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CASE REPORTS

A case of primary Sjögren syndrome masquerading as post-COVID Bickerstaff encephalitis

[1]Shawn Zhi Zheng Lin, [1]Hua Chan Ling, [1,2]You-Jiang Tan

[1]Department of Neurology, National Neuroscience Institute, Singapore General Hospital Campus, Singapore; [2]Duke-NUS Medical School, Singapore

Abstract

We present a case of acute external ophthalmoplegia, hypersomnolence, and ataxia occurring 5 days after an episode of SARS-CoV-2 upper respiratory tract infection. The patient's serum returned positive for anti-GD1a antibodies. Guided by precedent cases, she was empirically started on a course of intravenous (IV) immunoglobulin for possible para-infectious Bickerstaff brainstem encephalitis (BBE). However, she failed to respond and subsequently developed autoimmune hemolytic anemia as well as renal tubular acidosis (type 1). Corroborative history from her family elucidated constitutional and sicca symptoms and she was eventually diagnosed with primary Sjögren syndrome (pSS) complicated by brainstem and cerebellar involvement. She was treated with IV cyclophosphamide and rituximab, after which her neurological deficits completely resolved at two months.

Keywords: Bickerstaff brainstem encephalitis, Sjögren syndrome, SARS-CoV-2

INTRODUCTION

Primary Sjögren Syndrome (pSS) is a well-known mimicker and can present with a wide variety of neurological manifestations affecting both the peripheral and central nervous systems. Its recognition remains vital despite its rarity due to its propensity for significant disability. To the best of our knowledge, this is the first case of SARS-CoV-2 virus triggering the neurological manifestations of primary Sjogren's syndrome and producing a polyclonal humoral response which led to the detection of anti-GD1a antibodies in the serum.

CASE REPORT

A 69-year-old female without any prior medical history, presented with painless binocular horizontal diplopia with hypersomnolence (sleeping 19-20 hours daily). These symptoms began five days after an episode of SARS-CoV-2 upper respiratory tract infection. Examination was significant for up-beating nystagmus and impaired abduction of both eyes, bilateral facial weakness, and ataxia of the trunk and upper limbs. Fatigability was absent, and the limbs' deep tendon reflexes were normal. Brain magnetic resonance imaging (MRI) revealed regions of non-enhancing T2-weighted hyperintensities over the dorsal pons and cerebellar peduncles (Figure 1A). Ancillary neurophysiological investigations including nerve conduction studies, repetitive nerve stimulation, and single-fibre electromyography yielded unremarkable results. Cerebrospinal fluid examination revealed lymphomonocytic pleocytosis with elevated protein levels (0.49g/L), but the microbiologic assays and cultures, cytology and flow cytometry were otherwise normal. Serological tests were undertaken and returned positive for anti-GD1a antibodies (titre 79.084; range 0-50). Otherwise, tests for anti-acetylcholine receptor, anti-muscle specific tyrosine kinase, and paraneoplastic antibodies (Hu, Yo, Ri, CV2, amphiphysin, Ta, recoverin, SOX1, titin, zic4, GAD65, and Tr(DNER)) were negative. Guided by precedent cases[1], a preliminary diagnosis of para-infectious Bickerstaff brainstem encephalitis (BBE) from SARS-CoV-2 infection was made. She was treated with intravenous (IV) immunoglobulin (0.4g/kg/day for five days) but displayed no clinical improvement.

Address correspondence to: Shawn Zhi Zheng Lin MBBS (Singapore), MRCP(UK), Department of Neurology, National Neuroscience Institute, Singapore General Hospital Campus, Outram Road, Singapore 169608. Tel: (+65) 9749 3914, Email: shawn.lin@mohh.com.sg

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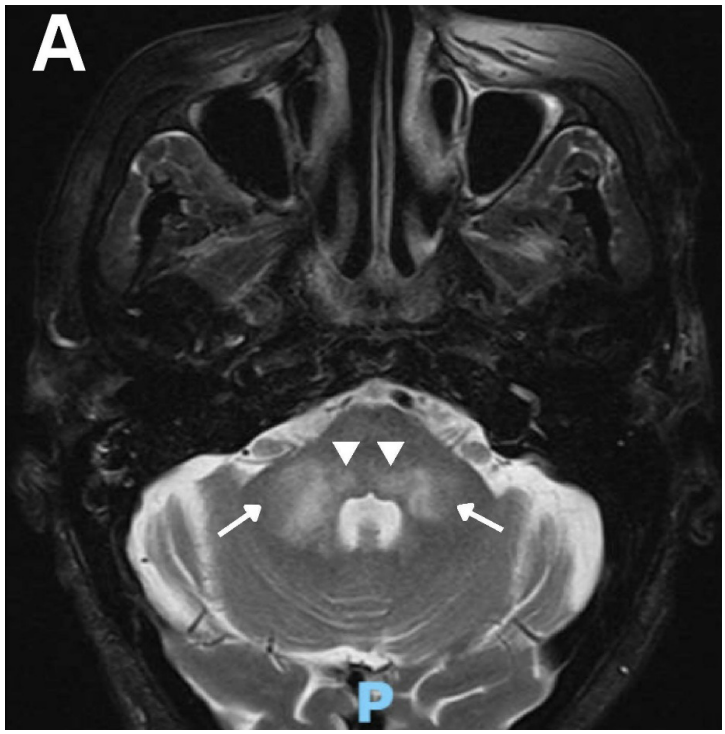

Figure 1A. T2-weighted axial MRI of the brain demonstrating white matter hyperintensities involving the dorsal pons (arrowhead) at the level of the facial colliculus and bilateral middle cerebellar peduncles (arrows)

Corroborative history from her family elucidated further symptoms of unintentional weight loss, xerostomia, and xerosis over the past year. Schirmer's test was positive on the right eye, and serological tests returned positive for anti-Ro and anti-La antibodies. Atrophic parotid, submandibular and lacrimal glands were demonstrated by Computed Tomography (CT) of the neck, thorax, abdomen, and pelvis. She soon developed autoimmune haemolytic anaemia and renal tubular acidosis (type 1) and was eventually diagnosed with primary Sjögren syndrome (pSS).[2] A second brain MRI showed progression of the T2-hyperintensities within the brainstem now involving the cerebellar peduncles and the cerebellum, consistent with progressive neuro-Sjögren syndrome (Figure 1B).[3] She was treated with IV cyclophosphamide and rituximab, after which her hypersomnolence and ophthalmological symptoms completely resolved at two months.

DISCUSSION

pSS is an autoimmune connective tissue disease that primarily affects the exocrine glands of the body. Neurological disorders are one of the most common extra-glandular manifestations of pSS with available data estimating a prevalence of 8.5-70%[4], the most common being a sensory peripheral neuropathy while complications of the central nervous system (CNS) are rarer (2-25%).[5,6] CNS manifestations include cognitive impairments, disseminated encephalopathy, aseptic meningitis, seizures, headaches, transverse myelitis, optic neuritis and other multiple sclerosis-like manifestations. How pSS affects the nervous system is not fully known but the underlying pathomechanisms have been postulated to be in part due to the vasculitic processes triggered by the secretion of pro-inflammatory cytokines by dendritic cells and T-lymphocytes.[7] Viral infections have also been thought to activate the autoimmune processes that underlie pSS via multiple mechanisms including molecular mimicry, bystander activation, the production of superantigens and viral cytokines, which in turn causes hyperactivation of B cells with autoantibody production.[8]

In retrospect, our patient's ophthalmological deficits and hypersomnolence may be explained by the inflammatory perturbations involving her dorsal pons, middle cerebellar peduncles, and her cerebellum. To the best of our knowledge, no preceding cases of patients with acute and prominent neurological manifestations of pSS

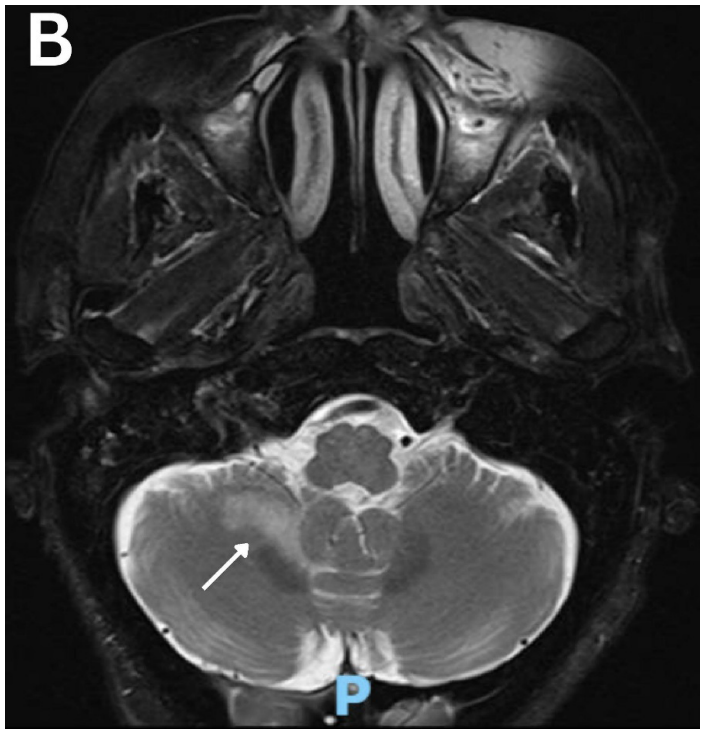

Figure 1B. T2-weighted axial MRI of the brain demonstrating white matter hyperintensities extending into the right cerebellar hemisphere (arrow)

after SARS-CoV-2 infections have been reported, much less one which mimics BBE and with seropositivity for anti-GD1a. In sum, our case elegantly illustrates how the clinical history, examination findings, and ancillary investigations, remains important components of the diagnostic processes, especially when facing diseases notorious for having diverse and non-specific clinical features such as pSS.

DISCLOSURE

Ethics: Informed consent was obtained from the patient.

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Conflict of interest: None

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