Magnetic resonance imaging of hypertrophic olivary degeneration

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Abstract

Objective: To review the pathophysiologic mechanisms involved in hypertrophic olivary degeneration, with attention to epidemiological and clinical aspects and especially to imaging findings.

Material and methods: We reviewed 5 patients diagnosed with hypertrophic olivary degeneration at our center from 2010 through 2013, analyzing relevant clinical, epidemiological, and radiological findings.

Results: In all cases, a hyperintensity was seen in the inferior olivary nuclei in FLAIR and T2-weighted sequences. No signal alterations were seen on T1-weighted sequences, and no enhancement was seen after intravenous injection of contrast material. In the cases studied by diffusion-weighted imaging, no significant alterations were seen in these sequences. Olivary hypertrophy was seen in all patients except in one, in whom presumably not enough time had elapsed for hypertrophy to occur. The alterations were bilateral in two of the five cases. Only one case exhibited the typical clinical manifestations.

Conclusion: Given that patients may not present clinical manifestations that can be attributed to hypertrophic olivary degeneration, it is important to recognize the characteristic radiologic signs of this entity.

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Núcleo olivar; Núcleo rojo; Núcleo cerebeloso; Bulbo raquideo; Cerebelo

**Material y métodos:** Se revisaron 5 pacientes diagnosticados de degeneración olivar hipertrófica en nuestro centro entre los años 2010 y 2013, analizando los aspectos clínicos, epidemiológicos y radiológicos relevantes.

**Resultados:** En todos los casos se vio una hiperintensidad en los núcleos olivares inferiores en las secuencias FLAIR y T2. Las secuencias potenciadas en T1 no mostraron alteraciones de señal ni tampoco se observó realce tras inyectar contraste intravenoso. En los casos en los que se realizó una secuencia de difusión, no hubo alteraciones significativas. Salvo en un paciente, en el que presumiblemente no había pasado el tiempo necesario, en todos los restantes se vio una hiperтроfía olivar. Las alteraciones fueron bilaterales en dos de los cinco individuos. En solo un caso las manifestaciones clínicas fueron típicas.

**Conclusión:** Dado que los pacientes pueden no presentar manifestaciones clínicas atribuibles a la degeneración olivar hipertrófica, resulta importante reconocer los signos radiológicos característicos.

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**Introduction**

Hypertrophic olivary degeneration (HOD) is an uncommon pathological entity characterized by trans-synaptic degeneration secondary to lesions in the dento-rubro-olivary tract or "the Guillain–Mollaret triangle" discovered in 1931 by Guillain and Mollaret. The expression "trans-synaptic neuronal degeneration" makes reference to the alteration of a group of neurons when a destructive process interrupts the majority of its afferent impulses. The degeneration can occur in other locations yet the HOD has been considered a unique morphological type where hypertrophy of the degenerated neurons occurs. The lesions in this tract are caused most often by diseases of vascular origin (ischemic or hemorrhagic) but it can also be the cause of a trauma or a tumor or due to surgical manipulation, infections, demyelinating or degenerative diseases. A percentage of cases, which in some series is around 40%, is of unknown cause or without any visible lesions. We presented a series of five patients with hypertrophic olivary degeneration with special emphasis on the clinical and epidemiological aspects and magnetic resonance (MR) findings.

**Materials and methods**

The dento-rubro-olivary tract (Fig. 1) connects the red nucleus of the mesencephalon, the inferior olivary nucleus of the medulla oblongata and the dentate contralateral nucleus of the cerebellum. Fibers originating in the red nucleus descend through the central tegmental tract until they reach the inferior ipsilateral olivary nucleus. In turn, the olive projects fibers to the contralateral dentate nucleus through the inferior cerebellar peduncle crossing the midline at the height of the inferior olivary nucleus. To complete the triangle, efferent fibers of the dentate nucleus ascend through the superior cerebellar peduncle and they decussate until they synapse in the contralateral red nucleus. HOD is due to lesions that affect the central tegmental tract or the dento-rubral tract of the Guillain–Mollaret triangle which will cause olivary disconnection. We have reviewed the relevant clinical, epidemiological and radiological aspects of 5 patients diagnosed with HOD at our hospital from 2010 through 2013. All of them were examined through an MRI, two for the control of the underlying disease (ependymoma and pontine hemorrhage) and three because they showed clinical syndromes (cerebellar syndrome and cognitive deterioration). The studies were conducted in a Siemens MAGNETOM Symphony Maestro Class 1,5T (Siemens Medical Systems, Erlangen, Germany). In four patients FLAIR axial, axial T2-weighted sequences were acquired and axial T1-weighted sequences with and without intravenous contrast, and diffusion with apparent diffusion coefficient map.

**Figure 1** Sketch of the dento-rubro-olivary tract or "the Guillain–Mollaret triangle". 1: olivary nucleus. 2: dentate nucleus. 3: red nucleus. 4: central tegmental tract. 5: dentorubral tract. 6: dento-olivary tract.
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In the fifth patient, a cranial base MRI was performed through axial T2, high resolution axial T2 and axial and coronal T1 sequences with IV contrast. The images were reviewed paying special attention to the size and the signal of the bulbar olives and the location of the source lesion. All patients were examined by one neurologist and three of them were also seen by a neurosurgeon. They underwent a thorough physical and neurological examination and except for one case in which cognitive deterioration prevented it a correct anamnesis could be performed.

Results

The epidemiological characteristics, the clinical manifestations and the MRI findings are presented in Table 1. All

![Figure 2](image-url)  
**Figure 2** Unilateral hypertrophic olivary degeneration (left). (a) Axial T2-weighted image showing one hyperintense left bulbar olive (white arrow). (b) Axial T2-weighted image showing affectionation of the left superior cerebellar peduncle (white arrow) due to ischemic attack in the territory of the superior cerebellar artery.
patients were women and their average age was 55 years. In all cases the inferior olivary nuclei were hyperintense in the T2-weighted sequences whereas the T1-weighted sequences did not show any signal alterations or enhancement with IV contrast either. Four of the patients were examined with a diffusion sequence that was normal. Except for one case in which presumably not enough time had elapsed (Fig. 2) in all cases it was possible to see an olivary hypertrophy (Figs. 3–6). In two individuals the source lesion was located in the cerebellum (ischemic ictus and intraparenchymatose hematoma, respectively) being the olivary affection contralateral (Figs. 2 and 6). In another patient the affection was unilateral but secondary to the resection of an ependymoma of the fourth ventricle that presumably damaged the central ipsilateral tegmental tract (Fig. 4). The alterations were bilateral in two patients. One of them suffered a pontine hematoma while in the other the cause was unknown (Figs. 3 and 5). In one case (patient 4) a control MRI was performed at 5 months that did not show any significant changes with respect to the MRI that diagnosed the HOD. Only in one individual the clinical manifestations were typical (rubral tremor).

**Discussion**

There are three HOD patterns depending on the tract affected by the primary lesion. In the ipsilateral olivary hypertrophy, the primary lesion affects exclusively the central tegmental tract. The contralateral olivary hypertrophy occurs when the primary lesion is located in the cerebellum, either in the dentate nucleus, or in the superior cerebellar peduncle. The olivary hypertrophy is bilateral if both the central tegmental tract and the dento-rubral tract are damaged, or if both dento-rubral tracts are damaged in the decussation. In two cases of our series the lesion was located in the cerebellum being the HOD contralateral. In another the affection was unilateral but secondary to the resection of an ependymoma of the fourth ventricle, which presumably damaged the ipsilateral central tegmental tract. However in our study the cerebrovascular disease was the most common cause which coincides with what has been published.

The main pathologic characteristic of HOD is hypertrophy in response to a lesion in the dento-rubro-olivary tract. The mechanism proposed to explain it is an atypical form of trans-synaptic degeneration. It is atypical because the loss of functional synapse in HOD leads to neuronal hypertrophy with cytoplasmatic vacuolar degeneration, astrocytosis and glial hypertrophy as opposed to the best known Wallerian degeneration which implies degenerative changes in

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**Figure 3** Bilateral hypertrophic olivary degeneration. Axial T2-weighted image showing two (2) hyperintense enlarged bulbar olives (double white arrow).

**Figure 4** Unilateral hypertrophic olivary degeneration. (a) Axial T2-weighted image showing one hyperintense enlarged right bulbar olive (white arrow). (b) Axial T1-weighted image with IV contrast showing a fourth ventricle ependymoma before surgical exeresis (white arrow).
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the distal portion of the axon. Based on postmortem pathological studies by Goto and Kaneko, six HOD stages are described: (1) there are no noticable changes during the first 24h; (2) the olivary amiculum (white matter capsule making up the olive periphery) degenerates between the second and seventh day; (3) neuronal hypertrophy in approximately three weeks; (4) the maximum period of olivary enlargement secondary to the hypertrophy both of the neurons and of the astrocytes, after 8.5 months approximately; (5) pseudo-hypertrophy in which the neurons degenerate but the large gemistocytic astrocytes prevail; (6) atrophy of the olivary nucleus several years after the lesion.

According to Goyal et al., hyperintensity shows in the T2-weighted sequences during the first month after the lesion persisting for several years (at least 3 or 4) or else it can be permanent. Olivary hypertrophy usually appears 10–18 months after the lesion to disappear 4 years later. Likewise three evolutionary stages of the inferior olivary nucleus were established in the MRI sequences. The first stage is characterized by hyperintensity in T2 sequences without olivary hypertrophy in the first six months. In the second one both appear and it finishes when the hypertrophy is resolved, that is, 3–4 years after the lesion. In the third stage hypertrophy starts to disappear and is characterized by T2-weighted hyperintensity only and usually remains indefinitely. All of our patients, except for one who belonged presumably in the first stage would belong to the second evolutionary stage.

Figure 5 Bilateral hypertrophic olivary degeneration due to pontine hematoma maybe due to lesion of the bilateral central tegmental tract and possibly due to lesion of the bilateral dento-rubral tract. (a) Axial T2-weighted image showing two (2) hyperintense and enlarged left bulbar olives (double white arrow). (b) Axial T2-weighted image showing one hyperintense lesion with a hypointense halo (hemosyderine) corresponding to the pontine hematoma (white arrow).

Figure 6 Unilateral hypertrophic olivary degeneration (right) due to left cerebellous hematoma due to lesion of the left dentate nuclei and dento-rubral tract. (a) Axial T2-weighted image showing one hyperintense enlarged right bulbar olive (white arrow) and one hematoma in the left cerebellous hemisphere (black arrow). (b) Axial FLAIR T2-weighted image showing one hyperintense enlarged bulbar olive (white arrow).
Other sequences and MRI techniques have also proven useful to diagnose this entity. The magnetic susceptibility sequences allow us to detect the degeneration of the red nucleus in HOD patients.\(^7\) In MRI studies of cerebral perfusion it has been possible to describe the hyperfusion of the hypertrophic inferior olivary nuclei with an increase of both the brain blood volume (BBV) and the brain blood flow.\(^8\) Ultimately tensor diffusion MRI studies have described an increase of radial diffusivity, which represents demyelination, and an increase of the axial one that translates neuronal hypertrophy.\(^9\) These parameters can reflect temporal–spatial evolution of HOD-associated transneuronal degeneration in a consistent manner with anatomic-pathological stages.

The clinical manifestations associated to this entity include, among others, palatal and ocular myoclonus, and dentorubral or Holmes’ tremor. The oscillations of the oculo-palatal tremor originate in the hypertrophic inferior olive and they are amplified by cerebellum.\(^7\) In our series however, we did not see palatal myoclonus, and only one patient presented with a finding typical of the disease–dentorubral tremor. This may be due to the fact that palatal myoclonus, the main clinical finding in this disease, and other brainstem nucleus-dependent myoclonus are very variable.\(^4\)\(^,\)\(^5\)\(^,\)\(^7\)\(^,\)\(^8\)\(^,\)\(^15\) Thus in a series of 29 patients with DOH confirmed anatomic-pathologically only two individuals had palatal tremor.\(^12\)

Differential diagnosis is considered with the diseases that can manifest with hyperintensity of the inferior olivary nucleus in T2-weighted sequences, including tumors (astrocytoma, metastasis and lymphoma), ischemia, demyelinating, infectious (tuberculosis, HIV and rhomboencephalitis) and inflammatory diseases (sarcoidosis). Tumor and infectious lesions differ from HOD in the contrast uptake. Although some infarctions can enlarge the olive, most affect the posterolateral bulb. The decrease in size in subsequent examinations allows us to rule out several diseases. But the main diagnostic key is affection of one or both inferior olivary nuclei with a lesion in the ipsilateral tegmental tract, the ipsilateral red nucleus, the contralateral dentate nucleus or the contralateral superior cerebellar peduncle.\(^7\)\(^,\)\(^10\)\(^,\)\(^15\)

In sum hyperintensity in FLAIR and T2 and the size increase of the inferior olivary nucleus associated with a lesion affecting the Guillain–Mollaret triangle, are the key characteristics to diagnose HOD. The patients may not show the typical clinical manifestations so it is important to recognize the characteristic radiologic signs.

### Ethical responsibilities

**Protection of people and animals.** The authors declare that no experiments with human beings or animals have been performed while conducting this investigation.

**Data confidentiality.** The authors declare that in this article there are no data from patients.

**Right to privacy and informed consent.** The authors declare that in this article there are no data from patients.

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### Conflict of interests

The authors declare no conflict of interests.

### References

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