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CASUISTIC PAPER

A rare case of hypertrophic olivary degeneration in a patient with pontine hemorrhage

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ABSTRACT

Introduction and aim. Hypertrophic olivary degeneration (HOD) is an extremely rare disease that affects the inferior olivary nucleus (ION) in the medulla oblongata and is also referred to as hypertrophic degeneration of the inferior olives. This type of degeneration is characterized by trans-synaptic degeneration resulting from the blocking of afferent impulses in the ION, which is distinct from HOD. In this report, we present a clinical case of bilateral HOD that was identified and confirmed by neuroimaging two months after pontine hemorrhage.

Description of the case. A 52-year-old male was admitted to a university hospital because of gait imbalance, difficulty in swallowing and speaking, psychomotor agitation, visual hallucinations, and full vertical and horizontal gaze paralysis. He had a history of hypertension, hyperlipidemia, and obesity. The patient received symptomatic supportive treatment, without surgery. Ten weeks after the vascular incident, neurological examination revealed six cases of right cranial nerve palsy, vertical pendular nystagmus, dysarthria, decreased throat reflexes, and lingual and pharyngeal paresthesia. Repeated magnetic resonance imaging revealed bilateral hyperintense foci of 15×6 mm in the medulla oblongata, as detected by T2-weighted and fluid-attenuated inversion recovery. Two months of treatment with clonazepam, carbamazepine, and vestibular exercise resulted in no positive changes. Rehabilitation and psychotherapy were then continued.

Conclusion. Contrast MRI is required to confirm HOD, whereas non-contrast magnetic resonance imaging is the only method used for imaging and is not always reliable because it can cause neoplasia, infarction, demyelinating disorders, infections, and other similar problems.

Keywords. dentato-rubral-olivary pathway, hypertrophic olivary degeneration, magnetic resonance imaging, pendular vertical nystagmus, pontine hemorrhage

Introduction

Hypertrophic olivary degeneration (HOD) is an extremely rare disease that affects the inferior olivary nucleus (ION) in the medulla oblongata and is also referred to as hypertrophic degeneration of the inferior olives.[1] This type of degeneration is characterized by trans-synaptic

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degeneration resulting from the blocking of afferent impulses in the ION, which is distinct from HOD.[1]

The hypertrophic appearance of HOD is caused by enlargement of neuronal bodies and vacuolization in the ION.[1] Three-dimensional T_2-weighted and fluid-attenuated inversion recovery imaging clearly demonstrate these changes, including enlarged ION and augmented signals on the affected side.[2,3]

HOD is frequently caused by a lesion in the dentato-rubro-olivaris pathway, also known as the Guillain-Mollaret triangle (GMT). This pathway involves afferent fibers from the dentate nucleus, which travel through the dentarubral tract to the upper part of the cerebellum, cross the midline, and reach the red nucleus on the contralateral side of the brain.[4] Any lesion involving any segment of this pathway from the dentate nucleus to the ION can lead to HOD. The olivo-dentatus tractus fibers enter the lower peduncle of the cerebellum and do not cause HOD because they are non-afferent fibers that originate from the ION to the contralateral dentate nucleus.[4]

HOD can be bilateral or unilateral. Bilateral HOD can result from various genetic and anatomical abnormalities.[5] A Chinese study found that out of 151 patients, nine had HOD related to genetically determined nervous system lesions, one patient had unilateral HOD, and the other eight had mitochondrial diseases caused by POLG and SURF1 gene mutations.[2]

The underlying cause of HOD remains unknown in many patients.[2,6,7] In most cases, patients exhibit soft palatal tremors and progressive ataxia.[8] Similar findings were observed in patients with bilateral HOD without any new structural damage to the GMT. The majority of these patients did not undergo genetic testing for SURF1 and POLG mutations, and further studies are needed to evaluate genetic neurological diseases. All the patients in these studies had bilateral idiopathic HOD due to undiagnosed hereditary disorders. However, POLG and SURF1, which are associated with Alexander's disease,[9] and autosomal dominant spinocerebellar ataxia type 20 (SCA20),[10] can cause bilateral HOD.

Aim

Further research is needed to understand the epidemiology and etiology of HOD, including its unilateral and bilateral variations. Although the mechanism and treatment efficacy are unclear, continued research on this condition is essential. In this report, we present a clinical case of bilateral HOD that was identified and confirmed by neuroimaging two months after pontine hemorrhage.

Description of the case

A male patient, aged 52, was admitted to the stroke department of the university clinic on April 29, 2023, complaining of sudden onset of nausea, dizziness, tinnitus, and noticeable gait imbalance, as well as difficulty swallowing and speech. Upon neurological evaluation, the patient exhibited cognitive impairment, with psychomotor excitation, disorientation, visual hallucinations, full vertical and horizontal gaze paresis, mild left nasolabial asymmetry, decreased pharyngeal reflexes, dysarthria, dysphonia, dysphagia, and moderate neck stiffness.

Computed tomography and magnetic resonance imaging (MRI) without contrast revealed a hematoma measuring 18×15×24 mm in size in a pontine projection. MR angiography revealed normal magistral blood vessels within the brain (Fig. 1). Laboratory tests, including complete blood count, urinalysis, and blood chemistry panel, revealed nonspecific inflammatory changes, hyperlipidemia, and impaired kidney function (GFR 40 mL/min/1.73 m^2). Carotid Doppler ultrasonography showed atherosclerotic plaques in the internal carotid artery with 68% right-sided stenosis and 30% left-sided stenosis. Transthoracic echocardiography and chest radiography revealed atherosclerotic degeneration of the ascending aorta and aortic valve, and dilatation and hypertrophy of the left ventricle.

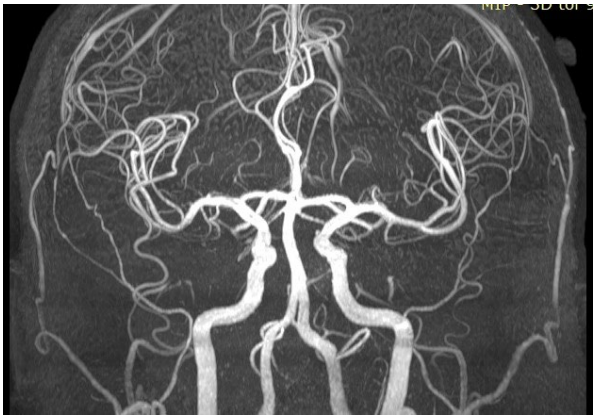

Fig. 1. MR angiography showed normal magistral blood vessels within the brain

After a week, the patient exhibited partial recovery, enabling him to stand and walk with assistance. However, walking remains challenging owing to diplopia, oscillations, and trunk imbalance. A repeat neurological examination revealed partial recovery of symmetric eye movements, with sequelae of right-sided convergent strabismus, vertical and horizontal divergence of the eyeballs, and limited rightward abduction of gaze. A neurosurgeon, vascular surgeon, and rehabilitation specialist advised the patient not to perform surgical interventions for long-term indications. The in-hospital management involved treatment with dehydration, antipsychotics, and hypotensive medications. The patient was discharged with recommendations for hypotensive, hypolipidemic, antiplatelet, and sedative medication.

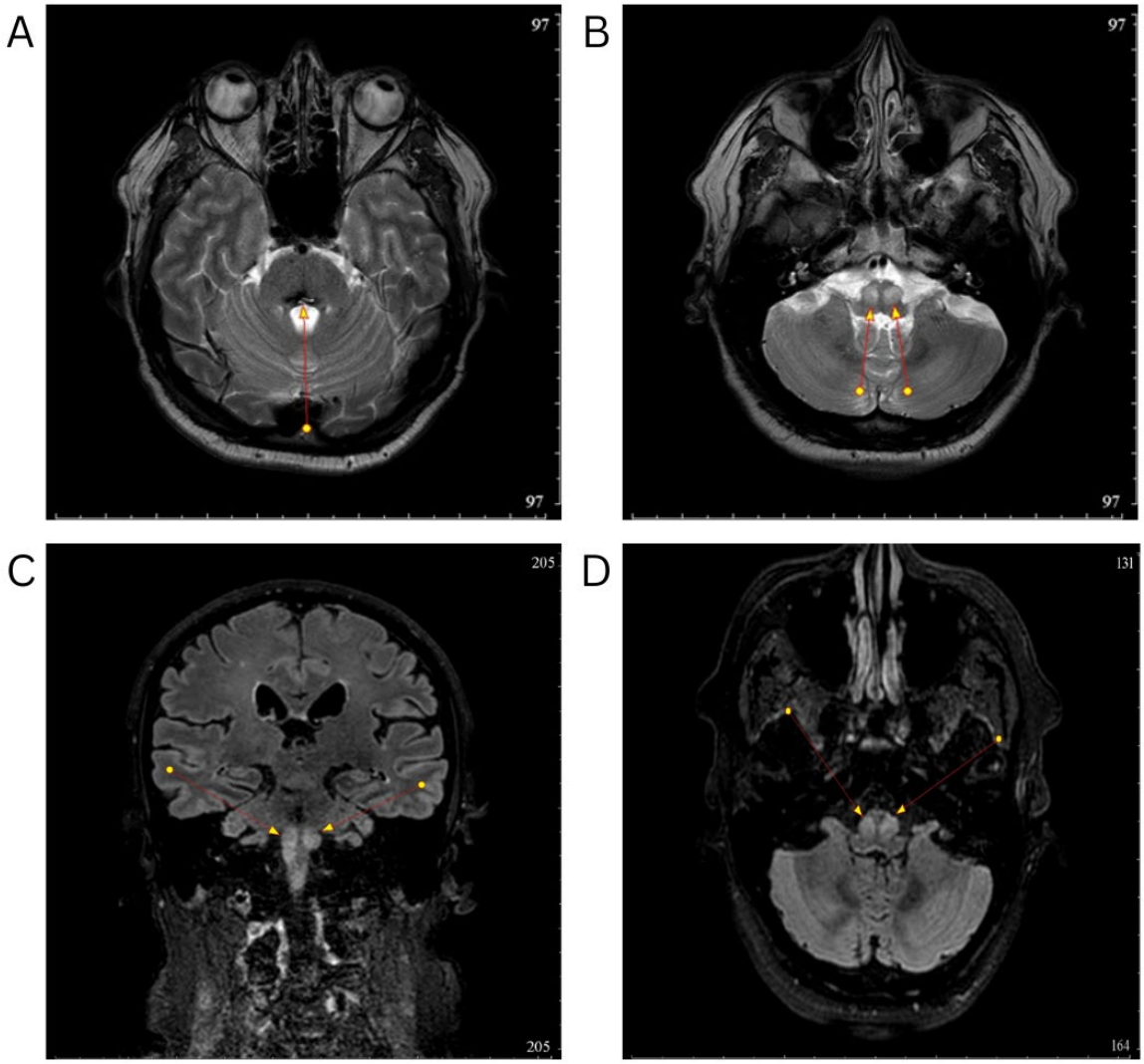

Fig. 2. A: MRI showed images in coronal T1w, B: frontal T1w, C: coronal T2w, and D: frontal T2w, pons is decreased in size and post-hemorrhagic cystic mass (9×3×10 mm) with hemosiderin deposits in the tegmentum and bilateral area of high signal intensity observed in the T2w MR image (15×6 mm)

At the 10-week follow-up, the patient still experienced diplopia, right convergent strabismus, limited rightward abduction of gaze, and a positive Romberg sign without severe dysmetria. Vertical pendular nystagmus was observed in all directions of ocular motion, and was not suppressed by fixation. Visual acuity remained unchanged from right to left, and the pupils were uniform and responsive to light. Fundoscopy revealed hypertensive microangiopathy. The saccades, convergence, and smooth horizontal and vertical tracking were normal. The ocular-cephalic reflex and head jerk test results were within normal ranges. The patient could not walk independently because of oscillopsia and diplopia. Dysarthria, decreased throat reflexes, and lingual and pharyngeal paresthesia were observed with no palatal myoclonia. No abnormalities in somatosensory sensitivity or reflexes were detected.

Permanent pendular vertical nystagmus was also present with no suppression of gaze fixation during ocular motion in any direction. The saccades, convergence, and horizontal and vertical tracking were unaffected. The patient continued to experience severe oscillopsia and diplopia, which prevented independent walking.

Repeated MRI with contrast revealed the presence of a post-hemorrhagic cystic mass with hemosiderin deposits in the pons and bilateral hyperintense foci of size 15×6 mm in the medulla oblongata, as detected by T_2-weighted and fluid-attenuated inversion recovery imaging. These findings were indicative of Wallerian degeneration (Fig. 2).

Discussion

This particular case involved clinical and neuroimaging examinations of a post-stroke patient with HOD. Bilateral post-pons hemorrhage HOD is uncommon and exhibits diverse clinical symptoms and MRI results, necessitating individualized patient monitoring and MRI assessment changes.In a retrospective study, 76% of patients exhibited bilateral HOD.[11]

Despite an unknown cause, bilateral HOD is disproportionately more prevalent in males. In some cases, both prominent and unexpectedly identified asymptomatic forms of HOD were detected by MRI.[12] Prominent forms of HOD were identified in 23% of cases with unilateral lesions and 39% with bilateral lesions.[13]

The precise causes of the clinical signs associated with HOD remain unknown.[14] The number of functional neurons in the ION and their afferent fibers, as well as the severity of the underlying illness, can influence the onset, severity, and progression of these symptoms.

Patients with HOD degeneration often experience palatal tremor, cerebellar ataxia (dysmetria, indistinct speech, and walking ataxia), nystagmus, ophthalmoplegia, ocular myoclonia, and other involuntary eye movements.[15] In our clinical case, HOD presented with ophthalmoplegia, nystagmus, dysarthria, and ataxia.

MRI is the most effective diagnostic tool for validating and confirming the diagnosis of HOD, as it provides a thorough delineation of the morphopathologic structure of the affected areas.[16]

To date, patients with bilateral HOD have been found to harbor various gene mutations. POLG mutations have been linked to a range of clinical signs, including bilateral HOD.[5] Leigh syndrome, a severe neurological disorder characterized by cytochrome C oxidase deficiency that typically affects neonates, is caused by SURF1 mutations. Bilateral HOD is often observed on MRI in patients with mutations in SURF1, TTC19, and AIFM1.[11,17] In the absence of other clear causes, mitochondrial dysfunction may be the reason for bilateral HOD, particularly in cases of hearing loss.[18] This is particularly true when both conditions occur simultaneously. Patients with SCA20 also exhibited signs of bilateral HOD.[19] Genetic testing can aid in the precise diagnosis of patients with bilateral HOD who have a family history of the disease or present with neurological and physiological signs indicative of SCA or mitochondrial disease.

As previously mentioned, HOD is characterized by the microscopic features of neuronal body enlargement and vacuolization, astrocytic hyperplasia, and proliferation with glyosis and demyelination.[1] These characteristics are indicative of trans-synaptic degeneration resulting from the loss of afferent fibers in the hilum of the ION.[1]

The literature on HOD consists mostly of case studies.[16,20] Previous studies have reported that HOD can occur unilaterally or bilaterally.[6,7,21,22] However, recent research has challenged the idea that HOD is consistently associated with GMT lesions. In fact, many patients with HOD do not have lesions in the GMT, and a small number of patients may have non-lesional HOD.[6,21] Some studies suggest that non-lesional HOD is mostly bilateral. [6,21,22] However, there is limited documentation of these cases. Therefore, we present a patient with bilateral HOD who exhibited a clinical picture that, although not entirely unique, had sparse documentation in larger investigations and not in individual case reports.

The standard therapy for HOD comprises gabapentin, memantine, botulinum toxin injections, and deep brain stimulation, with psychotherapy being beneficial for patients with chronic illnesses. However, some patients may show self-limited recovery, necessitating avoidance of overtreatment. Oculomotor or nonsensory tremors often persist throughout life, but some may experience improvement after several years.[23] The efficacy of HOD treatment is unclear because of its unclear pathological mechanisms. Our patient underwent rehabilitation for pontoon hemorrhage and later received pregabalin and clonazepam without symptom improvement. Further research is needed to clarify the pathological mechanism of HOD, particularly in cases of recurrent hemorrhage and bilateral HOD.

The results of this study did not include diffusion tensor imaging and MRI data, which are necessary to verify changes in brain structures within the GMT when MRI findings are inconclusive. Additional prospective monitoring of the patient, in conjunction with biopsy analysis, is needed to confirm the observation and uncover the pathological basis of the neuroimaging nature.

Conclusion

In this report, we describe an unusual case of pontine hemorrhage with early onset HOD in the brainstem. Contrast MRI is required to confirm HOD, whereas non-contrast MRI is the only method used for imaging and is not always reliable because it can cause neoplasia, infarction, demyelinating disorders, infections, and other similar problems. Remarkably, this type of degeneration results in hypertrophy, rather than atrophy. A case of HOD with radiological diagnosis may have many pathological phenotypes.

The literature on HOD reveals inconsistencies and gaps, particularly in the areas of epidemiology, illness comprehension, and therapy. Despite the patient's intricate medical history, this case showed a broad spectrum of symptoms experienced by a patient with HOD. Here, we discussed possible alternative diagnosis and uncertainties surrounding this condition. Further studies are required to address this issue.

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Declarations

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Author contributions

Conceptualization, E.M. and G.B.; Methodology, T.A.; Software, N.M.; Validation, E.M., T.A. and N.M.; Formal Analysis, M.S.; Investigation, N.C.; Resources, M.B.; Data Curation, E.M.; Writing – Original Draft Preparation, G.B.; Writing – Review & Editing, N.M.; Visualization, N.C.; Supervision, M.B.; Project Administration, M.S.; Funding Acquisition, E.M.

Conflicts of interest

The authors declare no competing interests.

Data availability

Not applicable.

Ethics approval

The authors reported that they acquired the necessary informed consent form from the patient, who consented to the publication of their photo, video materials, and other clinical information. The patient was informed that confidentiality would be ensured.

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