

Chylothorax: Case Report and Review of Literature

K L Tan,*^{MRCP (UK)}, L C Lim,**^{MRCP (UK)}, A A L Hsu,***^{M Med (Int Med), MRCP (UK)},

P Eng,****^{FAMS, M Med (Int Med), FCCP}, Y Y Ong,†^{FAMS, M Med (Int Med), FRACP}

Abstract

Chylothorax is a relatively uncommon condition. We report a case of a 53-year-old Chinese man with chylothorax who presented with cough, breathlessness, loss of weight and generalised lymphadenopathy. He was initially diagnosed as having tuberculosis based on histology and cultures of the cervical lymph node. However, immunophenotyping of the pleural fluid by flow cytometry showed the presence of a monoclonal B cell population with Kappa light chain expression suggesting an underlying lymphoproliferative disorder. A repeat lymph node biopsy showed malignant lymphoma (follicular small cleaved type). In spite of aggressive measures which included bilateral tube thoracostomy drainage, a low fat diet, medium chain triglyceride diet, totalparenteral nutrition, chemotherapy and mediastinal irradiation, his chylothorax persisted. Hence, we report a patient with persistent chylothorax and generalised lymphadenopathy who was subsequently diagnosed to have concurrent tuberculosis and malignant lymphoma. The literature on chylothorax is reviewed.

Ann Acad Med Singapore 1997; 26:225-8

Key words: Flow cytometry, Lymphoma, Treatment, Tuberculosis

Introduction

Chylothorax is defined as the accumulation of chyle in the pleural space.¹ It is a relatively uncommon condition.² Chyle is rich in triglycerides and is characterised by the presence of chylomicrons which imparts its milky appearance. Naked eye differentiation of chyle versus pseudochylothorax is usually difficult and sometimes requires lipoprotein electrophoresis. The presence of chylomicron in the pleural fluid by lipoprotein analysis confirms the diagnosis of chylothorax.³ Pseudo-chylothorax is the accumulation of a high concentration of cholesterol and/or lecithin-globulin complexes in a long-standing pleural effusion.⁷ It is important to differentiate chylothorax from pseudo-chylothorax as the prognosis and management of these two conditions are different.⁷ Biochemical criteria for the diagnosis of chylothorax usually require the triglyceride level of the pleural fluid to be greater than 1.24 mmol/L (110 mg/dL).⁴ In contrast, the cholesterol level in the pleural fluid in pseudochylothorax is usually greater than 6.45 mmol/L (250 mg/dL).⁵ Another differential diagnosis of chylothorax is that of empyema which

when packed with white blood cells can appear milky white.²

Case Report

A 53-year-old Chinese man, a chronic smoker, presented in April 1995 with cough and breathlessness associated with weight loss of a year's duration. He had a history of pulmonary tuberculosis treated thirty years previously. Clinical examination revealed the presence of generalised lymphadenopathy involving the cervical, axillary and inguinal regions, right pleural effusion and ascites. Apart from the right pleural effusion, the chest roentgenogram at presentation did not show any other abnormality.

Pleural aspiration yielded chylous fluid. The biochemical composition of the pleural fluid was as follows: total protein 42 g/L, lactic dehydrogenase 165 U/L, triglyceride 4.08 mmol/L, cholesterol 1.87 mmol/L. Serum levels of triglyceride and cholesterol were normal. Serum β_2 microglobulin measured 3099 μ g/L (normal range 878 to 2000 μ g/L). Computed tomographic (CT) scan of the thorax and abdomen revealed a right pleural

*Registrar

***Senior Registrar

****Consultant

† Senior Consultant and Head

Department of Respiratory and Critical Care Medicine

* * Senior Registrar

Department of Haematology

Singapore General Hospital

Address for Reprints: Dr Tan Keng Leong, Department of Respiratory and Critical Care Medicine, Singapore General Hospital, 1 Hospital Drive, Singapore 169608.

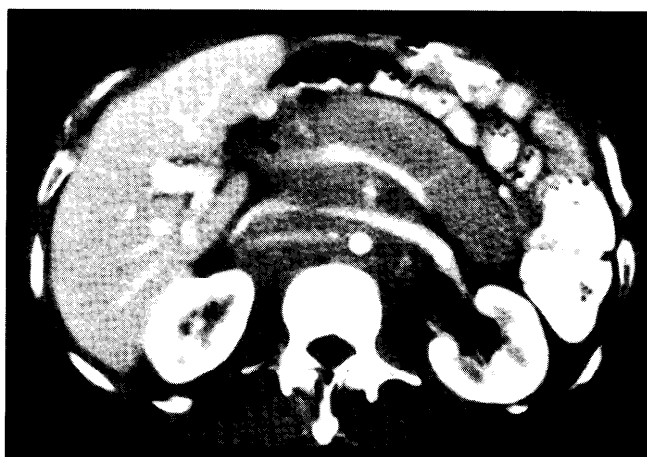


Fig. 1. Computed tomographic scan of the abdomen showing massive intra-abdominal lymphadenopathy.

effusion and multiple enlarged axillary, para-aortic, retroaortic, retrocaval, mesenteric, peripancreatic, prevertebral and inguinal lymph nodes (Fig. 1).

He underwent excision biopsy of the cervical lymph node in April 1995. Histology was reported as lymph node reactive hyperplasia with the presence of a small granuloma. As the specimen submitted for histological examination was small, a repeat biopsy was recommended by the pathologist in view of the clinical findings of generalised lymphadenopathy. Stains for acid fast bacilli and fungi of the lymph node were negative but cultures of the lymph node (which were subsequently reported in July 1996) grew *Mycobacterium tuberculosis* sensitive to streptomycin, isoniazid, rifampicin and ethambutol.

The patient defaulted repeat biopsy and follow up after April 1995. He presented again seven months later in late November 1995 with progressive abdominal swelling and dyspnoea. He was commenced on anti-tuberculous treatment comprising of isoniazid, rifampicin and pyrazinamide in late November 1995. He had bilateral pleural effusion which was aspirated and again found to be chylous (Fig. 2). Flow cytometry of the pleural fluid (Table I) showed the presence of B cell monoclonal population with Kappa light chain expression. Southern blot analysis of the pleural fluid for monoclonality was positive for B cell clonality. Infective processes such as tuberculosis are usually a polyclonal process; hence the demonstration of a monoclonal B-lymphocyte population here suggested an underlying lymphoproliferative disease. Pleural fluid cytology later showed lymphomatous cells. Excision biopsy of a right axillary lymph node in early December 1995 confirmed malignant lymphoma (follicular small cleaved type). Bone marrow trephine biopsy showed lymphomatous involvement. Human immunodeficiency virus serology was negative. He was diagnosed to have stage IV non-Hodgkin's lymphoma with concurrent tuberculosis.

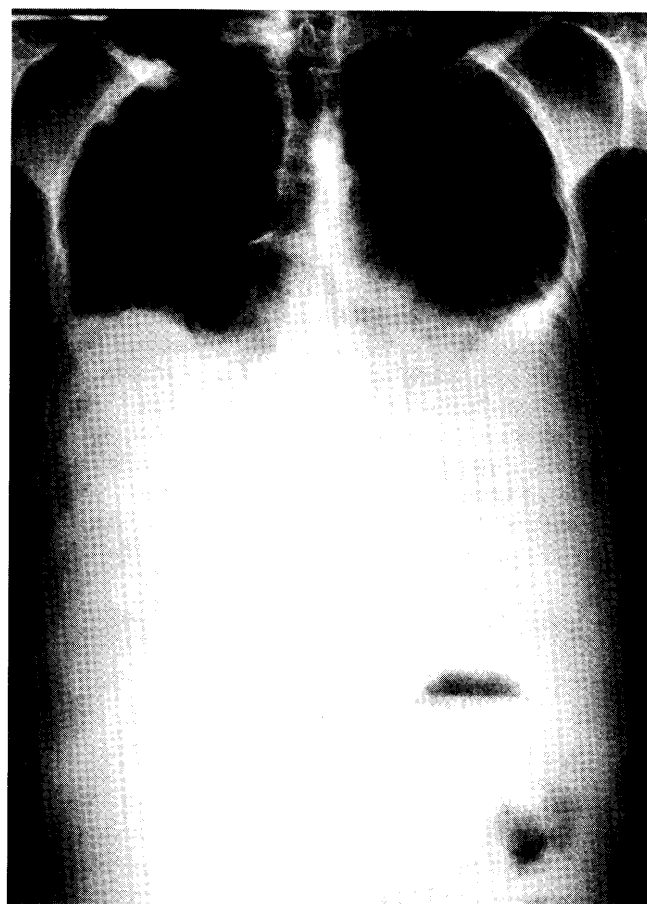


Fig. 2. Chest roentgenogram showing bilateral pleural effusion

TABLE I: FLOW CYTOMETRY OF THE PLEURAL FLUID

Lymphoid Markers	%
CD3	18.0
CD5	17.6
CD20	86.0
CD19	85.9
CD10	5.6
Surface membrane Ig	79.1
Kappa	78.8
Lambda	0.4
Other Markers	
HLA-D/DR related Ia-like antigen	28.7
CD23	68.7

Note: Surface markers are expressed as percentages of antigen-expressing cells.

The patient had bilateral chest tube insertion and drainage of the chylous effusion in December 1995. Despite a low fat diet, modified diet consisting of medium chain triglyceride, total parenteral nutrition, chemotherapy and mediastinal irradiation, the drainage of chyle persisted for 57 days. Following the failure of conservative management, surgical intervention was considered but he was deemed too ill. He continued to

deteriorate and eventually succumbed to *Klebsiella septicaemia* in January 1996.

Discussion

Chylothorax results from either an obstruction to or a disruption of the thoracic duct.⁶ Chylothorax can be classified as congenital, traumatic iatrogenic, traumatic non-iatrogenic or spontaneous.⁶ Most commonly, the causes of chylothorax are trauma and neoplasm. Traumatic causes of chylothorax may be either accidental (e.g. penetrating and non-penetrating injuries to the neck, thorax and upper abdomen) or iatrogenic (e.g. following surgical procedures such as thoracoplasty, oesophagectomy, lobectomy, pneumonectomy and corrective surgery for congenital heart disease). Malignancies,⁷ especially lymphoma,⁸ are the primary cause of spontaneous chylothorax. Tuberculosis⁹ has been reported to cause chylothorax. The postulated mechanism is thought to be obstruction of the cisterna chyli and thoracic duct by enlarged lymph nodes leading to dilatation of the lumbar lymphatic channels and opening of collateral anastomoses between the thoracic duct system and the azygos, intercostal and lumbar veins. The increased pressure in the system results in the transudation of chyle into the pleural space.⁹ Other uncommon causes of chylothorax include congenital chylothorax, filariasis, amyloidosis, sarcoidosis, cirrhosis, intestinal lymphangiectasia, tuberous sclerosis and pulmonary lymphangiomyomatosis.² Interestingly, our patient had lymphoma and tuberculosis; both possible causes of chylothorax. We believe the cause of his persistent chylothorax was malignant lymphoma likely resulting from extrinsic compression of the thoracic duct¹⁰ or direct invasion of the thoracic duct by the tumour.⁸

In the management of chylothorax, a review of the history and clinical examination is essential to evaluate the setting in which it developed. While surgical or traumatic causes are obvious, nonsurgical causes require special attention with regards to the search for an underlying aetiology. Lymphoma is the most common cause of chylothorax in the nonsurgical setting.² Useful investigations include a computed tomographic scan of the chest and abdomen for evaluation of mediastinal and intra-abdominal nodes and lymphangiography for locating the site of leakage or obstruction of the thoracic duct.

Immunophenotyping of cytologic specimens by flow cytometry is well established as an ancillary technique in the diagnosis of haematopoietic neoplasm.¹¹ In our patient, the immunophenotyping of the pleural fluid by flow cytometry led to the suspicion of lymphoma prior to histologic confirmation by excision biopsy of the enlarged lymph node. Hence as part of the investigative work-up for the aetiology of pleural effusion, flow

cytometry of pleural fluid should be considered if a diagnosis of underlying lymphoproliferative disorder is entertained.

Chylothorax is a potentially life-threatening disorder that has profound respiratory, nutritional and immunologic consequences. Prolonged loss of chyle results in severe nutritional depletion, water and electrolyte loss and lymphopenia with T-cell suppression.^{12,13}

Current treatment of chylothorax involves conservative therapy initially, consisting of bed rest, aggressive nutritional support (e.g. medium chain triglyceride diet and total parenteral nutrition), tube thoracostomy drainage and treatment of the underlying cause which led to the development of the chylothorax.¹⁴ The rationale for nutritional intervention in chylothorax is to prevent malnutrition and to diminish chyle production and thereby promote spontaneous closure of the thoracic duct leak.¹⁵ Thoracic duct lymph flow decreases during starvation and increases with ingestion of fat especially long-chain fatty acids. Fifty per cent of cases of traumatic chylothorax would resolve spontaneously.¹⁶ Surgical intervention for chylothoraces that fail to respond to initial conservative measures will be required in a minority of patients.¹⁷

Thoracic duct ligation is the mainstay of surgical treatment.¹⁸ In the management of postoperative chylothorax, early thoracic duct ligation has been recommended in recent literature.¹⁹ Other alternatives that have been tried include pleuroperitoneal shunts, thoracoscopic fibrin glue, chemical or talc pleurodesis, pleurectomy and mediastinal radiation.¹⁷ Norum and Aasebo²⁰ reported satisfactory control of chylothorax due to lymphoma with intrapleural bleomycin combined with systemic chemotherapy.

Mortality rates of 50% and 100% for traumatic and non-traumatic chylothorax respectively have been reported. In non-traumatic chylothorax the prognosis is determined by the underlying disease.

REFERENCES

1. Light RW. Pleural Diseases. 3rd edition. Baltimore: Williams and Wilkins, 1995:284-98.
2. Valentine V G, Raffin T A. The management of chylothorax. Chest 1992; 102:586-91.
3. Seriff N S, Cohen M L, Samuel I', Schulster P L. Chylothorax: diagnosis by lipoprotein electrophoresis of serum and pleural fluid. Thorax 1977; 32:98-100.
4. Staats B A, Ellefson R D, Budahn L L, Dines D E, Prakash U B S, Offord K. The lipoprotein profile of chylous and non chylous pleural effusions. Mayo Clin Proc 1980; 55:700-4.
5. Coe J E, Aikawa J K. Cholesterol pleural effusion. Arch Intern Med 1961; 108:763-74.
6. Teba L, Dedhia H V, Bowen R, Alexander J C. Chylothorax review. Crit Care Med 1985; 13:49-52.
7. MacFarlane J R, Holman C W. Chylothorax. Am Rev Respir Dis 1972; 105:287-91.

8. Strausser J L, Flye M W. Management of nontraumatic chylothorax. *Ann Thorac Surg* 1981; 31:520-6.
 9. Vennera M C, Moreno R, Cot J. Chylothorax and tuberculosis. *Thorax* 1983; 38:694-5.
 10. Lowe D K, Fletcher W S, Horowitz I J , Hyman H D. Management of chylothorax secondary to lymphoma. *Surg Gynecol Obstet* 1972; 135:35-8.
 11. Moriarty A T, Wiersema L, Snyder W, Kotylo P K, McCloskey D W. Immunophenotyping of cytologic specimens by flow cytometry. *Diagn Cytopathol* 1993; 9:252-8.
 12. Machleder H I, Paulus H. Clinical and immunological alteration observed in patient undergoing long term thoracic duct drainage. *Surgery* 1978; 84:157-65.
 13. Breaux J R, Marks C. Chylothorax causing reversible T-cell depletion. *J Trauma* 1988; 28:705-7.
 14. Fairfax A J, McNabb W R, Spiro S G. Chylothorax: A review of 18 cases. *Thorax* 1986; 41:880-5.
 15. Jensen G L, Mascioli E A, Meyer L I, Lopes S M, Bell S J, Babayan V K, et al. Dietary modification of chyle composition in chylothorax. *Gastroenterology* 1989; 97:761-5.
 16. Rubin J W, Moore H V, Ellison R G. Chylothorax: therapeutic alternatives. *Am J Surg* 1977; 43:292-7.
 17. Marts B C, Naunheim K S, Fiore A C, Pennington D G. Conservative versus surgical management of chylothorax. *Am J Surg* 1992; 164:532-5.
 18. Paes M L, Powell H. Chylothorax: an update. *Br J Hosp Med* 1994; 51:482-90.
 19. Sieczka E M, Harvey J C. Early thoracic duct ligation for postoperative chylothorax. *J Surg Oncol* 1996; 61:56-60.
 20. Norum J, Aasebo U. Intrapleural bleomycin in the treatment of chylothorax. *J Chemother* 1994; 6:427-30.
-