International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Encephalopathy in Sjogren's Syndrome: A Distinct Neurological Presentation

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Abstract

Sjogren's syndrome (SS) is an autoimmune disorder characterized by lymphocytic and plasma infiltration of exocrine glands, resulting in dry mouth and kerato-conjunctivitis sicca. The clinical symptoms may range from mucosal dryness to more systematic complaints. Sjogren's syndrome (SS) may be complicated by neurological manifestations.[1]

We report a 36-year-old woman presenting with quadriparesis, started as lower limb weakness which progressed to the upper limbs, having Guillain-Barre syndrome like pattern. MRI brain showed altered signal intensity in the brainstem, predominantly centered in the pons labelled as autoimmune brainstem encephalitis with distal RTA. With differentials as clippers, autoimmune disease and de-mylinating disease patient underwent an Autoimmune panel which showed Antinuclear Antibody showing speckled SSA/RO pattern and antibodies to SSB/LA were positive suggestive of Sjogren's syndrome. The diagnosis was confirmed with a minor salivary gland biopsy from the lower lip which was definitive of Sjogren's syndrome. Patient showed excellent improvement on pulsed steroid therapy. Therefore, this case illustrates a rare, heralding manifestation of Sjogren's syndrome as brainstem encephalitis with definitely diagnosis based on minor salivary gland biopsy showing complete recovery on early detection and management.

Keywords: Sjogren's Syndrome 1, encephalitis 2, oral biopsy 3

1. Introduction

Primary Sjogren's syndrome (SS) is an autoimmune disorder with a prevalence of approximately 0.5 to 1% in the adult population. Sjogren's syndrome is characterized by mononuclear cell infiltration and destruction of salivary and lacrimal glands, resulting in dry mouth and keratoconjunctivitis sicca (dry eyes).[2] The clinical manifestations of SS are of broad spectrum, ranging from mucosal dryness to more systemic complaints. Among the neurological presentations, the involvement of the peripheral nervous system is seen more commonly with a frequency of around 10 to 20%.[1] The central nervous system (CNS) involvement is not well established, with a rate varying from 1.5 to 25%.[1] The CNS manifestations can be in a diverse spectrum and may manifest at onset or later during the disease.[3] The diagnosis of SS is challenging due to its complicated clinical manifestations and non-specific signs. Salivary gland biopsy plays an important role in the diagnosis of SS, especially with anti-Sjögren's syndrome antigen A (SSA) and anti-SSB antibody negativity. Histopathology based on biopsy has clinical significance for disease diagnosis, stratification and prognosis evaluation, such as risk assessment for the development of non-Hodgkin's lymphoma.[4]

Here, we report a rare presentation of SS, manifesting as brainstem encephalitis with reversible magnetic

resonance image (MRI) findings showing altered signal intensity in the brainstem, predominantly centered in the pons which was a clinical dilemma, finally diagnosed after a positive minor salivary gland biopsy with a definitive diagnosis of Sjogren's Syndrome and treated with intravenous steroids.

2. Case study

A 36-year-old female presented with quadriparesis, which started as lower limb weakness and progressed to the upper limbs, having Guillain-Barre syndrome like pattern. On examination, the patient was drowsy and disoriented. The cranial nerve examination was unremarkable. Muscle bulk was normal. Power was mildly intact (2/5) on analysis. Reflexes were brisk, and plantar reflexes were bilateral flexors. The sensory system evaluation was of no note. There was no evidence of ataxia, gait imbalance, or involuntary movements. Cognitive function tests were suggestive of impaired orientation.

Her attendants complained of fluctuating consciousness with periods of profound disorientation. Her cognition declined rapidly. There was no significant past medical or family history. She was a non-smoker and non-alcoholic. The attendants denied a history of prolonged fever, headache, vomiting, and seizures. The patient did not report any hallucinations, psychosis, or depressive symptoms. Attendants denied symptoms of joint pain, arthralgia, and skin rash. They refused exposure to drugs or toxins. Patient was started on intravenous immunoglobulins infusion since working diagnosis was sort as Guillain Barre Syndrome based on the clinical presentation. Patient was planned for an MRI Brain and spine Screening, which showed no significant intracranial abnormality. Blood gas analysis showed hypernatremia (S. Sodium-141) and hypokalaemia (S. Potassium-1.3) ,dyselectrolytemia was corrected with potassium supplementation and I.V Sodium bi-carbonate infusion. USG whole abdomen was done which showed borderline liver enlargement (15cm) with normal echogenicity, borderline spleen enlargement (12.8cm) and multiple echogenic foci were seen in both kidneys. Patient was diagnosed with distal Renal tubular acidosis and due to raised serum sodium (163) was planned for haemodialysis and intubation was done in view of decreasing Glasgow Coma Scale and fall in blood oxygen saturation. MRI(Magnetic resonance imaging) brain with contrast was repeated which showed altered signal intensity in the brainstem, predominantly centered in the pons and extending bilaterally to the cerebellar peduncles, medulla oblangata, cerebral peduncles, posterior limb of internal capsule and corona radiata. There was FLAIR(fluid attenuation inversion recovery) hyperintensity with restricted diffusion appearing hyperintense on DWI(Diffusion weighted imaging), and hypointense on ADC map (apparent diffusion coefficient). SWI(susceptibility weighted imaging) showed peripheral curvilinear areas hypo-intensity in the region of pons. Post contrast scan showed subtle punctate enhancement in the central pons. Therefore the MRI was suggestive of brainstem encephalitis with differentials of CLIPPERS/AUTOIMMUNE DISEASE /DEMYLINATING DISEASE). Patient was subjected to intravenous Methylprednisolone 500mg twice daily after MRI suggestive of autoimmune encephalitis. Patient was planned for EEG which showed diffuse theta slowing over both hemispheres and there was no evidence of NCSE(Nonconvulsive status epilepticus) or burst suppression pattern. Nerve conduction velocity testing was done which was suggestive of non-uniform axonal polyneuropathy. Autoimmune panel was sent, dsDNA(Double stranded DNA) was negative (2.4), ANA (Antinuclear Antibody) showed speckled SSA/RO pattern >1.2 titre, antibodies to SSB/LA were positive (22) which was suggestive of Sjogren's syndrome. Patient was planned for cerebo-spinal fluid (CSF) analysis, which was 15ml in volume, colourless and clear, showed normal viscosity, clot/cob web was absent, mild pleocytosis (5 cells) with raised CSF glucose (131) and protein (76.9). CSF encephalitis panel and autoimmune panel showed no positive findings. Electrolytes

showed improvement after repeated dialysis and desmopressin 0.1mg twice daily. . Haemoglobin was low (7.7), for which patient was given pRBCS transfusions. The haematological parameters, including total leucocyte count, platelet count, and blood cells revealed normal study. Patient was subjected to serum immunofixation electrophoresis to rule out multiple myeloma which could be cause of encephalitis secondary to Fanconi's syndrome , but it showed no M spikes. The renal function test and liver assessment were unremarkable after starting treatment. Her serum electrolyte were in the improving trend. Repeat Electroencephalography(EEG) showed normal study.

To confirm the diagnosis a minor salivary gland biopsy from the lower lip was taken and sent for histopathological examination which showed parenchymal and ductal changes with disappearance of acini, lymphocyte infiltration and proliferation of the lining cells, and formation of epimyoepithelial cell islands with focal inflammation in salivary gland tissue and acinar atrophy, ductal dilatation, and fibrosis. There was presence of adipose which was all consistent with Sjogren's Syndrome.

The diagnosis of autoimmune brainstem encephalitis associated with Sjogren's syndrome with distal RTA showing dyselectrolemia was confirmed , and after starting intravenous methylprednisolone 1 g daily for 5 days patient showed improvement in GCS and cognition. Patient was discharged on oral steroids.

On follow up, the patient had complete resolution of all signs and symptoms, clinically as well as radiologically. Patient was advised to seek consultation from nephrology department and rheumatology department for further treatment.

3. Discussion

Sjogren's Syndrome is an autoimmune disorder characterized by lymphocytic and plasma cell infiltration of the exocrine glands. The extra-glandular features include both the peripheral, as well as central nervous system involvement. Peripheral nervous system involvement in SS is well studied, which manifests as cranial nerve palsies, pure or predominantly sensory polyneuropathy, sensorimotor polyneuropathy, and mononeuritis multiplex.[5] Distal axonal sensory or sensorimotor polyneuropathy occurs most commonly and accounts for more than 50% of cases with peripheral nervous system involvement.[6] On the other hand, CNS manifestations are heterogeneous and can be focal or diffuse. The diffuse pattern usually manifests as a recurrent, "subacute encephalopathy," with patients presenting with memory loss, cognitive dysfunction, and deficiencies in concentration and attention. The focal neurological manifestations include motor/sensory deficits, dysarthria, cerebellar ataxia, or seizures. Spinal cord involvement may be present and is usually manifested as transverse myelitis, neurogenic bladder, or with features of lower motor neuron disease. The CNS involvement shows a bimodal temporal pattern of distribution, presenting at onset, as well as later, during the course of illness. In approximately 25 to 60% of cases, the neurological manifestations are known to precede the diagnosis of SS by 2 years.[7] In pSS, sicca symptoms are present in only 50% of patients with neurologic involvement. Anti-Ro/SSA and anti-La/SSB antibodies are positive in only 50% of patients.[8] Thus, the neurologic symptoms of SS are present in the absence of oral/ocular dryness. In such cases, the clinicians should have a high index of suspicion for SS and consider autoantibody testing.

There have been only a handful of case reports associating SS with brainstem encephalitis. In the case series published by Çoban et al, the authors described three cases of SS presenting with acute encephalopathy. The patients had features suggestive of limbic encephalitis but had either mild sicca symptoms/signs or were known cases of SS.[9]

Finelli and Inoa described a case of limbic encephalitis, later diagnosed as a case of SS based on Schirme-

r's test and pathological examination of the lip biopsy specimen.[10]

Unlike the previously published cases, our patient did not have any subjective or objectives signs of sicca complex making the diagnosis more perplexing. Body weakness and distal RTA were the sole complaints of the patient. Recognizing the association with brainstem encephalitis, patient was promptly evaluated for an infective, paraneoplastic, and autoantibody related process. An extensive search for an underlying malignancy and alternative autoimmune, infectious, and metabolic etiologies proved unfruitful and consequently the diagnosis was established as autoimmune brainstem encephalitis associated with SS based on the autoimmune profile and minor salivary gland biopsy. The patient was labeled as a case of SS based on the ACR/EULAR classification criteria.

Though the patient did not have objective or subjective signs of ocular or oral dryness, he met the inclusion criteria as the patient scored ≥1 on the Sjögren's Syndrome Disease Activity Index (ESSDAI).

A confirmatory diagnosis was based on biopsy of the minor salivary gland from the lower lip which helped in starting early steroid treatment and led to faster recovery.

Our patient showed excellent response to methylprednisolone pulse therapy; thereby, we can conclude that the subacute encephalopathy related to Central nervous system(CNS) involvement in SS seems to be a reversible condition. CNS involvement in SS is thought to be a poor prognostic marker and is related to a more aggressive pattern of progression. However, our patient showed remarkable improvement with steroid pulse therapy. Keeping in mind the association of CNS involvement with increased severity of SS, such patients should be regularly followed-up.

4. Conclusion

To conclude, Central nervous system involvement in Sjogren's Syndrome is a relatively rare complication and can manifest in a variety of ways. The CNS involvement can occur at any stage of illness and presents as a diagnostic challenge for the clinician. In diagnosing brainstem encephalitis ,we should consider Sjogren's syndrome as an underlying disease, even though its rare and is ruled out with an excisional minor salivary gland biopsy.

FIGURE 1- Oral biopsy taken from lower lip, excisional biopsy of the minor salivary gland and sent for biopsy to rule out Sjogren's Syndrome

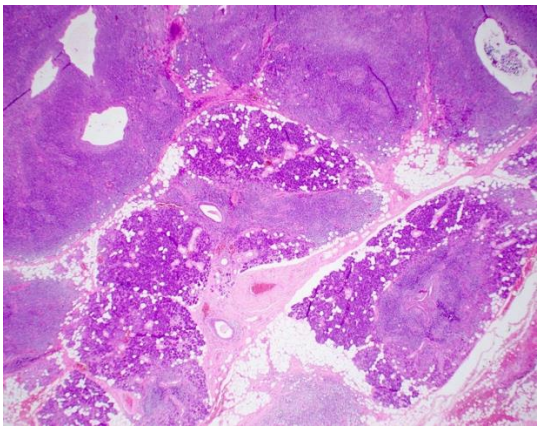

FIGURE 2- Histopathological slide showing lymphocytic infilterate around the minor salivary gland ducts suggestive of Sjogren's Syndrome

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