CHYLOTHORAX AS A RARE COMPLICATION OF SYSTEMIC LUPUS ERYTHEMATOSUS – CASE STUDY

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Abstract. *We present a case of systemic lupus erythematosus (SLE), which was diagnosed before 7 years, and antirheumatic therapy was prescribed. However, following relief of the initial symptoms, the patient stopped taking medications and presented again, after being symptom-free for three years, with chylothorax and symptoms, which were entirely different from the first visit. The patient was treated with a combination of hydroxychloroquine, prednisolone and azathioprine following ruling out of malignancy and infections and responded well to the therapy.*

Key words: *SLE, chylothorax, rare complication*

Introduction

Pulmonary symptoms are a common entity in SLE patients, however, chylothorax is a rare finding and reported sparingly in the literature. So far, only 26 cases of chylothorax, with or without chylous ascites or protein losing enteropathy, in SLE, are found in Medline search, and 14 of them were having exclusively chylothorax [1-10]. Usually, chylothorax accompanying SLE is observed either during disease as a complication [1, 2, 4, 6-10], while the patients were on therapy or as an initial presentation [3, 5]. However, we are describing here a patient who was initially on therapy for SLE and later discontinued treatment on her own decision following relief of symptoms. The patient remained symptom-free for around 3 years and presented in the emergency room with respiratory distress due to chylothorax.

Case description

A 16-year-old female patient presented to the rheumatology clinic in2013 with main complaints of pain and swelling in various joints, easily tiring and febrile. Clinical examination showed swelling in the elbow and knee joints. Laboratory evaluation showed leucopenia (leucocyte counts 3400/mm^3). Direct Coombs test was positive; antinuclear antibody (ANA) was significantly high at a titre of 1:160 with a homogenous pattern; anti-double stranded DNA (Anti-dsDNA) antibodies were also positive. She was diagnosed asa definite case of SLE based on the clinical and immunological criteria (6 of 17 on SLICC criteria) at her first visit to the rheumatologist [11]. Therapy with hydroxychloroquine200 mg daily in two divided doses and prednisolone 10 mg daily per os was started and the patient improved quickly. However, after a gap of symptom-free period,shestopped these medications as well as follow-up in 2016 against the advice of her rheumatologist.

After a period of approximately three years, on 22 July 2019, the same patient, now 23-year-old married woman, presented to the emergency department with shortness of breath. Her present condition started before nine months with dyspnea of grade 2 (according to the New York Heart Association (NYHA)), which was gradually progressive, increased with activity and decreased at rest. Hersymptoms of respiratory distress worsened over the last three months and hampered her daily routine activity with development of new symptoms including dry cough, orthopnea and paroxysmal nocturnal dyspnea. There is no history of hemoptysis, fever, night sweats, chest pain or lower limbs edema. She had never undergone surgery or suffered chest trauma in the past. She had no history of smoking and recent travel. *She is married with one child.*

On physical examination,the patient was dyspneic withoxygen saturation 93% on room air by pulse oximetry. Except for decreased bilateral air-entry on auscultation, the remainder of the examination was unremarkable.

Laboratory findings were mild leukocytosis with microscopic hypochromic anemia. We obtained a very high C-reactive protein (CRP) level and raised erythrocyte sedimentation rate (ESR). ANA and Anti-dsDNA antibodies were positive, whereas C3 and C4 levels were low [Table 1]. Arterial blood gas showed elements of hypoxia and hypoventilation. Urine dipstick wasnegative for protein and blood.

Chest radiography showed a massive bilateral pleural effusion. Electrocardiogram was unremarkable withsinus tachycardia. Echocardiography showed normal ejection fraction, mild pericardial effusion and normal pulmonary artery systolic pressure. On computerized tomography (CT) of chest, abdomen and pelvis with intravenous contrast showed an extensive bilateral pleural effusion (Figure 1A,1B) associated with left lower lobe collapse consolidation causing mass effect on the lung and heart with no parenchymal abnormalities, lung cysts or mediastinal lymphadenopathy. No abdominal mass or ascites was seen on CT.

Diagnostic as well as therapeutic thoracocentesis was performed as an initial step. Pigtail tube, size 8 French, was inserted bilaterally and milky white fluid was drained over a period of 6 hours from the left (1600 ml) and right (700 ml) sides, respectively.The chest physician replaced Pigtail tube with a bilateral chest tube(24 Fr). Pleural fluid examination showed 160 mg/dl of triglycerides and 16.2 mg/dl of cholesterol (Table 1).

We observed reactive mesothelial cells, inflammatory cells, which were predominantly lymphocytes and plasma cells, on cytological examination, Figure 2. Acid-fast bacilli (AFB) smear and culture of pleural fluid was negative. Left- and right-sided pleural biopsy following thoracoscopy revealed chronic inflammation with no malignant cells, and AFB staining was negative. No evidence of granuloma was observed in the examined tissue. After careful consideration of details, we made a diagnosis of SLE, with 1 clinical and 3 immunological criteria based on SLICC, with bilateral chylothorax. She was treated with hydroxychloroquine 200 mg, prednisolone 30 mg, and azathioprine 50 mg orally once a day. She had significant improvement; as the last follow-up in chest clinic on November 2020 revealed that she is stable, with no dyspnea. On a follow-up chest radiography, fluid collection was not observed.

Table 1. Levels of various analytes in patient's serum as well as pleural fluid

Variable (unit)	Values	Reference Ranges
Leucocyte count	11.4	4.5-10
Hemoglobin (gm/dL)	10.4, microcytic and hypochromic erythrocytes on peripheral smear	11.5-16.5
Platelet counts	217	150-400
Sodium	137	135-153
Potassium	4	3.5-5.3
Blood Urea Nitrogen	1.4	2.6-6.4
Creatinine	36	50-115
Bilirubin	6.5	0-17
Alkaline Phosphatase	130	50-137
Aspartate aminotranferase	30	15-37
Alanine aminotransferase	22	10-50
Total protein	69	64-82
Lactate dehydrogenase	162	
C-reactive Protein	849	0.0-0.3
Eryhtrocyte Sedimentation Rate	44	
Thyroid Stimulating Hormone	2.16	0.27-4.2

Antinuclear antibody	Positive	
Anti-double stranded DNA Antibody	Positive	
C3 and C4	Low	
C-ANCA	Negative	
P-ANCA	Negative	
Anti-SSA (Ro)	Negative	
Anti-SSB (La)	Negative	
Anti-Jo-1	Negative	
Anti-SCL-70	Negative	
Anti-cardiolipin	Negative	
Anti-CCP	Negative	
TTG	Negative	
Beta-2-glycoprotein-1	Negative	
Anti-histone-ABS	Negative	
HIV-1,2 Ab, Ag	Negative	
Hepatitis B	Negative	
Hepatitis C	Negative	
Anti RNP	Negative	
Pleural Fluid Examination		
Appearance	Milky	
Total Protein	44	
Lactate Dehydrogenase	655	
Glucose (mmol/L)	6.8	
Amylase (U/L)	40	
Triglyceride (mg/dL)	160	
Cholesterol (mg/dL)	16.2	

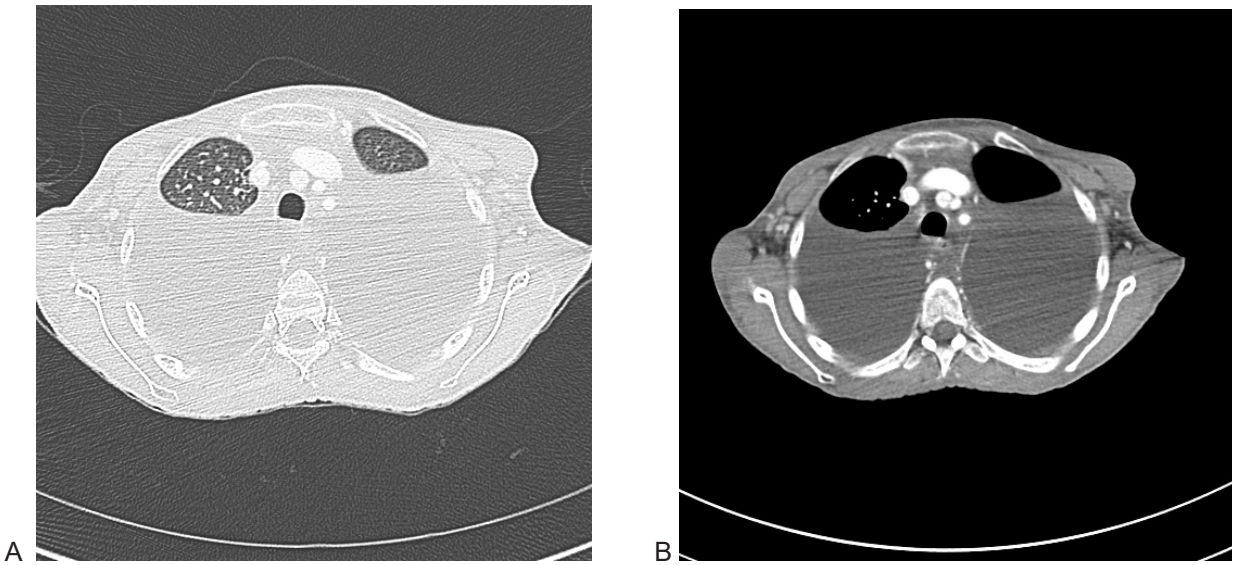

Fig. 1A and 1B. Bilateral massive pleural effusion

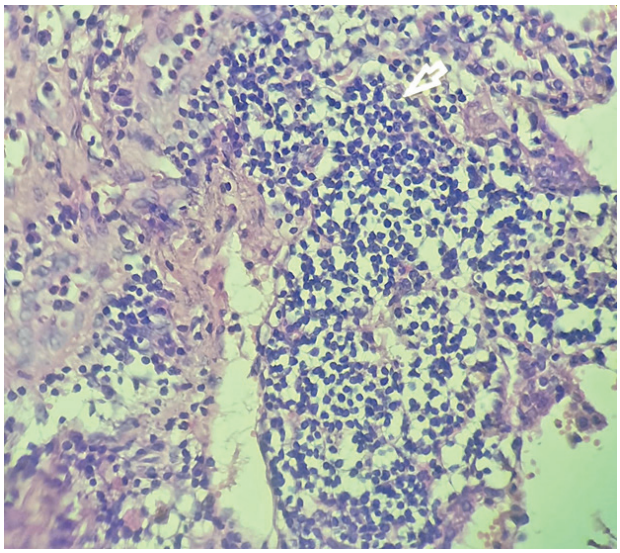

Fig. 2. Dense chronic inflammation below pleura in lung tissues

Discussion

Chylothorax is commonly seen in either trauma, whether non-surgical or surgical, malignancy, especially lymphoma, or infections [5]. The mechanism of chyle accumulation in the pleural space is either because of injury to the lymphatic channel or inflammation, which may result in improper drainage. Its presence in SLE is rare and the underlying reason for such manifestation is obscure. Chylothorax is diagnosedin clinical settings, when pleural fluid contains triglyceride level (more than 110 mg/dl) or chylomicron or both [1].

Our patient is the first case of chylothorax secondary to SLE among Arab ethnicities. Additionally, 80% (21 out of 26) of the previously reported cases come from Asia, including one patient from Turkey [2-4, 6, 8, 10]. On the other hand, only three cases from the United States [1, 7, 9] and one from Argentina [5] and, interestingly, no cases, so far, from Europe and Australia, are reported. It might be possible that majority of the reported cases were random observation andthis specific and rare complication of SLE is not associated with an ethnic predilection. However, in Asia, almost all the cases were from China, Taiwan and South Korea, and this observation needs future studies to discern any association of chylothorax (in SLE) with genetic and/or environmental factors in these regions or ethnicities.

In our case, there was no prior history of surgery, trauma, and we had ruled out malignancy as well as other infectious etiologies. The patient is a known case of SLE, and had stopped medications on her own, against the advice of concerned clinicians. Additionally, her laboratory evaluations including imaging and histopathology reports support her present diagnosis of chylothorax secondary to SLE.

Chylothorax as a presenting symptom in SLE is mentioned only in two cases in the past [3, 5]. The first case had a very short history of dry cough [3], whereas the other case was initially diagnosed as discoid lupus (treated for three years) and progressed to SLE [5]. However, except for one case with no information available regarding progression/presentation [1], the remainderof the cases developed the complication, i.e., chylothorax, during the course of their disease. Further, among these 23 cases, 12 were treated surgically with adjuvant immunosuppressive agents [1, 4, 8, 10] and 11 patients were managed conventionally with steroids (six achieved full remission, while one died due to infection, and four were lost during follow-up) [2, 6, 10]. Interestingly, even though none of these patients stopped their SLE therapy in the course of the disease, in all of them chylothorax developed. However, in our patient chylothorax occurred only after discontinuation of therapy, as opposed to the other cases reported earlier. Additionally, she improved swiftly on medications, however, most of the reported cases were refractory to conservative management, as surgical intervention was employed in more than half of them. Further, the cases managed conventionally by medications showed poor response to therapy. It could be due to younger age of the patient and lesser duration of the disease in our case, however, the actual reason cannot be ascertained due to the lack of comparison.

The pathophysiology of chylothorax in SLE is still not clear but we think that inflammatory process is the key factor. Inflammation of the cisterna chyli and lymphatic vessels leads to obstruction and backflow pressure which may lead to alteration of pleural membrane permeability and decreased lymphatic drainage at pleural edge.

Conclusion

The case mentioned here is a rare complication of SLE. Additionally, it demonstrates that chylothorax may be a presenting feature in SLE especially with an intervening symptom-free period of as long as three years.

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