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Case Report

Hypertrophic olivary degeneration secondary to a Guillain Mollaret triangle cavernoma: Two case report☆,☆☆

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ABSTRACT

Hypertrophic olivary degeneration (HOD) is a rare form of transsynaptic degeneration. It is caused by a damage at the Guillain-Mollaret triangle (GMT), which is defined by three anatomical structures: the dentate nucleus, the red nucleus, and the inferior olivary nucleus (ION). Clinically, it may be revealed by palatal myoclonus. On MRI, it appears as a unilateral or bilateral enlargement of the inferior olivary nucleus which shows a high signal intensity on T2-weighted images, with sometimes a cerebellar atrophy. Here we report 2 cases of healthy patients which present hemorrhagic brainstem cavernomas, complicated later by the development of palatal myoclonus and cerebellar ataxia, with MRI features corresponding to an (HOD) secondary to a (GMT) cavernoma. The purpose is to explain the mechanism of (HOD) subsequent to lesion in (GMT), and to describe magnetic resonance imaging features.

Introduction

Hypertrophic olivary degeneration (HOD) is a rare form of transsynaptic degeneration [1,2]. It was first described by Oppenheim in 1887 [3]. HOD is caused by lesions of the dentato-rubro-olivary pathway or Guillain-Mollaret triangle (GMT), leading to inferior olivary nucleus (ION) transneuronal degeneration. It seems to appear more frequently in men. HOD presents classical symptoms of palatal myoclonus and other rhythmic involuntary movements [4].

We present rare cases of hypertrophic olive degeneration (HOD) resulting from hemorrhagic brainstem cavernomas, reveled by palatal myoclonus and cerebellar ataxia.

The rarity of this clinical case is attributed to the infrequency of cavernomas located within the Guillain-Mollaret

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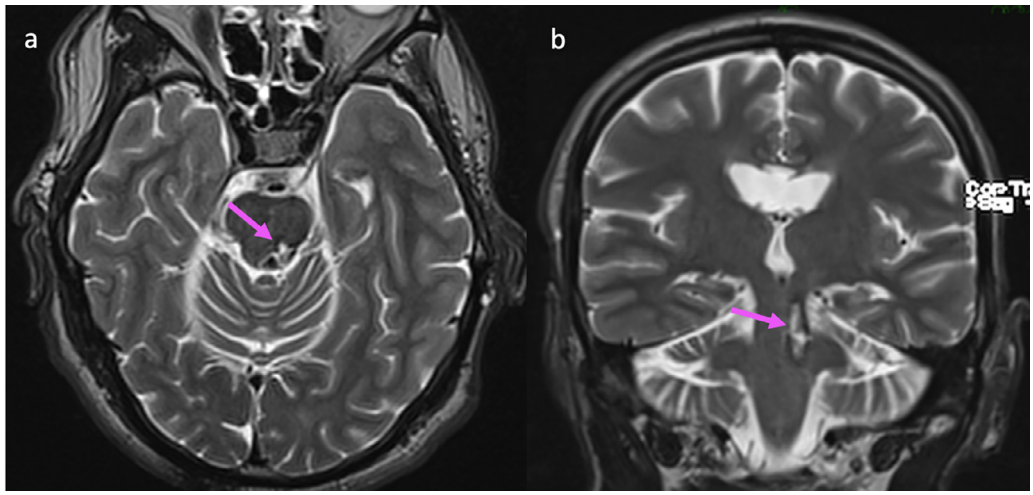

Fig. 1 – Brain MRI imaging on axial (A) and coronal (B) T2-weighted section which reveals a left tegmental pontine cavernoma extending to the left superior and middle cerebellar peduncles (Pink arrow) that appeared as an oblong T2-high-intensity mass in the dorsal pontomesencephalic part, with surrounding hypointensity which represents hemosiderin and ferritin deposited from an old hemorrhage.

triangle, as well as the uncommon occurrence of hypertrophic olivary degeneration. Rare cases involving this association have been described in the literature.

Case report 1

The first case is about a 19-year-old man with a history of pontomesencephalic hemorrhage that occurred 5 months ago. Currently, the patient exhibits a palatal myoclonus with cerebellar ataxia. On clinical examination, the patient had a finger-nose dysmetria, dysarthria, and a gaze-evoked nystagmus which seems to be synchronous with palatal tremor. A Brain MRI was performed, it showed an heterogenous hyperintense T2 hemorrhagic cavernoma centered on the central tegmental tract of the left pontine side, extending to the homolateral superior and middle cerebellar peduncles, and reaching the region of the inferior colliculus (at the lower posterior midbrain) (Fig. 1), bilateral swollen hyperintense inferior olivary nuclei (ION) more pronounced on the left side (Fig. 2), with a discrete cerebellar atrophy (Fig. 3).

Case report 2

The case is about a 58-year-old man without significant medical history, admitted for a 1-year history of rhythmical movement of the palate, speech disorder, and progressive difficulty in walking. On clinical examination, the patient presented an explosive dysarthria with cerebellar ataxia. The rest of examination revealed no abnormalities.

Investigations revealed normal routine blood analysis. EMG and nerve conduction studies showed no abnormalities. Evoked potentials were normal. Brain MRI revealed a heterogenous hypointense T1 and T2 cavernoma centered on the left tegmentum mesencephali, extending to the homolateral superior cerebellar peduncle, blooming on SWI (Susceptibility-Weighted Imaging) (Fig. 4), bilateral swollen hyperintense inferior olivary nuclei (ION) more pronounced on the left side (Fig. 5), with no restricted diffusion or Gadolinium enhancement, and a moderate cerebellar atrophy (Fig. 6).

The combination of clinical and radiological findings in both patients is highly suggestive of hypertrophic olivary degeneration secondary to destruction of a portion of the dentatorubral-olivary pathway, or Guillain- Mollaret triangle (GMT).

Both patients were treated by levetiracetam with significant myoclonus reduction.

Discussion

The olivary bodies are a pair of prominent oval lamellar nucleus located in in the anterior lateral medulla oblongata. They consist of 2 parts: The superior olivary nucleus, and the inferior olivary nucleus (ION) which is the largest nucleus. The latter is mainly involved in the normal integration of posture and motion [5].

Hypertrophic olivary degeneration (HOD) is caused by a lesion that damages the neuronal connections between the dentate nucleus of the cerebellum, the red nucleus, and the inferior olivary nucleus: the dentatorubral-olivary pathway or Guillain-Mollaret triangle (GMT) [7].

The dentate nucleus and the contralateral red nucleus are connected by the superior cerebellar peduncle (dentatorubral tract), with fibers crossing in the decussation of the peduncle at the level of the inferior colliculus in the posterior lower midbrain [8]. The red nucleus and the ipsilateral inferior olivary nucleus are connected by the central tegmental tract (Fig. 7) [6,9,10].

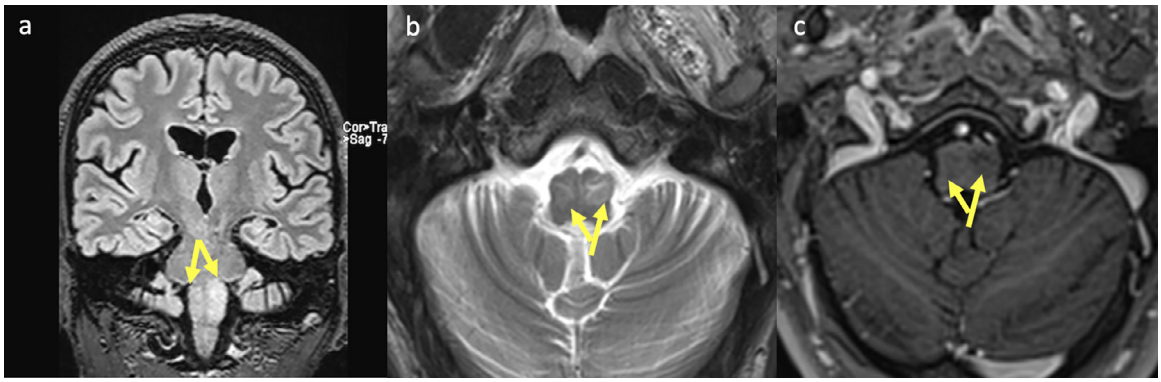

Fig. 2 – Brain-MRI images obtained more inferiorly on coronal (A) and axial (B) T2-weighted sections, and enhanced axial (C) section showed a bilateral enlargement of the anterior medulla with high signal intensity, more pronounced on the left side, non-enhanced with contrast product (Yellow arrows), corresponding to bilateral hypertrophic inferior olivary nuclei degeneration (HOD).

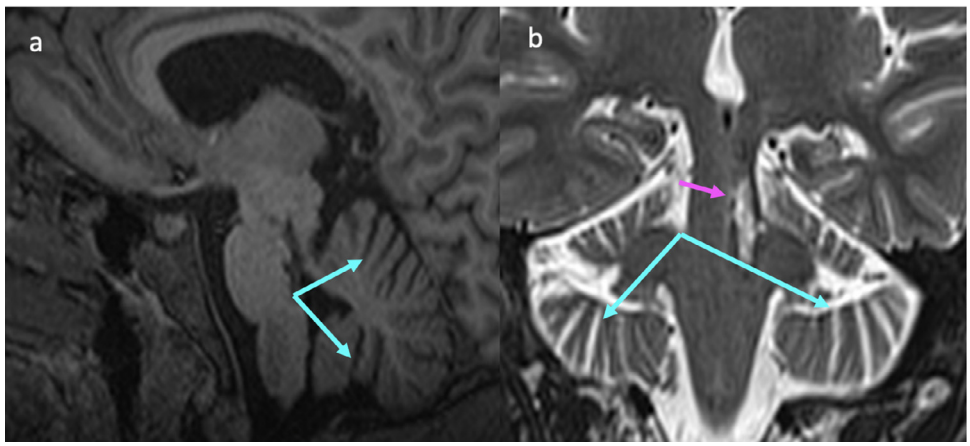

Fig. 3 – Cerebellar-MRI images on sagittal T1 (A) and coronal T2-weighted (B) sections reveal a discrete enlargement of the cerebellar cortical sulci (Blue arrows), corresponding to a cerebellar atrophy. Note the coronal section of the pontomesencephalic hemorrhagic cavernoma (Pink arrow).

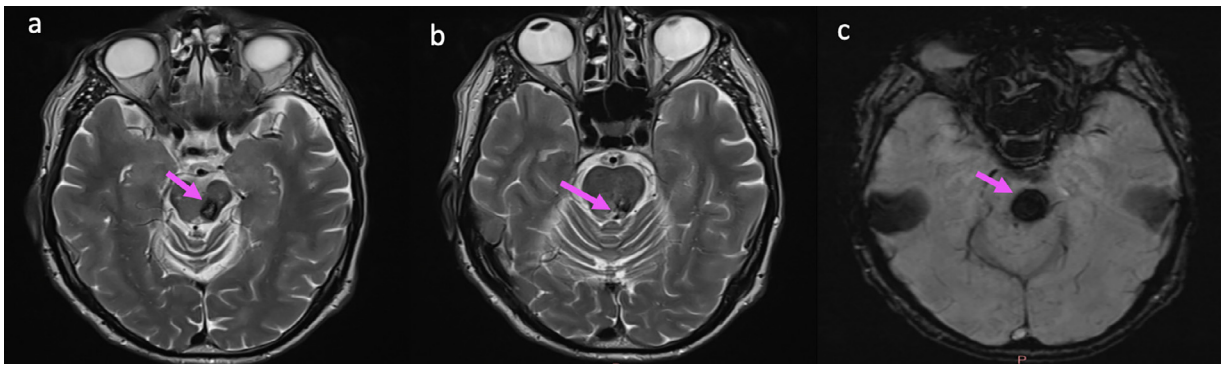

Fig. 4 – Brain MRI imaging on axial (A,B) T2-weighted section , and axial SWI (Susceptibility-Weighted Imaging) (C) , which reveals a cavernoma centered on the left tegmentum mesencephali extending to the left superior cerebellar peduncle (Pink arrow) that appeared as a heterogenous T2- low-intensity mass (A,B), with Blooming effect on (SWI) (C).

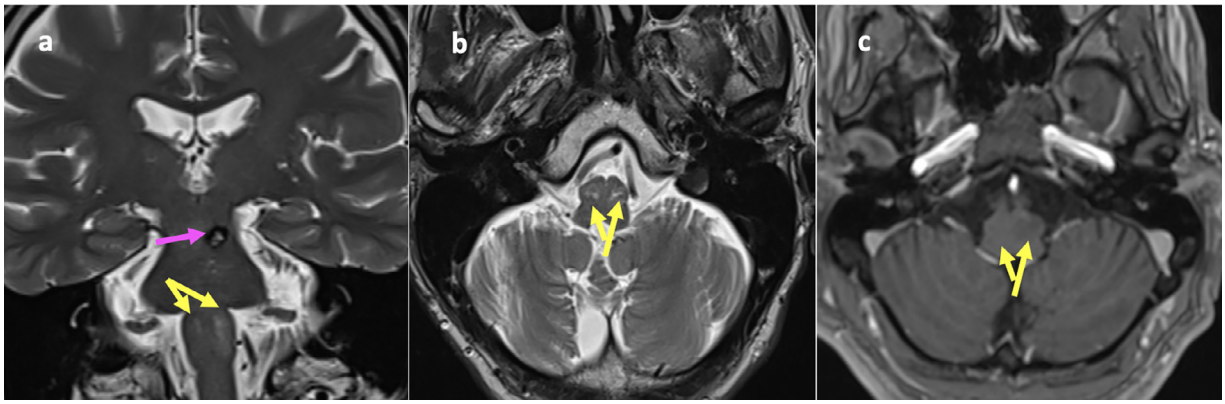

Fig. 5 – Brain-MRI images obtained more inferiorly on coronal (A) and axial (B) T2-weighted sections, and enhanced axial (C) section showed a bilateral enlargement of the olivary nuclei with high signal intensity, more pronounced on the left side, non-enhanced with contrast product (Yellow arrows), corresponding to bilateral hypertrophic olivary nuclei degeneration (HOD).

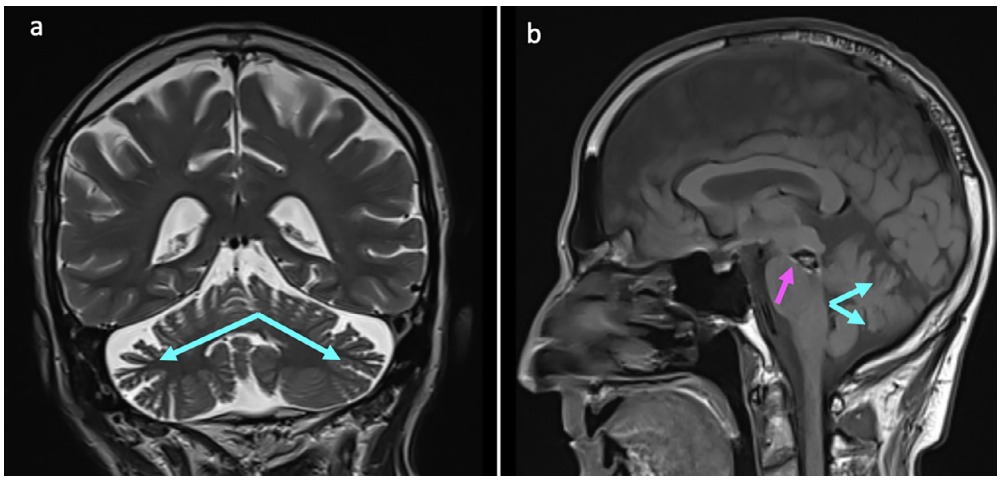

Fig. 6 – Cerebellar-MRI images on coronal T2-weighted (A) and sagittal T1-weighted (B) sections reveal an enlargement of the cerebellar cortical sulci (Blue arrows), corresponding to a cerebellar atrophy. Note the coronal section of the mesencephalic cavernoma (Pink arrow).

The loss of afferent input to ION cells results in the HOD degeneration.

In both of our reported cases, the involvement of the inferior colliculus, where fibers from the dentate nuclei decussate and project to the contralateral red nucleus and then the ipsilateral olivary nucleus (ipsilateral to the red nucleus), explains the bilateral involvement of the olivary nuclei.

HOD is considered a unique type of degeneration because it is associated with enlargement of the affected structure (the inferior olivary neurons). The olivary degeneration is initially hypertrophic, with atrophy observed only a few years later [11].

The major pathologic changes of affected olivary nuclei include vacuolar degeneration of the enlarged neurons, hypertrophy of the astrocytes, and gliosis [5].

In case of posterior pontine hematoma or hemorrhagic cavernoma, the blood products interrupt the white matter pathways between the red nucleus and the ipsilateral ION, pathway that involved in the control of fine voluntary movements. Disruption of Guillain and Mollaret triangle results in three potential forms of HOD. Ipsilateral ION involvement is the result of central tegmental tract affection by lesions targeting the brain stem tegmentum, while contralateral ION degeneration by lesions affecting the dentate nucleus or the superior cerebellar peduncle. Lastly, a paramedian pontine lesion near the superior cerebellar peduncle results bilateral ION degeneration due to simultaneous involvement of the central tegmental tract and the superior cerebellar peduncle [6] (Fig. 8).

In our patients, the predominant involvement of the left central tegmental tract explains the marked degeneration of the homolateral olivary nucleus. The extension of the lesion to the superior cerebellar peduncle and the inferior colliculus, accounts for the less pronounced degeneration of the con-

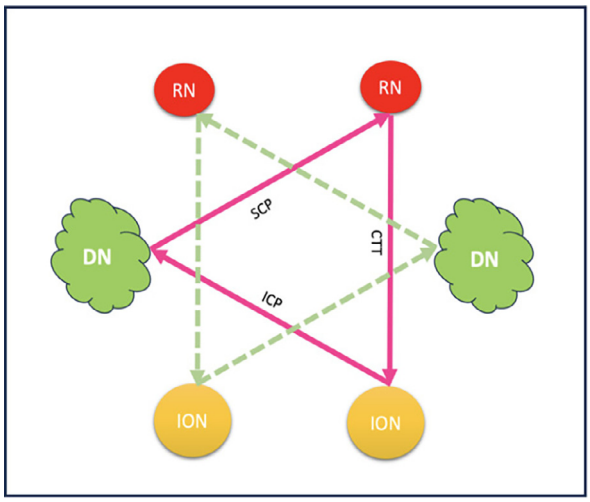

Fig. 7 – Simplified anatomy of the Guillain–Morlet triangle, Red nucleus (RN), dentate nucleus (DN), inferior olivary nucleus (ON), superior cerebellar nucleus (SCP), inferior cerebellar peduncle (ICP), central tegmental tract (CTT), Adapted from [6].

tralateral olivary nucleus. This, in turn, substantiates the bilateral olivary abnormalities observed in our patient's MRI.

Olivary hypertrophy is not seen immediately after the brainstem insult [8]. Goto et al described 6 neuropathological stages of HOD in patients after pontine hemorrhage: hypertrophy was observed initially from 3 weeks after the ictus to about 9.5 months [12]. It can be seen 5-15 months after the onset of ictus [5] and exist even 8 years later [5].

Clinically, HOD is commonly accompanied by palatal myoclonus [5]. The latter is characterized by recurrent dysrhythmic contractions of the soft palate, which are often accompanied by synchronous involuntary contractions of muscles from the branchial arches and diaphragm, tongue, or limbs [5]. Other clinical manifestations include ocular myoclonus or nystagmus, Holmes tremor, cervical muscle and diaphragm contractions, or brainstem lesion [4]. Holmes tremor is rare in HOD – 5 in the 151 HOD cases found by Wang et al. [13].

On MRI, HOD associates an enlarged ION with a proton density and T2 hypersignal without enhancement after injection of Gadolinium [2].

The high signal intensity in the inferior olivary nucleus is caused by the increased water content caused by gliosis and the structural anomalies described above [5].

The hypersignal of the ION can be observed 3 weeks after the onset of the causal lesion [14]. But it may appear later. This hypersignal then increases for a few months, until 15 months [15]. Then there is a progressive involution of the signal [3].

It is possible to observe cerebellar atrophy due to neuronal degeneration caused by the same deafferentation mechanism as that of olive degeneration. As is the case for our both patients, it can be seen as an enlargement of cerebellar cortical sulci.

Morphological MRI sequences (Proton density, T1, T2, and FLAIR) are generally sufficient to make the positive diagnosis.

Diffusion and injection of Gadolinium can help to eliminate differential diagnoses.

As a magnetic resonance imaging (MRI) technique specifically designed to study anomalies in white matter, diffusion tensor imaging with tractography enables the detection of interruptions within dentatorubral-olivary pathway [4].

The most frequent etiology of structural brainstem or cerebellar lesion is vascular and more often hemorrhagic than ischemic [16,17]. Other etiologies include brain trauma, brainstem tumors, surgical or gamma knife removal of brainstem cavernoma [18], multiple sclerosis (MS), and a broad range of other unspecific lesions [19]. It is assumed that, to be causative, this primary lesion has to be destructive, a condition that is most easily satisfied by vascular, neurosurgical, or gamma knife lesions [20].

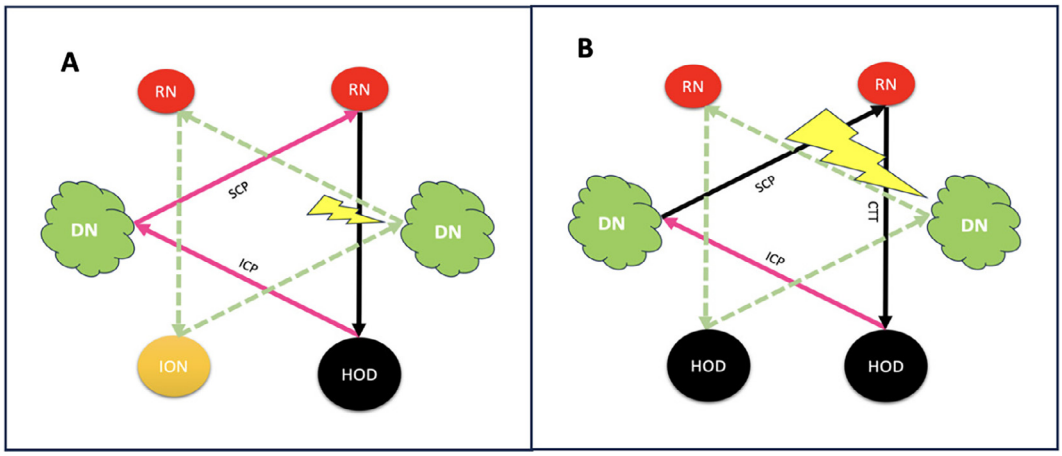

Fig. 8 – Simplified diagram of Guillain–Morlet triangle and possible patterns of hypertrophic olivary degeneration (HOD) related to location of the lesion, adapted from [6]. Red nucleus (RN), dentate nucleus (DN), inferior olivary nucleus (ON), superior cerebellar peduncle (SCP), inferior cerebellar peduncle (ICP), central tegmental tract (CTT): (A) Injury at cerebellar tegmentum involving the central tegmental tract (CTT) results in ipsilateral ION degeneration. (B) A paramedian lesion affecting both the central tegmental tract (CTT) and the superior cerebellar peduncle (SCP) results in bilateral degeneration.

Table 1 – Distinguishing Criteria for the Differential Diagnosis of Hypertrophic Olivary Degeneration.

	Clinical context	MRI Features	Associated MRI Signs
Bulbar hemorrhage	-Cardiovascular risk factors. -Acute onset of brainstem/ cervicomedullary dusfunction.	T1 hyperintensity (fresh blood). T2 hypointensity. Restricted diffusion of blood. Blooming on Susceptibility-Weighted Imaging (SWI) and T2* (gradient echo sequence). No enhacement	-Micro-bleeds. -Arteriovenous malformation (AVM) or aneurysm on MR angiography (MRA).
bulbar stroke	-Cardiovascular risk factors (atherosclerosis). -History of ischaemic cerebrovascular accidents.	T1 hypointensity (Chronic lesion) T2, FLAIR (Fluid Attenuated Inversion Recovery) hyperintensity. Restricted diffusion	-Lacunar and old infarcts. -Atrophy of the medulla oblongata and cerebellum (Chronic infarct) -Leptomeningeal or vascular enhancement. -Micro-bleeds and hemorrhagic transformation (rupture of the blood-brain barrier). -Posterior circulation large vessel (Vertebral artery) occlusion on MR angiography (MRA) : Dissection or atherosclerosis
Brainstem Trauma	-Brain trauma -Brainstem/ Cervicomedullary dysfunction.	T1 hyperintensity (fresh blood), T2 hypointensity. Blooming on SWI and T2*. Ischemic lesions (if traumatic artery dissection).	-Brain hemorrhagic contusions. -Pericerebral haematoma . -Subarachnoid hemorrhage -Vertebral artery dissection on MR angiography (MRA).
Demyelination	-Progressive demyelinating disease. -Long-standing of brainstem/ -Cervicomedullary / Cerebellar dysfunction.	-Hyperintense T2 and FLAIR demyelinating plaques. -Contrast enhancement for active lesions.	-Multifocal demyelinating lesions -Atrophy of the medulla oblongata and cerebellum.
Cervicomedullary and brainstem Tumours	-Long-standing of brainstem/ cervicomedullary dysfunction : -Hyperreflexia and cerebellar dysfunction (late in the progression of the disease.)	-Variable signal on T1, T2 and FLAIR. -Homogeneous or Heterogeneous gadolinium enhancement. -Restricted diffusion.	-Locoregional invasion with compression of the fourth ventricle and upstream hydrocephalus. -Metastasis +/-
Infection	Bacterial, viral, or fungal infection.	**Edema:** T2 hyperintensity. **Abscess:** -T1 hyointensity and T2 hyperintensity. -Restricted diffusion. -Peripheral enhancement.	-Thickening of the Leptomeninges. -Meningeal Enhancement. .Venous Sinus Thrombosis -Ventriculitis -Cerebral Edema
HOD (Hypertrophic olivary degeneration)	History of trauma, surgery or cerebrovascular accident involving the brain stem.	ION hypertrophy. T2 hyperintensity. T1 hypointensity. No restricted diffusion No enhancement, with gadolinium. No blooming on T2	-Lesion of MGT -Cerebellar atrophy (Late).

The differential diagnosis is essentially made with diseases that can cause palatal myoclonus with or without cerebellar ataxia. Palatal myoclonus can be also caused by acute lesions such as brainstem or cerebellar hemorrhage, infarction, or trauma [5]. In this case, the clinical context and imaging can eliminate these diagnoses.

HOD should not be confused with other bulbar lesions such as demyelination, tumor or infection, which also presents a high signal intensity on proton density and T2-weighted images, with possible enhancement after injection of Gadolinium. It may mimic the finding of HOD, whereas HOD never enhances and is always associated with a lesion of the Guillain-Mollaret triangle [3].

By combining the clinical context, non-enhancement after injection of contrast product and the existence of a lesion within Guillain-Mollaret triangle, we can differentiate HOD from other diagnosis. The table below elucidates the differentiation criteria among various hypertrophic olivary degenerations (Table 1).

Treatment is generally symptomatic, Therapeutic trials suggest anticonvulsants like gabapentin, levetiracetam or memantine as valuable drugs to treat eye oscillations in OPT.

Conclusion

Hypertrophic olive degeneration is a rare form of transsynaptic degeneration, which combines T2 hypersignal and hypertrophy of the inferior nucleus of the bulbar olive. It is secondary to damage to the Guillain-Mollaret triangle and can lead to palatal myoclonus. It is important to understand the mechanism by which it develops and to recognize its MRI features, so as not to confuse it with another lesion (inflam-

matory, tumoral, or vascular) of the inferior nucleus of the olive.

Patient consent

Written informed consent was obtained from both patients for the publication of these cases.

Author's contributions

All authors contributed to this work. All authors have read and approved the final version of the manuscript.

Ethical approval and informed consent

Ethics approval does not need to be obtained:

This is a case report, based on the editor Guidelines-Ethics Approval and Informed Consent Statements: Ethics committee/IRB approval is often not required.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2024.04.078.

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