An atypical case of systemic lupus erythematosus presenting as fleeting hemorrhagic pleural effusion with normal complement level

Ochieng PO, Abrudescu A

Queens Hospital Center, Mount Sinai School of Medicine, Jamaica, New York

Abstract

Background: Systemic lupus erythematosus (SLE) is a multisystem disease that can be a diagnostic conundrum.
Case report: We describe a patient who presented with recurrent fleeting exudative and hemorrhagic pleural effusion. It took multiple visits over 3 months and renal biopsy to confirm the diagnosis of SLE.
Management: The patient was treated with immunosuppression.
Results: She had a favorable clinical response and continues to be followed up as an outpatient.
Conclusion: Systemic lupus erythematosus can be difficult diagnosis to make as it may present with atypical features.

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune multisystem disease with a myriad of presentation. The varying manifestations and progression make SLE a potential diagnostic challenge. We present an atypical case of SLE that was a diagnostic enigma.

Case report

Forty five year old black female first presented in March 2011 with acute onset right side pleuritic chest pain and fever. She reported a dry cough and no other symptom. At admission, she was in mild respiratory distress with respiratory rate of 20/min with the rest of the vitals normal. Chest exam was consistent with right pleural effusion and the rest of systemic examination was normal. Haemogram revealed normocytic anemia and leucocytosis. Urea, creatinine and electrolytes were within normal limits. Hepatic panel was unremarkable except for low protein and albumin. Chest X-ray (CXR) revealed right pleural effusion (Figure 1). On thoracocentesis the pleural fluid was hemorrhagic and exudative with parameters as shown in Table 1. Pleural cytology and microbiology tests were negative.

Antinuclear antigen (ANA) was positive with speckled pattern and titre of 1:160. Other connective tissue markers (Anti-Double strand DNA antibodies, anti-smith antibody, anti-Ro, anti-La and Rheumatoid factor) were negative. Hepatitis B and C and HIV screening were negative. Complement 3 and 4 levels were within normal limits with levels of 129 mg/dl and 29 mg/dl respectively. She was treated as with antibiotics for community acquired pneumonia with para pneumonic effusion and she improved and was discharged home.

In May 2011, she returned to the Emergency room with three days history of left side pleuritic chest pain and dyspnea. The pain was similar to her pain on previous admission but she had no fever or cough on this admission. Examination was consistent with left pleural effusion which was confirmed on CXR (Figure 2). Chest CT scan revealed pulmonary emboli in the left main pulmonary artery with no lung infarct and left pleural effusion (Figure 3). Pleural fluid was exudative and hemorrhagic with parameters on table 1. Pleural cytology revealed reactive mesothelial cells and no malignant cells and microbiology studies were negative. Repeat connective tissue work-up was again negative except for ANA titers that increased to 1:640. Complement 3 and 4 levels were normal at 79 mg/dl and 29 mg/dl respectively. Antiphospholipid and anti-beta 2 glycoprotein were negative. Urinalysis revealed proteinuria and 24 hour urine protein was 4.1g. Right kidney biopsy was consistent with membranous nephritis classified as lupus nephritis WHO class V (microscopy- glomerular capillary loops thickening with subepithelial spikes and no endocapillary proliferation or crescents. Electron microscopy- podocyte effacement with intramembranous, transmembranous and subepithelial immune deposits and

proliferation of basement membrane around the deposits. Immunopathology- glomerular capillary wall and mesangial nodular IgM/IgG and C3 depositis with tubular basement membrane, interstitium and blood vessel sparing)

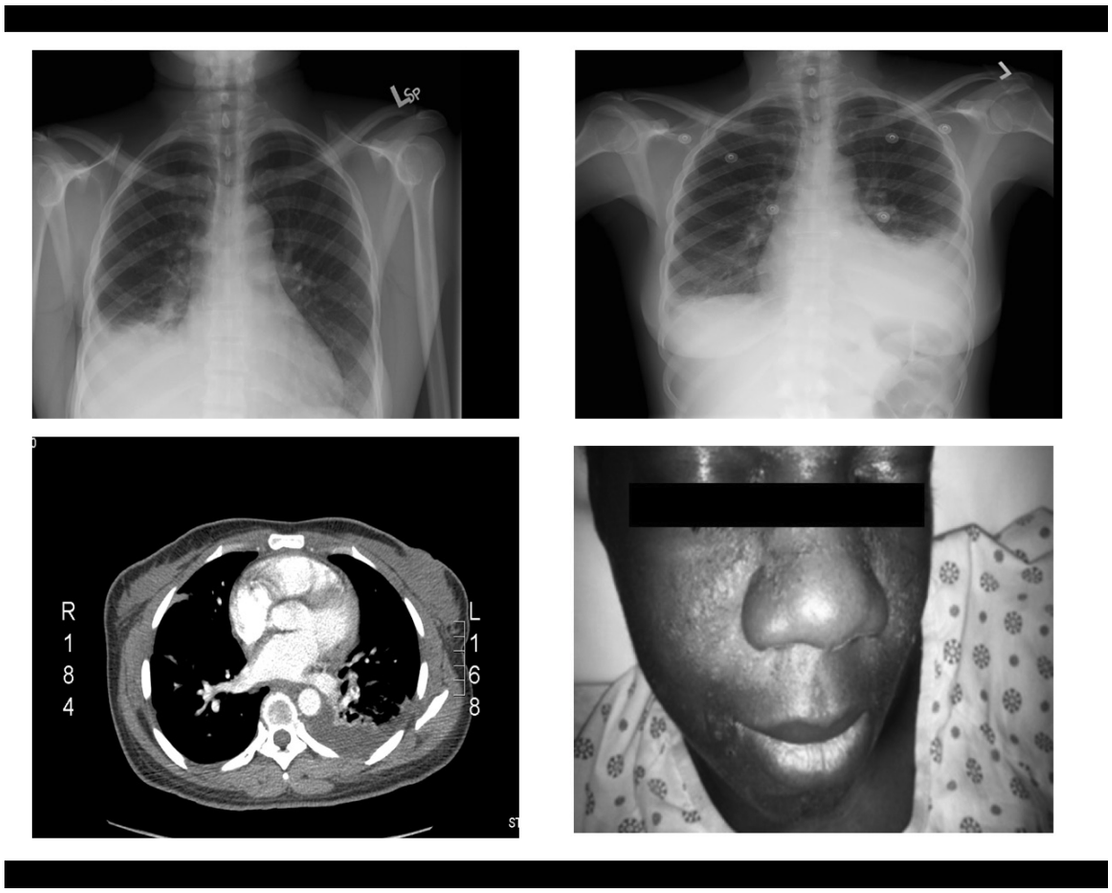
On follow-up, to discuss the renal biopsy results in June 2011, the pleural effusion had resolved spontaneously and proteinuria had improved (to 0.8g proteinuria in 24 hours) but she had developed atypical desquamating rash with malar distribution (Figure 4). At this point she was treated with steroids. On follow-up she had improvement of proteinuria and resolution of her rash. She continued with follow-up at the outpatient clinic.

Table 1: Pleural fluid analysis results

Date	PH	prot	alb	ldh	gluc	RBC	WBC	neut	lymp	mon	mes	mQ
22/3/11	7.43	3.8 (ser 6) Mg/dl	1.8 (ser 2.2) mg/dl	150 (ser 179) mg/dl	90 mg/dl	1020/ ml	2600/ ml	69%	21%	3%	1%	6%
13/5/11	7.2	4.1 (ser 5.7) mg/dl	1.7 (ser 1.9) mg/dl	584 (ser 206)	116 mg/dl	2210/ ml	2640/ ml	86%	9%	5%		

Key to abbreviations: Prot = Total protein, alb = Albumin, ldh = Lactate dehydrogenase, glu = Glucose, RBC = Red blood cells, WBC = White blood cells, neut = Neutrophils, lymph = Lymphocytes, mon = Monocytes, mes = Mesothelial cells and mQ = Macrophages

Figures 1 to 4: I (upper left) CXR in March, 2 (upper right) CXR in May, 3 (lower left) Chest CT scan in May and 4 (lower right) facial rash in june



Discussion

Although our patient did not meet the criteria for SLE during the first two admissions, she eventually had at least four of the diagnostic criteria including serositis, renal manifestation, positive ANA and malar rash. This took about 3 months from the initial presentation and underscores the fact that the American College of Rheumatology criteria was developed as a research criterion and not a clinical criterion.

Pleuropulmonary manifestations of SLE are vast entailing pleural, parenchymal, bronchial, pulmonary vasculature and diaphragmatic pathologies[1]. Pleural effusions have been recorded in up to 50% of patients with SLE with this number increasing to over 90% at autopsy [2, 3].

The fleeting nature of her pleural effusion that was initially on the right then left is not uncommon in SLE but hemorrhagic nature of the pleural effusion makes this case atypical. Only a few cases of hemorrhagic pleural effusion of SLE have been reported in literature with prevalence not documented. Other differential diagnoses considered for the pleural effusion included Pseudo-meigs' syndrome and pseudo-pseudo meigs' or Tjalma's syndrome but these were considered less likely with no ascites noted on imaging [4, 5]. Occult malignancy including lymphoma were also explored as a differential diagnosis with negative work-up.

Pathophysiology of SLE is postulated to entail uncontrolled autoreactivity of B and T lymphocytes leading to the production of autoantibodies against self-directed antigens and tissue destruction. The loss of self tolerance is an evolving area of medical knowledge and probably involves genetic factors, deficiency of regulatory T cells and B cells, hormonal factors and environmental factors [6]. Complement system is central in this pathogenesis process. Studies have revealed that reduced levels of hemolytic complement, C1q, C4, C3 in pleural fluid from lupus patient when compared to pleural effusions due to other conditions even after adjustment for the total protein content of the pleural fluid[7]. This makes this case atypical considering the normal complement levels during active serositis on both admissions. This normal complement is hard to explain and underscores the fact that knowledge on the complexity pathophysiology of SLE is in evolution. Another interesting phenomenon was paradoxical decline, albeit mild, in level of complement after the pleural effusion resolved and the proteinuria improved.

Conclusion

Differential diagnosis of SLE should be retained even in atypical cases particularly if no alternative diagnosis is made. It may also present with features not consistent with the conventional clinical and laboratory features.

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