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Case Report

Unraveling the Diagnostic Challenge: Primary Sjogren Syndrome Presenting with Recurrent Fevers and Hypotension

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ABSTRACT

Sjogren syndrome is a chronic autoimmune disease with multisystem involvement. The typical sicca symptoms of dry eyes and dry mouth are not always present, and patients may present with a wide range of extra glandular symptoms. In this report, we describe a 31-year-old female who presented with recurrent episodes of fever, malaise, difficulty in swallowing, tachycardia, and hypotension. Her presentation as sepsis led to an extensive investigation of the infectious process, which was negative. The autoimmune workup established the diagnosis of primary Sjogren syndrome. The patient was started on oral corticosteroids and discharged in a stable condition. This atypical presentation of Sjogren syndrome with recurrent fevers and hypotension has not been described before. The case highlights the challenge in diagnosing Sjogren syndrome due to its atypical presentation and multisystem involvement.

Keywords: Sjogren Syndrome; Fever; Hypotension; Diagnosis; Challenge

INTRODUCTION

Sjogren syndrome is a multisystem autoimmune disorder predominantly seen in middle-aged women [1]. The characteristic pathological feature is the lymphocytic infiltration and slow destruction of exocrine glands (mainly lacrimal and salivary glands) leading to the characteristic symptom of dry mouth and keratoconjunctivitis (dry eyes) [2]. Sjogren syndrome could manifest in the primary form without extra glandular manifestations or a multisystem form that overlaps with other autoimmune diseases, in particular Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA) [3,4].

Systemic involvement with extra glandular manifestations may be present in about one third of patients with Sjogren syndrome. This may include cutaneous vasculitis, Raynaud's phenomenon, pulmonary involve- ment, glomerulonephritis, neuropathy, cytopenia or lymphoma [5].

Severe fatigue and generalized pain are other characteristic features of Sjogren syndrome [6].

Autonomic nervous system dysregulation has been reported in primary Sjogren syndrome more often than any other autoimmune diseases manifesting as dysfunction of autonomic control of blood pressure and heart rate, gastrointestinal dysmotility or urinary retention [7-10].

Fever as a symptom of Sjogren syndrome is uncommon and there are a few case reports in literature where patients have presented as fever of unknown origin or periodic fevers [11,12]. But presentation as recurrent fevers and hypotension has never been described before.

Herein, we report a case of primary Sjogren syndrome with unique presentation posing a diagnostic challenge.

CASE PRESENTATION

A 31-year-old female with a past medical history of malaria one year ago was brought in by emergency medical services to the emergency department with complaints of fever, chills, malaise, palpitations, dizziness, dry cough, and difficulty in swallowing. The patient had been having these symptoms for three weeks. She was seen in another hospital before this visit and treated for an upper respiratory infection. On physical examination, the

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patient was conscious, oriented, febrile, and tachycardic with a temperature of 101.8°F, heart rate of 138/min, and blood pressure of 101/66 mmHg. The oral cavity examination showed dry mucous membranes with posterior pharyngeal erythema. The chest, cardiovascular, and abdominal exams were unremarkable. The laboratory examination revealed hemoglobin of 8 g/dL, leucocyte count of 3.8 × 10(3)/mcL, platelet count of 159 × 10 (3)/mcL, normal renal functions, hypoalbuminemia and mild transaminitis. The GenMark respiratory panel was negative. The HIV/Hepatitis panels were negative. The chest X-ray was normal, and the electrocardiogram showed sinus tachycardia. The patient was admitted for further evaluation and management and started on antibiotics. An infectious panel, including blood and urine cultures, malarial parasite, QuantiFERON plus TB, AFB sputum, MTB PCR, Epstein Barr-Virus, Streptococcal antigen, legionella/ Histoplasma/Brucella/Lyme serologies, HIV and Hepatitis panel were negative. Further, workup revealed TSH of 5.57 uIU/mL, ESR of 57 mm/hr, C-reactive protein of 132 mg/L, Rheumatoid factor of 32 IU/mL, Antinuclear Ab of 1:1280, speckled ANA IFA pattern, Sjogren's SSA Ab (RO) >8, Sjogren's SSB Ab (LA) >8, with raised immunoglobulin G and A levels, negative Anti dsDNA, Ab, Cyclic Citrullinated Peptide Ab, Centromere Antibodies, Antimitochondrial AB and normal C3/C4 complement levels. The soft tissue neck computed tomography revealed left posterior cervical lymphadenopathy, and the chest showed bilateral axillary reactive lymphadenopathy. The computed tomography abdomen/pelvis were normal. The patient responded to antibiotic therapy and improved clinically. She was discharged in stable condition with a plan for outpatient lymph node biopsy and rheumatology follow-up. Four days later, the patient presented to the emergency department with fever, chills, malaise, and dizziness. On physical examination, the patient was ill-appearing, febrile, tachycardic and hypotensive with temp 102.9°F, HR-142/min and BP-80/40 mmHg. The chest, cardiovascular, and abdominal examinations were unremarkable. After fluid resuscitation, the patient continued to be hypotensive, was started on vasopressors and antibiotics and was transferred to the intensive care unit as septic shock. The patient was worked up extensively to rule out infectious processes, malignancy, or autoimmune diseases. The infectious disease, hematology-oncology, and rheumatology services were involved. The infectious workup was negative. The serum cortisol and TSH levels were normal. The cervical lymph node biopsy showed reactive lymphadenopathy with, negative gram stain, and acid-fast bacilli. Autoimmune workup revealed raised inflammatory markers, positive Sjogren's SSA Ab (RO)/SSA Ab (LA), positive rheumatoid factor, speckled ANA and hypergammaglobulinemia. The Shirmer test was positive at 4 mm in both eyes reflecting severe aqueous deficiency. The patient improved clinically, was taken off antibiotics, started on oral corticosteroids and artificial tears. The patient remained stable during the hospital stay and was discharged with rheumatology follow up.

DISCUSSION

The etiology of Sjogren syndrome is unknown but is believed to involve a combination of genetic factors and an environmental trigger such as infections. Some infections may mimic Sjogren syndrome like tuberculosis, Epstein Barr virus, hepatitis, parvovirus B19, malaria, subacute bacterial endocarditis and HIV. Molecular mimicry has been hypothesized as the most important mechanism for infections induced autoimmunity [13].

Sjogren syndrome is a systemic disease with an extremely variable clinical spectrum. The typical symptoms of dry mouth and dry eyes are not always present, and the initial presentation might be misleading. Although our patient did not complain of dry mouth and dry eyes, her difficulty in swallowing might be attributed to decreased salivary gland secretions. The dry eyes in our case were confirmed by the positive Schirmer test.

The Schirmer test measures the total tear secretion and is done by placing a small strip of filter paper inside the lower eyelids. The eyes are closed for 5 min. The paper is removed, and the amount of moisture is measured. A Schirmer test result of <5 mm is indicative of aqueous deficiency, >10 mm is normal, and 5-10 mm is considered borderline [14].

Fever and hypotension requiring pressor support, in most cases, are due to the infectious process or malignancy which were ruled out in our case. However, an extensive work up is required to rule out other causes like connective tissue disorders, drugs or hyperthyroidism. Recurrent fevers in our case might represent an extra glandular manifestation of Sjogren syndrome, however, the initial response to antibiotic therapy is not explainable. There is a chance that an unidentified infectious agent might be a trigger in our case. Also, hypotension and tachycardia in our patient could not be explained but may be contributed to cardiovascular dysautonomia in Sjogren syndrome [7-10].

There are no specific diagnostic tests, but a combination of several tests can eventually diagnose Sjogren syndrome. Patients with Sjogren syndrome present a broad spectrum of serologic features (cytopenia, hypergammaglobulinemia, high erythrocyte sedimentation rate) and autoantibodies, of which Antinuclear Antibodies (ANA) are the most frequently detected and Anti-SSA/RO are the most specific [15]. Raised erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor, cytopenia, speckled ANA, hypergammaglobulinemia and positive Anti-SSA/RO, in our case, confirmed the diagnosis of Sjogren syndrome.

The most widely accepted current classification criteria for primary Sjogren syndrome are the American-European Consensus Group (AECG) criteria (American College of Rheumatology ACR-European League Against Rheumatism EULAR 2016 Classification Criteria). Patients with a total score ≥ 4 points meet the criteria for primary Sjogren syndrome (Table 1) [16].

Table 1: Classification criteria for primary Sjogren syndrome according to ACR-EULAR 2016 guidelines.

Item	Item to be scored	Weight
1	Labial salivary gland with focal lymphocytic sialadenitis and focus score of 1 foci/4mm	3
2	Anti-SSA/Ro positive	3
3	Ocular staining score >5 (or van Bijsterveld score >4) in atleast 1 eye	1
4	Schirmer's test <5 mm/5 minutes in at least 1 eye	1
5	Unstimulated whole saliva flow rate #0.1 ml/min	1

Our patient had a score of 4 based on positive Anti-SSA/Ro and Schirmer's test, which suggests primary Sjogren syndrome.

The treatment of Sjogren syndrome aims at providing symptomatic relief from dry mouth and dry eyes with artificial saliva, artificial tears and muscarinic receptor agonists (pilocarpine and cevimeline). For extra glandular manifestations, corticosteroids, immunosuppressive agents, intravenous immunoglobulins, and biologics are prescribed depending on the burden of the disease [17].

CONCLUSION

The extra glandular manifestations of Sjogren syndrome might be quite challenging. The presentation may range from mild symptoms of malaise and joint pain to more severe symptoms of recurrent fevers and hypotension, as in our case. It is important to consider Sjogren syndrome as one of the differential diagnoses, especially in young females with sepsis of unknown etiology.

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