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CASE REPORT

Intractable hiccups caused by syringobulbia and syringomyelia associated with intramedullary spinal hemangioblastoma

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Abstract
Introduction Hiccups caused by a neoplasm in the spinal cord are rare.
Materials and methods We report a case of intractable hiccups caused by syringobulbia and syringomyelia associated with cervical intramedullary spinal hemangioblastoma, which was successfully treated by surgical excision. A 60-year-old man was referred from the neurology department after presenting with hiccups for 1 year. The hiccups were aggravated 3 months ago and were sustained during eating or sleeping. Several doctors administered a muscle relaxant and an anticonvulsant, but they were ineffective. Spinal MRI revealed a huge syringomyelia from C2 to T2, associated with a highly enhancing intramedullary mass lesion at the C5 level. The hiccups were ceased after removal of the tumor through a right hemilaminectomy. The pathology of the specimen was hemangioblastoma. The size of the syringobulbia and syringomyelia decreased markedly on MRI checked 5 months after surgery.
Conclusions Intractable hiccups can be caused by syringobulbia associated with an intramedullary cord tumor in the cervical area and possible mechanisms of hiccups were reviewed.

Keywords Brain stem · Hemangioblastoma · Hiccup · Syringomyelia

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Introduction

Hiccups are usually associated with disorders in the abdomen, thorax, or neck. They are commonly associated with advanced internal organ malignancy [1–3]. Hiccups could be a main presenting symptom of a neurodegenerative disorder with a brain stem lesion such as neuromyelitis optica or multiple sclerosis. Hiccups are occasionally caused by a syrinx forming neoplasm such as hemangioblastoma in the cerebellum or a developmental anomaly of the central nervous system (CNS) such as Chiari malformation. However, hiccups caused by a neoplasm in the cervical spinal cord have never been reported. We report a case of intractable hiccups caused by syringobulbia and syringomyelia associated with an intramedullary hemangioblastoma in the cervical cord, which was successfully treated by surgical excision.

Case description

A 60-year-old man was referred from the neurology department after presenting with hiccups. The hiccups started about 1 year previously and had aggravated gradually. Three months ago, the hiccups began to be sustained during eating and sleeping without stopping and it disabled the patient's daily life. Although a neurological examination revealed a subtle gait disturbance and urinary incontinence, the deficits were so mild that it was not a concern. Several doctors treated with baclofen (5 mg tid), valproic acid (300 mg tid), and diazepam (2.5 mg tid), but the drugs were ineffective. The patient was sedated with 2 mg lorazepam to reduce the motion artifact for brain MRI, and his consciousness did not recover for several hours. Brain MRI showed extensive expansion of the central canal in the

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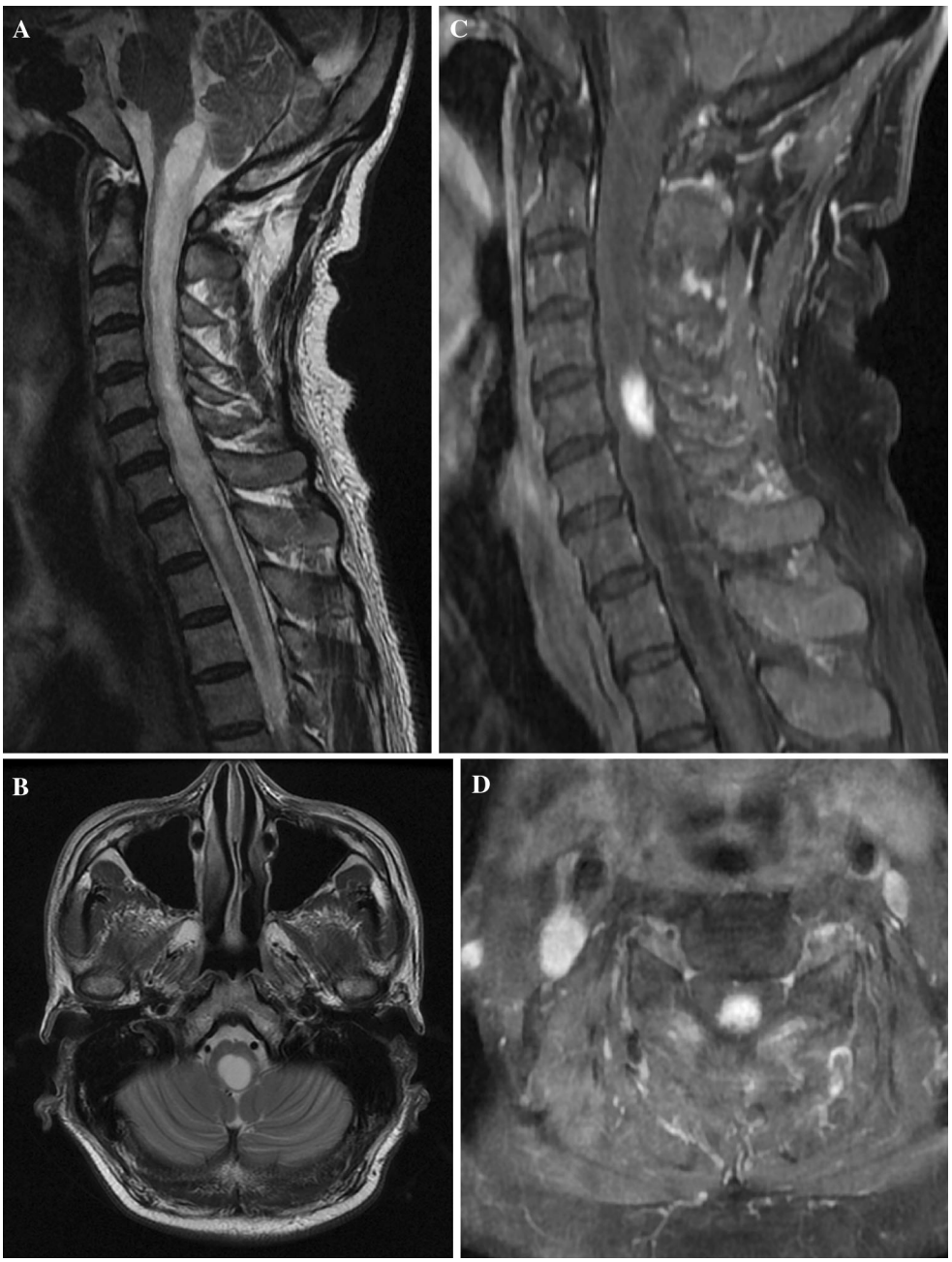

Fig. 1 **a**, **b** Preoperative T1 and T2-weighted sagittal magnetic resonance images (MRI) without contrast showing the syrinx from the brain stem to the T2 level. **b** Preoperative T2-weighted axial image showing the syrinx compressing the brain stem region. **c**, **d** Preoperative contrast enhanced T1-weighted MRI showing the enhancing mass located on the C5 spinal cord region

dorsal medullary region, which lead to a spinal MRI. The spinal MRI revealed that syringobulbia was connected to syringomyelia from C2 to T2 and associated with a highly enhancing intramedullary mass lesion at the C5 level (Fig. 1a–d). The lesion was removed through a right hemilaminectomy of the fourth and fifth cervical vertebra. A small amount of cerebrospinal fluid (CSF) gushed out during the midline myelotomy. A cherry red-colored mass was found near the center of the cord. The cord-tumor interface was well preserved, and dissection was not difficult. Copious CSF continuously spilled out from the upper and lower pole of the mass during dissection. Recovery from surgery was uneventful, and the hiccups disappeared immediately after surgery. The pathology of the specimen was compatible with hemangioblastoma (Fig. 2). The patient's gait and urinary symptoms improved gradually

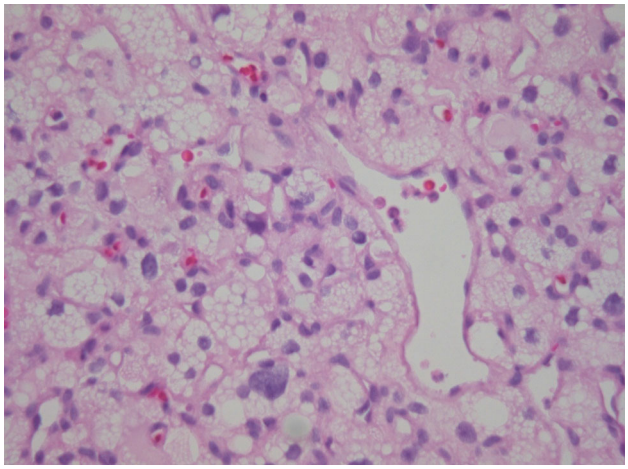

Fig. 2 The microscopic photography shows a rich capillary network in a stroma of clear vacuolated cell (hematoxylin-eosin, original magnification, ×400)

without sequelae. Mildly decreased proprioception of the right leg was observed. A MRI scan 5 months after surgery showed a marked decrease in the size of the syringobulbia and syringomyelia (Fig. 3). During the 2 years follow-up period, hiccups did not recur.

Discussion

Hiccups are repeated, myoclonic, synchronous, involuntary contractions of the diaphragm that can be accompanied by sudden closure of the glottis producing a clicking sound. Moreover, intractable hiccups are defined when they persist for >24 h, when the rate of contractions increases from 40 to 100 per min, or when they become refractory to usual treatment methods [4, 5].

The exact cause of intractable hiccups is obscure. The possible causes of intractable hiccups may be localized to the abdomen, thorax, neck, or CNS [6–14]. Hysteria, drugs, trauma, biochemical agents, infections, demyelinating diseases, tumors, and vascular disease have all been reported as causes of hiccups [15–22]. There have also been reports of familial cases without obvious etiology [4].

The hiccup reflex arc includes an afferent portion involving the vagus nerve, the phrenic nerve, and the sympathetic chain arising from T6 to T12 [23]. The efferent limb consists primarily of the motor fibers of the phrenic nerve [24]. Hiccup centers are believed to be located in the hypothalamus, medullary reticular formation, brain stem near the respiratory center, medial and dorsal medullary nuclei, and the cervical spinal cord between the C3 and C5 segments [5, 24]. Autopsy case reports have indicated that the nucleus tractus solitarius is a critical structure for hiccups. Kumral and Acarer [25] described an unusual case of primary medullary hemorrhage in the right medial medullary region, with mild dorsal extension, that was associated with intractable hiccups. One report describing a case of intractable hiccups associated with extensive syringomyelia and a Chiari malformation in the medulla oblongata have been published [5]. Recently, intractable hiccup developed by cavernous hemangioma in the medulla oblongata itself was reported [26]. Interestingly, the location of hemangioma described in this article is same area of maximal dilated portion of syringobulbia in the current case. Hiccups caused by a lesion on the cervical cord without a lesion on the medulla oblongata have been reported [27, 28]. Nevertheless, considering the hypothesis that the hiccup center is in the medulla or cervical cord along this pathway any lesion affecting this center or pathway may also evoke intractable hiccups. Considering hemangioma in the medullar and syringobulbia which is chronic lesion causing repetitive hemorrhage or gradual expansion of syrinx, hiccups are thought to be related to stimulation rather than destruction of one or more points of the hiccup reflex arc [29]. In the case of hiccups caused by a CNS lesion, the lesions are located mostly in the area postrema of the dorsal medulla oblongata. It has been suggested that there may have been susceptibility or hyperirritability of the hiccup center in some patients in whom such kinds of irritations lead to intractable hiccups.

Hiccups caused by many disease entities can be controlled by medical treatment. Baclofen, haloperidol, carbamazepine, chlorpromazine, gabapentin and methylprednisolone, particularly in patients with advanced cancer or neuromyleitis optica, have been recommended for treating intractable hiccups [4]. However, it is often difficult to treat intractable hiccups. In our case, intractable hiccups associated with hemangioblastoma accompanying syringobulbia and syringomyelia were successfully treated by surgical excision of lesion itself. Therefore, when persistent intractable hiccups occur, with or without neurological deterioration, a brainstem lesion should be suspected.

Conclusion

Intractable hiccups were caused by syrinx forming spinal tumor such as hemangioblastoma in the cervical cord and

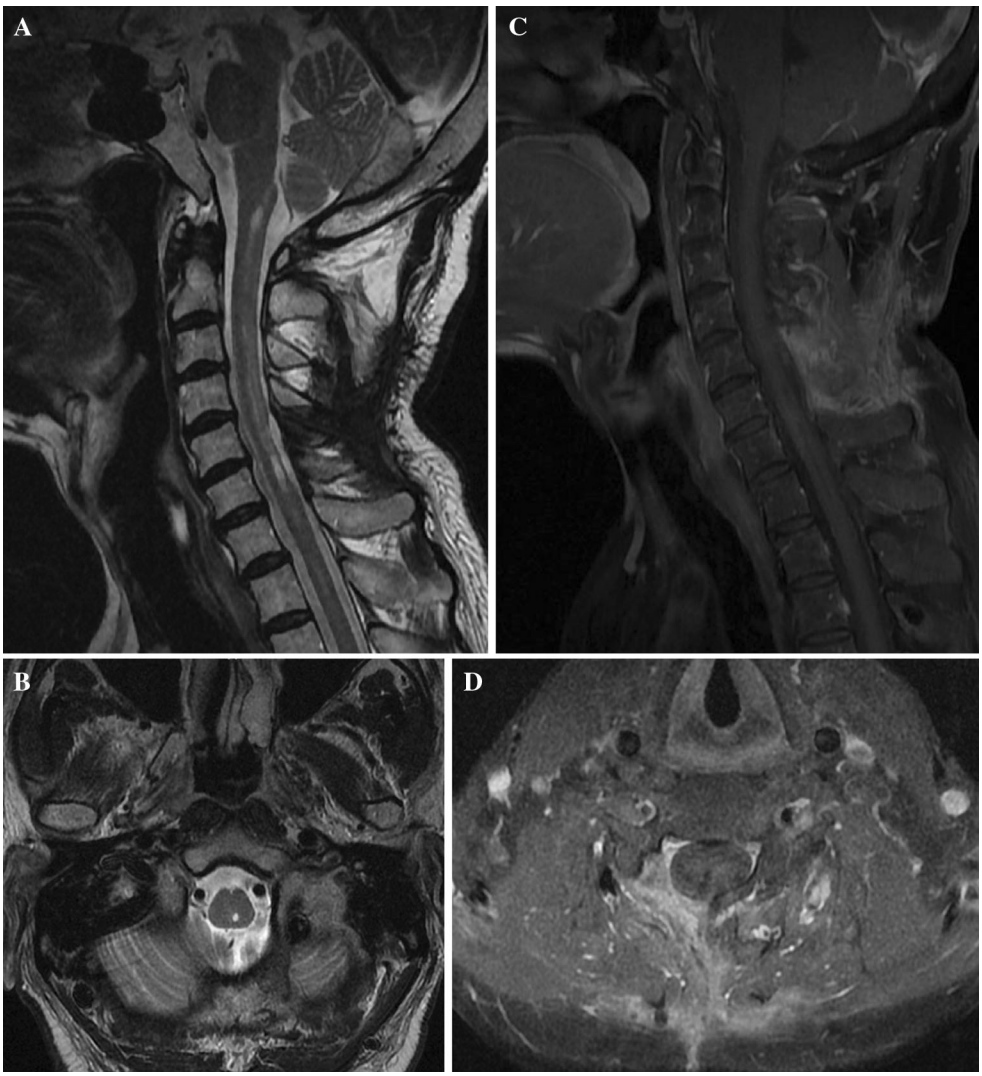

Fig. 3 **a**–**d** Postoperative magnetic resonance imaging (MRI) scans of the cervical spine obtained 5 months after surgery. **a** T2-weighted MRI scan in the sagittal plane demonstrating decompression of the brain stem. The cervical syringomyelia decreased slightly in size but remains. **b** T2-weighted axial MRI scan obtained at the brain stem level. The syringobulbia at the level of the brain stem diminished markedly. **c** Enhanced T1-weighted axial MRI scan obtained at the level of the removed hemangioblastoma

were treated effectively by surgical excision of only tumor itself.

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Conflict of interest None of the authors has any potential conflict of interest.

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