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Case Report

Reproducible occurrence of hiccups during resection of a large pontine cavernous malformation

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ABSTRACT

Background: Various brainstem pathologies cause hiccups.

Case Description: A 45-year-old man with cerebral cavernous malformation (CCM) in the pons, identified at the age of 25 years, experienced an exacerbation of left hemiparesis. The patient presented with left oculomotor and facial nerve paresis, trigeminal pain, and swallowing disturbances, though hiccups were not observed. Cerebral magnetic resonance imaging revealed a hemorrhagic mass occupying the dorsal pons, predominantly on the right side, along with multiple hemosiderin deposits in the cerebral and cerebellar hemispheres. The patient underwent a microsurgical CCM resection. Intraoperatively, traction maneuvers on the CCM, which severely adhered to the right lower pons, reproducibly caused intense hiccups. The hiccups resolved within minutes of the release of traction. Genomic analysis of CCM identified *CCM1* mutation. Postoperatively, the patient had no recurrence of hiccups.

Conclusion: Surgical resection of large pontine CCMs can cause intraoperative hiccups, potentially hindering the continuation of surgery. Despite common genomic mutations, multiple CCMs may exhibit diverse biological behaviors.

Keywords: Brainstem, Cavernous malformation, Hiccup, Neural circuit of hiccups

INTRODUCTION

Hiccups, a common biological phenomenon caused by sudden spasms of the diaphragm, are believed to be a respiratory reflex involving the corticobulbar tract, brainstem respiratory centers, phrenic nerve nuclei, medullary reticular formations, and hypothalamus.[1,6] Cerebral cavernous malformations (CCMs) are hamartomatous vascular malformations that can develop anywhere in the central nervous system, with a high affinity for veins. The annual hemorrhage rate of brainstem CCMs has been estimated at 7.0%, which is significantly higher than that of those occurring in other locations.[8] In rare instances, CCMs arise in multiple forms. In most cases, such CCMs are thought to develop based on genomic mutations and follow a stable clinical course.[3,15]

CCMs located in the dorsal medulla oblongata have been documented to cause hiccups.[7,9,10,14] Besides CCMs, various other pathologies are linked to hiccups, including nonruptured cerebral

aneurysms, embolized cerebral aneurysms, cerebral infarcts, diffuse pontine gliomas, and neuromyelitis optica spectrum disorders.[2,4,5,12,13] The susceptibility-weighted imaging is considered the most sensitive magnetic resonance imaging (MRI) sequence for detecting CCMs as hypointense lesions.[11]

Herein, we report a unique case of pontine CCM presenting with hiccups that reproducibly occurred during resection maneuvers.

CASE PRESENTATION

A 45-year-old man experienced an exacerbation of the left hemiparesis. He had first developed slight left hemiparesis at the age of 25 and was radiologically diagnosed with pontine CCM. Since then, he has been monitored with fully independent activities of daily living. At presentation, he exhibited left oculomotor and facial nerve paresis, trigeminal pain, and swallowing disturbances, along with the left hemiparesis corresponding to 4/5 on the manual muscle test. Hiccups were not noted. Cerebral MRI showed a less enhancing mass occupying the pons. The lesion showed heterogeneous intensity on both T1- and T2-weighted sequences, with a hypointense rim on T2, measuring 35 mm × 28 mm × 28 mm. In addition, an intra-axial lesion, suggestive of a cavernous malformation, was identified in the left ventral pons [Figure 1]. On susceptibility-weighted imaging, the large pontine mass appeared hyperintense, whereas multiple smaller hypointense lesions, indicative of previous hemorrhages from CCMs, were found in the cerebral and cerebellar hemispheres [Figure 2]. The patient underwent microsurgical resection of the pontine mass through the suboccipital approach. The fourth ventricle floor was considerably swollen, predominantly on the right side. An incision was made in the floor, at the rostral site of the right facial colliculus, and exposed clots. Evacuation of the clots revealed a capsulized vascular lesion [Figure 3]. Maneuvers applying traction to the lesion, which was severely adhered to the right lower pons, reproducibly caused intense hiccups. Once the traction was released, the hiccups resolved within a few minutes [Video 1]. The intense hiccup developing in the prone position made it difficult to safely continue surgery, in addition to refractory to medical management. Consequently, the resection maneuver was abandoned with a subtotal resection. Microscopic examination of the resected specimen confirmed a CCM [Figure 4]. Postoperative MRI performed on day 30 revealed a residual lesion in the right pons [Figure 5]. The patient underwent genomic analysis for *CCM* mutations that identified a *CCM1* mutation [Figure 6]. The postoperative course was uneventful, with no additional neurological deficits or hiccup recurrence. The patient was transferred to a rehabilitation facility on postoperative day 41.

DISCUSSION

In the present case, the patient did not experience hiccups before surgery. Presurgical MRI revealed a large mass involving the dorsal lower pons. During the resection maneuver, traction applied to the lower pons reproducibly caused intense hiccups, which resolved promptly on release of traction. Therefore, we assumed that the surgical maneuver may have mechanically stimulated the neural circuits involved in hiccup reflexes located within the dorsal medulla oblongata.[1,6] While cases of CCM-associated hiccups have been documented in the literature, to the best of our knowledge, this is the first case of intraoperative hiccups observed during resection of a pontine CCM.[7,9,10,14] Given the transient nature of hiccups in this case, it is likely that the neural circuit of hiccups responsible for the reflex was adjacent to the CCM but remained uninjured during the surgery. Intraoperative hiccups are challenging complications, particularly when the patient is in a prone position, as they can hinder the progression of surgery. In such cases, as was in our case, immediate discontinuation of surgery is recommended to ensure patient safety.

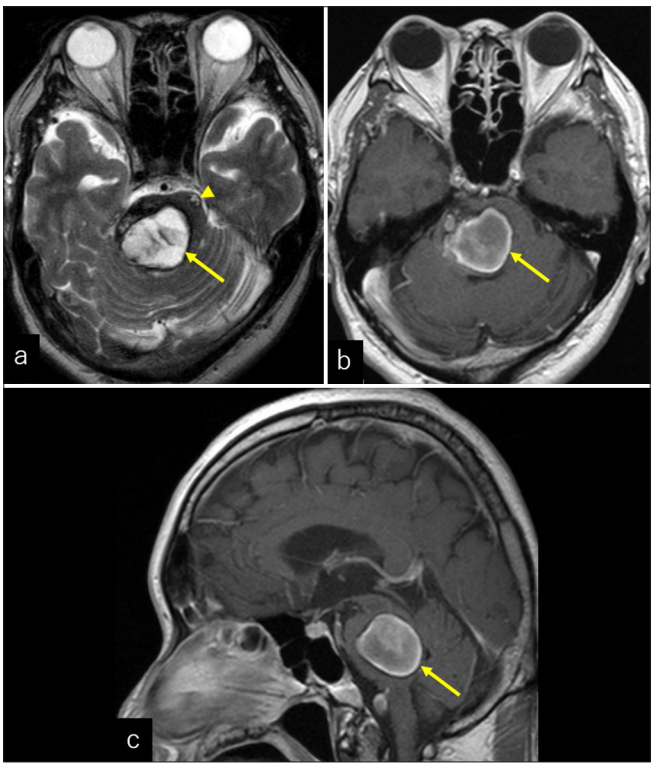


Figure 1: (a) Axial T2-weighted and contrast-enhanced (b) axial and (c) sagittal T1-weighted cerebral magnetic resonance images showing a less-enhancing mass occupying the dorsal pons, predominantly on the right side. It appears heterogeneous intensity and is accompanied by a hypointense rim (a-c, arrow). There is another lesion, suggesting cavernous malformation, identified in the left ventral pons (a, arrowhead).

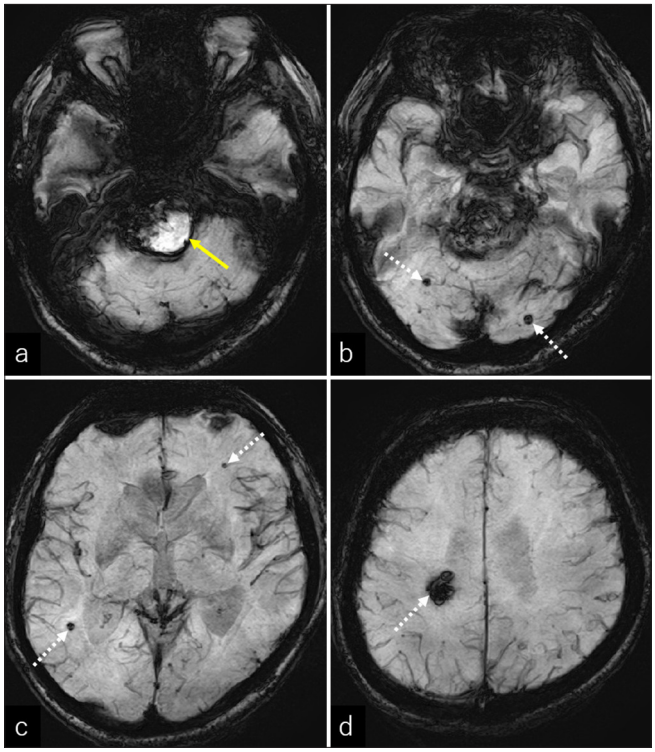


Figure 2: (a-d) Serial sections of axial susceptibility-weighted magnetic resonance imaging showing a hyperintense mass in the pons (a, arrow), in addition to multiple hypointense lesions suggesting hemosiderin depositions (b-d, dashed arrow).

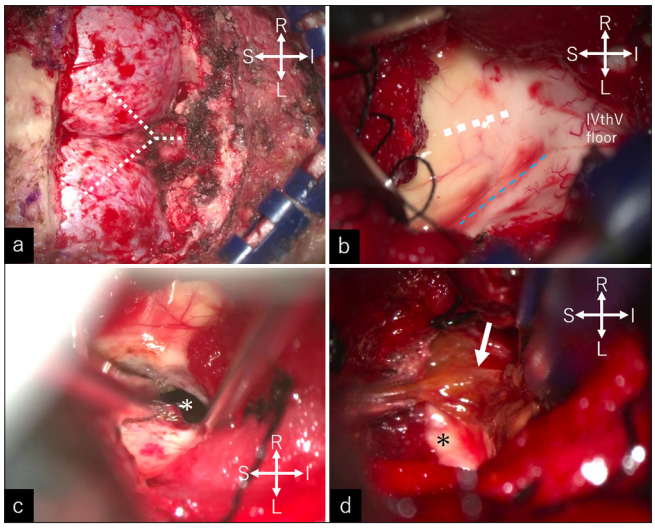


Figure 3: (a and b) Intraoperative photos. (a) A Y-shaped incision was made to the suboccipital dura mater (dashed lines). (b) An incision was made to the swollen floor of the fourth ventricle (thick dashed arrow) at the rostral site of the right facial colliculus. Thin dashed arrow: Median sulcus. (c) Clots are exposed below the fourth ventricle floor (asterisk). (d) Capsule of the lesion (arrow) severely adhered to the right lower pons (asterisk). I: Inferior; L: Left; R: Right; S: Superior; IVth V: Fourth ventricle.

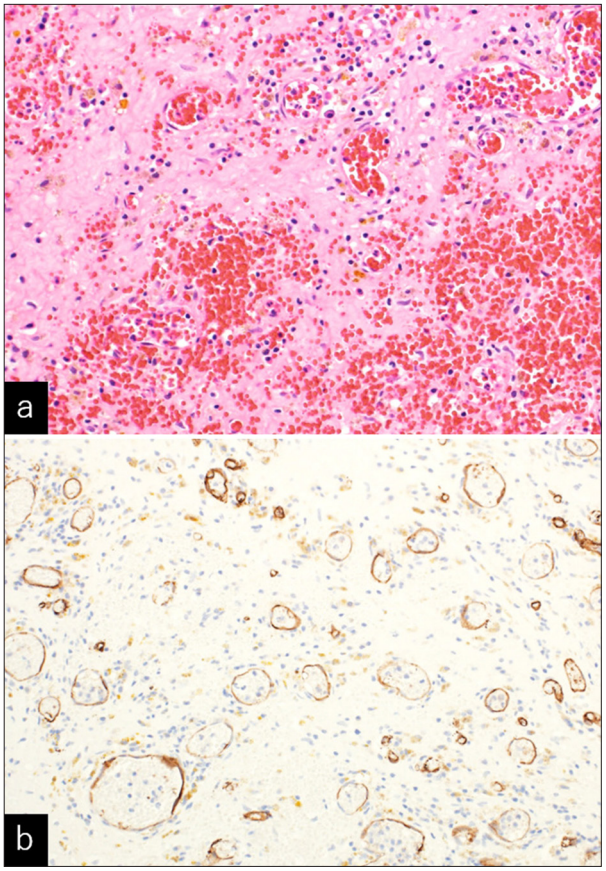
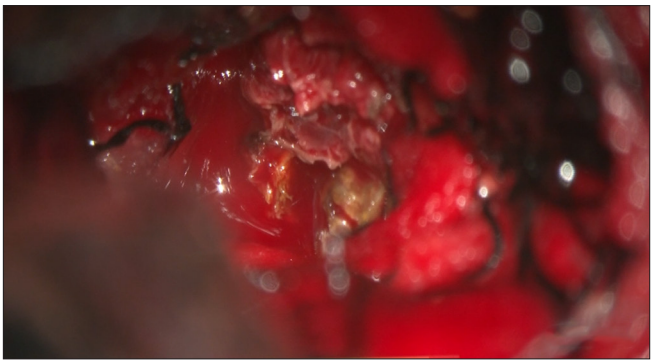


Figure 4: Photomicrographs of the resected specimen showing the proliferation of thin-walled vessels of varying diameters with fibrous interstitial tissue. (a) Neither cell atypia nor mitotic figures are observed. (b) Cells comprising the vessel walls are stained for CD34. (a) Hematoxylin and eosin stain, ×200; (b) CD34, ×200.



Video 1: A short intraoperative movie showing hiccups occurred by resection maneuver.

In this case, the offending CCM caused recurrent hemorrhages and appeared hyperintense on susceptibility-weighted imaging at presentation, whereas other CCMs distributed over the cerebral and cerebellar hemispheres

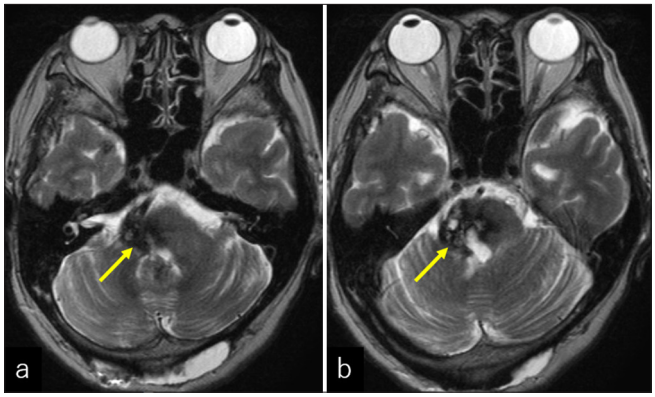


Figure 5: Axial T2-weighted magnetic resonance images at the level of (a) lower and (b) middle pons, performed on postoperative day 30, showing residual lesion (arrow).

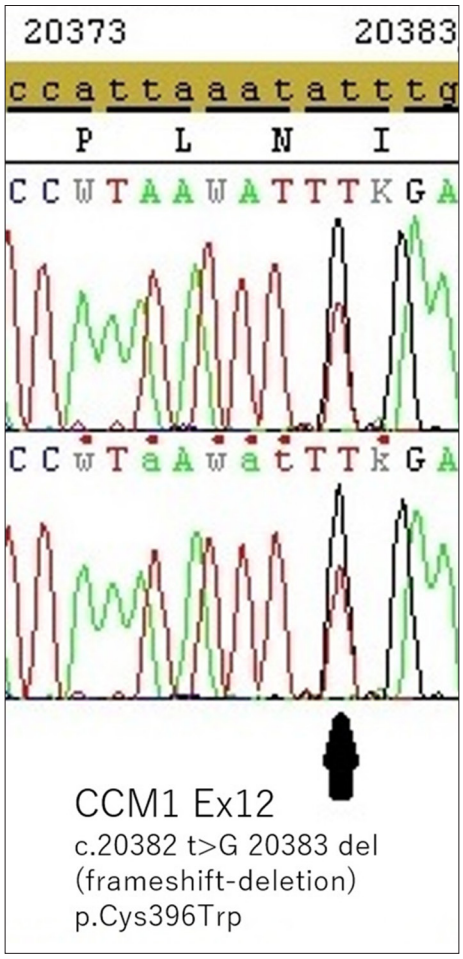


Figure 6: Result of genomic analysis showing the site (arrow) and detail of the mutation.

demonstrated a stable clinical course, consistently appearing hypointense on the sequence. Moreover, among the two identified pontine CCMs, only the offending one caused recurrent hemorrhages. Genomic analyses revealed the presence of a *CCM1* mutation. A previous study suggested that multiple CCMs arising based on a genomic mutation typically follow a stable clinical course.[15] However, the present case suggests that multiple CCMs arising from a common genomic mutation may not exhibit homogeneous biological behavior. Our patient exhibited neurological deterioration after a stable course lasting 20 years. Therefore, careful observation over a sufficiently extended period is recommended.

CONCLUSION

Surgical resection of large pontine CCMs can cause intraoperative hiccups, complicating the continuation of surgery. Despite common genomic mutations, multiple CCMs may not exhibit homogeneous biological behaviors and require careful long-term observation.

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