Primary Sjogren's syndrome presenting as autoimmune cytopenia

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Abstract

Sjogren’s syndrome (SS) is a chronic systemic autoimmune disease, characterized by lymphocytic infiltration of lacrimal and salivary glands. Although extra glandular manifestations are uncommon, they can occur with the musculoskeletal, renal, pulmonary and hematological disease. We report the case of a 35-year-old woman presented to us with persistent unexplained bicytopenia (anemia and thrombocytopenia). Antinuclear antibody and direct Coombs test were positive. Anti-Ro/SSA and anti-La/SSB antibodies were also positive in high titer. The final diagnosis of primary SS with autoimmune cytopenia was made. Cytopenias in SS are rarely reported. Our case illustrates that clinically significant cytopenias may present as an extraglandular manifestation of SS.

Introduction

Sjogren’s syndrome (SS) is a systemic autoimmune disease characterized by dry eyes and dry mouth. Lymphocyte infiltration of salivary and lacrimal glands is the common feature of SS. Common extraglandular presentations of SS are arthralgia, gastrointestinal symptoms, peripheral neuropathy and renal disease. The hematological abnormalities in primary SS (pSS) are not infrequent. Anemia of chronic disease is the most common presentation. However, clinically significant cytopenias are uncommon in SS. Leukopenia is usually mild with differential white blood cell counts are mostly normal, which do not require hospitalization. Though, newly developed cytopenia in an established patient of SS can be a sign of developing lymphoma. The pathophysiology and prevalence of cytopenia in SS is still an area of ongoing research. Sometimes a patient can present with severe hemolytic anemia, leukopenia or thrombocytopenia prior to the development of sicca symptoms. Autoimmune cytopenia associated with SS is rarely described in the literature. We herein report a case of pSS presented as immune hemolytic anemia with thrombocytopenia.

Case Report

A 35-year-old woman presented to us with complaints of generalized weakness, increasing fatigue for last 1 year. There was no history of fever, rash, weight loss, diarrhea or pain abdomen. The patient was not suffering from any chronic illness in past. On general examination, lower palpebral conjunctiva was pale, mild icterus was also present. There was no lymphadenopathy. Spleen was palpable 3 cm below left costal margin. Rest systemic examination was unremarkable. Complete blood count revealed a hemoglobin level of 7.0 g/dL, white blood cell count (WBC) of 6.8×10^3/µL (differential: N 63%, L 22% M 13%) and platelet count of 44×10^3/µL. Biochemical analysis showed total protein 9.55 g/dL, albumin 2.95 g/dL, total bilirubin 2.1 mg/dL, urea-28 mg/dL, creatinine 1.2 mg/dL, sodium 135 mmol/L and potassium 3.46 mmol/L. On further investigations, autoimmune profile revealed antinuclear antibodies positivity in high titer (1:1280, speckled). Anti-dsDNA antibodies were negative. In addition, Anti-Ro/SSA and Anti-La/SSB antibodies were also present in high titer. Peripheral blood film was suggestive of normocytic normochromic red blood cells (RBC) with few tear drop cells, serum Lactate dehydrogenase was 788 IU/L. Bone marrow examination was normal. Both direct and indirect Coombs tests were positive. When asked specifically about sicca symptoms, our patient admitted having dry eyes and mouth for past few months. Ophthalmological examination showed a positive Schirmer’s test (2 mm in right and 3 mm left eye). Our patient fulfilled the diagnostic criteria (2016 ACR-EULAR Classification Criteria for pSS) for pSS. Based on these investigations, we made a final diagnosis of pSS with autoimmune bicytopenia.

The patient was put on oral prednisolone (1 mg/kg). After 1 month of follow-up, she was symptomatically improved with hemoglobin of 9.2 g/dL, WBC 6.6×10^3/µL and platelets count - 110×10^3/µL. At 3 months of follow-up, corticosteroid was tapered successfully with remission of hemolytic anemia and thrombocytopenia.

Discussion

SS is a multisystem autoimmune chronic disorder, predominantly involving salivary and lacrimal glands. pSS is not associated with other diseases whereas secondary SS usually overlap other rheumatic disorders which include rheumatoid arthritis and systemic lupus erythematosus. Lymphocytes aggregation in salivary and lacrimal glands leads to xerostomia (dry mouth) and xerophthalmia (dry eyes) respectively in SS. Extra glandular involvement may occur, which include, musculoskeletal symptoms, vasculitis, pulmonary, renal, and hepatic disease and increased risk of lymphoma. Intestinal nephritis and tubular acidoses are the common renal manifestations in SS. Some of these systemic manifestations are due to autoimmune inflammation of ductal epithelial structures in various organs, like in intestinal nephritis. The hematological manifestations can occur with leukopenia is the most common cytopenia, reported in 15% of patients of SS, but clinically significant cytopenias requiring hospitalization, transfusion or immunosuppressant has been rarely reported in the literature. According to a report described by Ramakrishna et al., Coombs positivity can be a common feature of SS (22-47%), but frank hemolysis is rare. There are case reports of pure red cell aplasia and immune-mediated thrombocytopenia with SS. According to Yu et al., pancytopenia can present as a complication of SS. Cytopenias may develop prior to typical sicca symptoms or as a sole presenting feature in SS (Table 1), which can delay the diagnosis of SS. Similar to these
reports, our patient presented with thrombocytopenia and immune hemolytic anemia. Mild anemia usually occurs due to cytokine-mediated chronic inflammation however, the mechanism of hemolysis and bone marrow suppression in SS is still debatable. Immune-mediated thrombocytopenia, similar to systemic lupus erythematosus may be possible in SS. We speculate the presence of autoantibodies against different cell lineage is the triggering factor for cytopenias. According to some reports, antineutrophil and anti-RBC antibodies were observed in 45% and 22% of patients with SS respectively. fasting. Qing et al. hypothesized that deficient erythropoiesis in SS is attributed to the disorder of iron metabolism. Immunosuppressive therapy with corticosteroids is the treatment of choice for autoimmune cytopenias in SS. Azathioprine, cyclophosphamide has been used in some cases in past with mixed response. The response of rituximab in immune cytopenias with SS was described by one report. Similar to its effect in immune thrombocytopenia, rituximab use was shown to improve cytopenia in the patients with SS.

**Conclusions**

As illustrated by our case, cytopenias may present prior to sicca symptoms in SS. Mild asymptomatic normocytic anemia is a frequent presentation, but as our case suggests, clinically significant hemolytic anemia and thrombocytopenia may present as occult pSS without predominant sicca symptoms. Although our patients improved with corticosteroids, long-term follow-up is needed to know more about the clinical course of hematological disease in these patients. SS should be considered as an important differential while evaluating unexplained cytopenias.

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