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Collision in the inferior olive: hypertrophic olivary degeneration complicated by radiation necrosis in brainstem primitive neuroendocrine tumor

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Abstract

Hypertrophic olivary degeneration (HOD) is caused by disruption of the triangle of Guillain and Mollaret. We describe a child with a primitive neuroendocrine tumor who developed an expansile nonenhancing lesion in the olive after surgery and radiation therapy. Diffusion tensor imaging and tractography showed disruption of the central tegmental tract consistent with HOD. Subsequent transient enhancement of the olive was consistent with early radiation injury. Knowledge of coexisting complications such as HOD and radiation injury is essential for proper management.

Keywords

Hypertrophic olivary degeneration; Primitive neuroendocrine tumor; Diffusion tensor imaging; Radiation injury

1. Introduction

Hypertrophic olivary degeneration (HOD) is a unique phenomenon caused by disruption of the triangle of Guillain and Mollaret [1], which connects the red nucleus, inferior olivary nucleus, and contralateral dentate nucleus. Injury to the afferent limbs causes transsynaptic degeneration of the inferior olive with hypertrophic neuronal swelling and vacuolation [2,3], rather than the atrophy usually observed after neuronal injury. MRI shows increased olive signal on T2-weighted images as early as 1 month after injury that may persist for many

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years [4]. Hypertrophy appears at about the same time and resolves after several years [5]. HOD is most common after brainstem or cerebellar hemorrhage. We report a case of HOD in a child with a brainstem primitive neuroendocrine tumor (PNET) after surgery and radiation therapy (RT), whose course was further complicated by early radiation necrosis.

2. Case report

A 4-year-old girl presented with new onset of falls, asymmetric gait, right gaze palsy, and left eye drooping. Imaging revealed a dorsally exophytic, well-circumscribed, expansile nonenhancing T2 hyperintense mass lesion in the right pons (Fig. 1). She experienced progressive left-sided weakness and ataxia before undergoing subtotal resection of 85% of the tumor. Pathology revealed a PNET with abundant neuropil and true rosettes. The patient underwent external beam RT with the craniospinal axis receiving 2340 cGy in 13 fractions —although treated as high risk due to the residual tumor, the standard 3600 cGy dose was reduced due to her young age and lack of disseminated tumor. The brainstem including the inferior olive was boosted with 3420 cGy in 18 fractions to a total dose of 5760 cGy. Concurrent chemotherapy consisted of daily carboplatin as a radio-sensitizer and weekly vincristine, and adjuvant chemotherapy of cisplatin and cyclophosphamide.

MRI performed 1 month after completion of RT revealed a surgical cavity in the dorsal right pons medial to the brachium pontis and stable mild adjacent nonenhancing tumor. A new separate expansile T2 hyperintense lesion was found in the ventral right medulla in the inferior olive. This lesion was not diffusion restricted, excluding an infarct. This lesion was nonenhancing but thought not to represent tumor that was also nonenhancing, because the lesion was discontinuous from the tumor. As the surgical cavity extended through the region of the medial and dorsal longitudinal fasciculi into the medial lemniscus and central tegmental tract, the new ipsilateral ventral midbrain lesion was postulated to represent HOD from the interruption of the central tegmental tract.

Diffusion tensor imaging (DTI) was also acquired using a spin-echo echo-planar sequence on a 1.5-T magnet (Signa Excite, GE Healthcare, Waukesha, WI, USA) in 15 directions with TR/TE of 11,000/108 ms, matrix of 128×128, in-plane resolution of 1.88×1.88 mm, slice thickness of 3 mm, b value of 1000 s/mm², and NEX of 1. Tractography was performed using DTI Studio v. 3.0.3 (H. Jiang and S. Mori, Johns Hopkins University, Baltimore, MD, USA). All possible tracts in the brain were reconstructed using the brute force technique and the fiber assignment by continuous tracking algorithm [6]. Regions of interest were placed in the red nuclei and inferior olives to segment the bilateral central tegmental tracts. The directionally encoded color fractional anisotropy maps and tractography demonstrated discontinuity of the ipsilateral central tegmental tract at the level of the surgical cavity (Fig. 2).

Three months later, the patient developed new ill-defined hyperintense changes in the pons and medulla and new patchy enhancement in the medulla. Both these changes involved the inferior olive; the enhancement occurred in the inferior olive only (Fig. 3). Because the patient remained asymptomatic, and the original tumor had been nonenhancing, the new signal changes and enhancement were postulated to represent early radiation injury. Another

2 months later, there was complete resolution of these new T2 hyperintense changes and enhancement, with residual expansile T2 hyperintensity of the inferior olive stable from the initial post-RT MRI. This was consistent with resolution of early radiation injury, and stable underlying HOD. The patient is doing well now 6 months after completion of RT. No myoclonus or palatal tremor was found during the patient's course.

3. Discussion

Demonstration of an enlarged inferior olive with increased T2 hyperintense signal and no enhancement or diffusion restriction is usually diagnostic for HOD, particularly when the evolution of findings follows the typical course and an inciting lesion(s) is found in the triangle of Guillain and Mollaret [1]. We report a case of HOD after resection of a brainstem PNET and radiation therapy. We postulate that the HOD was caused by surgical disruption of the central tegmental tract that connects the red nucleus and the inferior olive. Other investigators have also reported development of HOD after surgery [7,8]. RT may have played a contributory role, as HOD has been described after targeted radiosurgery [9], although a pure radiation effect is thought unlikely, as are direct effects on the triangle from the tumor itself or from chemotherapy.

The patient's course was further complicated by early radiation injury of the medulla at 3 months that spontaneously resolved by 6 months. Enhancement has not been described in any stage of HOD. These signal changes and enhancement are not likely to represent tumor, since they developed then resolved during the same course of adjuvant chemotherapy. A recent review described the risk of radiation injury after irradiation as small with doses 5400 cGy to the entire brainstem or 5900 cGy to the partial brainstem, but markedly increased with doses >6400 cGy [10]. The poor survival of most patients with brainstem tumors may inflate the apparent safety of the reported brainstem doses. The patient's enhancement was limited to the inferior olive—it is unclear whether this was incidental, or whether areas of neuronal degeneration are more susceptible to radiation injury and blood–brain barrier disruption. Further work is necessary to better understand the maximum tolerable doses in the brainstem and to optimize tumor volumes and fractionation schedules.

Despite the well-described conventional MRI characteristics of HOD, few descriptions of DTI exist in the literature [11,12]. DTI and tractography of the central tegmental tract in this case showed disruption of the tract ipsilateral to the abnormal olive and supported the mechanism and diagnosis of HOD rather than tumor progression.

In conclusion, we report a case of HOD in a child with a brainstem PNET, whose course was complicated by enhancement of the inferior olive due to early radiation injury. Awareness of the characteristic imaging and temporal features of these treatment complications, and possible coexistence, is critical for recognizing nontumoral entities and enabling appropriate clinical management decisions.

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Fig. 1.

(A–C) Axial T2-weighted images. At presentation (A), there was an expansile right eccentric tumor centered in the dorsal pons. One month after completion of RT (B), a dorsal right pons surgical cavity was present with stable residual nonenhancing tumor. A lower image (C) showed a new discontinuous expansile T2 hyperintense lesion in the ventral right medulla, in the expected location of the inferior olive.

Fig. 2.

Directionally encoded color fractional anisotropy map (A) (blue=craniocaudal orientation, red=transverse, green=anteroposterior) shows normal contralateral central tegmental tract (arrow). Tractography overlaid on a contrast coronal T1-weighted image (B) demonstrates discontinuity of the ipsilateral central tegmental tract (green fibers) at the level of the surgical cavity. Note the normal contralateral central tegmental tract (purple fibers). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Fig. 3.

(A) Axial T2-weighted image shows new ill-defined hyperintense changes in the pons and medulla, and (B) contrast T1-weighted image reveals new patchy enhancement in the right medulla limited to the inferior olive. (C) Two months later, T2-weighted image demonstrates complete resolution of these new T2 hyperintense changes and enhancement, with residual expansile T2 hyperintensity of the inferior olive stable from the initial post-RT MRI. This was consistent with resolution of early radiation injury, and stable underlying HOD.