. Summary of all cases of isolated chylopericardium in the paediatric population

References	Year	Case number	Sex, age	Diagnosis	Post-op onset (days)	Management
Pollard et al[8]	1981	1	M, 4.5 years	VSD	10	Conservative
Pugliese et al[7]	1984	2	F, 10 months	TAPVR	Unknown	Conservative
Tchervenkov and Dobell[9]	1985	3	M, 12 years	AVS	34	Conservative
Pereira et al[10]	1988	4	F, 4 years	ASD	17	Thoracic duct ligation
Danfield et al[11]	1989	5	M, 9 months	ASD, TGA	180	Conservative
Campbell et al[3]	2001	6	M, 3 months	TOF	7	Continuous pericardial drain
		7	F, 3 months	AVSD	23	Continuous pericardial drain
		8	M, 7 months	Vascular ring, TEF	11	Continuous pericardial drain
		9	M, 10 months	TOF	9	Continuous pericardial drain
		10	M, 1 years 2 months	AVSD	35	Continuous pericardial drain
		11	F, 1 year 7 months	TA	17	Continuous pericardial drain
		12	M, 1 year 7 months	TOF, AVSD	28	Continuous pericardial drain
Shanmugam et al[4]	2003	13	F, 8 years	ASD	10	Conservative, continuous pericardial drain, re-exploratory surgery
Kumar and Sinha[12]	2005	14	F, 8 years	ASD	3	Conservative, continuous pericardial drain, re-exploratory surgery
Kan et al[1]	2007	15	M, 1 year	AVSD	10	Conservative
		16	M, 3 years	ASD	3	Conservative
		17	M, 4 months	VSD	4	Conservative
		18	M, 2 years	TOF	14	Conservative
Kanemoto et al[13]	2008	19	M, 4 months	AVSD	9	Conservative, continuous pericardial drain
Gowani et al[5]		20	M, 1 month 5 years	VSD	30	Conservative, continuous pericardial drain
Arabi	2019	21	F, 4 years	PAPVR	6	Conservative, continuous pericardial drain

ASD = atrial septal defect; AVS = aortic valve stenosis; AVSD = atrioventricular septal defect; PAPVR = partial anomalous pulmonary venous return; TA = tricuspid atresia; TAPVR = total anomalous pulmonary venous return; TEF = transesophageal fistula; TGA = transposition of the great arteries; TOF = Tetralogy of Fallot; VSD = ventricular septal defect.
Conservative treatment consists of dietary modifications such as low-fat diet and middle-chain fatty acid supplements.

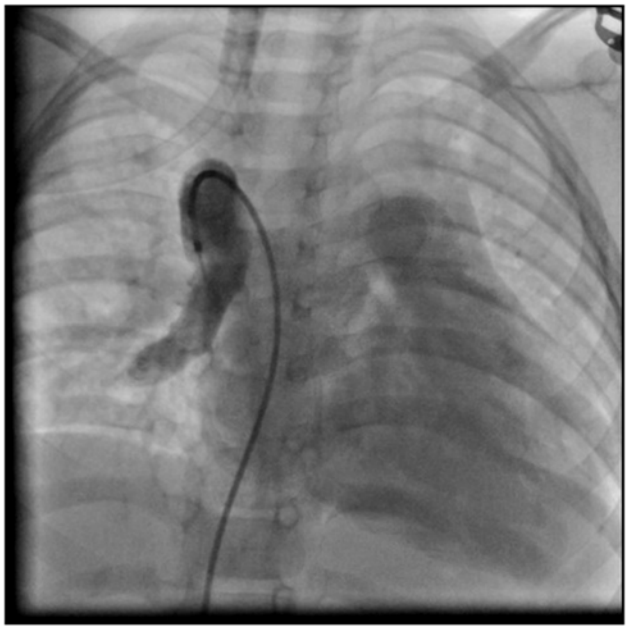

Figure 1. Angiography showing right pulmonary vein draining into the superior vena cava.

the paediatric population (under 18 years of age), but no limitations were made on year of publication or country of origin. The search consisted of MeSH terms and keywords: chylopericardium, chyle, chylous, chyle leak, milky fluid, lymph, lymph fluid, and lymphatic fluid. This was combined with MeSH terms and keywords for: pericardial effusion, effusion, tamponade, pericardial drain, and pericardial tube. A total of 11 published articles were retrieved and summarised in Table 1.

Case presentation

During a routine follow-up, a 4-year-old girl was found incidentally to have a soft systolic murmur on routine physical exam. Echocardiography showed right atrial and right ventricular enlargement. Partial anomalous pulmonary venous return was suspected, so this was followed by cardiac catheterization, which revealed that the right pulmonary veins were draining into the superior caval vein (Fig 1). The left upper pulmonary vein was draining into an ascending vein that was communicating superiorly with the innominate vein. The left lower pulmonary vein was draining into the left atrium directly. The right-sided pulmonary veins were draining very high into the superior caval vein close to the superior caval vein innominate vein junction. There was no

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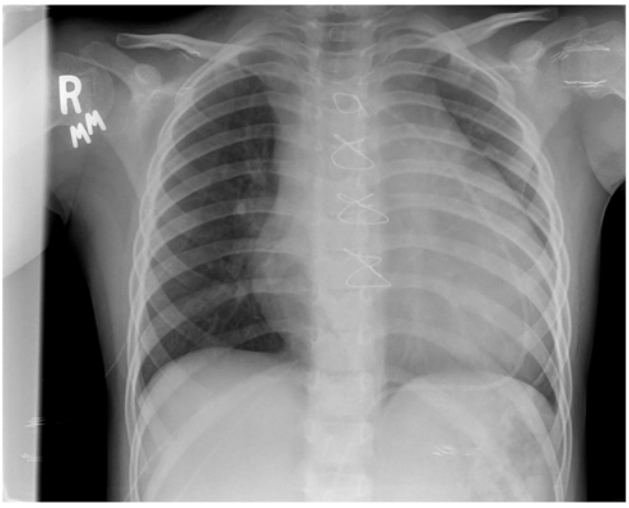

Figure 2. Chest X-ray of the patient showing a cardiothoracic ratio of 0.71 on post-op day 6.

communication through the inter-atrial septum. Pulmonary artery pressure was 21 mmHg at the time. As such, surgical repair was performed. The chest was entered through a median sternotomy incision, the thymus gland was totally removed with no potential for residual lymphatic leak, and the aorta was cross-clamped. A patch of autologous pericardium was harvested and utilised to tunnel within the superior caval vein the anomalous right pulmonary veins back to the left atrium through the created atrial septal defect. The superior caval vein was augmented utilising autologous right atrial flap. The left upper pulmonary vein was repaired by closing the vertical connection. In the immediate post-operative settings, the patient achieved haemodynamic stability. Transthoracic echocardiography revealed good surgical results showing superior caval vein divided into two tunnels connecting right pulmonary vein to left atrium and superior caval vein to right atrium. On post-op day 6, follow-up echocardiography showed a small pericardial effusion. Follow-up chest X-ray revealed a cardiothoracic ratio of 0.71 (Fig 2). The patient was started on ibuprofen, furosemide, and captopril. At the time, C-reactive protein measured 45.9 mg/L. Echocardiography on post-op day 9 revealed moderate pericardial effusion. On post-op day 19, the patient started to have shortness of breath, and a repeat echocardiography revealed increased pericardial effusion with early signs of tamponade (Fig 3). Her white blood cell count was 19,400/cu.mm. The patient was started on maintenance dextrose-5% half normal saline 50 ml/hour. The decision was taken to perform pericardiocentesis that immediately drained 750 ml of white milky fluid. Analysis of the fluid revealed a triglyceride level of 1410 mg/dl. There was no pleural effusion, and this further confirmed the diagnosis of isolated chylopericardium. Once the diagnosis of chylopericardium was ascertained, we started the patient on a strict fat-free diet after consultation with our dietitian. The patient was kept on a fat-free diet since the diagnosis for initially 2 weeks. However, we extended that duration for another 2 weeks. During these 4 weeks, we supplemented the patient with medium-chain fatty acid oil supplements. The patient was started on 5 ml of middle-chain triglyceride oil three times daily which was escalated to 10 ml three times daily and then to 14 ml three times daily as tolerated by the patient. These middle-chain triglycerides oil supplements were taken with food. After these 4 weeks, we switched the patient to a low-fat diet that stayed for 6 months after the diagnosis and we stopped middle-chain triglycerides oil supplements. Initially, the pericardial drainage improved. On post-op day 30, we had initially assumed that the drainage has completely ceased. Unfortunately, simple drain manipulation unveiled drain obstruction which has then continued draining. The pericardial drain was left in place, and the patient drained a daily estimate between 300 and 450 ml of chyle. On post-op day 34, the drainage had substantially increased and the IV was increased to 30 ml/hour. On post-op day 35, the patient was started on twice-daily prednisone (2 mg/kg/day) with a decrease in drainage noted thereafter (Fig 4). After 24 hours of initiating the steroids, an improvement in the patient's condition was noted and this improved continued until the day of discharge. Two days later, echocardiography revealed only trace pericardial effusion. Prednisone was decreased to 15 mg twice daily for 1 week. The patient was discharged on tapering doses of steroids. One week after discharged, she was given steroids 10 mg twice daily for another week and then tapered down to 5 mg twice daily for the 3rd week. At her 4th week, she was given 5 mg once daily for 1 week. No chylous drainage occurred thereafter until the day of discharge. Outpatient follow-up echocardiography showed absence of pericardial effusion, 70% ejection fraction, and normal venous return to left atrium. As our patient was discharged on tapering doses of oral prednisone, furosemide, and aldactone, no recurrence was noted.

Discussion

Isolated chylopericardium as a complication of paediatric cardiac surgeries is very rare. It occurs in 0.2–0.5% of all surgeries, which, if left untreated, can lead to catastrophic consequences.[3,6] A review of all the paediatric cardiac surgeries performed via the Children's Heart Center at the American University of Beirut Medical Center was conducted. This centre is a major referral centre with multi-disciplinary teams committed to provide a full range of cardiology services to patients with CHD and acquired heart disease from the Middle East region and beyond. Around 2000 surgeries were performed between 2008 and 2018 with only one case of post-operative isolated chylopericardium. This is concordant with the scarce literature on the matter. A thorough review of the literature was carried out on reported cases of isolated chylopericardium after cardiac surgeries in children and yielded 20 cases since first reported[1,7–13] (Table 1). The most common indications for cardiac surgeries were CHDs such as atrial septal defect and ventricular septal defect, followed by surgeries for Tetralogy of Fallot, transposition of great arteries, and others. The only incidence of isolated chylopericardium following repair surgery for total anomalous pulmonary venous return was reported in 1984,[7] and in our paper, we present the details of the first case of isolated chylopericardium following partial anomalous pulmonary venous return repair that was treated non-surgically and successfully with corticosteroids.

The control of potential chylous leaks at the time of the diagnosis is crucial for the patient's prognosis. The diagnosis demands a high degree of suspicion and prompts intervention. The presence of chylopericardium is indicated by the discovery of a milky, and opaque, pericardial effusion during pericardial fluid sampling, performed either with pericardiocentesis or surgical pericardial drainage. Isolated chylopericardium is difficult to diagnose as it can be mistaken for post-pericardiotomy syndrome which can present with similar signs and symptoms. This causes

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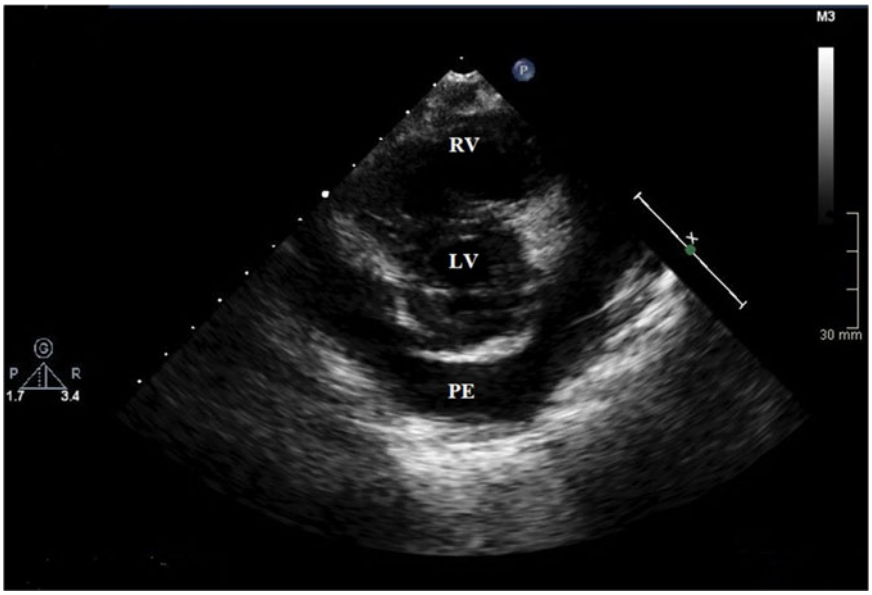

Figure 3. Short-axis view of the heart showing a large pericardial effusion. LV = left ventricle; PE = pleural effusion; RV = right ventricle.

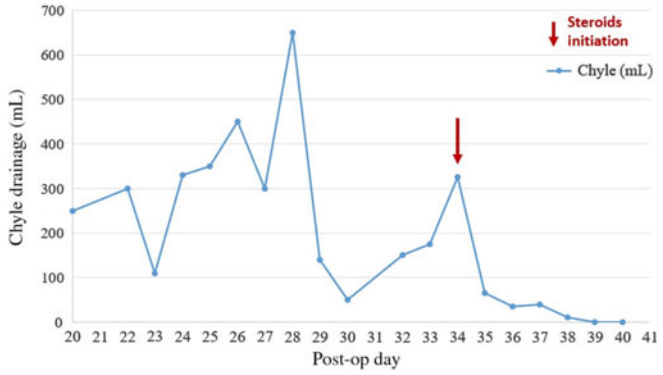

Figure 4. Graph showing decreasing chyle drainage after corticosteroids initiation.

further delay in diagnosis and treatment.[3,14] The pericardial effusion commonly has a high triglyceride level, with analysis of the fluid typically revealing: triglyceride level higher than 500 mg/dl (5.65 mmol/L), cholesterol/triglyceride ratio of less than 1, negative cultures and cytology, lymphocyte predominance on cytological examination, or fat globules seen on Sudan staining.[3,14,15] Other modalities that can be utilised to identify injuries of the thoracic duct or its tributaries are contrast-enhanced CT together with lymphangiography or lymphangioscintigraphy to identify an injury or blockage of the thoracic duct and scintigraphy after the oral administration of I-131 triolein.[16,17]

Unfortunately, the etiology of the chylous collection in the pericardial cavity after cardiac surgeries in children remains controversial and unclear. Chylopericardium might result from obstruction or injury of the thoracic duct, but in other times the culprit is not truly apparent.[5] Normally, the chyle is filtered by intestinal capillaries into the intestinal space and eventually to the thoracic duct. Afterwards, the duct passes near the aorta and azygous vein to terminate near the junction of the left subclavian artery and jugular vein. It is generally accepted that direct injury to the thoracic duct might result in chylothorax rather than isolated chylopericardium mostly because the thoracic duct is anatomically located in the region of the descending aorta, thus making direct injury during an intrapericardial procedure highly unlikely.[1] There is usually sufficient back pressure from an elevated systemic venous pressure that overwhelms the capacity of the major mediastinal lymphatic vessels. In turn, this elevated pressure is transmitted back to smaller lymphatic vessels commonly present within the pericardial space that may have been inadvertently injured during the cardiac surgery.[5] This process is further complicated by the fact that lymphatic capillaries lack a basal lamina which makes the endothelium much more permeable to large molecules, and cellular debris.[1,18,19] Moreover, the thymus is very rich in lymphatic tissue in children, in contrast to adults where the thymus is nearly devoid of lymphatic tissue at all. It has also been reported that there exist distinct anatomical variations of the terminal portion of the thoracic duct. This predisposes this part of the duct to unintended injury during thoracic or mediastinal surgical procedures. With the further opening of the pericardium, this presents an additional trigger and explanation for post-operative chylopericardium.[18–20] Other factors that may increase the likelihood of chylopericardium development are damage to the thoracic duct valves, and abnormal communication between thoracic duct and pericardial lymphatics.[14]

A review of the literature of all the different methods underwent to treat post-operative chylopericardium is outlined in this paper. Initially, the treatment for chylopericardium depends on the presence or absence of cardiac tamponade and the haemodynamic stability. If patients have signs and symptoms of cardiac tamponade, urgent fluid removal through either pericardiocentesis or surgical drainage is critical. If patients do not have signs and symptoms of impending cardiac tamponade, they are treated with conservative treatment.[1,3,21] For a trial of a minimum of 2 weeks, the patient can be started on oral medium-chain triglycerides because they are absorbed through the portal vein only and avoid entering the lymphatic system. In addition, a diet that is low-to-zero fat or nothing-by-mouth can be initiated. Unfortunately, the conservative approach is only successful in 55% of the patients with chylopericardium.[2,21] If the patient develops further cardiac tamponade or if the symptoms continue or worsen with time, percutaneous pericardiocentesis is required to decompress the pericardial space. When conservative treatment as well as

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decompression fails to achieve tangible results, surgical interference may be necessary. If the thoracic duct can be visualised and identified intra-operatively, some studies reported ligating it at the diaphragmatic level. Some other studies reported using pleurodesis, pleurectomy, low ligation of the thoracic duct by video-assisted thoracoscopic surgery, thoracic duct embolisation, and pericardial–peritoneal shunting.[11,21–23] Few reports have been published on the off-label use of the long-acting somatostatin analog, octreotide, that is presumed to cause a reduction in chyle production and thoracic duct flow rate.[24–27]

The use of non-steroidal anti-inflammatory drugs has been the cornerstone in the treatment of patients with pericarditis, but no studies were published on its use in chylopericardium.[19,20] Similarly, the use of corticosteroids has been suggested in acute and chronic pericarditis, but its benefit in post-operative chylopericardium has not been deciphered.[28] The pericardial space is bordered by the visceral and the fibrous layers. Regardless of the causative agent, whether infectious or post-operatively, inflammation of these layers increases fluid exudate. Inflammation also decreases the normal process of pericardial drainage by the lymphatic ducts. As such, inflammation alone can cause pericardial effusion.[28] Corticosteroids are known to decrease inflammation and inflammatory markers. In that sense, it is reasonable to believe that its usage may be beneficial for patients with chylopericardium who did not respond to first-line treatment with dietary modifications and non-steroidal anti-inflammatory drugs. Two case reports have been published on the effective use of corticosteroids to relieve chylopericardium and chylothorax. Tanizawa et al reported the efficiency of corticosteroids to relieve chylopericardium in a 77-year-old male with non-small cell lung cancer. This patient had chylopericardium that recurred 4 weeks after diagnosis. At that point, corticosteroids were given at 2 mg daily for 2 weeks, and the patient improved without being on chemotherapy or other anti-neoplastic regimens.[29] Miura et al reported on the effective use of corticosteroids when administered early in a newborn with congenital chylothorax.[30] Even though, to date, no other reports have been published, we have extrapolated from the available literature. Our patient was not improving on conventional therapy, and as such, we have administered steroids in the hope that the chylopericardium would resolve. As thus, we believe that oral steroids demonstrate efficiency in treating chylopericardium following cardiac repair surgery in patients who did not respond to standard therapy. While each patient may respond differently to corticosteroid treatment, we believe that physicians may start noticing improvement after 24 hours. Our results represent a unique attempt to treat chylopericardium that should be replicated in bigger studies for adequate assessment. We encourage physicians who are faced with similar dilemmas to consider this approach and report their findings.

Conclusion

Chylopericardium following paediatric cardiac surgeries is a very rare entity but one that is associated with high morbidity and mortality if left untreated. While the cause may not always be clear, any injury to the thoracic duct tributaries or small lymphatic channels is sufficient to cause chylous collection inside the pericardial space. We describe an effective conservative approach of steroid therapy in successfully treating post-operative chylopericardium without resorting to surgical intervention. We understand that chylopericardium is a rate entity by itself and treating it may be difficult. We present an approach that may be successful in patients who did not respond to conventional therapy. More studies are needed in the future to properly assess the effectiveness of corticosteroids in treating chylopericardium. We hope that this approach can be duplicated in other centres and further research on its efficiency can be conducted on a larger sample size.

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Conflict of Interest. None.

Ethical Statement. The authors assert that all procedures contributing to this work comply with the ethical standards of the World Medical Association relevant guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the institutional review board (IRB).

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