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Rheumatoid Pleural Effusions and Trapped Lung: An Uncommon Complication of Rheumatoid Arthritis

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INTRODUCTION

Rheumatoid arthritis (RA) is a disease affecting approximately 1% of the population. It is familiarly defined as “chronic, symmetric, debilitating and destructive inflammatory polyarthritis characterized by proliferative synovial tissue (pannus) formation in affected joints” (1). Pain symptoms are typically worse in the morning, the disease affects females more than males, and ulnar deviation and swan neck deformities are common. Perhaps less well known is the extensive list of extra-articular manifestations (EAMs) that can occur at any time during the course of the disease. EAMs affect an estimated 18-41% of patients with RA (1). Renal, pulmonary, cardiovascular, nervous, and integumentary system manifestations have all been described. Our case is that of an RA patient with shortness of breath and pleural effusions.

CASE PRESENTATION

A truly pleasant 56-year-old female with RA presented to the hospital after approximately 12 hours of diarrhea accompanied by progressively worsening lower extremity weakness and pain that began soon after her first of seven loose bowel movements. The weakness and pain first started in her hips and ankles, then her wrists and hands. It progressed to the point that she was unable to bear weight. Due to a white cell count of 13,000 cells/mcL³ and heart rate greater than 90 beats/minute, Systemic Inflammatory Response Syndrome criteria were met. An infectious work up produced negative blood cultures and a urinalysis not concerning for urinary tract infection. A chest radiograph revealed large, bilateral, left greater than right pleural effusions with associated linear opacities. There was also concern for loculation from the appearance of the radiograph. The patient had originally denied shortness of breath, but after further questioning, she mentioned that she has chronic shortness of breath on exertion.

A left diagnostic thoracentesis was performed. The pleural pH was 7.147, pleural glucose 24 mg/dL (plasma glucose at the time was 155 mg/dL), pleural protein 4.5 g/dL (serum protein 6.9 g/dL), pleural LDH 1952 units/L (serum LDH 166 units/L). Gram stain and culture were negative for organisms, cytology revealed acute inflammatory cells and no malignant cells. Due to a pleural protein/serum protein ratio of 0.65 and a pleural effusion LDH/serum LDH of 11.8, the pleural effusions met exudative criteria. The very low pH, very low glucose, and negative Gram stain and culture of the pleural fluid were highly indicative of rheumatoid pleural effusions. Rheumatology was consulted and recommended prednisone 40mg daily for RA flare and associated rheumatoid effusions. The patient improved rapidly and was discharged on a steroid taper less than 48 hours after admission.

Five months later, our patient presented to the Emergency Department for shortness of breath of three weeks' duration. She was febrile at 38.9° Celsius, tachycardic at 118 beats/minute, and was desaturating to 89% on four

liters of oxygen. Her white cell count was 26,000 cells/mcL³. She complained of a productive cough with yellow and brown sputum. Blood and sputum cultures were negative. A chest radiograph again showed similar appearing large right and moderate left pleural effusions with pleural calcification (Image 1). There was concern for loculated right pleural effusion. She was empirically started on azithromycin, ceftriaxone, and vancomycin. A Computed Tomography (CT)-guided diagnostic thoracentesis of the right lung was performed the following day by Interventional Radiology, and 380 mL of dark, bloody fluid was obtained. The pH was 7.15, glucose

24 mg/dL (plasma glucose at the time was 155 mg/dL), pleural protein 4.5 g/dL (serum protein 6.9 g/dL), pleural LDH 1952 units/L (serum LDH 166 units/L). Gram stain and culture were negative for organisms, cytology revealed acute inflammatory cells and no malignant cells. Due to a pleural protein/serum protein ratio of 0.65 and a pleural effusion LDH/serum LDH of 11.8, the pleural effusions met exudative criteria. The very low pH, very low glucose, and negative Gram stain and culture of the pleural fluid were highly indicative of rheumatoid pleural effusions. Rheumatology was consulted and recommended prednisone 40mg daily for RA flare and associated rheumatoid effusions. The patient improved rapidly and was discharged on a steroid taper less than 48 hours after admission.

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Chest radiograph from our patient's second hospitalization demonstrating large, bilateral rheumatoid pleural effusions.

Cardiothoracic Surgery was consulted for recurrent pleural effusions and evaluation for video-assisted thoracoscopic surgery/decortication. CT chest demonstrated bilateral moderate pleural effusions with calcific fibrosis of the parietal pleurae (Image 2). The patient was taken to the operating room where a left chest tube was placed with spontaneous drainage of 700 mL of serosanguinous effusion. There was right thoracotomy and attempted decortication of the right lung. The operation note mentions a "white pleural peel with a very bumpy surface." The pleural surface was completely calcified. Each time there was an attempt to remove the calcified pleural peel, lung tissue was penetrated making decortication impossible. A second consulting surgeon agreed that the cortex was not surgically excisable. The lung was trapped secondary to extensive calcification rendering

re-expansion impossible. After hemostasis was achieved, a right chest tube was inserted. The following day, talc pleurodesis of the left lung was performed and the right chest tube was removed. The left chest tube was uneventfully removed before discharge. She was discharged home to finish her course of levofloxacin and another prednisone steroid taper per Rheumatology recommendations. Her respiratory status was back to baseline.



Chest computed tomography scan from our patient's second hospitalization showing a large right rheumatoid pleural effusion and smaller left rheumatoid pleural effusion. Note the bright line at the interface of the large right pleural effusion with visceral pleura on the right. This bright line represents the "Plaster of Paris" calcific plaque encountered in unsuccessful decortication.

CT chest one month after discharge redemonstrated the bilateral pleural effusions. The right had worsened, the left had improved after pleurodesis. She has followed up with Cardiothoracic Surgery, Pulmonary, and Rheumatology since her hospitalization. She had worsening shortness of breath at a clinic visit that again improved with prednisone taper alone. In the past, she has failed multiple different disease-modifying antirheumatic drugs secondary to side effects or recurrent infection. She was recently prescribed leflunomide and is being evaluated for rituximab for her refractory rheumatoid arthritis.

DISCUSSION

Clinically-evident rheumatoid pleural effusions (RPE) affect 3-5% of patients with RA (2). The actual prevalence of asymptomatic RPE in the RA population is likely much higher. Interestingly, though women are more likely to be afflicted with RA, men with the disease are more likely to develop symptomatic RPE (3). The main symptoms of RPE include pleuritic chest pain and dyspnea (2). Imaging studies will show pleural effusions which are not necessarily symmetric, as was the case in our patient. Other causes of pleural effusion should be considered as warranted by the patient's history and physical examination. Radiographic evidence alone is not sufficient to diagnose a RPE. There appears to be no strong correlation between RA flares and RPE development, though this was the case in our patient (2).

Diagnosis is accomplished by thoracentesis with pleural fluid analysis. The effusion will be exudative by Light's criteria as in our case, with one of the following criteria fulfilled: the pleural fluid protein-to-serum protein ratio greater than 0.5, the pleural fluid LDH-to-serum LDH ratio of greater than 0.6, or the pleural LDH greater than 2/3 the upper limit of normal. Characteristic of RPEs is a low pH (a range of 6.4 – 7.1 in most cases of one study, [4]) and low glucose level. A normal glucose level should call into question the diagnosis of a RPE (3). The pathophysiologic mechanism behind low glucose levels in RPE seems to be due to impaired glucose transport into the pleural space (4, 5). Pleural fluid analysis should reveal a negative Gram stain for organisms and culture of the fluid should be negative as well. In most cases, the pleural fluid white cell count will be above 3,000 WBC/mL (4). The cell differential most often shows a neutrophil predominance but lymphocytic predominance can occur often as well (4). In our review of the literature, there was not a consensus on the value of obtaining RF or anti-CCP levels in the pleural fluid of patients with suspected RPE. The main differential diagnosis for a sterile exudative effusion includes malignancy and tuberculosis. Cytology and acid fast stains should therefore be considered in the appropriate clinical context. Acid fast bacilli smear and culture of pleural fluid in our patient was negative. In summation, RPE can be confirmed in a patient with RA when pleural fluid analysis reveals a sterile exudative effusion with low glucose and low pH (generally < 7.2, [2]).

The course of a RPE may be protracted. Potential complications of RPE include empyema, pneumothorax and, if left untreated, pleural fibrosis and calcification that can lead to a trapped lung. Unfortunately, our patient's RPEs likely went years without treatment, leading to these more permanent complications. There is no broad consensus on the management of RPE once it has been diagnosed. Drainage alone may be curative but reaccumulation of the effusion may occur. For a large RPE that is compromising lung function, a chest tube may need to be placed for symptomatic relief. In the case of more complicated, infected, and loculated effusions such as our case, surgery with decortication may be warranted. Prevention of long-term recurrence can be attempted using the anti-inflammatory and disease-modifying drugs used in the treatment of RA. Some recurrent cases have been managed with surgery using pleurodesis to prevent further effusion development. For the hospitalist, once the diagnosis has been established, consultation with rheumatologists, pulmonologists, and cardiothoracic surgeons should be considered depending on the severity of the patient's symptoms (2-6).

CONCLUSION

Symptomatic rheumatoid pleural effusions are uncommon among the rheumatoid arthritis population, but they should be considered in RA patients who present with pleuritic chest or dyspnea and have supporting radiographic findings of pleural effusion. Diagnosis is confirmed with pleural fluid analysis. Multiple treatment modalities are available and should be tailored to each patient's individual presentation.

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