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Case Report

Collet Sicard syndrome secondary to granulomatosis with polyangiitis

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ABSTRACT

Granulomatosis with polyangiitis (GPA) is a systemic vasculitis that affects small to medium-sized blood vessels. Although uncommon, cranial nerve (CN) involvement can result in CN palsy. We present a clinical case of a female with collet Sicard syndrome (CSS), displaying left-sided CN IX, X, XI, and XII involvement, which we determined to be caused by GPA. Our patient met 7 points on the American College of Rheumatology 2018 (ACR) criteria for GPA with positive ANCA, bilateral mastoiditis, and decreased sensorineural hearing. Early identification of GPA is crucial due to systemic CN involvement, as it can lead to dysphonia, dysphagia, and other complications. Early treatment can improve the functional prognosis of patients, requiring intensive induction immunosuppression due to frequent bilateral progression and worse prognosis. Despite its infrequency, timely diagnosis is critical for better patient outcomes.

Keywords: Collet Sicard, Case report, CN palsy, GPA

INTRODUCTION

Granulomatosis with polyangiitis (GPA) is a systemic vasculitis that affects small and medium-sized blood vessels, with infrequent involvement of CN or hypophyseal infiltration. In 90% of patients, ANCA antibodies are positive. To induce remission, GPA is treated with immunosuppressive therapy using high-dose corticosteroids, cyclophosphamide, or rituximab. After achieving remission, patients are shifted to low-dose glucocorticoids.[1]

In comparison to generalized GPA, young patients are more likely to have limited disease with a predominance in females and ANCA negativity. Limited GPA is characterized by middle ear and respiratory tract impairment, such as otitis media, sinusitis, nasal collapse, and airway stenosis.[2,3]

The CSS is typically associated with malignancies, glomus jugular tumors, carotid artery dissections, trauma, and skull base osteomyelitis. However, middle ear infections can also be a less common cause of CSS.[4]

Although infectious and inflammatory causes are uncommon, there have been reported cases of CSS associated with polyarteritis nodosa, Trousseau syndrome, otitis media, Lyme disease, and varicella-zoster. CSS is a rare syndrome that results in palsy of all the lower four CNs, and it is a rare manifestation of skull base disease involving the jugular and hypoglossal foramina. The jugular foramen, located at the medial end of the skull base, contains CN IX to XI, while the hypoglossal canal houses CN XII. Compression at these levels can lead to the development of CSS.[5]

CASE REPORT

The female of 53-year-old who complains with weight loss of 18% over the last 6 months, which is attributed to dysphagia, hearing loss, and lower CN impairment. The examination revealed several abnormalities, including

tongue deviation to the left (CN XII), absence of gag reflex on the left side (CN IX), impaired elevation of the soft palate on the left side, dysphonia (CN X), and weakness of the left sternocleidomastoid muscle (CN XI). The patient's dysphagia was characterized by an inability to swallow pureed foods or liquids. Additionally, left tongue atrophy and fibrillations, left vocal cord paralysis, and wasting of the trapezius and sternocleidomastoid muscles were observed during the physical examination. Right sensorineural hearing loss was confirmed with audiometry, which is consistent with a diagnosis of CSS.

A cranial magnetic resonance imaging (MRI) was performed to assess the central nervous system (CNS) for any structural anomalies, which revealed the presence of bilateral mastoiditis and sinusitis. There was no evidence of any mass on the skull base, and both jugular foramina were found to be unobstructed, with both jugular veins being clearly visible. A lumbar puncture was performed but was normal, laboratory was remarkable for iron-deficiency anemia; serum creatinine elevation of 1.67 mg/dL (0.5-1 mg/dL), the urine study with evidence of proteinuria, with urine depuration that showed proteins of 109 mg/24 h (<80 mg/24 h). The renal ultrasound revealed bilateral chronic inflammatory structural changes, while a modified barium swallow study demonstrated poor peristalsis, vallecula and pyriform pooling, and silent aspiration. These findings, combined with the absence of infectious etiologies and structural CNS impairment, led to further investigation; the complementary immunology studies showed C3 88 mg/dl, C4 32 mg/dl (Low), rheumatoid factor 32.9 UI/ml (High), anti cytoplasm of neutrophil (c-ANCA) IFI 1:32 (<1:20), Anti cytoplasm of neutrophils (p-ANCA) IFI <1:10. Anti-proteinase-3 (PR3) antibodies measured by ELISA mildly elevated 6.9 (<2). Anti-myeloperoxidase (MPO) antibodies were not detected. Tumoral, infectious, metabolic, hormonal, viral panels were normal. This led to the suspicion of GPA with neurological presentation CSS based on the ACR criteria, our patient meets 7 points to GPA with positive c-ANCA, bilateral mastoiditis, and reduction in sensorineural audition.

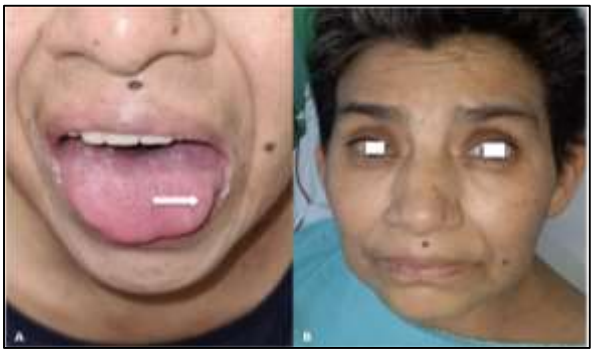

Figure 1: (A) Initial clinical picture of the patient, the patient's tongue was deviated to the right on protrusion, absent gag reflex on the left side. (B) Weakness of the left sternocleidomastoid muscle, and red eye on the right side.

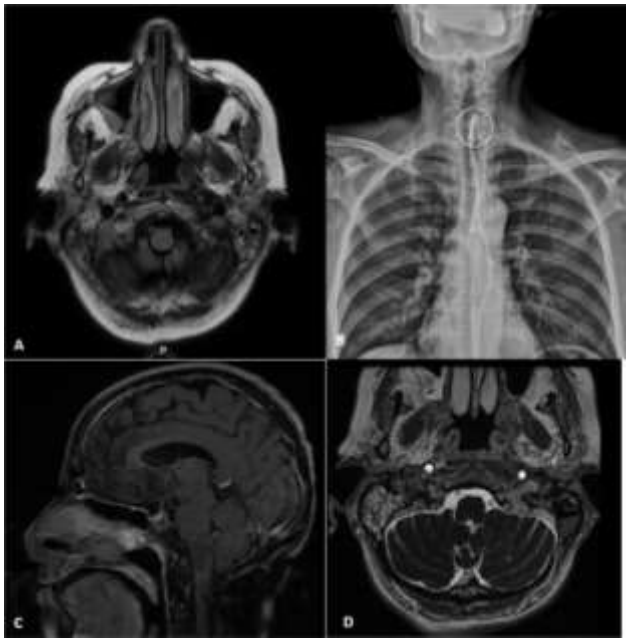

Figure 2: (A) Axial Brain MRI on the skull base with no evidence of neoplasm, bone lesion or jugular foramen occupation; (B) A modified barium swallow study, with silent aspiration; (C) Sagittal Brain MRI without evidence of lesion at brain stem, especially at midbrain level; (D) Axial Brain MRI with evidence of ethmoidal sinusitis.

Based on the severe neurological symptoms and the evidence of renal dysfunction, a clinical diagnosis of CSS was made. To address this condition, we initiated a treatment plan consisting of a three-day pulse of intravenous (IV) methylprednisolone in 1000 mg doses, along with IV cyclophosphamide in a dose of 600 mg (0.5 mg/BSm^2), followed by prednisone at a dosage of 1 mg/kg. After four weeks, the patient showed improvement in CN deficits, although dysphonia persisted.

DISCUSSION

The diagnosis of CSS underscores the importance of early recognition of GPA due to the systemic involvement of CNs, which manifested as dysphonia and dysphagia from glossopharyngeal involvement and vocal cord paralysis. These cases often require intensive induction immunosuppression, as bilateral involvement is common and can lead to a worse prognosis. Despite not being a frequent diagnosis, early identification is crucial for prompt treatment initiation and improvement of functional outcomes for patients.

Currently, there are numerous cases of GPA with intracranial involvement, primarily affecting the sellar region. However, approximately 57 cases of CSS have been reported, with most resulting from intracranial neoplasms or skull base trauma. Therefore, our patient can be regarded as an uncommon case.

Our patient exhibited atypical complications, including extensive CN palsies of CNs IX-XII, due to granulomatous infiltration of the skull base. This case report emphasizes several important takeaways. Firstly, it illustrates that localized GPA can be aggressive and result in significant morbidity. Additionally, assessment of disease severity is a crucial aspect of ANCA-associated vasculitis (AAV) management, as it influences treatment decisions.[6]

Despite having anatomically localized cranial GPA, our patient did not develop an organ-threatening disease. Nevertheless, she presented with vocal cord palsy, resulting in dysphonia. If prompt treatment had not been administered, this could have progressed to bilateral vocal cord palsy, leading to life-threatening airway obstruction. Additionally, glossopharyngeal, vagus, and accessory nerve palsies led to severe and progressive dysphagia.[7]

In a cohort of 128 GPA patients in Europe, 56 patients (44%) exhibited peripheral neuropathy (either symmetrical polyneuropathy or mononeuritis multiplex), whereas only 9 patients (7%) showed CNS involvement, with 6 of them presenting with CN palsies. At the Mayo Clinic, 21 out of 324 patients (6%) had CN palsies.[9]

CNS involvement in GPA occurs through contiguous spread of granulomatous tissue from adjacent sites in the middle ear and sinuses (as in the case of our patient), primary granuloma formation within the CNS, or vasculitis affecting the CNS.[10] The analysis of cerebrospinal fluid may show elevated protein and pleocytosis, but these findings are non-specific and can also be observed in other conditions such as sarcoidosis, IgG4-related disease, infections, and neoplasms, particularly lymphoma.[11]

The absence of a distinction between methotrexate and cyclophosphamide after 6 months may be due to the fact that patients in both treatment groups were still taking steroids at that time.[12]

Due to the patient's rapid clinical deterioration, treatment was initiated with cyclophosphamide. Studies such as RAVE and RITUXIVAS have demonstrated that rituximab is non-inferior to cyclophosphamide in treating AAV. However, in this case, high-dose corticosteroids and cyclophosphamide led to a significant improvement in the patient's condition.[13,14]

Considering our patient's disease course, it is worth noting that there has been only one recently published case that presents similar characteristics. Cranial neuropathies are commonly recognized as a complication of GPA, and the CSS represents a particular subset of CN palsies that affect nerves IX to XII. This condition can have intracranial or extracranial etiology, and the differential diagnosis includes neoplasms, infections, and inflammatory disorders.[15]

CONCLUSION

This case highlights the aggressive nature of localized GPA and its potential for significant morbidity, particularly when it manifests with extensive CN palsies. Prompt recognition and treatment are crucial to prevent life-threatening complications. Our patient's atypical presentation underscores the importance of considering GPA in cases of CN involvement, even without organ-threatening disease. Additionally, this case serves as a reminder that CNS involvement in GPA can occur through various mechanisms, necessitating a comprehensive diagnostic approach. Further research and awareness are needed to improve the understanding and management of this rare manifestation of GPA.

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