Sjogren’s Thrombocytopenia

Vasantha Kamath†, B Prabhakar†, Veena†, D Lachikarathman†

Abstract
Primary Sjogren’s is a multisystem autoimmune disease which predominantly affects the exocrine glands. pSS may occasionally present in an atypical way which may defy correct diagnosis for a considerable period of time. Clinically important immune-mediated cytopenia (or a combination of cytopenias) may be the first manifestation of an occult SS and have only been rarely described with Sjogren’s. This case exemplifies the atypical presentation of pSS and hence should be considered in the differential diagnosis of patients with unexplained cytopenias.

Introduction
Sicca symptoms are the sine qua non of diagnosis of primary Sjögren’s syndrome (pSS). However, extraglandular involvement is common and often causes highly varied manifestations which may preceede or overshadow the sicca symptoms and cause considerable diagnostic delay. Extraordinary tiredness and weight loss, peripheral neuropathy, proximal myopathy, interstitial lung disease or urolithiasis and renal tubular acidosis have all been reported as the initial manifestations of pSS. Mild normocytic normochromic anemia, leucopenia and thrombocytopenia are common. Hematological abnormalities as a mode of presentation have only been described rarely in individual case reports.¹ We report a patient with life threatening thrombocytopenia as an initial presentation.

Case Report
A 32 year old female presented with giddiness since one month, and bleeding tendencies in the form of bleeding per vagina, bleeding per rectum and generalized non-pruritic purpuric rashes and oral mucosal bleed since 15 days; no associated fever, diarrhoea, joint pains and prior history of drug intake; no history of repeated infections or similar illness in the past. On admission was found to have hypertension-stage 2 and was put on antihypertensives. She had pallor, generalized non palpable purpura, bleeding from gums and conjunctival haemorrhage. Her fundus examination revealed evidence of Bilateral Anemic Retinopathy. Rest of the systemic examination was normal. Schirmer’s test was negative; there was no salivary gland enlargement. Clinically, she was considered to have systemic vasculitis- SLE / Hemolytic urticarial syndrome.

Laboratory tests showed: (table 1)

Peripheral blood smear revealed polymorphous population with normocytic, micro and macrocytic population with anisopoikilocytosis; giant tear drop cells, ovalocytes and target cells, with normal WBCs and thrombocytopenia. Bone marrow examination revealed normal marrow morphology with mild erythropoietic hyperplasia with adequate iron stores and normal megakaryopoiesis. Direct and Indirect Coombs test were negative.

Urine analysis revealed 3+ albumin with SG of 1.020 and microscopy revealed plenty of RBCs with 2-3 EC/hpf, 6-8 PC/hpf. Urinary albumin to creatinine ratio revealed significant proteinuria. C3 levels were within normal range.

Ultrasound abdomen revealed bilateral contracted kidneys with corticomedullary differentiation being maintained and mild splenic enlargement.

HCV, HBsAg and HIV serology were negative.

Antinuclear antibody was positive (ANA); Profile analysis revealed Anti Ro, Anti Lo, Anti Ro S2 being positive. Anti ds DNA and other autoantibodies was negative. P- ANCA and Rheumatoid factor were negative.

On analysis of both clinical and laboratory data, a diagnosis of primary Sjogren’s with cytopenias was made.

Patient was given IV pulse Methyl Prednisolone therapy for 5 days and continued with oral steroids; Antihypertensives

Table 1: Investigations

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<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 30</th>
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<tbody>
<tr>
<td>Hb %</td>
<td>7.3 g%</td>
<td>6.4 g%</td>
</tr>
<tr>
<td>WBC (cells/cumm)</td>
<td>4500</td>
<td>7,100</td>
</tr>
<tr>
<td>DC</td>
<td>681.28 E 2 M1</td>
<td>70 1.28 M1 E3</td>
</tr>
<tr>
<td>Platelet (cells/cumm)</td>
<td>37,000</td>
<td>5000</td>
</tr>
<tr>
<td>Reticulocyte count</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>Anti platelet</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>antibodies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td>3min 20 sec</td>
<td></td>
</tr>
<tr>
<td>BT</td>
<td>6 min</td>
<td></td>
</tr>
<tr>
<td>B Urea (mg/dl)</td>
<td>74</td>
<td>40</td>
</tr>
<tr>
<td>S Creatinine (mg/dl)</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>LFT</td>
<td>Within normal limits</td>
<td></td>
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</tbody>
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*Professors, Department of Medicine, †Post graduates, Bangalore Medical College and Research Institute, Bangalore, Karnataka.
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and compatible platelet and blood component transfusions were given. She responded clinically as her bleeding tendencies stopped on 6th day after admission and her hypertension was under control. However she persisted to have low platelet counts (< 10,000 cells/cumm); during the course patient developed meningitis and was treated with parenteral antibiotics and dose of steroids was reduced. She recovered from the same. Renal biopsy was not contemplated in view of her severe thrombocytopenia.

Discussion

Primary SS is a common chronic inflammatory autoimmune disorder associated with B lymphocyte hyperreactivity, whose hallmark is that the salivary and lacrimal glands become infiltrated with lymphocytes and functionally impaired. Although most patients have exocrine glands involvement, their clinical presentation is not uncommonly quite non-specific and diverse. Only 36% present with sicca symptoms as initial complaint. An average of 8 yrs may lapse between the onset of first autoimmune symptom and sicca symptoms. The presence of anti SSB antibodies have high predictive value and underline the importance of serology.

Haematological abnormalities are common in patients with pSS. Leucopenia is the most frequently encountered cytopenia, being present in 14–42% of pSS patients (median 20%). Some patients develop a striking neutropenia or lymphopenia, possibly related to antineutrophil or anti-CD4 antibodies respectively. The prevalence of anaemia is about 11% and that of thrombocytopenia 5–15% (median 11%). The essentially asymptomatic course and fluctuating nature of the neutropenia and thrombocytopenia over many years appear to be characteristic of the autoimmune cytopenias of pSS.

Although thrombocytopenia is infrequent in pSS patients (5–16% only). Patients whose presentation may mimic that of idiopathic thrombocytopenia purpura should be screened for occult pSS. Immune-mediated platelet destruction similar to that of SLE is likely, and indeed, associated lupus and lymphoma, must be sought or may develop later.

Recent experimental evidence suggests that the mechanism that SSA and SSB are located in the nucleus of the resting cells, inaccessible to the circulating auto antibodies. Cell membrane expression of the same can be induced by variety of stimuli including UV radiation and viruses.

In the absence of ocular symptoms clinicians may not suspect Sjogren’s as a differential diagnosis of multisystem disorder and may hinder diagnosis, probably accounting for the rarity of reports of Sjogren’s and cytopenias.

It is therefore conceivable that a considerable number of patients with varying degrees of single or combined cytopenia, which are not due to other identifiable causes, may in fact have immune-mediated cell destruction and occult pSS and may be the first manifestation. This important presentation should be well recognized because pSS is a treatable condition, and because it carries an increased risk of associated diseases, such as lymphoma, an early diagnosis is necessary. Thus pSS should be considered in the differential diagnosis of all patients who have otherwise inexplicable cytopenias, whether silent or symptomatic.

References