

Recurrent Bifacial Neuropathy in a Case of Steroid Responsive Neurosarcoidosis: A Case Report



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ABSTRACT

Neurosarcoidosis is a rare or misdiagnosed disease that can be masked in a case with fleeting neurologic deficits, especially craniopathy. We present a 26-year-old Chinese-Filipino male who presented with recurrent facial neuropathy that was heralded by fleeting blurring of vision bilaterally. He was apparently responsive to corticosteroids (intravenous and oral methylprednisolone) from initiation to date. During the course, he also noted selective weakness of the right finger flexors. Nodules in the face eventually appeared that led to a biopsy disclosing a noncaseating granuloma. Apart from electrodiagnostic tests, a supportive diagnostic test for sarcoidosis was the presence of lymphadenopathies on his chest noted on Computed Tomography (CT) scan. Cerebrospinal fluid (CSF) and brain Magnetic Resonance Imaging (MRI) tests were not yielding. To our knowledge, this was the first reported Chinese-Filipino case of neurosarcoidosis involving cranial and peripheral nerves.

Keywords: case report, sarcoidosis, neurosarcoidosis, cranial nerve, neuropathy, noncaseating, granulomatous, steroid responsive.

INTRODUCTION

Sarcoidosis is a rare, often misdiagnosed, inflammatory multisystem disorder of unknown etiology with worldwide distribution (1,2). Neurosarcoidosis (NS) commonly affects the cranial nerves, hypothalamus, and pituitary gland, but also involves the meninges, parenchyma, brainstem, and spinal cord. The 7th cranial nerve is the most commonly affected cranial nerve. Histopathologic findings of non-caseating granulomatous infiltration of the meninges and underlying parenchyma are most frequently seen at the base of the brain (2-4). The process is either subacute or chronic in nature mimicking other granulomatous lesions and neoplasms. When the nervous system is involved as it is in about 5-13% of cases, NS can occur either in isolation or along with other features of systemic sarcoidosis (5,6). In a review by Lacomis (6), the mean age of onset is from 33 to 41 years. Women are more commonly affected. Neurologic manifestations usually occur within the first 2 years of illness.

CASE

A 26-year-old Chinese-Filipino male consulted because of inflammation to the left orbital area accompanied by blurring of vision in both eyes. Symptoms progressed leading to puffiness and swelling over the left orbital area which progressively increased in

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Figure 1. Images showing bilateral facial palsy in 2012 (a), 2013 (b) and 2014 (c). Note progression of weakness more on the left.

size leading to difficulty closing his eyes. This was accompanied by diplopia and dizziness. One year later, nodular skin lesions started to appear over his lip, cheeks, and forehead. Upon examination, there were unremarkable neurologic findings except for the bilateral peripheral facial palsy manifested as a weakness of orbicularis oculi muscles, difficulty closing his eyes, and facial asymmetry, noticeable more on the left (Figure 1).

Diagnosis and Treatment

The patient had several consultations. Electrodiagnostic tests showed reduced compound muscle action potential (CMAP) amplitudes of both facial nerves but with normal blink reflex as well as limb motor and sensory nerve conduction studies. A chest CT scan showed small calcified pulmonary nodules, anteromedial segment of the left lower lobe, subcentimeter prevascular space lymph node, and bilateral small axillary lymph nodes. Contrast-enhanced CT scan of the orbits, MRI with Magnetic

Resonance Angiography (MRA) and Magnetic Resonance Venography (MRV) of the brain (Figure 2) and CT scan of the whole abdomen were all unyielding. Autoimmune blood workups were unremarkable as well.

A diagnosis of NS was considered due to the presence of bifacial neuropathy with other cranial nerve symptoms such as diplopia, blurring of vision, and dizziness with lymphadenopathies on the chest CT scan (Figure 3).

During admission, CSF analysis had normal pressure, cellularity, protein, and sugar. Bacterial, viral, and fungal panels were not yielding. CSF determination of oligoclonal bands, aquaporin-4 antibodies, and protein immunoelectrophoresis was unyielding too. The patient was admitted and started on methylprednisolone pulse therapy at 1 gm/day for 5 days. Oral methylprednisolone was continued on an outpatient basis, initially at 16 mg/tab 2 tabs twice a day with signs of improvement. Two months post steroid pulse treatment and into oral steroid therapy, increase in the strength of bilateral facial muscles

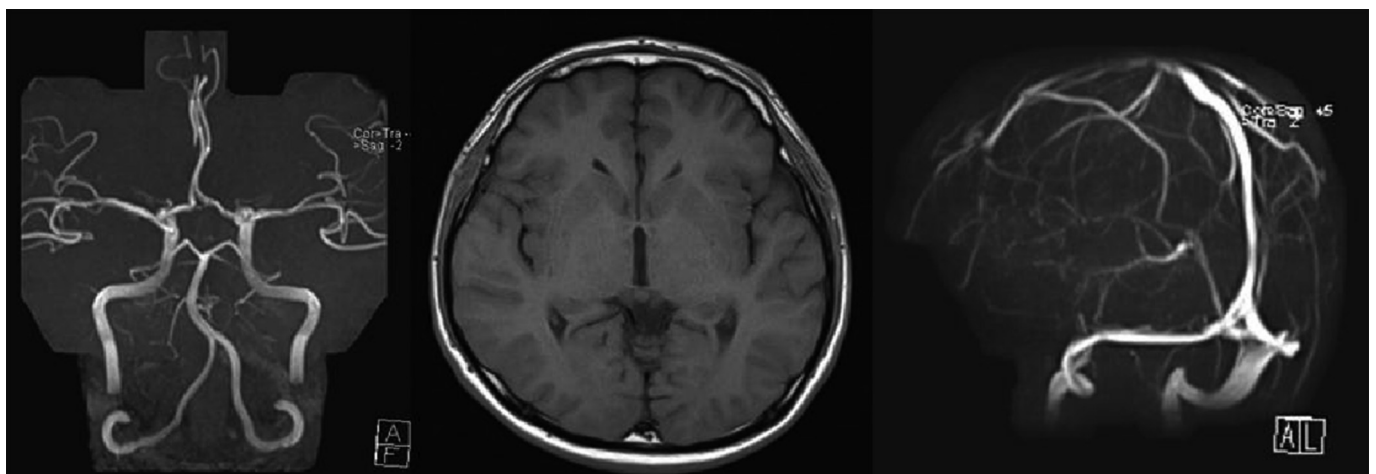


Figure 2. Cranial MRI with MRA and MRV of the patient showing normal results.



Figure 3. Post-contrast chest CT image of the patient showing lymphadenopathies.

were noted when the patient could resist passive eye opening. Eventually, oral steroids were tapered and discontinued. He had a recurrence of the same symptoms such as left facial asymmetry, dizziness, diplopia, and swelling of the right eye. Oral steroids were resumed and a steroid-sparing agent (Azathioprine 50 mg/tab once daily) was added to the treatment. Symptoms once again resolved and a trial of tapering steroids was once again performed.

When off steroids, new symptoms recurred such as weakness of finger flexors of the right hand and new nodules on the face (cheeks, eyelid, nose). Oral methylprednisolone at 16 mg/tab 2 tabs once a day was resumed. Biopsy of the upper and lower eyelid nodules was done and histopathology showed noncaseating chronic granulomatous inflammation (Figure 4).

Our patient presented mainly with bifacial neuropathy and also with other cranial nerve involvements, likely cranial nerves II, III, IV, and VI with unremarkable neuroimaging and CSF analysis but

with lymphadenopathies on chest CT scan and non-caseating granulomatous features in the histopathology of eyelid nodules. There was remarkable steroid response which when tapered and discontinued led to the occurrence of bifacial neuropathy and other cranial nerve involvement. The patient was too fearful to discontinue oral steroids, so he is currently maintained on methylprednisolone 16 mg/tab 1 tab daily and azathioprine 50 mg/tab 1 tab daily.

DISCUSSION

A published classification of NS diagnosis would be as follows (1):

Possible: The clinical syndrome and neuroradiologic evaluation are suggestive of NS. Infection and malignancy were not rigorously excluded or there is no pathologic confirmation of systemic sarcoidosis; **Probable:** The clinical syndrome and neuroradiologic evaluation are suggestive of NS and differential diagnoses have been made, especially malignancy and infection. There is pathologic evidence of sarcoidosis; **Definite:** Probable diagnosis + supportive nervous system pathology or response to therapy for NS over a 1- to 2-year observation period.

Using the criteria (1), our patient falls under a definite diagnosis of NS.

Neurologic Manifestations of NS

The most commonly involved cranial nerve is the facial nerve (CN 7) (1,2,5). If a patient presents with

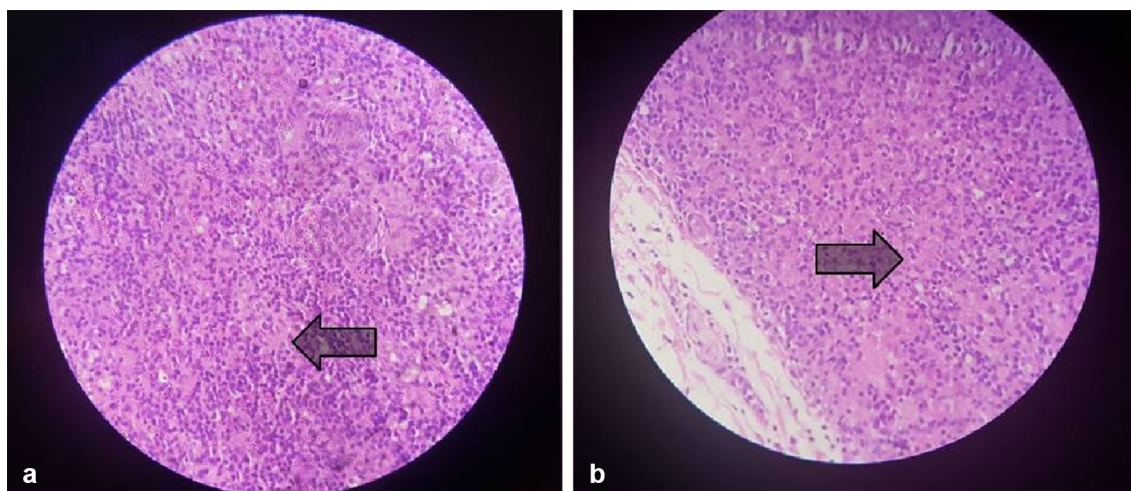


Figure 4. Images of the patient’s biopsy of the eyelid nodules. a and b. Granuloma formation with aggregates of epithelioid histiocytes (arrow) surrounded by chronic inflammatory cells.

bilateral cranial nerve palsy, NS should be strongly considered. Our patient presented with bilateral facial nerve weakness. In a study by Hoyle et al. (7), cranial nerve VIII is the third most commonly affected cranial nerve. The involvement of cranial nerve VIII may present as hearing loss or vestibular dysfunction secondary to acoustic neuropathy. In a case report by Imran et al. (2), they presented a patient whose primary symptom of NS is vertigo as also manifested by the patient in focus. The patient also complained of progressive blurring of vision. The optic nerve (CN 2) is also involved in up to 38% of patients with NS. This may present as progressive, painless or acute visual loss, papilledema, or optic atrophy (1,2). It is not present in our patient, but other presentations of NS may be the following: hydrocephalus and chronic meningitis (2,8), mass lesions (2), seizure (9), hypothalamic and pituitary involvement, and neuropsychiatric manifestations (5,9).

Imaging Studies in NS

Although not yielding in this case, a brain MRI is the preferred diagnostic imaging technique in the diagnosis of NS. T1-weighted images are useful in evaluating the optic chiasm, hydrocephalus, and spinal cord enlargement. Contrast studies for the evaluation of leptomeninges, parenchyma, and cranial nerves is important (1-3,9). Whole body Gallium (Ga) scanning or fluorodeoxyglucose PET scanning are ideal tests which were not performed on our patient and can be utilized to search the whole body for occult inflammation or neoplasia and therefore find suitable sites for biopsy (1,2). It is important to take note that whole body Gallium scanning is insensitive to central nervous system (CNS) lesions and shows uptake in only 5% of cases with CNS lesions, but may detect other systemic involvement in up to 45% of cases, and these cases usually have a concomitant CNS involvement (11). CT scan may be utilized as well but only shows findings in 40% of cases (6).

His chest CT scan showed a small calcified nodule and a subpleural bleb including axillary lymphadenopathies while his chest radiograph is unremarkable. Chest radiography and thoracic computed tomography scan may reveal intrathoracic involvement (1). However, cranial CT scan only shows findings, which may be hydrocephalus, calcifications or nodules, in 40% of the cases (6).

Diagnostics-CSF Analysis

Also, unyielding in the patient, CSF analysis is helpful in the diagnosis of NS. However, it is nonspecific. About one-third of patients with NS will have normal CSF analysis findings as was the situation in our present case (10). CSF analysis will be helpful in excluding CNS infections or malignancy (2,5,7). An elevated CSF protein level typically accompanies oligoclonal bands in patients with NS, but which was not found in this present case. In patients with leptomeningeal involvement, the CSF findings are as follows: 40-70% exhibit pleocytosis, 40-73% have elevated protein, and 10-20% have low glucose and oligoclonal bands, and an elevated IgG index is encountered in up to 53% (6). Our patient, therefore, does not appear to have leptomeningeal involvement.

Diagnostics-Histopathology

Our patient presented with multiple facial nodules (cheeks, eyelids, and nose) and a biopsy was warranted that would be helpful in the diagnosis of NS. The essential lesion in sarcoidosis consists of focal collections of epithelioid cells surrounded by lymphocytes with giant cells lacking caseation reflected in our patient's biopsy. In patients with a systemic disease like sarcoidosis, they may present with skin lesions, lymph node inflammation, and palpable nodules. A biopsy of these lesions is warranted. The sarcoid non-caseating granuloma may be found in all organs and tissues, including the nerve roots, peripheral, and central nervous systems (2-4, 11).

Differential Diagnosis

It is not only NS that presents with bilateral facial nerve neuropathy. Komurcu and Anlar (2015) (12) reported on a triad of repeating bilateral facial nerve paralysis, orofacial edema, and fissured tongue described as Melkersson-Rosenthal syndrome (MRS). MRS is also a non-caseating granulomatous disease like NS. Although biopsy was not done on the patient in their report, the patient was also treated and responded with steroids (12).

Evident in the patient's history and examination is the occurrence of right finger flexor weakness but this was not substantiated in the repeat electrodiagnostic test. Though not compatible with our patient, acute inflammatory demyelinating polyneuropathy (AIDP) is also a differential diagnosis of NS (6,7, 13).

In a report by Bhat (13) et al., they presented and worked up a patient with symptoms and results compatible with AIDP, until a brain MRI showed multiple meningeal enhancements, and brain biopsy showed non-caseating granulomas negative for acid-fast bacilli and who had marked improvement with high dose steroids. Polyneuropathy in sarcoidosis may present as chronic sensorimotor axonal polyneuropathy, multiple mononeuropathies, and sensory polyneuropathy including small-fiber neuropathy (6). Since 1975, sarcoidosis had already been studied in the context of myopathy (14). Hewlett and Brownell presented four cases of patients with proximal muscle weakness in which muscle biopsy of all the patients showed well-defined, non-caseating, epithelioid granuloma with giant cells, 3 of which were responsive to steroids (14). Though in some studies, they state that myopathy in NS may happen and be asymptomatic (1,4), but it was ruled out in this present case with normal CK and EMG findings.

Therapeutic Focus and Assessment

As with other systemic diseases, the mainstay of treatment for NS is the administration of corticosteroids (2,4). The present case is maintained on methylprednisolone 16 mg/tab 1 tab daily. Tapering of steroid was attempted before, but there would be a recurrence of symptoms. Hence, azathioprine, an immunosuppressive agent, started at 50 mg/tab 1 tab daily, was added to the regimen and maintained. The recent onset of neurologic symptoms indicating an active phase of the disease is the most certain indication for steroid therapy. In the study by Hoitsma et al. (2010), an initial dose of methylprednisolone at 1 mg/kg/day is recommended. In severe cases, high doses (500-1000 mg) of intravenous methylprednisolone may be used for a few days to obtain a high initial loading dose. Therapy is to be given for several months. In many cases, it may last for several years.

If patients become resistant or intolerant to corticosteroids, immunosuppressive agents or anti-Tumor-Necrosis-Factor (anti-TNF) drugs are to be added to the regimen. Immunosuppressive or cytotoxic agents are helpful for refractory cases to corticosteroids (2,4). Azathioprine, as used in our patient, requires monthly liver function tests and blood cell counts. Other immunosuppressive agents are Methotrexate, Mycophenolate, and Cyclophosphamide. Anti-TNF agents may also be used such as Infliximab and Etanercept (1-10).

Prognosis

Patients may have different responses to steroid treatment. The patient in focus presented with a good response upon taking steroids. Some patients also treated with steroids may show improvement in findings in MRI, but may not show clinical improvement and vice versa. It has to be taken into consideration also that steroid treatment comes with its own side effects. Mortality rates were 18% in a series of 37 patients and 31% developed steroid side effects related to the high dose of steroids and longer duration of therapy (1).

CONCLUSION

In this present case, the diagnosis of NS was supported by the following: recurrent multiple cranial nerve palsies, the bifacial neuropathy being the most prominent, facial nodules with non-caseating granuloma on histopathology, lymphadenopathies on chest CT scan with the rest of the workups unyielding. Another highlight in this present case is the strong response to corticosteroids (IV and oral methylprednisolone). Having presented this case, NS may be rare and hard to diagnose but is definitely one to highly consider, especially in cases of recurrent cranial neuropathies, with the facial nerve affected.

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