Posterior Fossa Brain Tumors and Arterial Hypertension

Review

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Abstract

Hypertension caused by arterial compression of the rostral ventrolateral medulla is well described. Much less information is available on the association between neurogenic hypertension and posterior fossa brain tumors. To date, multiple reports have supported the impression that a small subpopulation of patients with posterior fossa tumors can present with arterial hypertension, and many of those patients achieved significant improvement of their hypertension after tumor resection and medullary decompression. To review the relationship between posterior fossa brain tumors and hypertension, we detail the history, basic science, and clinical reports along with an illustrative case regarding this topic.

Key Words. Posterior fossa tumors, brain stem, arterial hypertension, essential hypertension

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Introduction

Approximately 20% of adults worldwide will develop hypertension, and 90% of them have essential hypertension (EHTN), an idiopathic form of the disease [6]. Among patients with apparent EHTN, a neurogenic cause has been suggested for a small subgroup with chronic elevation of sympathetic tone [10, 13, 23, 24, 31, 36]. It has been postulated that compression of the pressor center at the rostral ventrolateral medulla (RVLM) results in a chronic overstimulation of the sympathetic nervous system, leading to systemic hypertension [18]. Many studies have shown an association between arterial compression of the RVLM and EHTN [9, 12, 22, 28] and the role of microvascular decompression (MVD) in the treatment of hypertension in this subset patients. However, much less information is available on the association between posterior fossa tumors and hypertension, which presumably is mediated through the same mechanism of medullary compression. In this review, we summarize the basic science and clinical reports relating posterior fossa brain tumors and neurogenic hypertension, and we describe an illustrative case of a patient with complete resolution of her hypertension after total resection of her fourth ventricular ependymoma.

Illustrative Case

A 39-year-old woman presented with a 3-month history of headaches, nausea and vomiting, neck pain, and newly diagnosed hypertension. She was being treated with a single antihypertensive, triamterene/hydrochlorothiazide (Maxzide), at the time of presentation but had failed treatment with three other agents (metoprolol, valsartan, and hydrochlorothiazide) since the diagnosis of her hypertension 3 months earlier. Her neurological examination was unremarkable. Magnetic resonance imaging (MRI) revealed an enhancing lesion in the fourth

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ventricle that originated from the medulla (Figure 1). An ependymoma was completely resected. Postoperatively, the patient became normotensive with the cessation of all medications and remained so at her last follow-up 18 months after surgery (Figure 2).

Historical Review

Since the late 19th century, physicians have been well aware of the integral role that the central nervous system plays in the regulation of systemic blood pressure. In the early 1870s, Dittmar demonstrated that arterial blood pressure would drop to levels seen after spinal cord transaction when the neuraxis was interrupted below the level of the pons [11]. In 1946, Alexander concluded that the medulla contains neurons that are responsible for the maintenance of sympathetic tone and arterial blood pressure [2]. It was not until the 1970s, however, that clinical reports relating systemic hypertension and medullary compression emerged [8]. Jannetta and Gendell reported one of the first clinical series connecting EHTN and vascular compression of the brain stem [18]. In that report, 16 consecutive patients with EHTN underwent surgery for microvascular cranial nerve compression syndromes. At surgery, all were found to have vascular compression of the medulla between the ninth and tenth cranial nerves and the inferior olive, and such anomalies were not noted in 30 similar patients without EHTN. During the same period, clinical reports relating systemic hypertension and medullary compression by posterior fossa tumors also emerged. In 1970, Cameron and Doig reported 2 cases of cerebellar tumors with brain stem compression presenting with malignant hypertension [3]. Their paper was one of the first to connect systemic hypertension and posterior fossa tumors.

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Basic Science and Pathophysiology

Animal studies using various models have confirmed the presence of a subpial neuronal group (C-1) in the RVLM, which produces a transient pressor response when stimulated electrically, chemically, or mechanically [4, 5, 19, 32]. Its effect is mediated through its outflow to preganglionic neurons of the intermediolateral columns of the spinal cord [32-35]. This neuronal group in the RVLM contains the adrenaline-synthesizing enzyme phenylethanolamine N-methyl transferase and is an integral part of the medullary baroreflex pathway. Apart from adrenaline, nitric oxide [15, 17, 37], glutamate [38], and various neurotransmitters and neuropeptides [29] in the VLM have also been implicated in systemic blood pressure regulation. The afferents to the C-1 area originate from the solitary tract nucleus, which in turn is the termination site of arterial baroreceptors from the aortic arch (via the glossopharyngeal nerve) and carotid sinus (via the vagus nerve). In humans, histochemical studies of medulla at autopsy showed a similar population of catecholamine neurons in the subpial regions of the retro-olivary sulcus (ROS) near the root entry zone of the ninth and tenth cranial nerves bilaterally [1, 14]. This anatomic finding correlated with a recent physiologic study that mapped the C-1 area in humans to the VLM surface in the mid-ROS anterior to the nerve rootlets. In that study, intraoperative stimulation of the RVLM produced an increase in mean arterial pressure [30]. Interestingly, in the same study, areas mapped to the caudal ROS, both anterior and posterior to the nerve rootlets, responded to stimulation with a marked decrease in mean arterial pressure and heart rate, suggesting the role of a depressor in the caudal human medulla. It appears that the caudal RVLM exerts a direct inhibitory effect on the rostral pressor region.

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Although the above animal models and human studies supported the role of medullary stimulation and systemic hypertension, the laterality of the cardiovascular control center is still somewhat controversial. Evidence for left-sided dominance in cardiovascular regulation has been suggested by the authors of several studies. Naraghi and coauthors reported in both cadaveric and radiographic studies that patients with EHTN and medullary compression tend to have a left-sided compression [25-27]. Kleineberg et al. reported similar findings using angiography and topographic brain maps [20] and postulated that the efferent and afferent fibers of the left heart, the dominant chamber, are controlled by the left VLM. Nevertheless, others failed to show laterality regarding the cardiovascular center. In a recent study, Nicholas et al. reported that among hypertensive patients with medullary neurovascular compression, 56% were on the left side and 44% were on the right side [28].

With posterior fossa tumors, direct mechanical compression on the pressor zone in the rostral ventrolateral medulla is likely responsible for the pressor response observed. Although the animal studies described above have confirmed the pressor response obtained from direct mechanical stimulation of the rostral medullary pressor area, there is no experimental data on the minimal pressure or compressive force required to elicit the response. However, based on the reported cases along with our present case, it appears that both essential and malignant hypertension could result from posterior fossa tumors with various degrees of medullary compression, and its presence, rather than the extent of compression, appears to be more important in the pathogenesis of hypertension.

In addition to direct medullary compression, other factors may contribute to the pathogenesis of hypertension. Raised intracranial pressure and posterior fossa crowding may cause further disturbances of the vasomotor center through medullary ischemia, the

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mechanism thought to be responsible for the Cushing's response. This in turn can lead to a further activation of the sympathoadrenal pathways and systemic hypertension. It is also postulated that in certain cases, the abrupt rise in blood pressure can result in cerebral hyperemia and further the cycle of raised intracranial pressure. Furthermore, certain tumors were found to contain vasoactive neuropeptides, raising the possibility of a humoral connection between posterior fossa tumors and hypertension [16].

Interestingly, only a small number of patients with posterior fossa tumors develop essential hypertension, and the majority of reported patients were adults. We do not know why hypertension does not develop more often in young patients. Although posterior fossa tumors are more prevalent in children, most cases of essential hypertension associated with medullary compression from posterior fossa tumors actually occurred in adults, who are in general more prone to the development of hypertension.

Surgery, Operative Findings, and Outcomes

As more was learned about the pathophysiology of EHTN from medullary compression, case series began to emerge addressing the potential surgical correction of the disease. In 1985, Jannetta et al. reported the first clinical series on MVD for EHTN in 53 hypertensive patients undergoing craniotomy for other cranial nerve compressive syndromes [19]. Of those, 51 patients were found to have microvascular compression of the left RVLM by arterial loops at the time of surgery, and 42 of them underwent MVD of the left RVLM in addition to their primary decompression. In the follow-up period, 31 patients were normotensive. Subsequently, Jannetta and colleagues reported a study on 12 patients who underwent MVD of the left RVLM for severe medically refractory hypertension as a primary

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indication without concomitant cranial nerve compressive syndromes [21]. Eight patients noted improvement and 6 of them remained normotensive through their last follow-up. Geiger et al. reported similar findings in a prospective study [12]; in their study, 50% of patients became normotensive after surgery and required reduced doses of medications one year after surgery.

To date, only isolated case reports are available with regard to posterior fossa tumors and systemic hypertension. Cameron and Doig first reported 2 patients who presented with a cerebellar tumor with medullary compression and malignant hypertension in 1970 [3]. Postoperatively, one patient was borderline normotensive at her last follow-up 4 years after surgery and the other patient also noted improvement in his hypertension, although he later succumbed to tumor recurrence. Shortly thereafter, Evans et al. described a child who presented with a medullary astrocytoma and systemic hypertension associated with elevated urinary catecholamine metabolites [7]. Again, the child had significant improvement of his hypertension after radiation and chemotherapy. Interestingly, all three patients were initially thought to be harboring a pheochromocytoma, because of their malignant hypertension, episodic headaches, and the lack of neurological findings.

Complete resolution of systemic hypertension after surgical excisions of posterior fossa tumors has been reported by other authors in more recent cases (Table 1). Hedderwick et al. described a 29-year-old woman with persistent arterial hypertension that resolved following the excision of a posterior fossa hemangioblastoma [16]. Similarly, Yagil et al. also reported a patient whose malignant hypertension resolved completely after the resection of a posterior fossa medulloblastoma [39]. Our illustrative case was consistent with such reports, and our patient remained normotensive with no medications 18 months after surgery.

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In all cases, the hypertension, either essential or malignant, that coincides with tumor diagnosis was treated initially with appropriate antihypertensives to minimize end-organ damage. The antihypertensive regimen was only weaned judiciously in the postoperative period after a sustained and substantial decrease in blood pressure was observed.

Conclusions

Well-documented clinical evidence now indicates that compression of the RVLM can lead to hypertension in a small subpopulation of patients. Although most of these compressions arise from arterial loops in the medullary area, posterior fossa tumors can also be a source of medullary compression, leading to systemic hypertension. In both cases, medullary decompression through MVD or tumor resection has led to successful improvement in systemic hypertension in patients.

Acknowledgments

We thank Kristin Kraus for her editorial assistance in preparing this manuscript.

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Table 1. Reported cases of posterior fossa tumors and arterial hypertension

Case	Age/ Sex	Preoperative Blood Pressure	Preoperative Medications	Postoperative Blood Pressure	Postoperative Medications	Pathology	End Organ Damage
Yagil et al	30 M	190/135	HCTZ, propranolol, prazosin	140/90, four weeks after surgery	vasodilator and diuretic	Medulloblastoma	LVH, retinopathy
Mackay et al	46 M	240/140	Prazosin	Deceased	Never underwent surgery	Not available	Retinopathy, LVH
Evans et al	10 M	190/150	None	110/70	Phenoxybenzamine and hydralazine	Medullary astrocytoma	None
Hedderwick et al	29 F	200/105	None	123/84, two months after surgery	Cessation of all medications	Hemangioblastoma	None
Cameron et al	58 F	205/120	None	145/85, four years after surgery	Not available	Hemangioblastoma	Retinopathy
Cameron et al	31 M	250/135	None	160/90, immediately in the postoperative period	Not available	Medulloblastoma	Mild proteinuria
Kan and Couldwell	39 F	160/104	Triamterene/HCTZ, but has failed metoprolol, HCTZ, and valsartan	118/80, one month after surgery	Cessation of all medications	Ependymoma	None

Key: HCTZ=hydrochlorothiazide; LVH=left ventricular hypertrophy

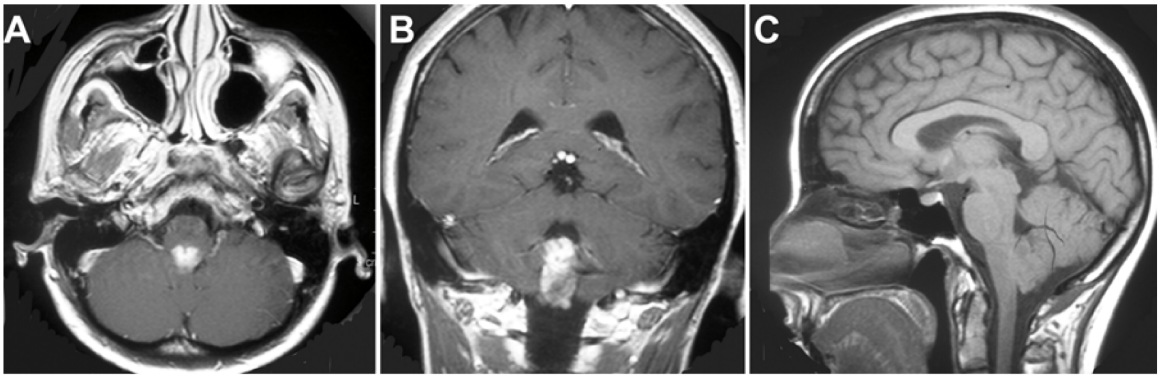

Figure 1. Axial (A), coronal (B), and sagittal (C) magnetic resonance imaging with gadolinium revealed a fourth ventricular tumor originating from the medulla.

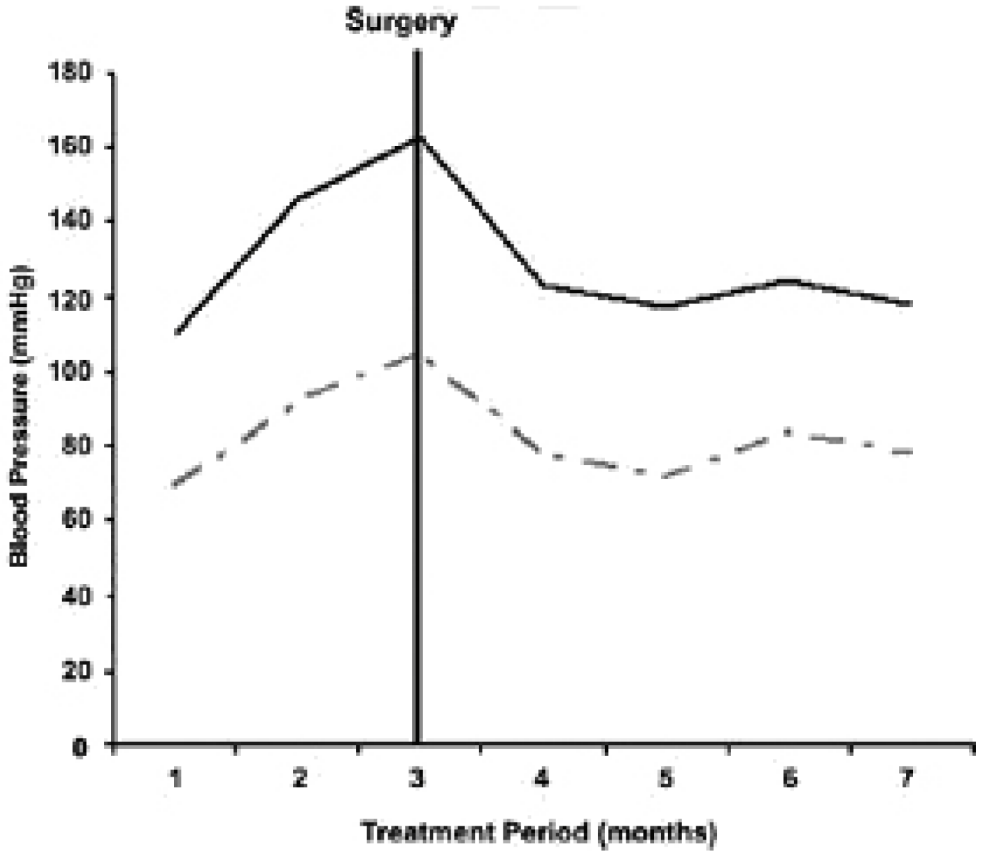

Figure 2. Blood pressure trend over the course of treatment. Solid line: systolic pressure; broken line: diastolic pressure.

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