Granulomatosis with Polyangiitis and Pontine Hemorrhage Resulting in Plus-Minus Lid Syndrome. Case Report and Literature Review

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Abstract

Granulomatosis with polyangiitis is a systemic vasculitis with uncommon central nervous system involvement. Stroke, which is the primary manifestation in this subgroup, presents with a wide clinical spectrum depending on its location. The plus-minus lid syndrome consists of unilateral ptosis and contralateral eyelid retraction following a lesion of the midbrain affecting the third nerve fascicle. We present a patient with granulomatosis with polyangiitis who developed a pontine hemorrhagic stroke probably secondary to vasculitis activity, which extended to the midbrain affecting the third nerve fascicle with a consequent plus-minus lid syndrome. This is the first case in literature reporting both entities.

ABBREVIATIONS

GPA: Granulomatosis with Polyangiitis; CNS: Central Nervous System; CT: Computed Tomography; MRI: Magnetic Resonance Imaging

INTRODUCTION

Granulomatosis with Polyangiitis (GPA) is a systemic vasculitis with a wide range of features; however, ear, nose and upper airway are the uppermost. Central nervous system (CNS) is affected in 2-8% of all patients. Stroke is the primary manifestation in 12% of this subgroup [1]. The unfrequent stroke manifestation makes difficult to determine a predominant location in patients with GPA. However, among general causes of stroke, the vertebrobasilar system accounts for 20%, more commonly the pons than the medulla or midbrain [2,3].

The plus-minus lid syndrome consists of unilateral ptosis and contralateral eyelid retraction (Hering’s law). This is the result of a unilateral lesion of the third nerve fascicle with extension rostrally and dorsally to involve the nucleus of the posterior commissure (NPC) or its connections [4].

CASE PRESENTATION

A 65-year-old man presented to the emergency room of our hospital after a sudden onset of right side weakness followed by slurred speech. His medical history is remarkable for 6 years of GPA under maintenance therapy with low dose of prednisone and azathioprine.

On physical examination, the patient was alert, with a blood pressure of 130/80, heart rate of 85 beats per minute and temperature of 37.5 ºC. Neurological examination revealed pupils with normal photomotor and consensuate reflexes, primary gaze deviation, left side ptosis and contralateral lid retraction (Figure 1). The patient presented left central facial paresis, anarthria and tongue deviation to the right side on protrusion. We also found weakness of right side trapezius and sternocleidomastoid. Motor examination revealed right side paralysis and hyperreflexia with Babinski sign. Rest of the examination was normal.

Following examination, we performed a CT scan of the brain with intravenous contrast, which showed an area of high attenuation in the right lateral region of the pontine tegmentum, which was consistent with the findings during the neurological examination. In laboratory studies, erythrocyte sedimentation rate elevated at 149 mm/h, complete blood count, blood glucose, albumin, electrolytes and coagulation systems were normal; due to technical issues, we could not perform a brain MRI or an angiogram. Relying on the brain imaging, history and examination, we concluded a diagnosis of pontine hemorrhage probably secondary to GPA vasculitis of the central nervous system. The patient was admitted for observation and initiated...
induction therapy with prednisone and cyclophosphamide. He reported improvement in motor function, except for the ophthalmoparesis, which persisted all his stay; no other manifestations of the disease were reported whatsoever. He was discharged with no further complications, and will continue follow-up by the neurology outpatient services.

**DISCUSSION**

GPA is a systemic necrotizing vasculitis associated with anti neutrophilic cytoplasmic antibodies with systemic involvement. Neurological involvement is present in 33.6% of the patients, with peripheral neuropathy and orbital masses as the most frequent neurological complications of GPA [1,5]. CNS involvement is relatively rare, and is reported in 7-11% of the patients [6]. The fact that our patient did not display any other manifestation of systemic vasculitis may represent a drawback to our primary hypothesis, given the fact that CNS manifestations have been predominantly reported in severe cases of GPA [7], however, spontaneous intracranial hemorrhage is not unusual in GPA patients [8]. Furthermore, it has been proposed that the location of the hemorrhage may indicate vasculitis as the underlying etiology [9]. Hemorrhage located in the perimesencephalic region may elicit it as well as in our patient’s case.

Our patient presented with a hemorrhagic stroke of the vertebrobasilar system at the pontine tegmentum, affecting fibers of the third nerve fascicle with a consequent plus-minus lid syndrome. The plus-minus lid syndrome is an uncommon finding, which can follow hydrocephalus, tumors, trauma, and multiple sclerosis, among other causes. Cases secondary to central lesions are exceptional [11]. The original report by Gaymard et al., stated a midbrain stroke as the underlying cause [4], however, our patient’s features were consistent with a pontine lesion which may have extended to the midbrain sufficiently to affect oculomotor fibers to the levator palpebrae. Only another reported case matches with this underlying pathophysiology [12]. This explains why, contrary to previous reports, our patient did not present a nuclear third nerve syndrome.

Although, CNS involvement is an uncommon manifestation of GPA, we must be aware that cerebral vasculitis can affect any territory, and elicit infrequent findings such as the plus-minus syndrome. Although the anatomical substrate of this syndrome is a midbrain lesion, we must be considering that lesions in the perimesencephalic region may elicit it as well as in our patient’s case.

**REFERENCES**


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