Case report

Persistent hiccup as presenting symptom in medulla oblongata cavernoma: a case report and review of the literature

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Abstract

A rare case of persistent intractable hiccup as presenting symptom of cavernous angioma in the medulla oblongata is reported. Pathophysiologic hypotheses about the triggering mechanism of hiccup are discussed, with special reference to the causes affecting the central nervous system. A review of the literature concerning medullary lesions presenting with persistent hiccup is also reported. Finally we have included some brief considerations about cavernous angiomas and the patterns of their clinical presentation, focusing on those located in the medulla oblongata. © 2000 Elsevier Science B.V. All rights reserved.

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1. Introduction

The etiology of persistent intractable hiccup is obscure and several hypotheses have so far been proposed regarding its pathophysiology. Hiccup is defined intractable when it persists for 24 h, lasting in some cases more than 25 years. Other terms as ‘chronic’ [1,2], ‘persistent’ [3] and ‘obstinate’ [4] were used to describe such a long duration.

The afferent pathway of hiccup reflex arc comprises the sensory branches of the phrenic and vagus nerves as well as dorsal sympathetic fibers; its main efferent limb causing spasm of the diaphragm is mediated by motor fibers of the phrenic nerve [5]. Hiccup may be triggered by central nervous system (CNS) lesions or by the irritation of the phrenic and vagus nerves [5]. Recently, more attention was focused on its ‘central’ etiology, in particular on those lesions located in the brainstem, interfering with specific neuronal circuits in the dorsal-lateral aspect of the medulla oblongata [6–10].

2. Case report

A 46-year-old man complained of some episodes of violent vomiting and nausea that remitted spontaneously. After a few days a persistent and intractable hiccup occurred and led to severe insomnia and a seven pounds weight loss. He was examined in another hospital with gastroscopy and thoracic–abdominal CT-scans. They were normal. CT-scan of the brain showed a hyperdense lesion, not enhanced after contrast infusion, in the medulla oblongata. Two months after the onset of the symptoms the patient was admitted to our Department and neurological examination showed diplopia in upward gaze and persistent hiccup refractory to chlorpromazine, metoclopramide and cusaprid. MRI of the brain confirmed a well-circumscribed dorsal medullary lesion, hyperintense with an isointense nucleus in T1-weighted images, without Gadolinium-enhancement, beneath the caudal floor of the fourth ventricle (Fig. 1). A cavernous angioma was suspected.

The patient was operated on by the senior author (AB), in a semi-sitting position. Suboccipital median craniectomy and C1-laminectomy were carried out. The dura was opened in a Y-shaped fashion, the cerebellar...
tonsils were gently retracted laterally and the floor of the fourth ventricle was exposed. A red mulberry-like cavernous angioma was raised from the obex, at the right side of calamus scriptorius, exophytic in the lower third of the fourth ventricle (Fig. 2a). It was easily reduced and radically removed including its gliotic-haemosiderin wall (Fig. 2b), avoiding rough traction to the brainstem. Bleeding was slight and there were no abnormalities in respiration and blood pressure, although severe bradycardia was observed transiently during the debulking of the mass. Interrupted suturing was used for a watertight closure of the dura. The muscles and skin flap were closed in the usual manner.

Hiccup resolved from the day after surgery and the patient no longer complained of diplopia in the upward gaze. At discharge neurologic examination was normal. Pathology confirmed the lesion as a cavernous angioma. After 1 year the patient was hiccup free.

3. Discussion

Hiccup or singultus is a repeated, myoclonic, synchronous and involuntary contraction of the diaphragm. Inspiratory (external) intercostal muscle contractions are followed (in 35 ms) by a sudden closure of the glottis, stopping the air exchange abruptly and producing the typical ‘hic’ [11,12].

Etiology of persistent hiccup is still unknown and several folk [13–15], pharmacological [16–25], not invasive [26–28] and extremely invasive [29–32] therapeutic remedies were tried.

Generally the causes of hiccup could be divided into ‘peripheral’ and ‘central’. Peripheral is any factor outside the CNS that may produce afferent nerve impulses which finally reach the phrenic motor fibers. Central are all those causes which act directly upon the CNS to stimulate the phrenic motor fibers [33].

Hiccup was considered a gastrointestinal reflex [12] whose center should be located in the spinal cord at the cervical-thoracic level. However, a well-coordinated contraction suggests the relay by a supraspinal polysynaptic center of coordination.

Hassler [34] thought that hiccup could be the subcortical equivalent of myoclonus possibly generated at the level of the ponto-medullary so-called myoclonic triangle of Guillan–Mollaret: inferior olive, dentate nucleus, red nucleus. Other authors [35–38] developed, for palatal myoclonus, the concept of denervation supersensitivity caused by a disfunction of the inferior olivary complex, nucleus ambiguous and adjacent postero-lateral reticular formation of medulla oblongata due to medullary lesions. Al Deeb et al. [6] and De la Fuente-Fernandez [8] proposed a similar genesis for the hiccup.

Few reports exist in the literature regarding persistent intractable hiccup due to lesions located in the medulla oblongata [1,6,7,9,10,39–43]. Fisher et al. [40], in 1961, and other authors [6,7] more recently, reported dorsal and lateral medullary infarctions presenting with persistent hiccup. Kumral and Acarer [42] described an unusual case of primary medullary haemorrhage with intractable hiccup. Vascular anomalies with neurovas-

Fig. 1. Preoperative MRI. T1-weighted images on the sagittal (left) and axial (right) planes showing a well-circumscribed bleeding lesion in the dorsal aspect of the medulla oblongata, beneath the caudal floor of the fourth ventricle.
We report a rare case of persistent intractable hiccup as the presenting symptom of a cavernous angioma located near the obex of the medulla oblongata, dorsally exophytic in the fourth ventricle.

Houtteville (personal communication, 1998) showed a similar clinical onset for a cavernous angioma associated with a venous angioma at the ponto-medullary junction. Porter et al. [44], in their recent review of 100 brainstem cavernous malformations, reported hiccup as the presenting symptom in three cases, but they did not provide the exact location in the brainstem of the cavernomas nor a pathophysiological explanation of hiccup.

Moreover, cavernous angiomas were associated with other movement disorders. Akbostanci et al. [45] described a case of hemidystonia, reviewing 11 previous cases of other movement disorders. Five cavernous angiomas were located in the brainstem, one of which was beneath the floor of the fourth ventricle: this case was associated with oculopalatal myoclonus and synchronous movements of the face, jaw, tongue and the diaphragm.

Cavernous angioma is a hamartomatous berry-like collection of vascular spaces lined by thin walls devoid of smooth muscle [46–48]. No brain tissue intervenes between these vascular channels. Surrounding neural tissue is often gliotic and haemosiderin-stained, and may contain small low-flow feeding arteries and draining veins [45,46,49]. Cavernous angiomas are properly vascular malformations but in the brainstem they were considered vascular tumours [50] because they represent real mass-lesions [50–55]. Most frequently clinical presentations of intracranial cavernomas are seizures, focal neurological deficits, and haemorrhages [51–56]. Regarding brainstem cavernous angiomas, long-tract signs or cranial nerves deficits are due to mass effect in such densely eloquent area [53,55,57–59]. The symptoms described for medullary cavernous angiomas, are headache, diplopia, truncal ataxia, paresis of facial nerve, weakness of arms and/or legs, dysphagia, numbness of the face or body, dizziness, nausea and vomiting [50,54–57,59–61] but hiccup has rarely been reported.

According to previous pathophysiological considerations, we believe that the slow growth of the cavernous angioma, in the dorso-lateral aspect of the medulla oblongata, in our case caused the irritation of the muscular contacts determining persistent hiccups were advocated [9,10,41]. Most reports describe persistent intractable hiccup elicited by brainstem tumours: low-grade gliomas [39,43], ependymoma [1], choroid plexus papillomas of the fourth ventricle [7,9] and tuberculomas [6] were reported. In all cases the lesions developed slowly and were located near the dorso-lateral aspect of the medulla oblongata. Among them, in four cases [1,6,39,43] an involvement or extension to the region of the obex was documented.

Fig. 2. (a) Intraoperative photograph. Medullary cavernous angioma dorsally exophytic from the obex in the fourth ventricle. (b) Intraoperative photograph. The floor of the fourth ventricle after total removal of cavernous angioma.
centrally mediated pathways for hiccup which remained primarily for such a long time prior to the development of localizing neurological signs. Experimental studies of electrical stimulation in medulla oblongata of cats [62,63] showed that the sites where the hiccup-like responses are generated are located in the medullary reticular formation lateral to the nucleus ambiguous, at the rostrocaudal level between 1 and 2.5 mm rostral to the obex. Moreover it was demonstrated that the nucleus raphe magnus have GABA-containing cells and it could be the source of the GABAergic inhibitory inputs to the hiccup reflex arc. Thus we hypothesize that the cavernoma in our case was most likely to interfere with the neuronal connections between the nucleus raphe magnus and those hiccup-evoking sites near the obex, which could discharge when released from the higher inhibitory control.

4. Conclusion

This case illustrates a very unusual presentation of brainstem lesions and makes this etiology one of the important considerations in the differential diagnosis of persistent intractable hiccup. When neurological examination is normal, the diagnosis is easily missed. The patient undergoes a large series of radiological examinations of the gastrointestinal tract and is treated uselessly with a lot of palliative drugs or extremely invasive procedures, like ablative procedures of the phrenic nerve. However, when persistent intractable hiccup occurs with or without a slow neurological worsening, a brainstem lesion should be suspected. MR-imaging is mandatory. Diagnosis of benign brainstem tumour brings seriously surgery into the available treatments.

References


