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Case study

A rare neurological complication of Waldenstrom's Macroglobulinemia

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ABSTRACT

Bilateral and simultaneous facial nerve palsy (FNP) is a rare clinical condition occurring in 0.3–2.0% of facial palsy cases and is typically a manifestation of an underlying systemic disease. We here describe a case of a 67-year-old Hispanic man with a known history of Waldenstrom's Macroglobulinemia (WM) who presented to the clinic with a sub-acute onset of bilateral facial weakness. No alternate etiology for the facial weakness was identified after a thorough diagnostic approach. WM is a rare hematological condition due to low-grade B cell lymphoma, where lymphoplasmacytoid cells infiltrate different tissues and secrete monoclonal IgM. Peripheral neuropathy develops in 15–30% of the cases, being usually a chronic, progressive, symmetric, predominantly distal polyneuropathy. Facial nerve impairment is unusual; however, it could be caused by anoxic damage as a result of an increased blood viscosity from IgM monoclonal gammopathy, direct nerve infiltration of tumorous cells and an antibody (anti-MAG) mediated demyelinating process. Treatment is directed to the established mechanism for neural injury. This report highlights a rare condition (WM) with a rare complication (bilateral facial nerve palsy) and illustrates the broad differential comprised by this presenting complaint.

1. Introduction

Unilateral facial nerve palsy (FNP) is a common neurologic disorder with an estimated incidence of 25 patients per 100,000 population; it is often idiopathic and referred to as Bell's palsy [1]. On the contrary, bilateral FNP is an extremely rare clinical entity, usually due to an underlying systemic medical condition, and is seen only in 0.3–2% of all FNP cases [1,2]. In this paper, we present a case of bilateral FNP attributed to an underlying Waldenstrom's Macroglobulinemia (WM) and discuss the differential diagnosis. To our knowledge, this is the second report in the literature that comments on this association [3].

2. Case description

A 67-year old Hispanic male with a past medical history significant for WM, hypertension and latent tuberculosis infection (LTBI) was followed by Neurology for longstanding, painful, progressive length-dependent, axonal small fiber neuropathy. This involved his hands and feet and predated the WM diagnosis. Initially it was thought that this condition could be due to WM, but it was unresponsive to treatments directed to his WM, specifically the administration of chemotherapy (i.e. rituximab and cladribine), despite improvement of other features of the disease. Initial evaluations for his neuropathy included: anti-ganglioside panel, anti-MAG antibody, serum protein electrophoresis (SPEP), free kappa light chains, vitamin D levels, cryoglobulins, erythrocyte sedimentation rate (ESR) and rheumatoid factor (RF). All were negative. EMG showed marked interval amplitude reduction in all sensory responses with evidence of a distal left ulnar mononeuropathy at the level of the canal of Guyon.

Without change in his painful neuropathy, he presented to urgent care with a new onset left facial nerve palsy. Other cranial nerves were normal. He was diagnosed with left Bell's palsy and was started on valacyclovir and prednisone. Gradually, the facial weakness on the left side progressed to inability to close the eye and total paralysis of the left lower face. Two weeks later, he developed right facial weakness that followed a similar course. Around the same time, he also noted constant left sided pressure-like headache with some discomfort on the left side of his neck. He denied any change in mentation, dysgeusia, hypo/hyperacusis or diplopia. He had no additional neurological complaints. On examination, he had mild tenderness of the left paracervical muscles without meningismus or tenderness to palpation along the spine and paraspinal muscles. There was pronounced bilateral lower-motor-neuron pattern facial weakness with inability to raise the eyebrows bilaterally with partial closure of the lids, better on the right than the left. He had mild decrease in vibratory, light touch,

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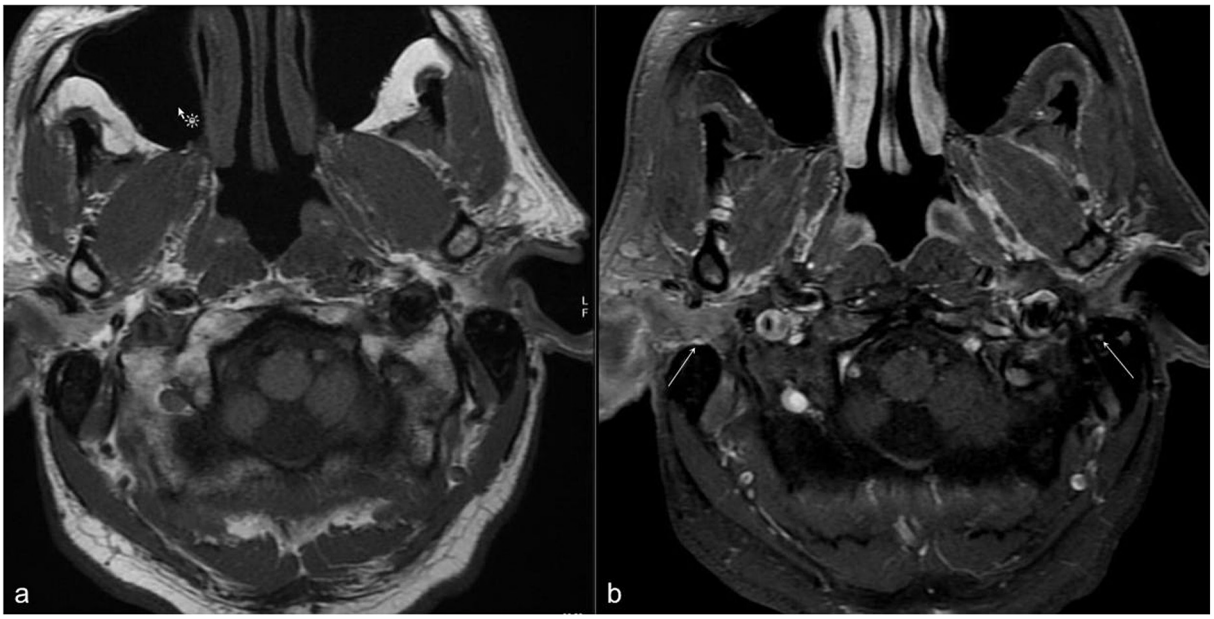

Fig. 1. Magnetic resonance imaging, T1 weighted axial cuts with (a) and without gadolinium (b) showing bilateral VII cranial nerve enhancement (white arrows), at the level of the mastoid segments.

and temperature sensations bilaterally, attributed to his known peripheral neuropathy.

Brain MRI with contrast was significant for a slight abnormal enhancement in both facial nerves, involving the meatal, labyrinthine, geniculate, tympanic, and mastoid segments, with no leptomeningeal enhancement (Fig. 1). Cerebrospinal fluid (CSF) was bland. HSV was not performed, but VZV, Lyme serology, syphilis and CSF cytology were negative. In blood, Lyme serologies were negative on two separate occasions, as was syphilis. Antiganglioside panel and CSF ACE levels were also unremarkable. CRP and ESR were markedly elevated, with negative cryoglobulins, ANA and anti-SSA/SSB. Infectious diseases (ID) consult ruled out TB reactivation. He was treated with chlorambucil, with decrease in serum viscosity without recovery of his facial neuropathy.

His clinical course was complicated. Three weeks after his lumbar puncture (LP) he developed symptomatic acute on chronic subdural hematoma, thought to be in the setting of intracranial hypotension from the LP, requiring evacuation. Following evacuation, he developed two further complications. The first was a right inferior temporo-parietal stroke with hemorrhagic transformation, thought to be secondary to his increased blood viscosity in the setting of his underlying WM, and to the dehydration induced by nausea and vomiting. The second was EEG-confirmed seizure activity with clinical correlate, controlled with levetiracetam. He was discharged to rehabilitation. He developed a right CN VI palsy as an outpatient 2 months later, with no new imaging or laboratory findings to explain this. Repeat LP was deferred given his subdural experience. Symptoms stabilized and he has been stable since, with gradual improvement in cranial neuropathies.

3. Discussion

Bilateral FNP is an exceedingly rare disease, and is usually explained by an underlying medical condition, warranting an extensive work-up for etiology. Among the differential diagnoses, Guillain-Barre Syndrome (GBS) and an infectious agent comprised the majority of causes for bilateral FNP [1,4]. Other etiologies are congenital, traumatic, metabolic, immunologic and neoplastic, leaving less than 20% as idiopathic [5].

GBS is associated with facial nerve impairment in up to 50% of the cases, and half are bilateral [5] and usually is followed by ascending limb weakness [1]. It is a diagnosis that should be sought whenever assessing a bilateral FNP not only because it is the most frequently associated etiology reported, but also because it carries a high mortality [3]. This concern in our patient was mitigated by his normal motor function, sensation and deep tendon reflexes with both CSF analysis and nerve conduction studies normal that made GBS an unlikely diagnosis.

Viral and bacterial infectious agents have been described in association with bilateral FNP; of these, the most common is the tick-transmitted spirochete *Borrelia burgdorferi* that causes Lyme disease. Nervous system involvement occurs in 10–15% of Lyme disease cases, and in adults usually consists of meningitis, accompanied by cranial neuritis (predominantly facial nerve palsy) and peripheral radiculoneuropathy [6]. This is sometimes referred to as Bannwarth syndrome. Close to 50% of the patients with meningitis will present with FNP, however FNP can also be an isolated finding in Lyme disease [7]. Facial palsy is present in 11% of the cases and nearly a quarter of them are bilateral. Despite the excellent prognosis of the paralysis, patients with bilateral disease could suffer persistent mild dysfunction or late recovery. Moreover, patients with bilateral FNP have a higher incidence of meningoencephalitis and CSF pleocytosis [7]. Even though antibiotic treatment does not appear to influence the outcome or the duration of the FNP, the diagnosis of Lyme disease in the context of a FNP should not be overlooked as early treatment usually prevents subsequent and more serious late complications of the disease [8]. Albeit our patient came from an endemic area he had no history of tick-bites. He tested negative twice for Lyme disease. Serological tests for other infectious causes of bilateral FNP, such as HIV and syphilis, were also unremarkable.

In ruling out other etiologies for bilateral FNP, we excluded structural causes such as skull abnormalities and brainstem tumors by head CT and MRI. The patient did not have a history, labs or imaging consistent with sarcoidosis. Normal blood glucose values excluded diabetes, which has been previously reported in 28.4% of patients with bilateral FNP [9]. Other remaining causes in the literature including amyloidosis, porphyria, poliomyelitis,

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