Continuous hypertension and tachycardia after resection of a hemangioblastoma behind the dorsal medulla oblongata: relationship to sympathetic overactivity at the neurogenic vasomotor center

Case report

Makoto Ideguchi, M.D., Ph.D., Koji Kajiwara, M.D., Koichi Yoshikawa, M.D., Shoichi Kato, M.D., Hideyuki Ishihara, M.D., Masami Fujii, M.D., Hirosuke Fujisawa, M.D., and Michiyasu Suzuki, M.D.

Department of Neurosurgery, Yamaguchi University Graduate School of Medicine, Ube, Yamaguchi, Japan

A very rare case of continuous hypertension and tachycardia after excision of a cerebellar hemangioblastoma at the dorsal medulla oblongata is presented. This 21-year-old man was admitted to the authors’ hospital with a headache and dizziness. Radiological examination revealed a tumor located behind the dorsal medulla oblongata and compressing it substantially. The tumor was completely resected, but after the surgery the patient experienced prolonged hypertension and tachycardia. Postoperative MR imaging showed a small injury at the dorsocaudal medulla that was located at the caudal site of the nucleus of the tractus solitarius (NTS). Because the NTS has been reported to play a central role in cardiovascular regulation along with the rostral ventrolateral medulla, the authors considered it possible that the NTS injury was the cause of the prolonged elevation of sympathetic tone.

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Key words • neurogenic hypertension • vasomotor center • sympathetic overstimulation • paramedullary tumor

Abbreviations used in this paper: BP = blood pressure; CVLM = caudal ventrolateral medulla; HR = heart rate; IML = intermediolateral cell column; NTS = nucleus of the tractus solitarius; RVLM = rostral ventrolateral medulla; VHL = von Hippel–Lindau.

It is very important to perform cardiovascular monitoring when manipulating a para- or intramedullary tumor because of possible damage to the vasomotor area of the medulla oblongata. We present a rare case of uncontrollable sympathetic overstimulation after removal of a paramedullary tumor, and speculate, after a review of the literature, that the patient’s symptoms were due to baroreceptor reflex circuit dysfunction.

Case Report

History and Examination. This 21-year-old man had suffered from anorexia and occasional dizziness for 6 years and had been found to be underweight during a health check-up at his school. He was referred to our hospital because of headache, accompanied by dizziness and loss of consciousness. His dizziness persisted after admission, but no neurological deficit was apparent. All vital signs were unremarkable. A Gd-enhanced MR imaging study revealed that a heterogeneous strongly enhancing mass lesion with an associated cyst was located behind the dorsal medulla oblongata (Fig. 1A and B). The medulla oblongata was strongly compressed ventrally by the tumor bulk in the fourth ventricle. Angiography of the bilateral vertebral arteries showed a strong tumor stain that was fed from the mainly bilateral posterior inferior cerebellar arteries, anterior inferior cerebellar arteries, and cortical branches of the bilateral superior cerebellar arteries (Fig. IC and D). The venous phase angiograms showed thick draining veins. The results of all laboratory tests, including testing for tumor markers, were within the normal range. The patient’s mean (± SD) preoperative BP was 111.8 ± 7.09/63.8 ± 8.30 mm Hg, which was also within the normal range.

Operation. The patient underwent bilateral suboccipital craniectomy with a C-1 laminectomy for removal of the tumor. Intraoperatively, the tumor bled profusely and was hard to separate from the parenchyma of the dorsal medulla oblongata because of its tight adhesion. During manipulation of the dorsal side of the medulla oblongata, the patient’s BP and HR suddenly rose to 190/95 mm Hg and 135 bpm, respectively, and the BP could not be stabilized for approximately 30 minutes thereafter.

Histological Findings. Histological examination

Abbreviations used in this paper: BP = blood pressure; CVLM = caudal ventrolateral medulla; HR = heart rate; IML = intermediolateral cell column; NTS = nucleus of the tractus solitarius; RVLM = rostral ventrolateral medulla; VHL = von Hippel–Lindau.
revealed 1) accumulation of abundant thin–walled and dilated vessels, and 2) foamy stromal cells that were distinguished by reticular variants. These findings were consistent with the diagnosis of cerebellar hemangioblastoma.

Postoperative Course. Antihypertensive agents (the \(\beta\)-blocker landiolol and the Ca-blocker diltiazem) were administered by constant intravenous infusion because the patient had hypertension and tachycardia of over 180/100 mm Hg and 120 bpm during the immediate postoperative period. His blood catecholamine levels remained elevated for 5 months after the operation (Table 1). Postoperative T2-weighted MR imaging revealed a small injury at the caudal dorsal portion of the medulla oblongata, as well as confirming that the tumor had been completely removed (Fig. 2). Azelnidipine treatment was initiated at approximately 5 months (148 days) after surgery, and was found to control the patient’s BP effectively (Fig. 3). This medication was chosen because it has an antihypertensive effect without reflex tachycardia and can also suppress the sympathetic overactivity caused by an abnormal baroreflex correlating with the injury to the dorsal medulla oblongata.15

Six months after surgery, the patient had no symptoms other than transient mild dysphagia and hoarseness caused by slight lower cranial nerve palsy.

Discussion

Neurogenic hypertension is associated with chronic elevation of sympathetic tone.1,9,12,20,23 It has been postulated that compression of the pressor center at the rostral ventrolateral medulla (RVLM) results in chronic overstimulation of the sympathetic nervous system, leading to systemic hypertension.15 There have been several reports on the association between posterior fossa tumors and hypertension, an association which was believed to be mediated through the same mechanism of medullary compression.4,14,30 In the majority of surgically treated cases, decompression (by means of vascular translocation or tumor resection) was associated with improvement of hypertension.4,8,10,14,30 Although our patient’s medulla was strongly compressed ventrally by the tumor mass and cysts, he demonstrated no remarkable sympathetic overstimulation before the operation, but experienced sudden and then chronic elevation of sympathetic tone during the intra- and postoperative periods despite complete decompression of the medulla. We therefore needed to consider the mechanism of sympathetic activation via neuronal mechanisms that regulate systemic arterial BP.

The NTS is the initial synaptic integration site for the afferent inputs from the aortic baroreceptor and arterial chemoreceptor from the carotid sinus (Fig. 4).5,7,25 These inputs powerfully inhibit the intermediolateral cell column (IML), which is composed of sympathetic preganglionic vasomotor neurons in the spinal cord via a multisynaptic pathway involving an excitatory projection from the NTS to the caudal ventrolateral medulla (CVLM), an inhibitory projection from the CVLM to the RVLM, and an excitatory projection from the RVLM to the IML (Fig. 4).13,26 In our patient, MR imaging showed injury to the dorsocaudal medulla in the area of the caudal NTS (Fig. 2C–F). In fact, given the sudden elevation of sympathetic tone, we may have caused some damage to the dorsocaudal medulla when separating the tumor from the brainstem parenchyma. It is now well established that peripheral baroreceptor input to the NTS is mediated by an excitatory amino acid neurotransmitter.7 Incomplete direct or indirect injury to the NTS by mechanical manipulation might elicit the inhibition of NTS activation via mediation by excitatory amino acids, the suppression of CVLM activation, the inhibition of RVLM suppression (which results in further RVLM activation), and finally, further activation of the IML in the spinal cord (Fig. 4).

We hypothesize that in our patient this phenomenon caused activation of the peripheral effectors in organs such as the heart, blood vessels, and kidneys, resulting in the continuous elevation of sympathetic tone. There are some reports supporting this hypothesis. The injection of GABA receptor antagonists into the NTS, which causes

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* Ref = reference.
indirect NTS activation, decreased BP in spontaneously hypertensive rats compared with normotensive control animals. Doba and Reis showed that bilateral lesions of the NTS in the rat, which produce central deafferentation of baroreceptors, result in the development of marked arterial hypertension in association with increased total peripheral resistance. In fact, in the present case, even 5 months after the operation, the patient’s blood norepinephrine level was still elevated at 637 pg/ml (Table 1).

It is common knowledge that hemangioblastomas develop in association with VHL disease. Our case was not associated with VHL disease, however; the patient’s retina was intact, he did not have a close relative suffering from VHL disease, and whole-body PET and CT revealed no abnormal lesion such as a pheochromocytoma. In light of these negative findings, we diagnosed incidentally occurring hemangioblastoma in the absence of VHL disease.

It is very important to regulate continuous activation of sympathetic tone such as occurred in our patient, because it is one of the most significant risk factors for a cardiovascular event. In addition, elevation of the HR is the mediator of sympathetic tone activation. Two large studies, the Framingham Study and a study from the Centre d’Investigation Préventives et Cliniques in France, showed that hypertensive patients with tachycardia are at high risk of death from a cardiovascular event. Although we first tried a β-blocker (landiolol) and Ca-blocker (diltiazem) intravenously in the immediate postoperative term, and thereafter used a β-blocker (bisoprolol or carvedilol) orally, it was hard to regulate the patient’s tachycardia (>100 bpm)—in contrast with the relatively controllable BP (Fig. 3). We next tried azelnidipine, a Ca-blocker that has been shown to decrease BP with a similar potency as other dihydropyridines, such as amlodipine, but without increasing the pulse rate. Moreover, because azelnidipine has been reported to suppress RVLM activation directly, this drug can suppress the central sympathetic outflow and ameliorate not only hypertension, but also tachycardia. One month after the initiation of azelnidipine therapy, the patient’s BP and HR were controlled within...
the upper limit of the normal range (Fig. 3). Careful clinical and radiological follow-up is still considered essential to assess the most appropriate antihypertensive therapy.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

References

Sympathetic overstimulation after paramedullary tumor resection


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