
Life threatening chylothorax in a patient with congenital thrombophilia: Case report

Gülay ÜLÜSAL OKYAY¹, Ezgi COŞKUN YENİGÜN¹, Gülbahar DARILMAZ YÜCE²,
I. Safa YILDIRIM¹, Sadık ARDIÇ²

¹ S.B. Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi, İç Hastalıkları Kliniği,

² S.B. Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi, Göğüs Hastalıkları ve Tüberküloz Kliniği, Ankara.

ÖZET

Konjenital trombofilili bir hastada hayatı tehdit eden şilotoraks: Olgu sunumu

Bu yazıda, heterozigot faktör V Leiden gen mutasyonuna ek olarak antitrombin III eksikliği saptanan ve yaygın trombüs oluşumu sonucu bilateral şilotoraks gelişen bir olguyu sunuyoruz. Hastaya bilateral göğüs tüpü takılarak, trombolitik ve oral antikoagülan tedavi uygulandı. Dört haftalık tedavi sonunda semptomları geriledi. Hasta 18 aydır semptomsuz olarak takibimizdedir.

Anahtar Kelimeler: Şilotoraks, konjenital trombofilili.

SUMMARY

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Gülay ÜLÜSAL OKYAY¹, Ezgi COŞKUN YENİGÜN¹, Gülbahar DARILMAZ YÜCE²,
I. Safa YILDIRIM¹, Sadık ARDIÇ²

¹ Department of Internal Medicine, Dışkapı Yıldırım Beyazıt Education and Research Hospital, Government of Health, Ankara, Turkey,

² Department of Chest Disease and Tuberculosis, Dışkapı Yıldırım Beyazıt Education and Research Hospital, Government of Health, Ankara, Turkey.

Yazışma Adresi (Address for Correspondence):

Dr. Gülay ÜLÜSAL OKYAY, S.B. Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi, 3. Dahiliye Kliniği,
06110 ANKARA - TÜRKİYE

e-mail: mdgulayulusal@hotmail.com

We reported here a case of bilateral chylothorax as a result of widespread thrombi formation in a patient who was heterozygote for factor V leiden gene mutation and who had antithrombin III deficiency. We performed bilateral chest tubes, thrombolytic and oral anticoagulant therapy. The patient responded to the therapy. She has been in follow up without symptoms for 18 months.

Key Words: Chylothorax, congenital thrombophilia.

Chylothorax is the collection of lymphatic fluid at the pleural region because of obstruction or damage of thoracic duct or its major branches. We suggested the chyle flow obstruction from thoracic duct to left subclavian vein, yielding chylous pleural effusion because of increased hydrostatic pressure due to thrombosis of nearby venous vessels. As far as our knowledge, this is the first case in literature which is presented with bilateral chylothorax due to two congenital thrombophilic deficiencies, so we found it noteworthy for the presentation.

CASE REPORT

A 16 year old female admitted to our emergency department with the complaints of gradually increased back pain and dispnea for one month. She had a normal past history. At physical examination the patient was normotensive, but tachycardic and tachypneic. The breath sounds were bilaterally diminished inferior to scapula and the percussion revealed dullness at these regions. The superficial abdominal collateral veins filling from down were remarkable. The homans sign was positive at right lower extremity. The plain chest radiography showed bilateral pleural effusions (Figure 1). Complete blood count findings were Hb: 9.1 g/dL, Htc: 29.4%, WBC: 10.000 /mm³, MCV: 71 fL, platelets: 662.000 /uL. Erythrocyte sedimentation rate was 34 mm/hour. Blood biochemistry and urine analyses were normal. ANA, anti-dsDNA, RF and HLA B51 were negative. Arterial blood gas analysis revealed pH: 7.43 (7.35-7.45), PaO₂: 65.4 mmHg (\geq 80 mmHg), PaCO₂: 28.4 mmHg (35-45 mmHg), oxygen saturation: 93.3% (\geq 95%). The thoracentesis yielded milky coloured chylous fluid. Its analysis revealed triglyceride: 115 mg/dL, cholesterol: 73 mg/dL, total protein: 2800 mg/dL, glucose: 126 mg/dL, cell count: 3800 /mm³; lymphocytes 70%, neutrophils



Figure 1. Bilateral pleural effusions in chest radiography.

30%. The fluid was sterile and negative for ARB and tuberculosis PCR. ADA level was within the normal limits. The fluid colour became clear with ether addition and there was no precipitation with centrifugation. Cytologic examination was consistent with class II lymphocytosis. The pleural biopsy specimen showed chronic fibrinous pleuritis without any malignant cells. With the diagnosis of bilateral chylothorax, bilateral intercostal chest tubes were applicated. The oral intake was ceased and total parenteral nutrition riched from middle chain fatty acids was initiated. Since the patient had positive homans sign and superficial abdominal collateral veins, doppler ultrasonographies were performed. At bilateral lower extremities subacute deep vein thrombi were determined. There was thrombus formation in a length of 8 cm throughout the lumen of inferior vena cava. Also in right renal vein, main and external iliac veins, bilateral jugular veins and right subclavian vein subacute

thrombi were determined. The calibration of left subclavian vein was reported as decreased. Abdominal ultrasonography showed minimal amount of ascites, without organomegaly or lymphadenopathy. Computed tomography of thorax revealed thrombi smaller than 1 cm at left pulmonary and left interlober pulmonary arteries (Figure 2). Although the pulmonary conus was prominent on chest radiography, transthoracic echocardiography showed normal left and right ventricular functions with normal leaflets, without pericardial effusion or thrombus formation. Because of extensive thrombosis, the coagulation studies were performed. Antithrombin III [41.1% (75-125%)] deficiency, activated protein C resistance [0.5 (0.86-1.1)] and heterozygote factor V Leiden gene mutation were established. Oral anticoagulation therapy was added to conservative treatment. But, the patient remained as hypotensive, tachycardic and seriously dispneic. Because of pulmonary thromboembolism, thrombolytic treatment with tissue plasminogen activator was applied. Afterwards oral anticoagulant therapy was rearranged. At clinical follow up, daily amount of chest tube drainage did not diminished. Moreover, at the end of the second week it was still about 500 mL. The patient was referred to another facility for the surgical intervention. There, she was kept on total parenteral nutrition for about two more weeks. The chest tubes were also preserved. Then, the treatment was continued with oral anticoagulant medication,



Figure 2. Thrombus at left pulmonary artery in thorax computed tomography.

on, without surgery. For about 18 months she is in our follow up with the significant clinical improvement and relief of symptoms. The repeated imaging studies yielded recanalized vessels and resumption of blood flow. Because of two congenital factor deficiencies and extensive thrombi formation she was decided to remain on oral anticoagulant therapy for life long period.

DISCUSSION

Chylothorax is the collection of lymphatic fluid at the pleural region because of the obstruction or the damage of thoracic duct or its major lymphatic branches. The chylothorax is diagnosed with the triglyceride level of pleural fluid greater than 110 mg/dL (1). In the presented case the pleural triglyceride concentration was 115 mg/dL. The ether and centrifugation tests, pleural fluid glucose level and cell count with lymphocyte predominancy, exclusion of tuberculosis and other nonspecific infections were in accordance with the diagnosis of chylothorax. The etiology is heterogenous for the development of chylothorax. Most commonly reported cases are those in the setting of cardiothoracic surgical procedures. Recently, some cases secondary to central vein thrombosis as a result of catheterization were reported. Seibert et al. and Curci et al. reported the cases with chylothorax related to superior vena cava obstruction secondary to catheterization (2,3). The thoracic duct pours to systemic circulation at the union level of left subclavian vein and left jugular vein. In our case, there were widespread thrombi formation including jugular veins. At left subclavian vein the calibration was found to be diminished in doppler ultrasonography. If the systemic venous pressure exceeds the pressure of the thoracic duct because of any reason, the back pressure in lymphatics will create a relative flow obstruction, prevent the chyle drainage from thoracic duct to subclavian vein and rupture of thoracic duct and/or its collaterals (4). For our patient, we suggested chyle flow obstruction from thoracic duct to left subclavian vein because of increased hydrostatic pressure due to thrombosis of nearby venous vessels, eventually yielding chylous pleural effusion. Pa-

tients with recurrent, widespread or early age thrombosis and those with positive family history should be screened for acquired and inherited thrombophilic risk factors (5). We performed the screening tests and established the congenital deficiencies without any identifiable acquired prothrombotic condition. She was heterozygote for the factor V Leiden gene mutation resulting activated protein C (APC) resistance. This hypercoagulable state increases the risk of thrombosis 3 times as compared to normal population (6). Additionally antithrombin III, one of the natural anticoagulants was also defective in our patient. Combination of APC resistance and one or more acquired risk factors is more common than combination of multiple hereditary risk factors at thromboembolic cases (7). However, in our case, two congenital abnormalities resulted in widespread thrombosis at an early age. As far as our knowledge this is the first case of chylothorax in literature with two congenital thrombophilic deficiencies. When the chylothorax diagnosis was established, immediately bilateral chest tubes were applied for the evacuation of chylous fluid from the pleural cavity. The patient oral intake was ceased and nourishment with total parenteral nutrition was initiated. Several authors had displayed that by ceasing oral intake and initiating total parenteral nutrition, thoracic duct leakages spontaneously closed in 10-14 days (1,8,9). Baghetti et al., reviewed 51 patients with chylothorax, mostly secondary to cardiotoracic surgery and reported that conservative treatment was successful in 80% of the patients with their management approach (10). Jhonestone et al. suggested that a minority of chylothorax will fail to resolve with conservative measures and surgical intervention is required to prevent chronic metabolic deterioration and death (11). In the absence of medically treatable disease, thoracotomy with ligation of the thoracic duct and/or pleurectomy or pleurodesis can provide substantial palliation for patients with nontraumatic chylothorax, even when a discrete source of lymph leakage cannot be localized or ascites is present (12). In our case with the conservative measures directed to chylothorax

the clinical improvement could not be achieved. She was hemodynamically unstable. We considered that the submassive pulmonary thromboembolism (PTE) was also a contributing factor for this dramatic outcome and we decided to supplement thrombolytic therapy. The main indications of thrombolytic therapy for PTE are more than 50% obstruction of pulmonary vascular bed and hemodynamic instability (13,14). Although not widely recommended, at patients with significant dyspnea or at patients with hemodynamic instability, regardless of thrombus size, thrombolytic therapy may be indicated (13). Bilateral chylothorax is a serious condition that can affect the cardiac and respiratory systems and be associated with cardiopulmonary collapse. So, we decided surgical intervention and referred her to another facility. But there, she was kept on conservative treatment for about two more weeks, so total four weeks reached and the clinical improvement was achieved without surgery. Le Coultré et al. displayed that in patients with chylothorax secondary to venous obstruction, the effusion persisted longer and was more difficult to treat (15). They suggested that the time limit for nonoperative treatment for these patients should be prolonged to four weeks (15). The clinical outcome of our patient with chylothorax secondary to venous obstructions was in accordance with their suggestion. After the discharge from the hospital, for about 18 months she was in our follow up with significant clinical improvement.

The presented patient is a rare case with bilateral chylothorax as a result of widespread thrombosis. The chylothorax and its life threatening complications were disentangled by the overall management approach based upon thrombophilia including fibrinolytic treatment, conservative protocols and systemic anticoagulation. This case should remind that, chylothorax may occur with central venous thrombosis in the presence of congenital coagulation system defects. Thus, patients should be investigated for this aspect in the absence of usually reported risk factors or well known underlying etiologies.

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