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Case Report

Unusual co-occurrence of hypertrophic inferior olivary degeneration with infratentorial cavernomatosis and orbital cavernous hemangioma ☆

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ABSTRACT

Hypertrophic olivary degeneration (HOD) is a rare condition resulting from a lesion in the Guillain-Mollaret triangle (GMT), causing transsynaptic degeneration and hypertrophy of the inferior olivary nucleus (ION). The GMT is composed of the dentate nucleus, red nucleus, and ION, and is commonly affected by ischemic and hemorrhagic strokes, vascular malformations, neoplasms, or surgical trauma. Cavernomas are a frequent type of cerebral vascular malformation associated with HOD, while orbital cavernous hemangiomas are another rare vascular malformation. The association of these two malformations is scarcely reported, with only one case previously documented. We report the case of a 26-year-old male presenting with right exophthalmos and palatal myoclonus, where brain MRI demonstrated HOD secondary to infratentorial cavernomatosis, along with a right orbital cavernous hemangioma. This case highlights a rare co-occurrence of infratentorial cavernomatosis and orbital cavernous hemangioma, emphasizing the importance of recognizing vascular malformations as potential causes of HOD.

Introduction

Hypertrophic olivary degeneration (HOD) is a rare clinical entity defined by pseudo-hypertrophy of the inferior olive following a lesion of the afferent fibers that comprise the Guillain-Mollaret triangle. This condition can occur with or without an identifiable causal lesion and can be unilateral or bilateral [1]. The first description of HOD was published by Oppenheim in 1887, and its development was further detailed by Guillain and Mollaret in 1931 [2]. HOD presents with classic symptoms of palatal myoclonus and other rhythmic involuntary move-

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ments [3]. The most appropriate imaging modality for diagnosing HOD is MRI [4]. The most common causes of brainstem lesions that may involve the dentatorubral-olivary pathway include hemorrhage secondary to hypertensive disease, head trauma, vascular malformations, and infarction [3].

We present a unique case of hypertrophic inferior olivary degeneration resulting from infratentorial and cerebellar cavernomatosis, revealed by exophthalmos secondary to an orbital cavernous hemangioma. The uniqueness of this clinical case lies in the rarity of cavernomas located within the Guillain-Mollaret triangle and, most notably, in the presence of an associated orbital cavernous hemangioma. This is the first known report describing a concurrent case involving this specific association in the literature.

Case presentation

A 26-year-old patient with no previous medical history presents with a progressively developing, non-pulsatile right exophthalmos. Clinical examination reveals a moderate decrease in visual acuity, bilateral nystagmus, and palatal myoclonus. A brain MRI was performed, revealing a large tissue signal lesion within the right intraorbital, intraconal space, situated between the lateral rectus muscle and the optic nerve, which is displaced medially without sheath involvement. This lesion is oblong with well-defined borders, measuring 56×25 mm, extending posteriorly to an enlarged orbital fissure and the spheno-cavernous region with a clear cleavage plane with the vasculonervous structures of the cavernous sinus. Anteriorly and superiorly, it expands to the pre-septal region. This lesion causes grade III exophthalmos and vascular remodeling of the sphenoid hemicorpus. It appears as a T1 hypointense, T2, and STIR hyperintense signal, with early discontinuous nodular enhancement after Gadolinium injection, revealing multiple ectatic draining veins in the anterior temporal region.

The brain MRI also shows multiple signal-void lesions on all sequences, not enhanced by Gadolinium, in the pons and cerebellum, typical of cavernomas. There is also a Flair hyperintense signal of the inferior olivary nuclei, indicating hypertrophic olivary degeneration. Additionally, dilated cerebellar veins draining into a dysplastic venous collector joining the right superior petrosal sinus are noted around the fourth ventricle. Scattered non-specific demyelination spots in the periventricular white matter are also observed, appearing as Flair hyperintensities Figs. 1 and 2.

Discussion

Hypertrophic olivary degeneration (HOD) is a rare pathology caused by a lesion in the Guillain-Mollaret triangle, leading to trans-synaptic degeneration resulting in degenerative hypertrophy of the inferior olivary nucleus (ION) [1]. It is a rare form of neuronal degeneration that occurs due to lesions disrupting the normal function of afferent fibers to the ION within the dentato-rubro-olivary pathways (Guillain-Mollaret triangle) [1]. The first description of HOD was published by Oppenheim in 1887, and its development was further detailed by Guillain and Mollaret in 1931 [2,5].

HOD results from an alteration in neuronal connections within the dentato-rubro-olivary pathway. This pathway, also known as the myoclonic triangle, connects the dentate nucleus to the contralateral red nucleus and the inferior olivary nucleus [3,5]. The dentate nucleus synapses with the contralateral red nucleus via the superior cerebellar peduncle (dentatorubral tract). Its fibers decussate in the medial inferior midbrain [4]. The red nucleus and the ipsilateral inferior olivary nucleus are connected by the central tegmental tract, located in the paramedian dorsal pontine region, immediately lateral to the medial longitudinal fasciculus and dorsal to the lateral aspect of the medial lemniscus [4]. The pathway is completed by the network of olivocerebellar connections linking the inferior olivary nucleus to the contralateral dentate nucleus [4].

There are three different patterns of olivary degeneration depending on the location of the primary lesion:

- If the primary lesion is located in the dentate nucleus or superior cerebellar peduncle (before the decussation of the dentatorubral tract), the olivary degeneration is contralateral [3].
- If the primary lesion is limited to the central tegmental tract, the olivary degeneration is ipsilateral [3].
- The degeneration is bilateral in cases involving both brainstem and cerebellar lesions [3]. This is the case for our patient who presents with left brainstem and cerebellar cavernomatosis (Fig. 3).

In the first stage of HOD, no abnormalities are detected in the inferior olivary nucleus (ION) [6]. The second stage, lasting up to 3 weeks, reveals mild neuronal hypertrophy. The third stage shows hypertrophy due to neuron and astrocyte proliferation over 6 months, likely from loss of GABA-mediated inhibition from the red nucleus [6]. The fourth stage shows ION hypertrophy, followed by pseudohypertrophy with neuronal dissolution lasting 3–4 years. In the final stage, neuronal loss leads to atrophy [6].

Clinical signs include nystagmus, palatal myoclonus, soft palate tremor, limb clonus, and ataxia, although palatal myoclonus is not always present [6]. HOD is caused by strokes, vascular malformations, neoplasms, surgery, infections (listerial rhombencephalitis, toxoplasmosis), and head trauma [7]. Idiopathic cases are rare, with other causes including Neuro-Behçet's disease, Wilson's disease, and PML [7,8].

MRI is the most effective imaging modality, showing hypertrophy of the ION with T2 hyperintensity and iso- to hypointense signal on T1 [9]. The condition progresses through three phases: early T2 hyperintensity without hypertrophy, pseudohypertrophy with increased T2 signal lasting 3–4 years, and eventual atrophy [2]. Diffusion tensor imaging (DTI) can help assess disease severity, but early detection through imaging remains challenging [6].

The differential diagnosis of T2-weighted hyperintensity in the ponto-medullary region includes tumors, strokes, demyelinating, infectious, and inflammatory diseases (Sánchez et al., 2013; Blanco et al., 2015) [7]. An initiating lesion in the contralateral cerebellum or ipsilateral brainstem strongly suggests HOD diagnosis. Ischemic infarction of the medulla

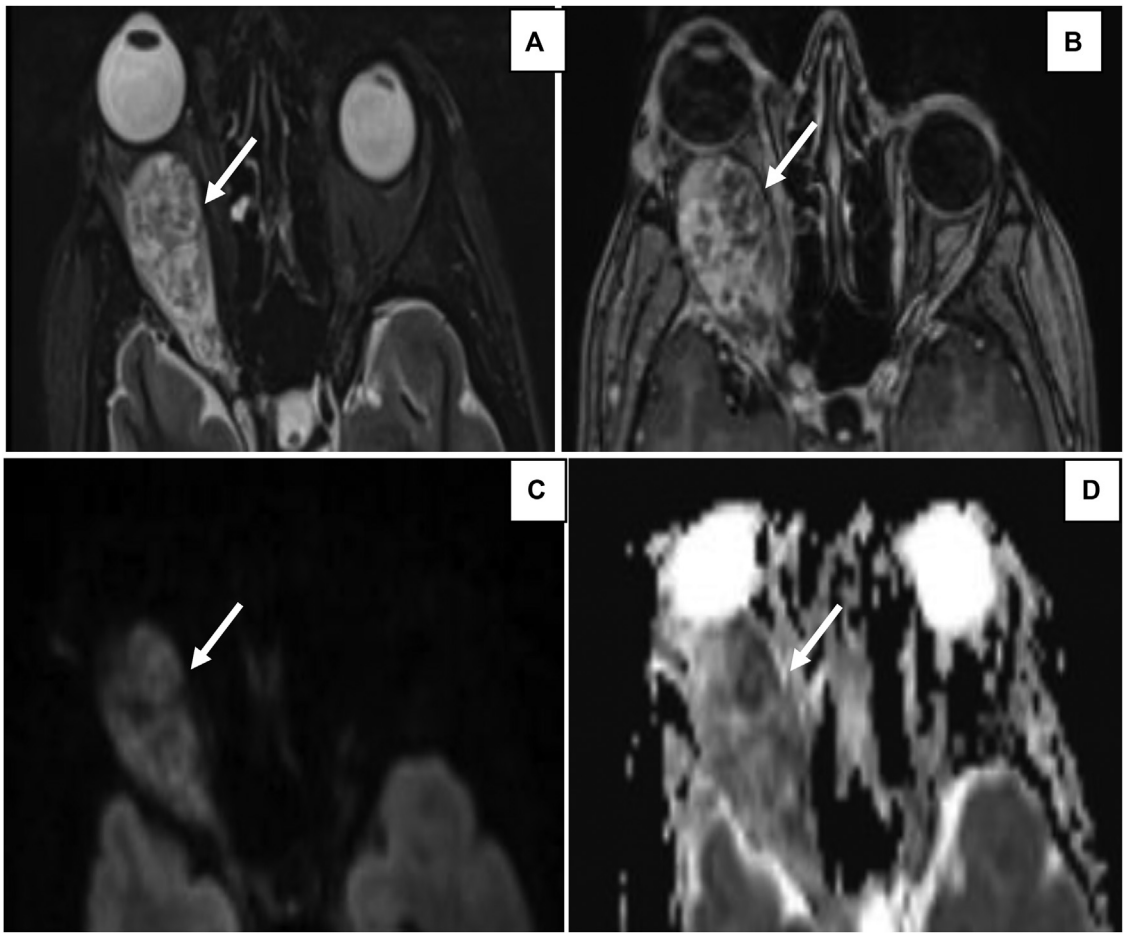

Fig. 1 – Intraorbital, intraconal tissue signal lesion process, right-sided, causing grade III exophthalmos and vascular-origin bone remodeling of the sphenoid wing. It demonstrates significant hyperintensity on STIR sequences (A), with early discontinuous nodular enhancement observed after gadolinium administration (B). There is no evidence of diffusion restriction (C), and the region exhibits a high ADC (Apparent Diffusion Coefficient) value (D).

oblongata can cause focal signal alteration, as can neoplastic processes such as astrocytoma, metastasis, or lymphoma (Macht et al., 2009) [7]. Additionally, demyelination associated with multiple sclerosis and inflammatory or infectious diseases like tuberculosis, sarcoidosis, acquired immunodeficiency syndrome, or rhombencephalitis should be considered. The lack of gadolinium enhancement in surrounding areas of the medulla distinguishes HOD from other lesions [7]. Tumors, inflammations, or infections differ from HOD by contrast enhancement, whereas HOD shows non-enhancement. Although some infarctions may lead to olive hypertrophy, most affect the lateral medullary bulb. Reduction in size of the inferior olive in follow-up exams helps exclude several conditions [7]. Olivary hypertrophy in HOD excludes chronic stages of multiple sclerosis or ischemic lesions [7]. In summary, hyperintense enlargement of the inferior olive on FLAIR and T2 without contrast enhancement, associated with a lesion affecting the Guillain-Mollaret triangle, are key features for diagnosing HOD. Recognizing these distinctive radiological features is important in patients without typical clinical manifestations [7].

Cerebral vascular malformations are traditionally classified into four categories: arteriovenous malformations (AVMs); cavernous cerebral malformations (CCMs), also known as cavernomas or cavernous hemangiomas; venous angiomas; and capillary telangiectasias, in decreasing order of incidence [10]. The majority of cavernomas (70-80%) are supratentorial, 10-20% infratentorial, with the remaining 5 to 10% found in the spinal column [10].

The locations of intracranial cavernomas can vary widely, from superficial structures such as the third ventricle, lateral ventricle, cavernous sinus, suprasellar region, pineal region, and dura mater, to deeper structures like the brainstem, thalamus, and basal ganglia [10]. Our patient presents with infratentorial and cerebellar cavernomatosis associated with developmental venous anomalies.

Orbital cavernous hemangiomas (OCHs) are benign vascular malformations with low flow, slow growth, and occasionally acute progression. Typically observed in middle-aged adults, they represent about 4 to 6% of all intraorbital masses [4,10]. Over 80% of OCHs are located intraconally, with progressive painless proptosis being the most common presen-

Fig. 2 – FLAIR hyperintensity is observed in the inferior olivary nuclei (A). The left cerebellar (B) and brainstem (C) cavernomas demonstrate heterogeneous FLAIR hyperintensity with a surrounding hypointense halo, consistent with hemosiderin deposition, and no enhancement following gadolinium administration (D). Additionally, dilated cerebellar veins are noted around the V4 segment, draining into a dysplastic venous collector (e, white arrow) that empties into the right superior petrosal sinus. Multiple ectatic draining veins are visible in the anterior temporal region (E, black arrow).

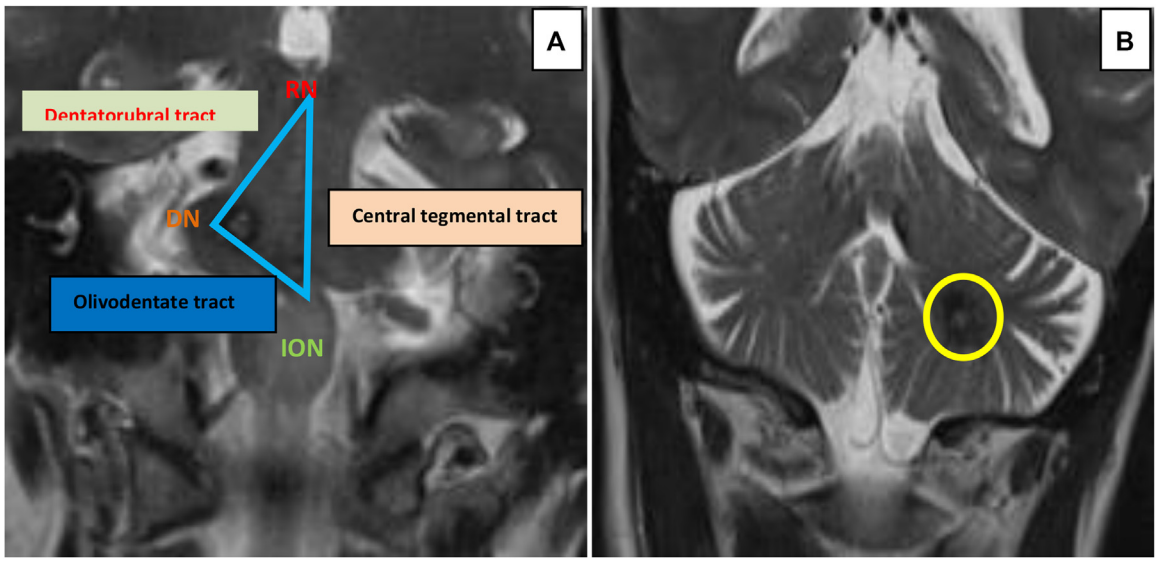

Fig. 3 – Coronal T2-weighted images (A, B) with a schematic of the Guillain-Mollaret triangle (A) showing secondary degeneration of the inferior olivary nucleus (ION) with T2W hyperintensity secondary to cavernomas in the Dentato-Rubro-olivary pathway (DN: Dentate Nucleus/RN: Red Nucleus) associated with a left cerebellar cavernoma.

tation [4,10]. In our case, the intraconal orbital cavernous hemangioma causes exophthalmos and bone remodeling of the sphenoidal hemi-corp.

Several studies have compared the nature of OCHs with that of CCMs in terms of pathology and clinical behavior. Hejazi et al. have extensively studied these two lesions and conclude that they differ clinically, histopathologically, and neuroradiologically [10]. Choudhri et al. demonstrated that cavernomas represent a spectrum of lesions characterized by sinusoidal cavities lined with endothelium, with varying wall thickness and tissue reaction depending on their location. Although these lesions share similarities, they maintain distinct characteristics based on the native tissue microenvironment [10].

To our knowledge, only one case has been reported in the literature associating an orbital cavernous hemangioma with cerebral cavernomas (Choudhri et al. 2014) [10]. To date, our case is unique in the literature, highlighting the association of hypertrophic inferior olivary degeneration with infratentorial cavernomatosis and orbital cavernous hemangioma.

Management of hypertrophic olivary degeneration (HOD) primarily involves addressing the underlying cause within the Guillain-Mollaret triangle. Symptomatic treatment may include medications for managing myoclonus and ataxia. Conservative management often leads to spontaneous resolution of symptoms. Drugs such as levodopa, carbamazepine, propranolol, tiapride, and clonazepam have been used for treatment [6]. Regular MRI follow-ups are recommended to monitor disease progression and response to treatment. In cases involving vascular malformations, such as cavernomas, surgical intervention may be considered. Stereotactic radiosurgery has been utilized with some success for treating lesions in critical, deeply seated locations [11]. Our patient received only symptomatic treatment for HOD.

Surgical treatment of orbital cavernous hemangiomas (OCHs) is recommended only for symptomatic patients. Lateral orbitotomy, the most common approach, provides excellent exposure for tumors located in the superior, lateral, or inferior compartments of the orbit [10]. Our patient underwent complete resection of the OCH.

Conclusion

Hypertrophic inferior olivary degeneration is a unique form of neuronal degeneration characterized by typical clinical manifestations and distinct imaging features. In our case, it is associated with infratentorial and cerebellar cavernomatosis, highlighted by exophthalmos secondary to an orbital cavernous hemangioma. This clinical case is notable for the rarity of cavernomas located within the Guillain-Mollaret triangle and, notably, for the presence of an associated orbital cavernous hemangioma. To our knowledge, this is the first reported case describing such an association in the medical literature.

Patient consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

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