

## Bilateral Chylothorax: Which is to Blame?

### Bilateral Şilotoraks: Etiyoloji Hangisi?

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#### ABSTRACT

Chylothorax is a rare condition in children with various traumatic and non traumatic etiologies. It is very important to determine the etiology for the management. Herein, we report a 16 year-old boy with a history of monosomy 7 positive refractory AML, stem cell transplantation, gastrointestinal graft versus host disease, invasive aspergillosis and bilateral chylothorax with multiple suspected etiologies.

**Key Words:** AML, aspergillosis, chylothorax, graft versus host disease, irradiation, stem cell transplantation

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#### ÖZET

Şilotoraks travmatik ve travmatik olmayan nedenlerle ortaya çıkan, çocuklarda nadir görülen bir durumdur. Etiyolojisini belirlemek tedavi açısından çok önemlidir. Bu yazıda, monozomi 7 refrakter AML olup kök hücre nakli yapılmış, gastrointestinal graft versus host hastalığı, invaziv aspergillozis ve birden çok şüpheli etyolojisi olan bilateral şilotorakslı 16 yaşında erkek bir hasta sunulmuştur.

**Anahtar Sözcükler :** AML, aspergillus, şilotoraks, graft versus host hastalığı, ışın tedavisi, kök hücre nakli

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#### INTRODUCTION

Chylothorax is the leakage of lymphatic fluid to the pleural space resulting from disruption or obstruction of the thoracic duct anywhere along its course (1). The fluid has characteristic features like high triglyceride content and milky white appearance. The etiology can be classified as congenital lymphatic abnormalities, trauma, high central venous pressure, malignancy or miscellaneous (2). Although there are various conditions that cause chylothorax, the etiology could not be identified clearly in some patients. Herein, we report a 16 year-old boy with bilateral chylothorax with multiple suspected etiologies.

#### CASE REPORT

A 16 year-old male was admitted with complaints of fever and weight loss. On physical examination he had mild pallor without organomegaly. Normocytic moderate anemia (Hb: 7.7g/dl, MCV: 85 fl), leukocytosis (WBC: 14.500/mm<sup>3</sup>), thrombocytopenia (Platelets: 14.500/mm<sup>3</sup>) and blasts in the peripheral smear were noticed. Bone marrow morphology (32 % myeloblasts), immunophenotyping (CD 11b, 13, 14, 33, 64, 117, CyMPO positivity) and cytogenetic tests (monosomy 7 positivity) lead to the diagnosis of acute myeloid leukemia (AML). Imaging studies (chest x-ray and abdominal ultrasound) were normal on admission.

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He was commenced on Medical Research Council; MRC-AML15 chemotherapy protocol and after 2 cycles no remission was achieved. As he received FLAG-ida (fludarabine, ARA-C, G-CSF with idarubicin) chemotherapy with remission failure again (15 % blasts in the bone marrow) he had undergone stem cell transplantation from a matched related donor with a cytoreductive, myeloablative conditioning (total body irradiation, ARA-C and cyclophosphamide). He was also given secondary prophylaxis with voriconazole as he had an invasive fungal infection during induction chemotherapy for AML. Graft versus host disease (GVHD) prophylaxis consisted of cyclosporine for three months. At 3 months after transplantation while he had 100% donor chimerism and monosomy negativity he was admitted with dysphagia, vomiting, anal pain and fever which prompted empirical antibiotic treatment. On the second day of treatment he experienced facial angioedematous like swelling which was resistant to steroids and antihistaminics (Figure 1).



Figure 1: Facial angioedematous like swelling of the patient.

There was no sign of extramedullary relapse in paranasal and neck computerized tomography scan (CT). Tranexamic acid was commenced for nonhistaminergic angioneurotic edema without any benefit. On the 7th day he developed 10-15 times/day diarrhea. Although rectal biopsy proved severe intestinal GVHD no immune suppressive therapy was started as diarrhea resolved. Fifteen days later liver function tests increased together with a maculopapular rash. Liver biopsy proved GVHD with severe hemosiderosis that lead to tacrolimus and short course steroid treatment. While performing liver biopsy milky appearing fluid was noticed. Perihepatic, perisplenic fluid was detected (6 mm) in abdominal ultrasound (US). The previous history of invasive aspergillosis and newly developing cough directed a thorax CT which showed bilateral pleural (20 mm in left, 24 mm in right) and pericardial effusion with fibrotic retractions and atelectasis areas in both lungs as well as 5 mm cavitory lesion in the left lung (Figure 2).

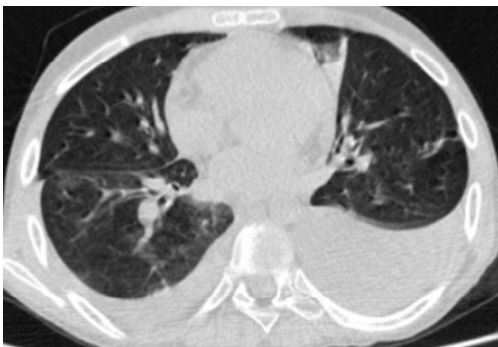


Figure 2: Thorax tomography of the patient depicting bilateral pleural (20 mm in left, 24 mm in right) and pericardial effusion with fibrotic retractions and atelectasis areas in both lungs as well as 5 mm cavitory lesion in the left lung.

Chylohemorrhagic fluid (Figure 3) with a triglyceride content of 1150 mg/dl and galactomannan and aspergillus PCR positivity were found in thoracentesis.



Figure 3: Milky chylohemorrhagic fluid of the patient.

Central venous line was removed for leakage suspicion. Liposomal amphotericin B (L-AMB) was started as new lesions under voriconazole treatment has emerged. A fat-restricted oral diet and octreotide was started. In the meantime, although morphologically in remission monosomy 7 positivity was detected that encouraged withdrawal of tacrolimus. At 1st month of octreotide and L-AMB treatment he developed fever with an increase in cough. Thorax CT showed ground glass appearance and increase in effusion (52 mm in left, 13mm in right). Thoracentesis drained 150 ml inflammatory fluid with a triglyceride content of 184 mg/dl. Caspofungin was added to L-AMB along with wide spectrum antibiotics. No microorganism was detected in further tests. Lymphoscintigraphy did not demonstrate any leakage. For the resolution of chylothorax besides octreotide he was commenced on total parenteral nutrition (TPN) for 10 days with nil by mouth which lead to a decrease in pleural effusions (7 mm in right, 12 mm in left). He received combined antifungal therapy for 8 weeks with resolution of the lesions on thorax CT. Repeated examinations showed morphological bone marrow remission and monosomy negativity. He is now 16th months after transplant and well with minimal pleural effusion receiving cyclosporine for upper GI GVHD and weekly octreotide.

## DISCUSSION

Chylothorax is an uncommon cause of pleural effusion in children. As treatment should be mainly based on determining and treating the underlying cause, it is of paramount importance to define the etiology. In the absence of apparent risk factors such as trauma the determination of etiology could be difficult. This is particularly challenging in the transplant setting since the etiology could be multiple as in our patient.

Chylothorax may be caused by infections, pleural involvement and lymphatic obstruction, central catheterization and rarely by radiotherapy in patients with malignancies (3,4). Granulomatous infections such as tuberculosis and histoplasmosis have been reported as the cause of chylothorax by compressive or other effects of mediastinal lymphadenitis (5,6). However all detailed microbiological investigations were performed in our patient, and only aspergillus which is a non-granulomatous infection was detected. Malignancies such as lymphoma, chronic lymphocytic leukemia, and metastatic cancers are the leading causes of non-traumatic chylothorax; none of them was relevant to our patient. Few studies reported the radiotherapy as the cause of chylothorax by narrowing of lymph vessels and consequent impaired lymph flow (7,8). Chylothorax after radiotherapy as a complication of treatment was reported in Hodgkin's lymphoma, soft tissue sarcoma, non-small-cell lung cancer, and oesophageal cancer (4,7-9). To our knowledge, currently there is no report about AML. Our patient also had upper gastrointestinal manifestations of acute GVHD such as dysphagia, vomiting that might also cause non iatrogenic trauma for chylothorax.

The management of chylothorax includes treatment of the underlying disease, pleural drainage, dietary modifications, pleurodesis, and thoracic duct ligation. Octreotide is a synthetic analogue of somatostatin that inhibits the secretion of growth hormone, glucagon, insulin and reduce the lymph fluid excretion. Octreotide also reduces splanchnic blood flow and secretion of water and electrolytes and it is highly efficacious in the conservative management of chylothorax (10). A fat restricted diet and octreotide were given and aspergillus infection was treated by antifungal agents in this patient. After non oral feeding by TPN he recovered rapidly.

## CONCLUSION

Although the beginning was chylous ascites the bilateral nature of chylothorax refrained us to consider it being the origin. We assume that the reason of bilateral chylothorax in our patient is iatrogenic trauma by total body irradiation as well as noniatrogenic trauma by forceful emesis and coughing owing to GVHD and aspergillus infection where all could be common in the posttransplant setting.

Although we could not clearly define the etiology and suggest a novel therapy model for this particular patient we believe that this case could be helpful for pediatric transplanters as well as other pediatric subspecialists who deal with such difficult cases.

**Conflict of interest**

No conflict of interest was declared by the authors.

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