DOI: https://doi.org/10.17650/1683-3295-2024-26-4-48-53

HYPERTROPHIC OLIVARY DEGENERATION IN THE LATE PERIOD AFTER RESECTION OF CAVERNOUS ANGIOMAS OF THE BRAIN STEM

I.V. Gubareva[1], A.V. Dubovoy[2]

[1]Sochi City Hospital, Ministry of Health of the Krasnodar Territory; 1 Tuapsinskaya St., Sochi 354057, Russia;
[2]Federal Center of Neurosurgery, Ministry of Health of Russia (Novosibirsk); 132/1 Nemirovicha-Danchenko St., Novosibirsk 630087, Russia

Contacts: Inga Vladimirovna Gubareva *inga1gubareva@gmail.com*

Hypertrophic olivary degeneration is a rare form of transsynaptic neuronal degeneration caused by damage to the dentato-rubro-olivary pathway also known as the Guillain–Mollaret triangle. In magnetic resonance diagnostics, this is manifested by increasing the size and hyperintensity of the inferior olivary nucleus in T2-weighted images. The article presents two clinical cases of hypertrophic olivary degeneration, which was caused by cavernous angiomas with hemorrhage in the brainstem. Knowledge about this pathological change in the olivary nuclei of the medulla oblongata and a correct diagnosis help to avoid wrong diagnostic and their consequences.

Keywords: hypertrophic olivary degeneration, cavernous angioma, stem hemorrhage, Guillain–Mollaret triangle

For citation: Gubareva I.V., Dubovoy A.V. Hypertrophic olivary degeneration in the late period after resection of cavernous angiomas of the brain stem. Neyrokhirurgiya = Russian Journal of Neurosurgery 2024;26(4):48–53. (In Russ.).
DOI: https://doi.org/10.17650/1683-3295-2024-26-4-48-53

BACKGROUND

Hypertrophic olivary degeneration (HOD) (synonyms: inferior olivary nucleus degeneration, hypertrophic degeneration of the olives, inferior olivary nucleus pseudohypertrophy) is a rare transsynaptic neuronal degeneration caused by injuries of the dentato-rubro-olivary pathway (anatomical Guillain–Mollaret triangle or myoclonic triangle (Fig. 1)). In studies using magnetic resonance imaging (MRI), HOD is identified through increased size and hyperintensity of the inferior olivary nucleus on T2-weghted images. Anatomical pathology is presented as increased volume of the inferior olivary nuclei due to cytoplasmic vacuolar dystrophy and increased number of astrocytes [1, 2].

HOD was first described in 1887 by a German neurologist H. Oppenheim who observed pathological enlargement of the inferior olivary nuclei in pathoanatomical studies. In 1931, G. Guillain and P. Mollaret discovered the dento-rubro-olivary pathway [3].

The causes of HOD include traumatic brain injury, consequences of surgical intervention, cerebral infarction, hemorrhage, cavernous malformations, space-occupying cerebral lesions (astrocytoma, metastatic lesions, lymphoma), demyelination of the brainstem, infectious and inflammatory processes, genetic abnormalities of the nervous system (Wilson's disease).

Clinical manifestations include involuntary muscle movements dependent on the cranial nerve (CN) nuclei in the brainstem; palatal tremor/myoclonus (rhythmic involuntary movements of the soft palate, uvula, pharynx and larynx; in severe cases, myoclonus of the diaphragm can develop); eye myoclonus; torsion nystagmus, dysarthria, ataxia; Holmes tremor (dentatorubral tremor, postural and dynamic tremor of the upper limbs) [4].

The pathological process is divided into 6 phases [2, 5]:
1) in the first 24 hours, olives do not change;
2) degeneration of the amiculum of olive 2–7 days later;
3) hypertrophy of the olives after 3 weeks;
4) maximal enlargement of the olives after 8.5 months;
5) pseudohypertrophy of the olives after 9.5 months;
6) atrophy of the olives after 3–4 years.

Macroscopically, HOD is characterized by local edema of the inferior olivary nucleus; in unilateral HOD, asymmetrical enlargement of the anterior medulla oblongata, paleness in the contralateral dentate body, atrophy of the contralateral cerebellar cortex are observed; in bilateral HOD, left-right asymmetry is absent.

Microscopically, changes in the inferior olivary nucleus affected by hypertrophic degeneration are observed (hypertrophy and thickening of axons, vacuolization of neurons, fibrillary gliosis, demyelination and astrocytic

proliferation of the white matter); in the contralateral cerebellar hemisphere, the number of Purkinje cells decreases; contralateral dentate body shrinks.

The literature describes a number of clinical observations with diagnosed HOD. HOD can develop 2 years after severe traumatic brain injury [1], as well as in patients with SANDO syndrome, Wilson's disease [1, 5].

The best visualization technique for this pathology is MRI (T2-weighted images in the coronal and sagittal projections). In T1-weighted images (acute phase), the inferior olivary nucleus is normal, primary injury of the brainstem is visible. After HOD development, enlargement of the inferior olivary nucleus is observed, the signal changes from isointense to slightly hypointense relative to the grey matter. The signal from the olives can slightly increase, residual lesion of the primary injury is also visible.

In T2-weighted images, 3 HOD stages are identified: 1) increased signal intensity without hypertrophy of the inferior olivary nucleus (in the first 6 months since the start of the disease); 2) increased signal intensity and hypertrophy of the inferior olivary nucleus (between 6 months and 3–4 years); 3) increased signal intensity only in the inferior olivary nucleus (is observed after resolution of hypertrophy and can persist indefinitely).

Magnetic resonance tractography: German authors propose diffuse-tensor imaging with tractography to identify injuries of the functional pathway along the tracts comprising the Guillain–Mollaret triangle [6].

Computed tomography allows to see the primary injury (for example, hemorrhage) in the midbrain tegmentum; HOD usually is not visualized.

Differential diagnosis of HOD includes neoplasms (astrocytoma, metastases, lymphoma), infections and inflammatory processes (tuberculosis, human immunodeficiency virus (HIV), sarcoidosis, rhombencephalitis), multiple sclerosis, ischemia [7, 8].

If primary injury is limited by the central tegmental tract, olivary degeneration is ipsilateral. If the brainstem and cerebellum are injured, degeneration is bilateral [2, 5].

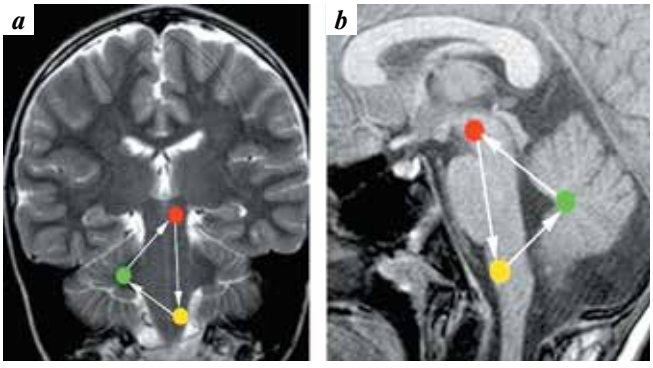

Fig. 1. *Coronal (a) and sagittal (b) sections of the midbrain, pons, and medulla oblongata. The triangle of Guillain–Mollaret is formed by the ipsilateral inferior olivary nucleus (yellow), dentate body of the contralateral cerebellar hemisphere (green), and ipsilateral red nucleus (red)*

Aim of this study is to investigate the current state of the HOD problem (causes, diagnosis and treatment), as well as presentation of 2 clinical observations from the practice of the Federal Center of Neurosurgery (Novosibirsk).

CLINICAL CASE 1

Female patient K., *born in 1990, was admitted to the Neurosurgery Division in April of 2020 with diagnosis of cavernous angioma of the pons with hemorrhages in January of 2018 and December of 2019; supranuclear palsy of the cranial nerve pair VI on the left. At the time of admittance, clinical symptoms included diplopia, stocking-glove neuropathy in both hands, instability in the Romberg's pose (Fig. 2).*

MRI of the brain showed cavernous angioma of the pons near the pontomedullary junction located centrally.

Surgery was performed consisting of midline suboccipital craniotomy, resection of cavernous angioma of the pons using bilateral telovelar approach through the floor of the rhomboid fossa along the midline. In the postoperative period, symptoms from the cranial nuclei increased in the form of development of bilateral internuclear ophthalmoplegia manifesting through horizontal gaze palsy. Additionally, sensory ataxia in the right limbs, hemihypesthesia on the right developed.

The patient was discharged on day 13 after surgery with partial regression of the symptoms which allowed her to live independently (modified Rankin scale (mRS) score 1). MRI performed in the early postoperative period showed total resection of cavernous angioma, no hemorrhagic or ischemic foci (Fig. 3).

Control MRI performed 1 year after surgery showed left-sided hypertrophy of the olive of the medulla oblongata (Fig. 4).

At the control examination 1 year after surgery, the patient was able to operate in everyday life, returned to her previous job; she underwent 2 surgeries to correct strabismus; persisting neurological symptoms include moderate sensory ataxia in the right upper limb, mRS score 1.

CLINICAL CASE 2

Female patient Ya., *born in 1982, was admitted in August of 2020 with a diagnosis of cavernous angiomas of the*

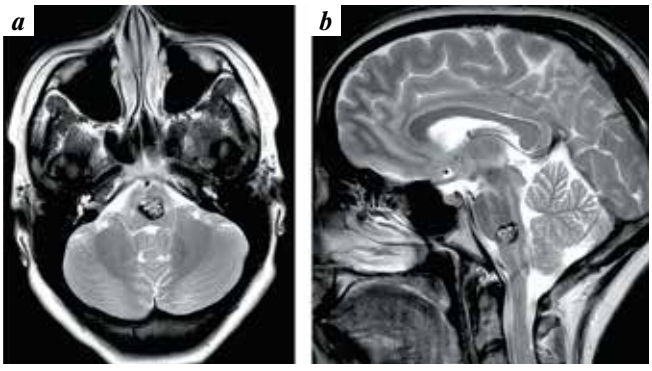

Fig. 2. *Brain magnetic resonance images of female patient K.: coronal (a) and sagittal (b) projections. Cavernous angioma of the pons Varolii*

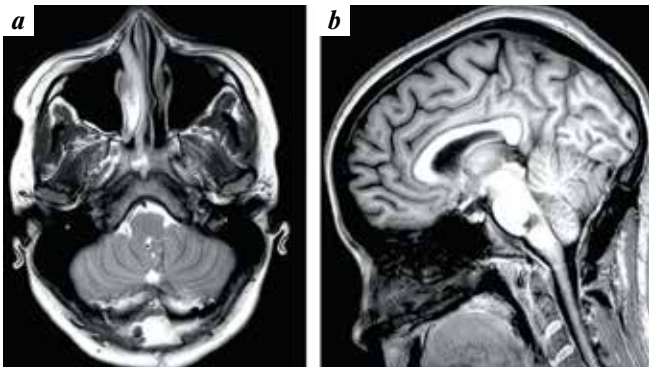

Fig. 3. *Brain magnetic resonance images of female patient K. in the early postoperative period: coronal (a) and sagittal (b) projections. Cavernous angioma was resected totally, no hemorrhagic or ischemic lesions*

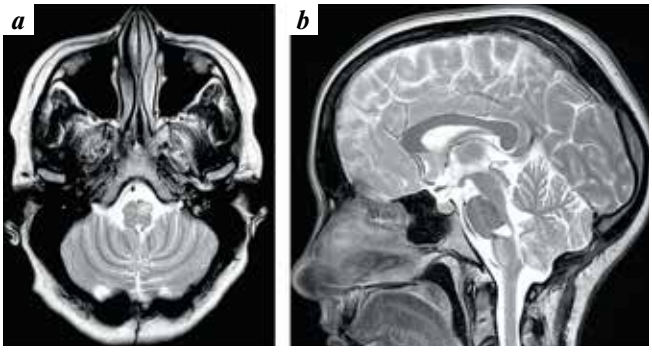

Fig. 4. *Brain magnetic resonance images of female patient K. one year after surgery: coronal (a) and sagittal (b) projections. Left-sided hypertrophy of the olivary body*

pulvinaria and corpora quadrigemina on the left with hemorrhages in May and June of 2020 (from cavernoma of the corpora quadrigemina). At admittance, gross vestibular ataxia, diplopia due to supranuclear palsy of the cranial nerve pair VI on the left were observed (Fig. 5).

In the hospital at the place of living in July of 2020, endoscopic perforation of the floor of the 3rd ventricle was performed to treat worsening obstructive hydrocephalus. supranuclear palsy of the facial nerve on the left (grade I per the House – Brackmann scale), hypesthesia in the face on the right and on the lateral surface of the tongue on the right, instability in the Romberg's pose were observed.

Surgical treatment was performed consisting of osteoplastic left-sided parasagittal craniotomy in the occipital region, resection of the cavernous malformations of the midbrain and thalamus through transtentorial approach. In the early postoperative period, symptoms worsened in the form of development of supranuclear palsy of the facial nerve on the right (grade V per the House – Brackmann scale), bilateral upward gaze palsy, paresis of the oculomotor nerve on the left, cranial nerve pairs VI and IV on the right, supranuclear palsy of the hypoglossal nerve on the right, right-sided hemiplegia, abnormalities in all types of sensitivity on the right. The patient underwent tracheostomy, nutrition was given through nasogastric tube, a week later gastrostomy was installed, mRS score 5. Control MRI did not show olivary degeneration, and no hemorrhage or ischemia (Fig. 6).

In the long-term postoperative period, partial regress of the neurologic symptoms was observed. The patient underwent decannulation; nutrition was taken independently through the mouth; right-sided hemiplegia, abnormal oculomotor function (cranial nerve pair III on the left, pairs IV and VI on the right) persisted; right-sided prosoparesis severity decreased to grade III per the House–Brackmann scale. The patient required nursing care, mRS score 4. Control MRI performed a year after surgery showed bilateral HOD, primarily on the left (Fig. 7).

DISCUSSION

In 2016, A. Elnekiedy et al. described cases of 6 patients (5 men and 1 woman aged between 39 and 69 years) with recently developed neurologic symptoms which could not be explained by primary stroke. In the 6 examined patients, variable old strokes including hematomas (1 patient), old infarctions (3 patients) and hemorrhagic vascular malformation (2 patients) involving afferent components of the Guillain–Mollaret triangle were observed [9].

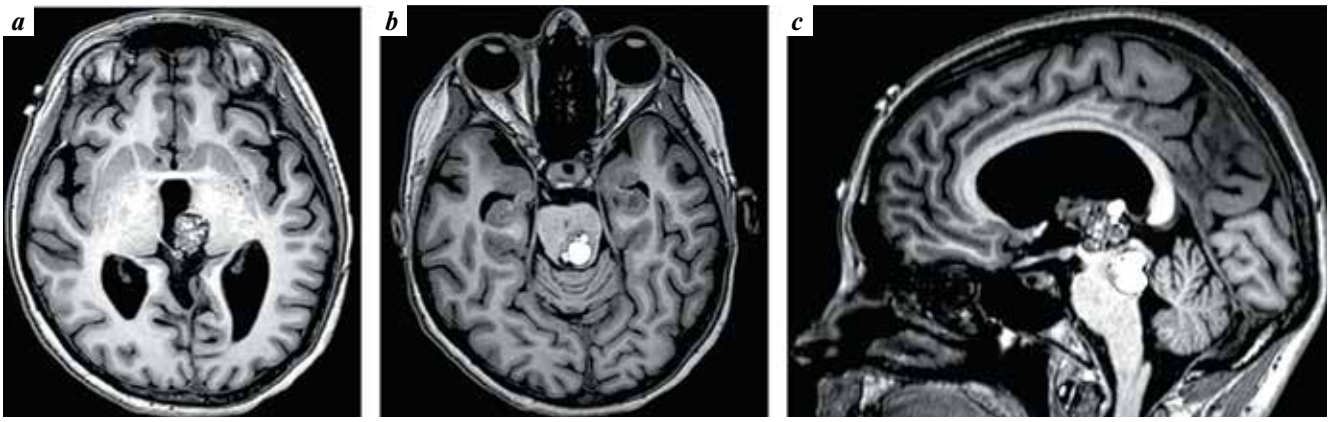

Fig. 5. *Brain magnetic resonance images of female patient Ya.: coronal (a, b) and sagittal (c) projections. Cavernous angiomas of the pulvinar nuclei and corpora quadrigemina on the left*

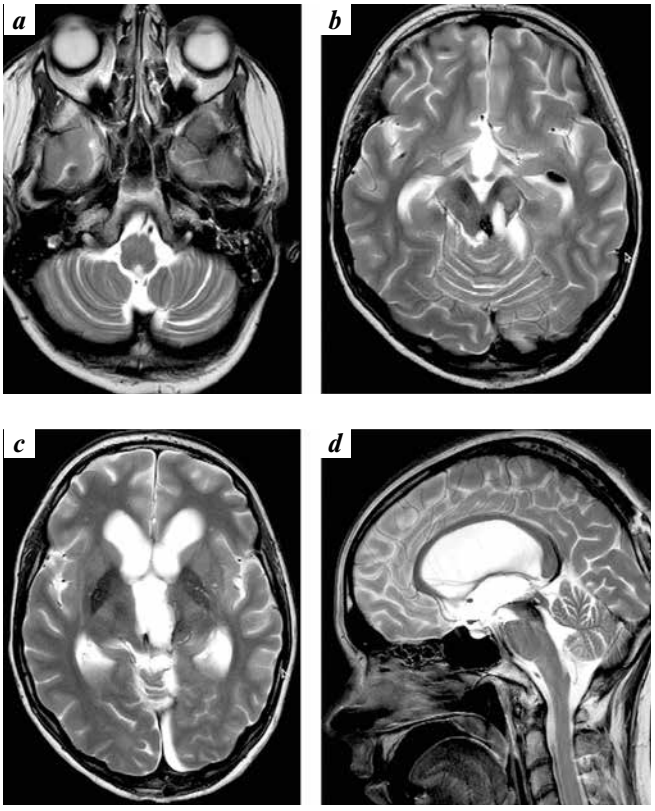

Fig. 6. *Brain magnetic resonance images of female patient Ya. immediately after surgery: coronal (a–c) and sagittal (d) projections. Degeneration of the olivary bodies, no signs of hemorrhage and ischemia*

In an article by E.Y. K. Tsui et al. from 1999, a clinical case of HOD development in a 43-year-old woman due to cavernous angioma with hemorrhage in the pons and middle cerebellar peduncles, palsy of the cranial nerve pairs VI and VII on the right, mild right-sided hemiparesis was described. Seven months after surgery, MRI showed bilateral HOD [10].

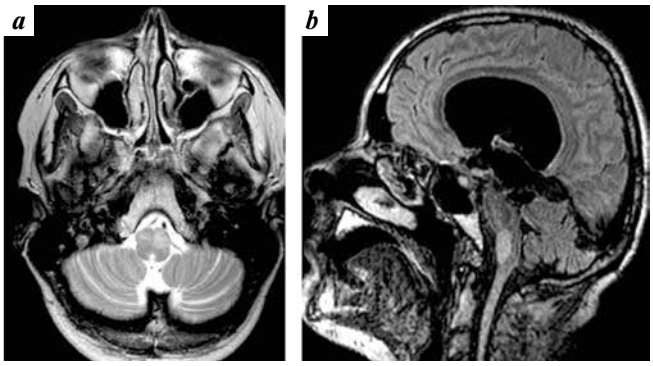

Fig. 7. *Brain magnetic resonance images of female patient Ya. in the long-term postoperative period: coronal (a) and sagittal (b) projections. Hypertrophic olivary degeneration on 2 sides, primarily on the left*

In 2018, S. Sato et al. reported 2 HOD cases in patients with diffuse large B cell lymphoma who underwent surgical treatment, chemo- and radiotherapy due to this disease without significant side effects. Both patients developed HOD (on days 26 and 166) [11].

Literature also described 6 cases of HOD development due to toxoplasmosis caused by HIV infection [12].

CONCLUSION

During literature review, we found descriptions of HOD developing 2 years after traumatic brain injury, hemorrhagic stroke, including hemorrhages from cavernous angiomas. Our own observations presented here are interesting because these changes (HOD) developed after surgical treatment of vascular malformations located in the brainstem and cerebellum including the Guillain–Mollaret triangle. Presence of vascular malformations inside this triangle allows to assume HOD development in the long-term postoperative period. Knowing the locations of conduction tracts comprising the Guillain–Mollaret triangle, a surgeon can plan approach preserving all the structures of this anatomical part to prevent HOD development.

REFERENCES

1. Konakova T.A., Zakharova N.E., Serkov S.V. et al. Magnetic resonance imaging in diagnosis of hypertrophic olivary degeneration (case reports and literature review). Radiologiya – Praktika = Radiology – Practice 2020;(2):46–58. (In Russ.)
2. Osborn A.G., Zaltsman K.L., Zaveri M.D. Radiation diagnostics. The brain. 3rd edn. Transl. from Engl. Moscow: Izd-vo Panfilova, 2018. Pp. 982–985. (In Russ.).
3. Diehl G.E., Wilmes E. [Etiology and clinical aspects of palatal myoclonus (In German)]. Laryngorhinootologie 1990;69(7):369–72. DOI: 10.1055/s-2007-998210
4. Uchevatkin A.A., Lisachenko I.V., Smagin S.S. et al. Hypertrophic degeneration of olives after bleeding in the brain stem (case report). Meditsinskaya vizualizatsiya = Medical Vizualization 2013;5:56–61. (In Russ.).
5. Suslin A.S., Seliverstov Yu.A., Kremneva E.I., Krotenkova M.V. Bilateral hypertrophic olivary degeneration in genetic neurological disordes. Annaly klinicheskoy i eksperimentalnoy nevrologii = Annals of Clinical and Experimental Neurology 2020;14(3):82–7. (In Russ.). DOI: 10.25692/ACEN.2020.3.11
6. Schaller-Paule M.A., Steidl E., Shrestha M. et al. Multicenter prospective analysis of hypertrophic olivary degeneration following infratentorial stroke (HOD-IS): evaluation of disease epidemiology, clinical presentation, and MR-imaging aspects. Front Neurol 2021;12:675123. DOI: 10.3389/fneur.2021.675123
7. Sánchez Hernández J., Paniagua Escudero J.C., Carreño Morán P., Asensio Calle J.F. Degeneración hipertrófica de la oliva por lesión del triángulo de Guillain-Mollaret. Presentación de 2 casos. Neurología 2013;28(1):59–61.
8. Asal N., Yılmaz Ö., Turan A. et al. Hypertrophic olivary degeneration after pontine hemorrhage. Neuroradiology 2012;54(4):413–5. DOI: 10.1007/s00234-011-0897-4

9. Elnekiedy A., Naguib N., Hamed W. et al. MRI and neurological presentation of hypertrophic olivary degeneration. Egypt J Radiol Nucl Med 2016;47(3):1019–29. DOI: 10.1016/j.ejrnm.2016.04.019
10. Tsui E.Y.K., Cheung Y.K., Mok C.K. et al. Hypertrophic olivary degeneration following surgical excision of brainstem cavernous hemangioma: a case report. Clin Imaging 1999;23(4):215–7. DOI: 10.1016/s0899-7071(99)00147-3
11. Sato S., Shibahara I., Inoue Y. et al. New radiological findings of hypertrophic olivary degeneration in two patients with Brainstem lymphoma. World Neurosurg 2018;123:464-68.e1. DOI: 10.1016/j.wneu.2018.11.161
12. Sabat S., Mannering N., Agarwal A. Hypertrophic olivary degeneration: case series and review of literature. J Neurol Sci 2016;370:180–6. DOI: 10.1016/j.jns.2016.09.055

Authors' contributions
I.V. Gubareva: data collection for analysis, analysis of the data obtained, patient monitoring, literature review on the topic of the article, writing the text of the article;
A.V. Dubovoy: performing surgical treatment, patients monitoring, data collection for analysis, analysis of the data obtained, literature review on the topic of the article, article writing.

ORCID of authors
I.V. Gubareva: https://orcid.org/0000-0001-5263-285X
A.V. Dubovoy: https://orcid.org/0000-0002-0927-2841

Conflict of interest. The authors declare no conflict of interest.

Funding. The study was performed without external funding.

Compliance with patient rights. The patients gave informed consents to the publication of their data.

Article submitted: 29.04.2022. **Accepted for publication:** 05.06.2024. **Published online:** 27.12.2024.