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Case report

Intractable hiccups resolved after resection of a cavernous malformation of the medulla oblongata

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1. Introduction

Hiccups are reflexive involuntary contractions of the respiratory muscles followed very early by sudden closure of the glottis. While common in the fetal stages of life they are usually benign, short-lived, self-limited and very commonly overlooked in adults. Rarely, hiccups can indicate significant neurologic disease [1].

Here, we present a case of a patient presenting with 3 years of intractable hiccups and a single medullary cavernous malformation whose symptoms resolved after resection of the lesion. We then discuss the available literature for medullary cavernomas presenting with hiccups and how surgical resection relieves symptoms likely by compromising the vagal activity.

2. Case report

The patient, a 36-year-old female, presented at the emergency room with headache followed by blurry vision, generalized weakness, numbness of her right extremities and unsteady gait. The headache had started the day prior and was described as of gradual onset, moderate to severe intensity, with associated nausea and an episode of vomiting. After reaching peak intensity within few hours, symptoms dissipated during the next day. She denied previous similar episodes but reported recurrent episodes of hiccups on and off for the past 3 years sometimes lasting for up to 1 month and unresponsive to medical treatment with gabapentin and chlorpromazine. She had noticed that in the last 2 months the hiccup bouts were almost continuous with no more than half an hour interruption between them. A gastro-intestinal (GI) work-up including upper GI tract endoscopy had revealed only mild erythematous gastropathy. On neurological exam she was found to have only mild sensory loss on the right side of her face and a wide based gait; otherwise her strength had recovered fully.

Brain CT scan showed a hemorrhagic lesion at the right posterolateral medulla, just caudal to the fourth ventricle floor (Fig. 1A and B). MRI findings suggested the lesion could be a cavernous vascular malformation (Fig. 2).

The patient was discharged after a week of observation with recommendation to follow-up at the neurosurgery clinic to discuss surgical options. Three weeks later the patient presented again to our emergency department with sudden-onset of a severe headache and unsteady gait. On physical exam she was noted to have nasolabial fold flattening on the left and mild spastic quadriparesis. Romberg test was positive, but no clear sensory deficits were elicited. And again all symptoms and signs, beside the hiccups, regressed in the next 24 h. Brain imaging showed a new

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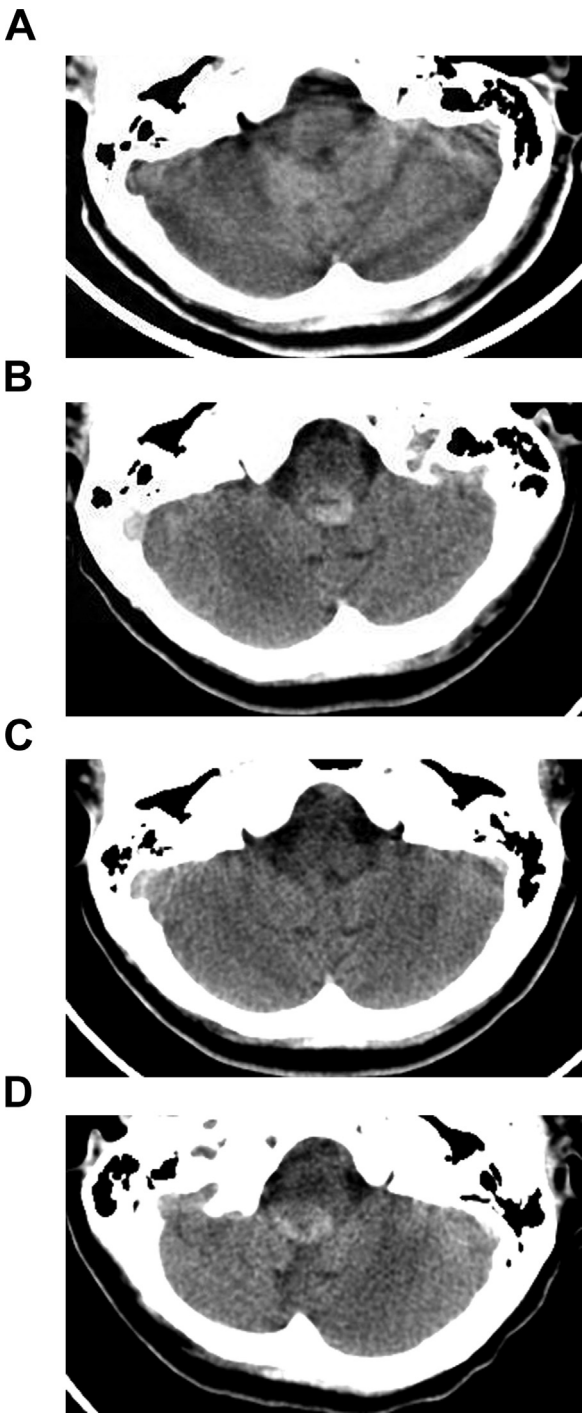

Fig. 1. Brain CT scan performed 5 years earlier, as part of work up for an episode of seizures, shows no abnormalities in the posterior fossa (A). CT scan performed on admission showed a round intra-axial hyperdense lesion, measuring 1.4 cm × 1.2 cm × 1 cm, at the right postero-lateral medulla, just caudal to the fourth ventricle floor (B). Repeat CT brain 14 days later, upon discharge, shows resolution of the hemorrhage (C). Upon second admission, there is a new hemorrhage at the same location (D).

intra-capsular bleed within the cavernoma (Fig. 1D) that was not present 3 weeks earlier, on the day of her discharge (Fig. 1C). Considering that this lesion had bled twice in a month decision was made to resect the lesion via a suboccipital inter-tonsillar approach. At operation, we observed the lesion to be located entirely within the fourth ventricle, extending inferiorly deep to the obex. It was visible as an area of xanthochromia on the right at the median aperture of the fourth ventricle. It was possible to dissect around the lesion, which was quite discrete and well demarcated from surrounding brain, typical of a cavernous malformation. There was evidence of recent and remote hemorrhage, with liquid hematoma and extensive surrounding xanthochromia. A gross total removal was effected (Fig. 2) and histopathology examination, confirmed it was a cavernous vascular malformation (Fig. 3).

The day after the surgery patient complained of dysphonia, dysphagia and quadriparesis, but noted that hiccups had resolved. Her postoperative stay was uneventful, showing good recovery of her strength. At 9 months after surgery the patient was free of hiccups, had recovered her strength fully and complained only of mild dysphonia and dysphagia. On physical exam we noticed minimal wasting of her lateral edge of the tongue on the right and video stroboscopic exam of the larynx showed normal appearance but immobile right vocal cord; findings consistent with lesions in the hypoglossal and ambiguus nuclei.

3. Discussion

Hiccups are a repeated well-coordinated primitive reflex of unclear benefit. The afferent arm of this reflex receives input from the distal esophagus, stomach, and the abdominal side of the diaphragm and travel centripetally via the phrenic nerve, the vagus, and sympathetic (T6–T12) chain branches, while the efferent arms travel within the phrenic nerve toward the diaphragm and the recurrent nerve from Nucleus Ambiguus of Vagus to glottis. Hiccups are considered intractable when symptoms persist for longer than 2 months. These patients usually share a common history with protracted systemic work-up and a long list of unsuccessful therapies. CNS pathologies account for about one in six intractable hiccups. Of those cases, about 70% are attributable to ischemic strokes, 13% to tumors and the rest divided between infectious, inflammatory and developmental anomalies. Tumors causing hiccups can be located anywhere along the cortico-bulbar tract, from the cortex to the lower medulla. Rare reported causes of intractable hiccups are medullary cerebral cavernous malformation [2–4].

Cavernomas are vascular lesions, either sporadic or of familial inheritance, composed of vessels lined by a single layer of endothelium lacking tight junctions and proper architecture that can be found anywhere in the brain. Brainstem cavernomas, unlike the ones found in cerebral hemispheres, tend to present with mass effect symptoms, due to limited space in the posterior fossa [5]. Such symptoms can be acutely aggravated during cavernoma's intracapsular bleeding, as happened in our case. In brainstem cavernoma series persistent/intractable hiccups were reported in 3 out of a 100 patients with brainstem cavernoma without specifying the exact location [4].

In this report, we present the fourth case to our knowledge of a medullary cavernoma resection that resulted in dissipation of previously intractable hiccups [2–4]. Common to all of these case reports was the fact that cavernoma causing hiccups was located on the floor of the forth ventricle, close to obex. Such location also harbingers the highest rate of surgical morbidity and therefore the benefits of surgery have to be weighed against such risk [5]. In our case, the decision to resect was determined by the aggressive nature of the lesion which bled twice in a month (Fig. 1); and the second episode presenting with more severe symptoms than the first. After surgery we noted the hiccups to be resolved and have not recurred ever since.

In our patient, as in the other cases, hiccups resolved immediately after surgery; a result most commonly seen with lesional surgery than recovery from long-term loss of function due to mass effect. How brainstem surgery dissipates hiccups remains a