Chylothorax in a Level III Neonatal Intensive Care Unit: A Case Series

Quilotórax numa Unidade de Cuidados Intensivos Neonatais de Nível III: Estudo de Série de Casos

Rita Barreira[1], Maria Inês Marques[1], Rita Valsassina[1], Kátia Cardoso[1], Anabela Salazar[1]

Corresponding Author/*Autor Correspondente:*
Rita Barreira [rita.cruzbarreira@gmail.com]
Estr. Forte do Alto Duque, 1449-005 Lisboa, Portugal

ABSTRACT

INTRODUCTION: Chylothorax is a rare potentially life-threatening condition characterized by accumulation of chyle in the pleural space. It can be responsible for metabolic, nutritional and immunological complications in newborn infants.

Our aim was to evaluate the clinical course and treatment of all cases of neonatal chylothorax admitted to a Portuguese tertiary perinatal unit.

METHODS: Retrospective analysis of institutional records of newborn diagnosed with chylothorax between 1st of February 2007 and 31st of January 2017 in a tertiary neonatal intensive care unit.

RESULTS: Six patients were included; two cases were congenital, one with prenatal diagnosis. The remaining cases were all secondary to trauma during thoracic surgery. All needed ventilation support with high positive end-expiratory pressure. Except for two cases, parenteral nutrition was implemented at diagnosis. Three cases did not improve with conservative treatment. One case was effectively treated with octreotide. Two patients died, one due to shock and multiorgan failure and the other one due to respiratory failure.

DISCUSSION/CONCLUSION: In our sample, trauma (from thoracic surgery) was the main etiology, reflecting our Unit´s collaboration with the pediatric cardiology department. Concerning diagnosis and treatment there are some algorithms, however, there are no national or international accepted guidelines and there are some aspects of the therapeutic approach that remain controversial.

KEYWORDS: Chylothorax; Infant, Newborn; Intensive Care Units, Neonatal

1. Unidade de Neonatologia - Serviço de Pediatria, Hospital de São Francisco Xavier - Centro Hospitalar de Lisboa Ocidental, Lisboa, Portugal.

Received/*Recebido*: 03/03/2018 - Accepted/*Aceite:* 21/05/2018

RESUMO

INTRODUÇÃO: *O quilotórax é uma condição rara e potencialmente fatal que se caracteriza pela acumulação de linfa no espaço pleural. Pode ser responsável por complicações metabólicas, nutricionais e imunológicas no recém-nascido.*
O nosso objetivo foi avaliar a evolução clínica e o tratamento dos casos de quilotórax neonatal admitidos numa unidade de cuidados intensivos neonatais.
MÉTODOS: *Análise retrospetiva dos processos clínicos dos recém-nascidos com o diagnóstico de quilotórax entre 1 de fevereiro de 2007 e 31 de janeiro de 2017.*
RESULTADOS: *Foram incluídos seis doentes. Dois dos casos eram congénitos, um com diagnóstico pré-natal. Os restantes quatro casos foram secundários a trauma durante cirurgia torácica. Todos necessitaram de ventilação por pressão positiva. Quatro recém-nascidos iniciaram nutrição parentérica ao diagnóstico. Metade dos casos não respondeu à instituição de medidas conservadoras, um dos quais foi eficazmente tratado com octreótido. Registaram-se dois óbitos, um dos doentes no contexto de choque e falência multiorgânica e o outro caso por insuficiência respiratória.*
DISCUSSÃO: *Na nossa série a etiologia traumática pós-cirurgia torácica foi a principal causa, refletindo a estreita colaboração da nossa unidade com o Serviço de Cardiologia Pediátrica. No que diz respeito ao diagnóstico e tratamento, existem alguns algoritmos, no entanto, não há guidelines universalmente aceites e há alguns aspetos da abordagem terapêutica que permanecem controversos.*

PALAVRAS-CHAVE: *Quilotórax; Recém-Nascido; Unidades de Cuidados Intensivos Neonatais*

INTRODUCTION

Chylothorax is a rare potentially life-threatening condition characterized by the accumulation of chyle in the pleural space. It can be responsible for metabolic, nutritional and immunological complications, as well as respiratory distress in newborn infants. The diagnosis of chylothorax is usually based on a pleural effusion characterized by a triglyceride level > 110 mg/dL and a cell count > 1000/µL with > 80% lymphocytes.[1,2] Without enteral fat intake, the distinction between chylous and non-chylous effusion is difficult because chylomicrons are absent from the pleural fluid. In non-feeding infants, the diagnosis of chylothorax is made through the identification of a high number of lymphocytes in the serous fluid.[2,3]

Chylothorax can be congenital or acquired. Congenital chylothorax is the most common type of pleural effusion during the neonatal period, with an estimated incidence of 1:7300-1:15 000 and a male/female ratio of 2:1.[1-5] The etiology of congenital chylothorax is often unclear. Association with congenital heart disease, chromosomal disorders (e.g. Down, Turner or Noonan syndromes), prenatal infections, birth trauma, superior vena cava thrombosis and abnormalities of the lymphatic system are described.[1,4,6] Most cases have no clear etiology and are considered as idiopathic congenital chylothorax.[2] Acquired chylothorax is most often a postoperative complication due to trauma to the thoracic duct during cardiac or thoracic surgery.[4-7]

Management practices are not standardized and vary among neonatal units, from conservative approach (diet modifications and positive end expiratory pressure during mechanical ventilation) to medical (somatostin or octreotide) or surgical intervention (thoracoscopic pleurodesis, pleuroperitoneal shunt, surgical abrasion and ligation of the thoracic duct).[2,7] None of these therapeutic modalities have undergone controlled clinical trials.[7] This study is a retrospective review of all cases of neonatal chylothorax admitted to a Portuguese perinatal unit and aimed to evaluate its course and treatment. Our unit provides tertiary level care for extremely premature infants and newborn infants with congenital heart disease.

METHODS

We carried out a retrospective review of our institutional records of newborn diagnosed with chylothorax between 1st of February 2007 and 31st of January 2017 in a tertiary neonatal intensive care unit. The following variables were evaluated: gender, gestational age, delivery mode, birth weight, Apgar score, etiology, age at diagnosis, associated pathologies, composition of pleural effusion, medical and surgical therapeutic and its complications. The inclusion criteria was the presence in a newborn of a pleural effusion characterized by > 1000 cells/µL with > 80% of lymphocytes and triglycerides greater than 110 mg/dL if they were on enteral feeding; while in non-feeding infants we used only the identification of a high number of lymphocytes (> 80%). Descriptive statistics were performed using Microsoft Excel®.

RESULTS

Six patients were included. Demographic data are summarized in Table 1.

Two cases (A and B) were congenital albeit only case A had a prenatal diagnosis at 21 weeks of gestational age, and no *in utero* intervention was needed. Case B, also congenital, was diagnosed during coarctation of the aorta repair surgery. Pleural effusions in congenital cases A and B were left sided and bilateral, respectively. Diagnosis was confirmed by cytochemical analysis of the pleural fluid, in which both had more than 80% lymphocytes. Case B had a triglyceride level > 110 mg/dL, however, case A had a lower value (19.2 mg/dL), because effusion drainage was performed on the first day of life before starting enteral nutrition (Table 2). In case A, a thoracentesis was performed at day 1 with resolution of the effusion. Due to high-volume and persistence, case B was managed by drainage and subsequent insertion of a thoracic drain. Both cases needed ventilation support with high positive end-expiratory pressure (Table 3). Congenital cases started parenteral nutrition at diagnosis. General measures, including adequate fluid and electrolyte replacement along with appropriate nutrition, permitted the resolution of case A. Case B did not respond to conservative treatment. In the context of diaphragmatic paralysis, we opted for the surgical intervention in the first place and a thoracic duct ligation was performed at day 43 of life. Recurrence of effusion occurred postoperatively and by day 50 octreotide was initiated for the following two weeks. As there was no improvement in the volume of the effusion as well as in the clinical status, the patient underwent right and left thoracoscopic talc pleurodesis at days 102 and 115 of life, respectively. Despite the multiple interventions, the patient died at 7 months with respiratory failure.

Remaining cases (C, D, E and F) were all secondary to trauma after thoracic surgery, three were on the left side corresponding to the intervened side and one was bilateral (case C). Diagnosis was made between day 7 and 20 postoperatively at the onset of symptoms of respiratory distress. Diagnosis was confirmed by cytochemical analysis of the pleural fluid (Table 2), in all cases lymphocytes were more than 80% of all cells and triglyceride levels > 110 mg/dL. Due to high-volume and persistence, all patients with postoperative effusion were managed by drainage and subsequent insertion of a thoracic drain. All cases needed ventilation support with high positive end-expiratory pressure (Table 3). Regarding nutrition, cases C and D initiated parenteral nutrition and cases E and F remained on enteral feeding without long-chain polyunsaturated fatty acids, with progressive medium-chain triglycerides supplementation. In cases secondary to trauma, general measures were effective in cases E and F. Cases C and D were treated with octreotide, with an initial dose of 1 µg/kg/h, up to a maximum of 10 µg/kg/h, although only case D was efficiently managed. Case C died due to persistent chylothorax, pulmonary hypertension, shock and multiorgan failure, on day 31 (Table 3).

Hypoalbuminemia was the most frequent complication. In case A, the most severe, the minimum value of hypoalbuminemia was 1.7 g/dL.

Regarding the long-term outcomes, no data are available because two patients were transferred to their local hospitals after clinical stability and cases D and E have been followed in pediatric cardiology, without sequelae related to chylothorax.

TABLE 1. Characterization of neonatal chylothorax cases.

	Case A	Case B	Case C	Case D	Case E	Case F
Gender	F	F	F	M	M	M
GA	33w+4d	39w+5d	25w+3d	37w+2d	35w	38w
Delivery mode	caesarean	caesarean	caesarean	caesarean	caesarean	forceps
WB (g)	2160	3240	623	3345	2020	2910
AS 1'/5'	1/7	9/10	5/7	9/10	8/9	9/10
Etiology	Congenital	Congenital	Post-surgery	Post-surgery	Post-surgery	Post-surgery
Age at diagnosis	21w	D15	D23	D26	D23	D14
Associated pathologies	Hydramnios Lung hypoplasia Malformation of cortical development	AVSD CoAo Diaphragmatic paralysis Noonan syndrome	PDA	ASD VSD CoAo Diaphragmatic paralysis	CoAo VSD	AVSD CoAo Down syndrome

F – female; M – male; w – weeks; d – days; GA – gestacional age; WB – weight birth; AS – Apgar score; D – day of life; PDA - persistent ductus arteriosus; ASD – atrial sept defect; VSD – ventricular sept defect; CoA – coarctation of the aorta; DP - diaphragmatic paralysis; AVSD - atrioventricular septal defect

TABLE 2. Characterization of pleural fluid.

	Case A	Case B	Case C	Case D	Case E	Case F
Cells (cells/µL)	300	8358	13000	10560	7088	18997
Lymphocytes (%)	87	93	81	98	93	98
Proteins (g/dL)	2.5	3.1	0.8	3.2	3.6	3.8
Triglycerides (mg/dL)	19.2	898	1523	2944	772	914

TABLE 3. Treatment and complications of neonatal chylothorax cases.

	Case A	Case B	Case C	Case D	Case E	Case F
Ventilatory support	Invasive	Invasive	Invasive	Invasive	Invasive	Non-invasive
Octreotide	No	Yes (D50-D64)	Yes (D29-D31)	Yes (D37-D52)	No	No
Surgical therapy	No	Yes	No	No	No	No
Complications	Hypoalbuminemia	Respiratory insufficiency Infection Hypoalbuminemia Hypogammaglobulinemia Death at 7 months	SVCS Hypoalbuminemia Infection Shock Death at D31	Respiratory insufficiency Hypoalbuminemia	Infection Hypoalbuminemia	Infection

D – day of life; SVCS – superior vena cava syndrome

DISCUSSION

In our series, the traumatic cause - thoracic surgery - was the main etiology, reflecting our Unit´s collaboration with the pediatric cardiology department.

Concerning treatment, namely the relief of respiratory symptoms, the use of positive end-expiratory pressure ventilation is advised as it may tamponade the injured duct, helping to decrease chyle flow.[8,9]

Dietary measures are a mainstay in the treatment of chylothorax. Using a fat-free diet without long-chain fatty acids but supplemented with medium-chain triglycerides (MCT's), reduces lymphatic drainage because MCT's are absorbed directly into the portal venous system, bypassing the lymphatic system.[4,10,11]

Cases that do not respond to a low-fat diet, as described above, might need parenteral nutrition with total enteric rest. Nevertheless, the risks associated with the use of a central venous catheterization in immunodeficient patients should be considered.[12-14] One of the main complications of chylothorax is secondary immunodeficiency, due to the loss of lymphocytes and immunoglobulins. In a group of 16 pediatric cardiac patients with postoperative chylothorax, there were B-cell and T-cell lymphopenia with a proportional decline of CD4+ and CD8+ cells.[15] Chyle also contains a high concentration of immunoglobulin and there are reports showing that persisting chyle losses can lead to hypogammaglobulinemia.[16,17] One study reported that four out of seven (57%) patients with congenital chylothorax developed nosocomial infections, this incidence of nosocomial infections is about three times higher than that in other neonatal patients.[18]

In a recent study, regardless of the heterogeneity of published reports, conservative management is appropriate as initial treatment for neonatal postsurgical chylothorax.[19]

Observational studies suggest that octreotide should be considered in the conservative treatment of chylothorax when other conservative measures were not fruitful. Bellini *et al* concluded in a recent systematic review that octreotide is a relatively effective and safe treatment option in neonates with chylothorax.[20] Nevertheless, there are no firm recommendations concerning the timing and duration of this therapy.[2,12-14] In our series, three patients were treated with octreotide: case C died two days after beginning due to shock and multiorgan failure, case D got better with this therapy (two weeks duration) and congenital case B did not improve at all. No side effects were registered.

Concerning surgical management of chylothorax, most studies recommend surgery if the effusion persists for more than three or four weeks despite conservative management. Surgery may, nevertheless, be anticipated

if the effusion volume is persistently high despite drainage or if there are severe metabolic or nutritional complications.[4,13,21] In cases that require surgical management, thoracoscopic approach should be considered.[19]

CONCLUSION

This is a small study which reflects the rarity of this pathology, and it would be helpful a multicenter study to increase the number of patients assessed. Concerning diagnosis and treatment there are some algorithms, however, there are no national or international accepted guidelines and there are some aspects of the therapeutic approach that remain controversial, namely the heterogeneity in dosing regimens, mode of administration, therapeutic duration and time to start medical therapy[22-24] as well as the indications and timing for surgery.[6]

CONFLICTS OF INTEREST: The authors declare that they have no conflicts of interest.

FINANCIAL SUPPORT: This work has not received any contribution, grant or scholarship.

CONFIDENTIALITY OF DATA: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

PROTECTION OF HUMAN AND ANIMAL SUBJECTS: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

CONFLITOS DE INTERESSE: Os autores declaram não ter qualquer conflito de interesse na realização do presente trabalho.

FONTES DE FINANCIAMENTO: Não houve qualquer fonte de financiamento na realização do presente trabalho.

CONFIDENCIALIDADE DOS DADOS: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

PROTEÇÃO DE PESSOAS E ANIMAIS: Os autores declaram que os procedimentos seguidos na elaboração do presente trabalho estão em conformidade com as normas das comissões de investigação clínica e de ética, bem como da declaração de Helsínquia e da Associação Médica Mundial.

REFERENCES

1. Downie L, Arun S, Atul M. Congenital chylothorax: associations and neonatal outcomes. J Paediatr Child Health. 2014;50:234-8.
2. Das A, Shah PS. Octreotide for the treatment of chylothorax in neonates. Cochrane. Database Syst Rev. 2010;9:CD006388.
3. Bengtsson BO. Outcome of neonatal chylous effusions: what do you tell the parents? A 10-year experience in a community hospital. Am J Perinatol. 2014;31:1037-42.
4. Biewer ES, Zürn C, Arnold R, Glöckler M, Schulte-Mönting J, Schlensak C, et al. Chylothorax after surgery on congenital heart disease in newborns and infants -risk factors and efficacy of MCT-diet. J Cardiothorac Surg. 2010;13;5:127.
5. Mery CM, Moffett BS, Khan MS, Zhang W, Guzmán-Pruneda FA, Fraser CD Jr, 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.
6. Matsuo S, Takahashi G, Konishi A, Sai S. Management of refractory chylothorax after pediatric cardiovascular surgery. Pediatr Cardiol. 2013;34:1094-9.
7. Tutor JD. Chylothorax in infants and children. Pediatrics. 2014;133:722-33.
8. Kurtz TW, Hsu CH. Resolution of chylothorax after positive end-expiratory pressure ventilation. Arch Surg. 1980;115:73-4.
9. Ragosta KG, Alfieris G. Chylothorax: a novel therapy. Crit Care Med. 2000;28:1208-9.
10. Straaten HL, Gerards LJ, Krediet TG. Chylothorax in the neonatal period. Eur J Pediatr. 1993;152:2-5.
11. Maia I. Abordagem Nutricional no Doente com Quilotórax. Rev Nutrícias 2013;19:32-4.
12. Panthongviriyakul C, Bines JE. Post-operative chylothorax in children: an evidence-based management algorithm. J Paediatr Child Health. 2008;44:716-21.
13. Beghetti M, La Scala G, Belli D, Bugmann P, Kalangos A, Le Coultre C. Etiology and management of pediatric chylothorax. J Pediatr. 2000;136:653-8.
14. Tallo E, Hernández R, Rodiño R, Rodríguez S, Escudero E. Quilotórax neonatal y tratamiento conservador. An Esp Pediatr. 2002;56:448-51.
15. Kovacikova L, Lakomy M, Skrak P, Cingelova D. Immunologic status in pediatric cardiosurgical patients with chylothorax. Bratisl Lek Listy. 2007;108:3-6.
16. McBride ME, Drass JC, Berkenbosch JW, Wilson WR, & Tobias JD. (2001). Hypogammaglobulinemia complicating chylothorax after cardiac surgery in two infants. Journal of Cardiothoracic and Vascular Anesthesia. 2001;15(3):358-361.
17. Orange J, Geha R, Bonilla F. Acute chylothorax in children: selective retention of memory T cells and natural killer cells. J Pediatr. 2003;143:243-249.
18. Wasmuth-Pietzuch A, Hansmann M, Bartmann P, Heep A. Congenital chylothorax: lymphopenia and high risk of neonatal infections. Acta Paediatr. 2004;93(2):220-224pmid:15046278.
19. Costa KM, Saxena AK. Surgical chylothorax in neonates: management and outcomes. World J Pediatr. 2018;14:110-5.
20. Bellini C, Cabano R, De Angelis LC, Bellini T, Calevo MG, Gandullia P, et al. Octreotide for congenital and acquired chylothorax in newborns: A systematic review. J Paediatr Child Health. 2018 (in press).
21. Shah D, Sinn JK. Octreotide as therapeutic option for congenital idiopathic chylothorax: a case series. Acta Paediatr. 2012;101:e151-5.
22. Jarir RA, Rahman SU, Bassiouny Iel S. Use of octreotide in the management of neonatal chylothorax secondary to repair of congenital diaphragmatic hernia: a report of two cases and review of literature. J Clin Neonatol. 2012;1:91-5.
23. Copons Fernández C, Benítez Segura I, Castillo Salinas F, Salcedo Abizanda S. Neonatal chylothorax: aetiology, clinical course and efficacy of treatment. An Pediatr. 2008;68:224-31.
24. Rocha G, Azevedo I, Guimarães H. Quilotórax no feto e no recém-nascido: Orientação do tratamento. Rev Port Pneumol. 2007;13:377-81.