Massive Serositis as the Initial Presentation of Systemic Lupus Erythematosus: A Report of Two Cases and Review of the Literature

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Abstract

Large volume effusions as a manifestation of active systemic lupus erythematosus (SLE) is rare, and when it does occur, it is usually associated with complications of chronic lupus disease, such as nephrotic syndrome, constrictive pericarditis, heart failure or Budd-Chiari syndrome. Massive serositis as a presenting feature of SLE is rare. We describe two adult cases of new onset SLE presenting with massive ascites in the first case, and large bilateral pleural effusions in the second case. The serositis in both patients responded well to high dose steroid therapy with significant improvement in symptoms. Only a small number of case reports describing massive ascites or large pleural effusions as initial manifestations of new onset SLE have been published. A literature review of these case reports and their treatment outcomes is described.

Keywords

Systemic lupus erythematosus, Lupus pleuritis, Lupus peritonitis, Lupus ascites, Pleural effusion

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease with heterogeneous phenotypes. Although serosal inflammation is common in SLE, massive pleural ascites and large volume pleural effusions as presenting features are unusual. Unlike most cases of lupus serositis, patients with these large effusions tend to require aggressive management with high dose steroids and steroid-sparing agents [1].

Methods

Two case reports of SLE presenting as serositis with large volume effusions are described.

A literature review was performed using a Pubmed search (1964-2015) for all reported cases of large volume ascites or pleural effusions as the presenting features of new onset SLE. The following search terms were used: SLE/Lupus serositis, ascites, pleuritis, peritonitis, pleural effusion, peritoneal effusion. Only adult cases in the English language were reviewed.

Case Reports

Case 1

A 50-year-old immigrant from Central America, was admitted with rapidly increasing ascites. Medical problems included hypertension, chronic hepatitis C with cirrhosis and portal hypertension (treated with an 8 month course of PEG-IFN one year prior to admission), and end-stage renal disease (ESRD) status post cadaveric renal transplant 10 years prior but complicated by transplant rejection and new hemodialysis requirement over the last two years.

On presentation, the patient was febrile with cervical lymphadenopathy, accompanied by massive non-tender ascites with hemodynamic compromise requiring serial large-volume paracentesis (Figure 1). The serum-ascites albumin gradient (SAAG) was < 1.1, which was inconsistent with portal hypertension ascites or possible nephrotic syndrome given the end stage renal disease. Ascitic fluid WBC counts ranged from 77-675/mm³ with a lymphocytic predominance. Peritoneal fluid bacterial, fungal,

Figure 1: Axial, contrast enhanced computed tomography (CT) image of the abdomen showing ascites.
and AFB cultures were negative and there were no malignant cells. Serum HIV, rheumatoid factor and cryoglobulins were negative. Tuberculin purified protein derivative (PPD) testing was negative as well. Hepatic or portal vascular thrombosis was ruled out with patent vessels seen on Doppler, and an echocardiogram noted preserved ventricular function. Serum ANA and anti-dsDNA antibodies were 1:2560 and 12,751 IU/mL, respectively (normal dsDNA is < 25 IU/mL). The patient was also leukopenic (WBC-2.7/mm³) and had severe hypocomplementemia (C3 = 12 mg/dL, C4 = 4 mg/dL).

A diagnosis of SLE with lupus peritonitis was made and treatment initiated with intravenous methylprednisolone 500 mg/day for a week followed by prednisone 1 mg/Kg/day and hydroxychloroquine 400 mg daily. This resulted in hemodynamic stability, significant improvement of the ascites, rise in complement levels and lowering anti-DNA titers. The small volume ascites that remained revealed a SAAG >1.1 which was then attributed to the known portal hypertension.

**Case 2**

An 80-year-old patient with history of congestive heart failure (CHF) and breast cancer in remission after a left radical mastectomy, radiation and chemotherapy presented with dyspnea. On arrival the patient required emergent mechanical ventilation for respiratory failure due to massive bilateral pleural effusions and ascites. Pleural fluid analysis was exudative with negative cultures and cytology

### Table 1: Case reports of ascites as the presenting feature of SLE.

<table>
<thead>
<tr>
<th>Year/Author (reference)</th>
<th>Clinical Presentation</th>
<th>SAAlb°</th>
<th>AsAlb°</th>
<th>ANA</th>
<th>anti-dsDNA</th>
<th>C3</th>
<th>C4</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mier [14]</td>
<td>24yo F with abdominal pain and distention x1 month</td>
<td>NR</td>
<td>3.9 g/dL</td>
<td>NR</td>
<td>13% binding (normal 0-2%)</td>
<td>30 mg/dL</td>
<td>4 mg/dL</td>
<td>Prednisone 60 mg/day</td>
<td>Resolution in 10 days</td>
</tr>
<tr>
<td>Ishiguro [10]</td>
<td>52yo F with fever, rash, abdominal distention x6 months</td>
<td>2.8 g/dL</td>
<td>2.2 g/dL</td>
<td>1:1280</td>
<td>36 U/mL (radio-immunoassay, normal &lt; 10 U/mL)</td>
<td>&lt; 20 mg/dL</td>
<td>&lt; 5 mg/dL</td>
<td>Prednisolone 50 mg, Methylprednisolone 1 g/day × 3 days (repeated twice) followed by taper</td>
<td>Massive ascites resolved after pulse dose steroids</td>
</tr>
<tr>
<td>Hammadoudeh [4]</td>
<td>27yo F with abdominal pain, n/v with new rash and joint pain</td>
<td>NR</td>
<td>Ascites</td>
<td>Protein 4.8 g/dL</td>
<td>1:1280</td>
<td>1:20</td>
<td>51 mg/dL</td>
<td>10 mg/dL</td>
<td>Sulindac 400 mg/day, Chloroquine 500 mg/day</td>
</tr>
<tr>
<td>Weinstein [2]</td>
<td>33yo F with sharp peri-umbilical pain and increasing abdominal girth x1 week</td>
<td>2.7 g/dL</td>
<td>1.9 g/dL</td>
<td>pos</td>
<td>pos</td>
<td>23.7 mg/dL</td>
<td>7.9 mg/dL</td>
<td>Methyl-prednisolone + Cyclophosphamide</td>
<td>Discharged with minimal ascites and mild AKI</td>
</tr>
<tr>
<td>Ro [11]</td>
<td>77yo F with pancytopenia and worsening ascites and lower extremity edema x3 months</td>
<td>2.2 g/dL</td>
<td>2.3 g/dL</td>
<td>pos</td>
<td>71 U/mL</td>
<td>20.4 mg/dL</td>
<td>9.4 mg/dL</td>
<td>Prednisolone 60 mg/day, Methylprednisolone 0.5 g/day × 3 days (× 2) tapered to 15 mg over by 2 months</td>
<td>Complicated by pneumonia, death</td>
</tr>
<tr>
<td>Trock [15]</td>
<td>80yo F with increasing abdominal girth and extremity edema over 3 weeks, found to have massive ascites and pericarditis</td>
<td>NR</td>
<td>NR</td>
<td>1:640</td>
<td>37 (crithidia assay, normal &lt; 25)</td>
<td>62 mg/dL</td>
<td>13 mg/dL</td>
<td>Methylprednisolone 60 mg followed by prednisone 20 mg bid, AZA 100 mg/day, Hydroxychloroquine 400 mg/day</td>
<td>Resolution without symptoms by 4 weeks, but recurred on 2 year follow up</td>
</tr>
<tr>
<td>Forouhar-Graff [7]</td>
<td>18yo F with n/v, diarrhea, abdominal distention x4 weeks</td>
<td>2.9 g/dL</td>
<td>1.9 g/dL</td>
<td>1:5120</td>
<td>1:80</td>
<td>53 mg/dL</td>
<td>4 mg/dL</td>
<td>Methylprednisolone 250 mg × 3 days, then 60 mg/day × 4 weeks</td>
<td>Over the course of 18 months, was still steroid dependent and AZA was started given 2 relapses</td>
</tr>
<tr>
<td>Prasad [8]</td>
<td>26yo F with 2.5 months of abdominal distention and fever postpartum</td>
<td>2.5 g/dL</td>
<td>1.72 g/dL</td>
<td>pos</td>
<td>115 U/mL</td>
<td>44.9 mg/dL</td>
<td>6.85 mg/dL</td>
<td>Prednisolone 1 mg/kg, hydroxychloroquine maintenance</td>
<td>Ascites resolved by 4 weeks; in remission at 3 months follow-up</td>
</tr>
<tr>
<td>Pott Junior [16]</td>
<td>47 yo F with increasing abdominal size x2 months and diffuse pain</td>
<td>2.5 g/dL</td>
<td>1.65 g/dL</td>
<td>1:160</td>
<td>neg</td>
<td>na</td>
<td>na</td>
<td>Prednisone 60 mg/day; chloroquine 250 mg/day</td>
<td>Ascites resolved and patient was asymptomatic at 3 months follow-up</td>
</tr>
<tr>
<td>Liu [18]</td>
<td>19yo M with abdominal pain/n/v x3 days</td>
<td>3.4 g/dL</td>
<td>NR</td>
<td>pos</td>
<td>pos</td>
<td>55 mg/dL</td>
<td>10 mg/dL</td>
<td>Prednisone 60 mg/day; chloroquine 250 mg/day</td>
<td>Symptoms resolved at 3 months follow-up</td>
</tr>
<tr>
<td>Zhou [1]</td>
<td>39yo F with abdominal distention and pain x20 days</td>
<td>3.2 g/dL</td>
<td>NR</td>
<td>1:800</td>
<td>neg</td>
<td>anti-Sm pos</td>
<td>65 mg/dL</td>
<td>5 mg/dL</td>
<td>Methylprednisolone 40 mg/day, taper to 10 mg/day; 0.2 g/day hydroxychloroquine maintenance</td>
</tr>
</tbody>
</table>

YO: Year Old; M: Male; F: Female; NR: Not Reported; n/v: Nausea and Vomiting; Neg: Negative; Pos: Positive; AZA: Azathioprine. aSAIb, serum albumin; bAsAIb, ascites albumin.
negative for malignant cells. An echocardiogram showed preserved ventricular function and a small pericardial effusion. A CT scan of the chest confirmed large bilateral pleural effusions. V/Q scan was low probability for pulmonary embolism. Bronchoscopic lavage had no growth from cultures and was negative for malignant cells. A rightsided heart catheterization was normal. After diuresis, the patient was extubated but required emergent chest tube placement for pleural fluid drainage.

Serologies revealed a positive serum ANA (1:320), anti-ds-DNA (119), and borderline complement levels (C3 = 89, C4 = 14). Acute renal failure subsequently developed and a renal biopsy revealed Class IV/V lupus nephritis (LN). After no response to prednisone 60 mg/day, methylprednisolone 500 mg/day for 3 days was started followed by a steroid taper, hydroxychloroquine 400 mg daily and mycophenolate mofetil titrated to 2 g/day. The renal function improved over the subsequent days and the pleural and peritoneal effusions resolved.

Discussion

Although serositis is found in 63% of SLE patients on autopsy, [2] massive ascites and large pleural effusions are uncommon in the lifetime of lupus disease, and are even more rare as the initial manifestation [2-4]. Pleural effusions occur in up to 50% of patients with SLE, but it is the presenting feature in only 1-5% of patients, with effusions usually small to moderate in size [5]. Unlike pleural involvement, the true prevalence of lupus peritonitis is unknown but presumably low, although probably overlooked despite several cases being published since Metzger’s initial case report in 1974 [6].

Large effusions are usually attributed to a complication from CHF, constrictive pericarditis, nephrotic syndrome, portal hypertension, Budd-Chiari, peritoneal carcinomatosis, infectious peritonitis or pneumonia. One of these etiologies is usually cited as the cause for the 8-11% of SLE patients that develop ascites during the lifetime of their disease [7,8]. It is nonetheless important to consider active SLE in the differential, as was the situation in the two cases described that had massive pleural effusions [19], case reports have been published suggesting that massive lupus serositis does occur and can be the main initial manifestation of the disease. Our case reports and review of the literature emphasize how appropriate evaluation and aggressive immunosuppressive therapy is often required to assure a positive outcome in these cases.

Table 2: Case reports of massive pleural effusions as the presenting feature of SLE.

<table>
<thead>
<tr>
<th>Year/Author</th>
<th>Clinical Presentation</th>
<th>Pleural Fluid WBC</th>
<th>ANA anti-dsDNA</th>
<th>C3</th>
<th>C4</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bouros [3]</td>
<td>2oyo M with dyspnea and fevers × 1 week</td>
<td>500 × 106 cells/L; 70% lymphocytes</td>
<td>1:350</td>
<td>pos</td>
<td>17.5 mg/dL</td>
<td>methylprednisolone 64 mg/day × 2 months then slowly tapered; cyclophosphamide 150 mg/day × 6 months, then 100 mg/day × 6 months</td>
<td>effusion resolved by 20 days, minimal pleural thickening remained</td>
</tr>
<tr>
<td>Mitra [12]</td>
<td>2oyo F with dyspnea × 7 days</td>
<td>200-1970 × 106 cells/L; 20-40% lymphocytes, 60-80% neutrophils</td>
<td>1:160</td>
<td>98 ng/dL</td>
<td>NR</td>
<td>prednisolone 1 mg/kg/day, maintained on chronic steroids</td>
<td>near complete resolution of pleural effusion at 4 weeks</td>
</tr>
<tr>
<td>Wan [5]</td>
<td>2oyo F with cough and chest pain x 1 week</td>
<td>NR</td>
<td>320X</td>
<td>1:620</td>
<td>35.5 mg/dL; &lt; 10 mg/dL</td>
<td>prednisolone 2 mg/kg/day; methotrexate 7.5 mg/wk - subsequently maintained on prednisolone 10 mg/day</td>
<td>effusion decreased dramatically by 1 month</td>
</tr>
<tr>
<td>Chang [17]</td>
<td>6oyo M with fever and dyspnea × 1-2 weeks despite levoquin for pneumonia</td>
<td>340-2950 × 106 cells/L; 3-16% lymphocytes and 49-92% neutrophils</td>
<td>1:1280</td>
<td>1:160</td>
<td>dcr</td>
<td>methylprednisolone 1 mg/kg/day</td>
<td>complete resolution of pleural effusion and symptoms</td>
</tr>
</tbody>
</table>

Y/O: Year Old; M: Male; F: Female; NR: Not Reported; Pos: Positive; DCR: Decreased Serum Complement Levels (taken from the original publication, actual serum level not reported).


