Intractable Hiccup as the Presenting Symptom of Cavernous Hemangioma in the Medulla Oblongata: A Case Report and Literature Review

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A case of intractable hiccup developed by cavernous hemangioma in the medulla oblongata is reported. There have been only five previously reported cases of medullary cavernoma that triggered intractable hiccup. The patient was a 28-year-old man who was presented with intractable hiccup for 15 days. It developed suddenly, then aggravated progressively and did not respond to any types of medication. On magnetic resonance images, a well-demarcated and non-enhancing mass with hemorrhagic changes was noted in the left medulla oblongata. Intraoperative findings showed that the lesion was fully embedded within the brain stem and pathology confirmed the diagnosis of cavernous hemangioma. The hiccup resolved completely after the operation. Based on the presumption that the medullary cavernoma may trigger intractable hiccup by displacing or compression the hiccup arc of the dorsolateral medulla, surgical excision can eliminate the symptoms, even in the case totally buried in brainstem.

Key Words: Brainstem · Cavernous hemangioma · Hiccup · Medulla oblongata · Surgery.
The lesion was covered by normal parenchymal tissue and made a bulging contour of the medulla oblongata with superficial abnormal draining veins (Fig. 2A). The shortest trajectory to the lesion was confirmed by neuronavigation (StealthStation S7®, Medtronic, Minneapolis, MN, USA) and a 2 cm longitudinal pial incision was made caudally from the obex. After dissecting a few millimeters deep, hemosiderin staining of the neural tissue was encountered (Fig. 2B). The plane of the dissection between the cavernoma and the parenchyma was well-distinguished (Fig. 2C). The lesion was removed en bloc. Histopathologically, the brain specimen revealed irregularly dilated vascular spaces without intervening neural tissue, which are typical features of cavernous hemangioma (Fig. 3). Additionally, there was reactive piloid gliosis with numerous Rosenthal fibers in the periphery of the lesion and occasional hemosiderin-laden macrophages. Hiccup resolved immediately after surgery. The patient had slight hemiparesis (motor grade IV+/IV+) and hemisensory changes that cleared entirely at the time of discharge.

**DISCUSSION**

The clinical manifestations of the brainstem CHs closely correlated with the anatomical location of the lesion. The common signs and symptoms include various types of cranial neuropathy, sensory/motor deficits, headache, diplopia, ataxia, vertigo, nausea/vomiting, dysarthria, dysphagia, and dysmetria, but
Hiccup has rarely been reported\(^1\). Porter et al.\(^{16}\), in their review of 100 cases of brainstem cavernous malformations, reported hiccup as the presenting symptom in three cases. Contrary to this, Ward et al.\(^{20}\) reported that intractable hiccup was not an infrequent clinical presentation in medullary cavernoma (5/18 cases, 27.8%). However, these case series did not reveal the detail description on the exact location, and clinico-radiological characteristics. For this reason, medullary cavernoma presenting as intractable hiccup has been reported as a single case report, with the explanation of unique clinical course (Table 1).\(^{1,11,12,15,18}\) Majority of reported cases were in male patients (female in only one case) with the mean age of 34.8 years, relatively younger than the patients with general brainstem CHs in a large series (41.8 years in brainstem CHs; 44.1 years in medullary CH).\(^{11}\) Main accompanying symptoms were sensory/motor deficits, followed by visual disturbance, headache or nausea and vomiting. Intralesional hemorrhage, related with sudden onset nature of hiccup, occurred in all cases and the size of the lesion varied (range from smaller than 1 cm up to 2.2 cm). Medullary CHs tend to be the smallest among brainstem CHs (mean diameter, 1.2 cm in medullary CHs vs. 1.8 cm in total brainstem CHs), while the preoperative hemorrhagic rate approaches 97% in the medullary CHs and in brainstem CHs as well\(^{11}\). The hiccup was immediately resolved after the surgical resection in all cases.

With regard to the pathomechanism of hiccup, Hassler assumed that hiccup could be the subcortical equivalent of myoclonus generated at the pontomedullary level of the triangle of Guillain-Mollaret (inferior olivary nucleus, dentate nucleus, and red nucleus).\(^{9}\) Other investigators proposed that hiccup could be resultant from denervation supersensitivity caused by dysfunction of the inferior olivary complex, nucleus ambiguus and adjacent reticular formation of medullar oblongata\(^{6,7,21}\). In animal studies, hiccup-like responses were generated by electrical stimulation in the medullary reticular formation, lateral to the nucleus ambiguus and rostral to the obex.\(^{7}\) Oshima et al.\(^{9}\) also showed that GABA-containing inhibitory cells in the nucleus raphe magnus could be the source of inhibitory inputs to the hiccup reflex arc.

Medullary lesions other than medullary CHs also reportedly induced hiccups in the dorsolateral aspect of the medullar oblongata\(^{7,21}\). In a study conducted by Park et al.\(^{14}\), 14% of patients with lateral medullary infarcts (seven out of 51) had hiccups, mainly when the lesion developed in the dorsolateral region of the middle medulla. All reported cases of medullary CHs, inducing intractable hiccup (except one case with ill-defined location), demonstrated laterally-located lesions in the medulla oblongata; three were superficial exophytic cavernomas and the other two, totally buried into medulla. In addition, the intractable hiccup in the report resolved immediately after surgery. The location of the former three exophytic cases seems to be in the dorsolateral medulla rostral to the obex, described by Arita et al.\(^{7}\), in which the pathophysiology may be related to

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**Table 1. Surgically resected medullary cavernomas presenting as intractable hiccup**

| Authors                        | Age/sex | Onset | Duration | Associated symptoms | Lesion characteristics | Operation related | Complication                  |
|--------------------------------|---------|-------|----------|--------------------|-----------------------|-------------------|-------------------------------|
| Eisenächer and Spiska          | 26/Male | Not defined | Midline SOC | Lateral | Midline SOC (exophytic) | Midline SOC | Hiccups immediately resolved after operation |
| Mattana et al.                 | 40/Male | Sudden | 3 months | Ocular headache     | Superficial (exophytic) | Midline SOC | Hiccups immediately resolved after operation |
| Musumeci et al.                | 46/Male | Sudden | 2 months | Nausea/Vertigo     | Superficial (exophytic) | Midline SOC | Hiccups immediately resolved after operation |
| Musumeci et al.                | 46/Male | Sudden | Several months | Sensory change | Lateral | Midline SOC | Hiccups immediately resolved after operation |
| Pechlivanis et al.             | 33/Male | Sudden | 3 years | Sensory change, headache, transient motor weakness and sensory change | Lateral | Midline SOC | Hiccups immediately resolved after operation |
| Thaci et al.                   | 36/Female | Sudden | 15 days | Subjective sensory change, transient weakness and motor weakness | Lateral | Midline SOC | Hiccups immediately resolved after operation |

*Presenting sudden deterioration in consciousness and respiration due to intralaminar hemorrhage. May be deep seated lesion based on representative MR image. Presumptive size of lesion based on representative MR image. Presumed and lasting up to 3 months. Presenting sudden developed quadriparesis, headache, unsteady gait and facial paralysis due to intralaminar hemorrhage. SOC: suboccipital craniotomy.
excitatory function for hiccup genesis. On the other hand, the latter two cases, including the current one, were located in the deep portion of the dorsolateral medulla caudal to the obex. Intractable hiccup in the latter ones may be induced by inactivation of the inhibitory function of GABA-containing neurons suggested by Oshima et al.\textsuperscript{13)} Considering the aforementioned hiccup pathogenesis and the case summary, we presume that the present medullary cavernoma may also have reduced the inhibitory function or induced a stimulatory signal on the hiccup reflex by displacing or compressing the hiccup arc of the dorsolateral medulla.

CONCLUSION

Cavernous hemangioma on the dorsolateral medulla can generate intractable hiccup by compressing or displacing the normal reflex arc. Even in totally buried cases like the current one, surgical excision could be performed for eliminating symptoms without a major neurological deficit.

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