CASE REPORT

Recurrent aseptic meningitis: A rare clinical presentation of Sjogren's syndrome

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Abstract

Sjogren's syndrome most commonly presents with dry eyes, dry mouth, joint pain and fatigue. However, recurrent aseptic meningitis, reported as the most uncommon initial symptom, was the presenting feature in our case. We present the case of a 19-year-old female with recurrent episodes of aseptic meningitis. She presented with fever, headache, vomiting and photophobia. Neurological examination showed neck stiffness. Fundoscopy was normal. On two previous occasions her cerebrospinal fluid analysis was consistent with meningitis; however, it was normal at this presentation. Review of system revealed history of fatigue and sicca symptoms since early childhood. Autoimmune workup showed antinuclear antibodies with a titer of 1:400 and positive anti SSA (Ro) antibodies that led to the diagnosis of Sjogren's syndrome. She responded well to intravenous steroids, followed by oral prednisolone and hydroxychloroquine. To conclude, diagnosis of Sjogren's syndrome may also be considered in a patient presenting with recurrent aseptic meningitis.

Keywords: Aseptic meningitis, Keratoconjunctivitis sicca, Sjogren's syndrome.

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Introduction

Sjogren's syndrome (SS) is an autoimmune disorder that presents with dryness of the eyes and mouth, arthralgia and fatigue.[1] SS can be a primary autoimmune disease or it can occur in association with other autoimmune disorders, the most frequent being autoimmune thyroid disease, rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE).[2] Rarely do patients with SS present with symptoms of central nervous system (CNS) or peripheral nervous system (PNS) as an initial manifestation.[3] SS on rare occasions present as recurrent aseptic meningitis and is a diagnostic challenge. About 20% of the patients with SS are known to present with CNS complications like aseptic meningitis and meningoencephalitis.[4] The acute presentations may vary with various meningitis features such as fever, headache, neck stiffness and rarely focal neurological findings and seizure.[3] This case is of special interest because of its SS association with aseptic meningitis that has been very rarely reported among young adolescent population.[5,6] To our knowledge, this is the first report of its kind from Pakistan.

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Case Report

A 19-year-old female, was admitted in the Department of Neurology, Shifa International Hospital, in January 2017, with episode of aseptic meningitis for the third time. Previously she had suffered two episodes of aseptic meningitis in 2010 and 2016. In July 2010, she was admitted for the first time in another hospital with high-grade fever, headache and vomiting for four days. The cerebrospinal fluid (CSF) analysis was consistent with meningitis (Table). Computed tomography (CT) of the brain without contrast was normal. Rest of her labs including CSF culture, Herpes simplex virus (HSV) 1 and 2 by polymerase chain reaction (PCR), Cryptococcal antigen and blood cultures were negative. She was treated for meningitis with intravenous (IV) ceftriaxone 2 gm twice daily for 10 days. She responded well to the treatment and remained asymptomatic for the next six years.

However, her initial presentation at our emergency department was in December 2016, with complaints of progressively increasing headache, photophobia and vomiting for five days. She also had neck and right shoulder pain for one day. On examination she had neck stiffness. CSF analysis was again consistent with meningitis (Table).

Brain magnetic resonance imaging (MRI) without contrast was normal. Blood and CSF cultures were negative. Mycobacterium tuberculosis GeneXpert was negative in CSF. She completed a course of IV ceftriaxone 2 gm twice daily for 14 days and acyclovir 500 mg three times a day till PCR study was negative for HSV 1 and 2. She remained asymptomatic for a month.

In January 2017, she again presented to us in the emergency department with signs and symptoms of

Table: CSF analysis comparison.

Characteristics	July 2010	December 2016	January 2017	Reference range
Color	Clear	Clear	Clear	Clear
WBC (cell count per microliter)	218	245	5	0-5
Differential count (%)	60 neutrophils, 40 lymphocytes	10 neutrophils, 90 lymphocytes	Not possible	0-6 neutrophils, 40-80 lymphocytes
Protein (mg/dl)	129	106	20	15-45
Glucose (mg/dl)	68	60	62	40-70
Cytology	Not Done	Not Done	Negative	Negative
Bacterial, fungal and AFB stains	Negative	Negative	Negative	Negative
CSF Culture	Negative	Negative	Negative	Negative
AFB culture or GeneExpert	Negative	Negative	Negative	Negative
HSV 1 & 2 PCR	Not detected	Not detected	Not detected	Not detected

WBC- white cell count; CSF- cerebrospinal fluid; AFB- acid fast bacilli; HSV- Herpes simplex virus 1 &2 by polymerase chain reaction.

meningism including headache, low-grade fever, photophobia and vomiting for three days. Detailed systemic evaluation was done which revealed a previous history of arthralgia. Rheumatology review was requested and past history of dry eyes and dry mouth for last 3 years and fatigue for 6 months was elicited. She denied any skin rashes, oral ulcers, hair loss, thromboembolic phenomenon or any other systemic symptoms. Musculoskeletal and systemic examination was normal. On examination she was febrile with a temperature of 38°C and had neck stiffness.

Investigations included a normal CSF analysis and CSF cytology (Table), C-reactive protein (CRP) 25 mg/L and erythrocyte sedimentation rate (ESR) was 40 mm/hour. Anti-nuclear antibodies (ANA) titer was 1:400. Her extractable nuclear panel (ENA profile) was strongly positive for Anti SSA (Ro) antibodies (52), and after excluding other differential diagnoses like immunodeficiency, complement deficiency, thyroid disorder, SLE, Hepatitis B and C, she was diagnosed with a case of SS presenting with recurrent aseptic meningitis.

Management included IV dexamethasone for two days followed by oral prednisolone 60 mg/day and hydroxychloroquine (HCQ) 200 mg/day. She had an excellent response to the treatment, with significant improvement in her headache. On her two-week follow up, she was asymptomatic and her ESR had reduced to 15 mm/hour from an initial 40 mm/hour. Steroids were gradually tapered off and she was started on oral azathioprine. At 11-months follow-up she was asymptomatic with normal ESR and CRP.

Informed consent was sought from the patient for using her laboratory values for reporting purpose.

Discussion

CNS involvement is rarely observed in primary SS and aseptic meningoencephalitis occurs in rare cases.[3] The prevalence of CNS manifestations is highly variable and estimated around 8.5-70% in available literature.[7] Other presentations included visual disturbances, transverse myelitis, ataxia, lower limb weakness, concentration deficit and cerebellar features.[8] ANA, RF, anti-Ro/SS-A antibodies and anti-La/SS- B antibodies can be elevated. Anti-Ro/SS-A antibodies are specially reported to be associated with CNS vasculitis secondary to SS, which explains the pathophysiology of meningitis.[9] The CSF can vary from normal to variablepleocytosis consisting predominantly of polymorphonuclear leukocytes at the onset, and then mononuclear cells. CT and MRI may be normal or show diffuse leptomeningeal and subarachnoid enhancement, which are not disease-specific findings.[10,11] Corticosteroids have been the mainstay of treatment of aseptic meningitis secondary to SS and most cases resolve with this therapy alone.[10,11] Cyclophosphamide, azathioprine, cyclosporine, methotrexate, chlorambucil and tacrolimus may also be effective as monotherapy or in combination with corticosteroids.[12,13] Lately, Anti-CD20 (rituximab) has been reported to successfully treat CNS manifestation of SS.[12] Plasmapheresis and intravenous immunoglobulin might be worth considering in refractory cases.[13]

Literature search revealed very few previously reported cases with similar presentation of recurrent aseptic meningitis associated with SS, and none reported from Pakistan except for one case series of childhood recurrent meningitis, which included a child with Mollaret's meningitis.[14] Our patient's diagnosis of SS was based on her sicca symptoms (symptoms of dry eyes and dry mouth lasting more than 3 months) and also positive anti-Ro antibodies with a total score of 3. She did not meet the 2016 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria, as a score of $\geq$4 is required to diagnose a patient

with SS.[15] This patient's Shirmer test, which constitutes part of the criteria, was negative, on the other hand the test was done several weeks into her treatment which probably affected the result. Another limitation in our patient's case was lack of labial gland biopsy as mandated by ACR/EULAR 2016 criteria, which we could not perform due to lack of patient's consent.

Conclusion

We suggest that SS should be considered in the differential diagnosis of recurrent aseptic meningitis, especially in a young female patient with recurrent symptoms.

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Conflict of Interest: None

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