Hypertrophic olivary degeneration following pontine haemorrhage: hypertensive crisis or cavernous haemangioma bleeding?

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The clinical and magnetic resonance (MR) features of hypertrophic olivary degeneration are described, along with a rare but treatable cause of this entity—pontine cavernous haemangioma. Hypertrophic olivary degeneration occurs after focal lesions to the dentato-rubro-olivary pathway, typically following a pontine haemorrhage involving the ipsilateral central tegmental tract, the contralateral superior cerebellar peduncle, or the dentate nucleus. Clinically, there is palatal myoclonus and an uncontrollable tremor, presumably caused by loss of inhibitory control. On MR imaging, hypertrophic olivary degeneration is characterised by a non-enhancing T1 isointense, T2 hyperintense enlargement confined to the olivary nucleus. Typically, haemorrhages following a hypertensive crisis are responsible for hypertrophic olivary degeneration. However, in the three reported cases, imaging findings within the former bleeding cavity suggested a cavernous haemangioma as the source of the haemorrhage.

Hypertrophic olivary degeneration occurs in lesions involving the dentato-rubro-olivary system. A unique finding in this form of transneuronal degeneration is enlargement rather than atrophy of the affected structure. Typically, haemorrhages following a hypertensive crisis are the cause of this pathological entity. However, other entities such as cavernous haemangiomas may also be responsible for a pontine bleed. We describe three patients in whom a pontine haemorrhage resulted in hypertrophic olivary degeneration. In all patients, at both the 12 month and the 18 month follow-up examinations in two of the patients, the former haemorrhagic cavity was localised in the tectum pontis. On both the 12 month and 18 month follow up visits after informed consent was obtained. All three patients were male, aged 45, 48, and 64 years, and suffered their initial haemorrhage in the brain stem between one and 12 months before the first MRI study. One patient had a history of long standing hypertension, though his blood pressure was within normal limits as he was on antihypertensive treatment; the other patients had no history of previous hypertension or other medical problems. The family history was unremarkable for cavernoma or brain haemorrhage in any of the three patients.

RESULTS

The bleeding episodes initially led to a nearly complete paresis of the ipsilateral facial muscles and the contralateral upper and lower extremities. Additionally all patients complained of the sudden onset of gait disorder, balance disturbance, and vertigo. The initial diagnosis was made after emergency computed tomography, after which all patients were monitored on an intensive care unit. They all underwent rehabilitation treatment approximately one month later, which improved the paresis slightly in two cases and markedly in one. Besides their paresis, the patients were still complained of vertigo and a moderate to severe gait disorder at this time. They all had a generalised intention tremor of the extremity contralateral to the former bleeding site, and palatal myoclonus. The tremor reportedly started eight months, nine months, and one year, respectively, after the bleeding occurred. Drug treatment to reduce tremor was initiated, but did not improve the symptoms. Normal life activities were affected because of the paresis and particularly because of the tremor in the upper contralateral extremity. Subjectively, the generalised tremor was rated the most disabling symptom.

In all patients MR examinations were undertaken at 12 and 18 months after the initial haemorrhage (fig 1); in addition one patient each was examined at the following time points: one month, 24 months, and 30 months after the initial event. The single patient who was scanned one month after the pontine haemorrhage showed bright hyperintense signals on both T1 and T2 weighted sequences, with a normal appearing olivary nucleus. In all patients, at both the 12 month and the 18 month follow-up investigations the following imaging characteristics were seen in the medulla: the ipsilateral olivary nucleus was markedly enlarged and protruded and showed homogeneous hyperintensity on T2 weighted images. On T1 weighted images the olivary nucleus presented with a hyperintense signal compared with the grey matter. Contrast enhancement was not present.

There were no changes of note between the 12 month and the 18 month follow up examinations in two of the patients, but the third showed slight diminution in size and a reduction in hyperintensity of the signal in the olivary nucleus. In all patients the former haemorrhagic cavity was localised in the tectum pontis. On both the 12 month and 18 month follow up

Abbreviations: FA, flip angle; TE, time of echo; TR, time of repetition

Methods

Patients were investigated using 1.5 T magnetic resonance (MR) scanners (Philips Gyroscan Intera and ACS NT, Best, Netherlands; Siemens Symphony, Erlangen, Germany). MR imaging consisted of standard spin echo T1 weighted sequences (TR/TE/FA, 530/20/90) before and after the intravenous administration of contrast material (Magnevist, Berlix Laboratories, Wayne, New Jersey, USA), T2 Turbospin-echo sequences (TR/TE/FA, 4400/120/90), fluid attenuated (FLAIR) sequences (TR/TE/FA, 11000/140/90), and T2* weighted gradient echo sequences (TR/TE/FA, 670/23/15) in various planes using thin sections.

We reviewed the clinical records and MR imaging (MRI) studies obtained up to 30 months after the bleeding had occurred. The patients were scheduled for a final clinical follow up visit after informed consent was obtained. All three patients were male, aged 45, 48, and 64 years, and suffered their initial haemorrhage in the brain stem between one and 12 months before the first MRI study. One patient had a history of long standing hypertension, though his blood pressure was within normal limits as he was on antihypertensive treatment; the other patients had no history of previous hypertension or other medical problems. The family history was unremarkable for cavernoma or brain haemorrhage in any of the three patients.

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ipsilateral inferior olivary nucleus, is called the Guillain–Barré syndrome. Other names for this nucleus are the ipsilateral dentate nucleus, the ipsilateral red nucleus, and the ipsilateral central tegmental tract. Efferent fibres from this structure, the lateral superior cerebellar peduncle, crosses the midline in the contralateral dentate nucleus, travels over the contralateral superior cerebellar peduncle to the ipsilateral red nucleus. This tract is the afferent pathway to the olive, which originates in the contralateral dentate nucleus. Pathologically, cell body enlargement, vacuolation of the cytoplasm, astrocytic hyperplasia and proliferation, demyelination, and fibrillary gliosis are seen.

These histopathological changes are reflected in the typical imaging appearance of hypertrophic olivary degeneration, with an increase in signal on T2 and proton density weighted images and an increase in size of the olivary nucleus. The size of the hypertrophic olivary nucleus is variable, depending on the time interval between the event and the scanning procedure, with a normal size in the acute stage. Olivary hypertrophy typically develops around six months after the event and resolves after three to four years. An increased signal on T2 and proton density images on the other hand typically appears early (around one month after the initial lesion) and persists indefinitely. The initial signal hyperintensity relates to the early phases of neuronal hypertrophy, with gliosis due to demyelination and an increased water content (vacuolisation). Subsequently, the hypertrophic olivary nucleus resembles the stage of hypertrophic precursors to cell death of both neurons and astrocytes. Finally, this leads to atrophy, neuronal disappearance, and olivary shrinkage.

Whereas the imaging characteristics of hypertrophic olivary degeneration resolve, the clinical appearance of the hallmark symptom of this disease—the palatal myoclonus and other involuntary movements—persists. Palatal myoclonus is characterised by rhythmic involuntary movements of the oropharynx. In addition, patients with hypertrophic olivary degeneration may suffer from a denitro-rubral tremor which is characterised by a delayed onset of muscle contractions at one to three cycles per second and which is not affected by voluntary control. These clinical symptoms presumably reflect loss of inhibitory control that is transmitted through the dentato-rubral pathway.

The differential diagnosis of signal hyperintensity on T2 weighted images within the pontomedullary region includes tumours, demyelinating lesions, infarction, and inflammatory processes (tuberculosis, sarcoidosis, or encephalitis). The lack of contrast enhancement, however, is against many tumorous entities or an infectious origin, while the additional enlargement of the olivary nucleus is against chronic stages of infarction or multiple sclerosis. Therefore, in the setting of a T2 hyperintense non-contrast enhancing lesion which is accompanied by enlargement of the olivary nucleus, hypertrophic olivary degeneration remains the sole diagnosis that explains all the imaging findings.

MRIs, a marked T1 and T2 hypointense rim was seen around the slit-like liquor isointense former haemorrhagic cavity. However, in addition a mulberry to nodular shaped T2 hyperintense structure close to the cavity could be visualised in all patients; this was isointense to slightly hyperintense on T1 weighted sequences. Within this structure, contrast enhancement was present in one patient. This nodular lesion did not vanish or change its imaging characteristics on the follow up examination done at 24 and 30 months after the haemorrhage.

DISCUSSION
Hypertrophic olivary degeneration is a rare finding secondary to focal lesions of the brain stem and can be explained by trans-synaptic degeneration. Most commonly, lesions involving the dentato-olivary tract are the cause of this pathology. This tract is the afferent pathway to the olive, which originates in the contralateral dentate nucleus, travels over the contralateral superior cerebellar peduncle, crosses the midline through the inferior colliculi, enters the ipsilateral red nucleus, and then traverses through the central tegmental tract to the olivary nucleus. Efferent fibres from this structure traverse out of the hilus medially, intermingling with medial lemniscus fibres while crossing the midline at the level of the olives, and enter the cerebellum through the inferior cerebellar peduncle. While hypertrophic olivary degeneration can be caused by any lesion involving the aforementioned structures, it is typically seen with focal lesions involving the ipsilateral central tegmental tract, the contralateral superior cerebellar peduncle, or the dentate nucleus.

While transneuronal degeneration associated with atrophy of the targeted structure is a common response to a confined lesion (for example, atrophy of the mammillary bodies in lesions involving the fornix), transneuronal degeneration resulting in hypertrophy of the targeted region is unique to the inferior olivary nucleus. Pathologically, cell body enlargement, vacuolation of the cytoplasm, astrocytic hyperplasia and proliferation, demyelination, and fibrillary gliosis are seen.

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Although one of our patients had a history of hypertension, the imaging findings were suggestive of a pontine cavernoma as the cause of the haemorrhage. If hypertension was the cause of the bleeding, one would have expected a different pattern of imaging findings in the late chronic stage. We found hyperintense nodules on both T1 and T2 weighted images, indicating extracellular methaemoglobin. Although no definite histological diagnosis could be obtained because of the location, a cavernous haemangioma would be a plausible cause for these imaging findings. On MR examination, cavernous angiomas appear as well defined circumscribed lesions of varying size, which have a hypointense rim on T2 or proton density imaging and an inhomogeneous, often hyperintense, centre on T2 weighted images. The reticulated core represents haemorrhage in different stages of evolution. Neighbouring tissue is typically gliotic and contains haemosiderin from continued oozing of blood. The free methaemoglobin seen even after a follow up of two to three years following haemorrhage is unusual for a parenchymal bleed and is more typical of continued oozing of blood that is typically present in a cavernous haemangioma.

Our cases demonstrate that, although hypertensive bleeding is a more common cause of pontine haemorrhages resulting in hypertrophic olivary degeneration, bleeding from a cavernous haemangioma may lead to the same morphological changes.

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