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Subepyndemal hemangioblastomas of the cervicomedullary junction: lessons learned in the management of two cases

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Abstract
Objective This retrospective case series analyzes two cases of hemangioblastomas in the cervicomedullary junction.
Methods A survey of the pediatric staff and of the operative reports from medical records with a review of the literature and medical records of patients with the condition was conducted.
Results Two patients were successfully treated surgically.
Conclusion Surgery is the treatment of choice for hemangioblastomas of the cervicomedullary junction. Careful monitoring for unique complications, treatment of the tumor as a vascular malformation, and screening for von Hippel Lindau must all be employed to safely care for this challenging group of patients.

Keywords Hemangioblastoma · Brain tumor · Brain stem · Cervicomedullary junction · Ondine's curse · Neurogenic hypertension · von Hippel Lindau

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Introduction

Hemangioblastomas are rare tumors of the central nervous system that make up less than 2.5% of all intracranial tumors [7]. They are benign neoplasms with a natural history of slow growth. Hemangioblastomas are approached technically like arteriovenous malformations, as they are composed of densely packed thin-walled blood vessels without intervening parenchyma. Seventy-five percent of hemangioblastomas are isolated, but 25% of the cases present as part of the von Hippel-Lindau (VHL) disease, an autosomal dominant neurocutaneous syndrome. Left alone, hemangioblastomas tend not to hemorrhage but are lethal in that they lead to death in 82% of von Hippel-Lindau patients [1, 2]. The tumor itself in any location presents a surgical challenge, as it is vascular malformation. However, when located in the brainstem, these lesions are particularly challenging and, historically, have been associated with high morbidity. Early studies noted a 33–50% operative mortality when attempts were made to remove hemangioblastomas from the brainstem due to the close proximity to cardiac and respiratory control centers in the medulla [7].

Material and methods

After approval from the institutional review board, pediatric neurosurgeons at our institutions were surveyed regarding brainstem hemangioblastomas under their care. The medical records department of our pediatric hospital was queried with key words "hemangioblastomas, brain tumor," and five cases were found. Hemangioblastomas of other areas of the brain were excluded from the study. Three cases had been previously published [3]. Two newer cases were

retrospectively reviewed with the original three, and the following case reports were established.

Patients

Two attending physicians at our institution have together treated five hemangioblastomas in the cervicomedullary junction over more than two decades. Three cases were reported in 1986, and two newer additions have been added to the series with updates in experience and technology.

Patient 1

This 19-year-old gentleman presented with difficulty swallowing. On MRI, T1 weighted images with contrast show two discreet masses, one at the obex of the fourth ventricle and one at the cervicomedullary junction with a cystic component. (Fig. 1). Axial images demonstrate the cyst anterior to the enhancing nidus of the hemangioblastoma. The young man was operated on first for the fourth ventricular tumor and then for the mass at the cervicomedullary junction in a second setting. A midline suboccipital approach to the posterior fossa was made both times. The masses were identified and slowly rolled in alternating directions as feeding vessels were coagulated, all the while maintaining the integrity of the tumor. The hemangioblastoma became progressively smaller as this was done. Eventually, the decrease in size made it possible to access the ventral primary feeding vessel and coagulate it, thereby removing the mass. After two surgeries, he made a complete recovery. The presence of multiple lesions by definition lead to a diagnosis of von Hippel-Lindau disease.

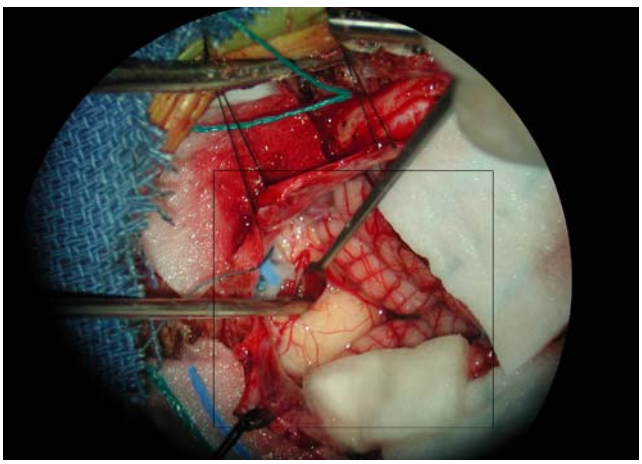

Fig. 1 Intraoperative photograph of mulberry like mass in patient 2. Upon recognizing this as a hemangioblastoma, decision was made not to biopsy

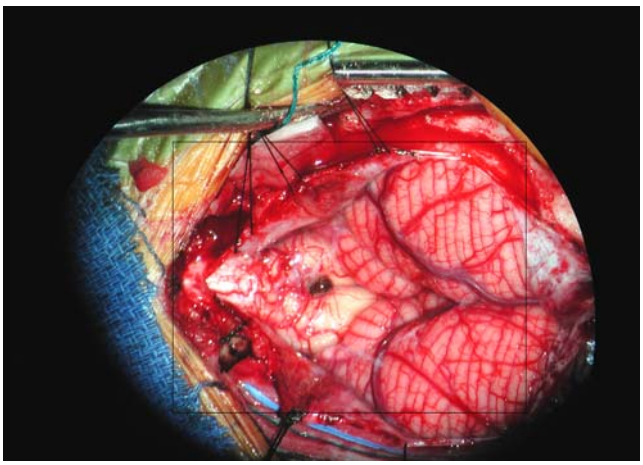

Fig. 2 Intraoperative photograph of isolated and coagulated vascular nidus of patient 2's hemangioblastoma

Patient 2

This 5-year-old child presented with an 8-month history of nausea and vomiting. She underwent a complete gastrointestinal work-up that was negative. Psychiatric causes were investigated as well but to no avail. Eventually, she developed dysphagia, and an MRI was obtained. A mass was found at the cervicomedullary junction (Fig. 2). T1 sagittal, axial, and coronal images show a contrast enhancing mass in a larger cystic component that is slightly hyperintense to cerebral spinal fluid. Preoperatively, it was thought the tumor was likely a juvenile pilocytic astrocytoma, as it was a homogenously enhancing mass with a cystic extension. Hemangioblastoma was considered less likely in the differential diagnosis because of the mural nodule associated with a cyst.

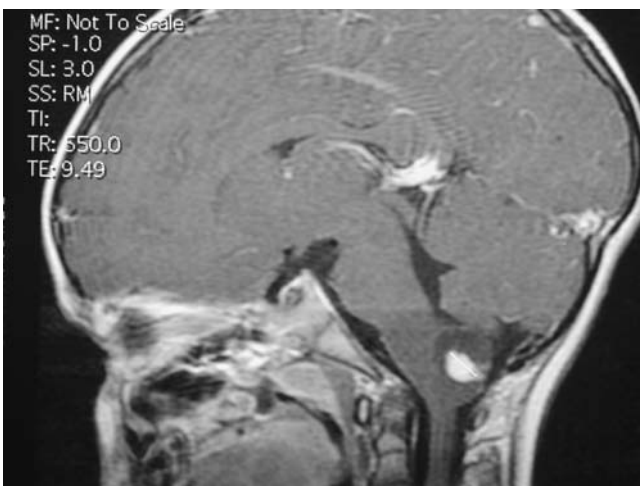

Fig. 3 T1 saggital contrast enhanced MRI of 5 year old with hemangioblastoma (patient 2)

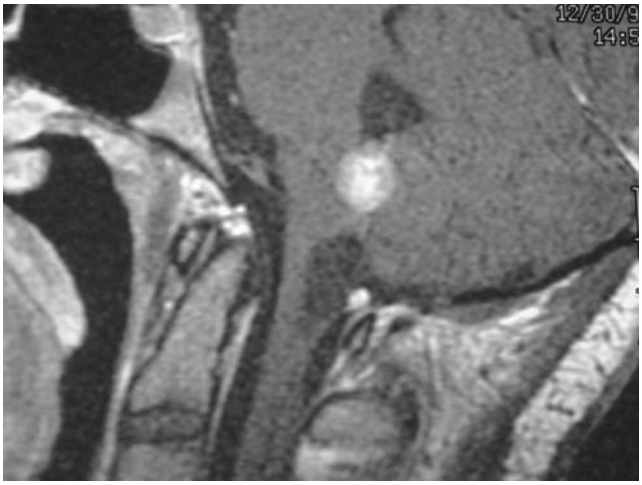

Fig. 4 T1 saggital contrast enhanced MRI of 19 year old with two hemangioblastomas (patient 1)

A midline posterior fossa approach with occipital craniotomy and removal of the posterior arch of C1 was undertaken. The dura was opened, and the cerebellum was retracted laterally and rostrally, exposing a cyst. To our surprise, when the cyst was opened, a bright red mulberry-like mass was in the center of the cavity (Fig. 3). The decision was made not to biopsy, as it was recognized as a hemangioblastoma. The mass was removed en bloc after isolating the nidus (Fig. 4). She made an uneventful recovery and remains asymptomatic. Screening for von Hippel-Lindau lesions was negative.

Results

This series adds two cases to complete a series of five who had operative management of hemangioblastomas in the brainstem. They are patients number 1 and 2 in Table 1. Two had von Hippel-Lindau disease. Two had perioperative neurogenic hypertension, and one experienced perioperative central sleep apnea. One of these patients has continued to have hypertension to this day. Of the other patients, one has had no change in his symptoms, whereas another patient has had continued progression of her symptoms.

Discussion

Successful surgical management of this tumor starts with consideration in the preoperative differential diagnosis. The classic appearance is a homogeneously enhancing mass that may have a cystic component. Hemangioblastomas are benign slow-growing neoplasms that carry a significant operative risk. According to Osborne, 90% of all hemangioblastomas are in the posterior fossa, but 20% occur at the brainstem. The obex is a common location for the presentation of a hemangioblastoma in von Hippel-Lindau disease but rare in spontaneous cases. The tumor itself is a well-circumscribed, sometimes-cystic lesion with a mural nodule. The nodule is composed of a tightly bound group of thin-walled blood vessels. Interspaced are clusters of large polygonal stromal cells whose origin is unclear [1].

Gross debulking of the nodule may lead to catastrophic hemorrhage. It must be technically treated as an arteriovenous malformation. The nidus must be identified. Its vascular supply must be isolated, controlled, and eliminated. In light of this, preoperative detailed vascular imaging such as angiography or MRA may be advantageous. Several authors reporting series of spinal and supratentorial hemangioblastomas have noted that failure to achieve gross total resection was often secondary to massive bleeding. It was found in our two most recent cases published in this paper that it is possible to successfully remove these tumors. They must never be biopsied. The tumor should be rolled back and forth in an attempt to gently create a plane between the intact nidus and the surrounding brain. Vascular feeders should be taken in an attempt to shrink the nidus and eventually remove it en masse. In our experience, total removal of the cyst capsule has not been necessary to prevent

Table 1 Summary of the Memphis brainstem hemangioblastoma series

	Age at presentation	Von Hippel Lindau	Presenting symptoms	Perioperative complications	Long-term morbidity
Patient 1	19	Yes	Dysphagia	None	None
Patient 2	5	No	Vomiting	None	None
Patient 3	28	No	Headaches ataxia	Hypertension	Hypertension, no decrease in Ataxia
Patient 4	28	No	Nausea, vomiting, and ataxia	Hypertension, Ondine's Curse	Ataxia, headaches—after reoperation by other institution for separate tumor
Patient 5	18	Yes	Neck pain, right hand numbness	None	Reoccurence of symtoms

recurrence, as long as the hemangioblastoma itself is completely removed.

Gross total resection of a brainstem tumor carries significant risks. Two that are particular to the anatomy at hand are Ondine's curse and neurogenic hypertension. Two of our patients experienced perioperative neurogenic hypertension, which in one case has persisted. This is believed to be due to the pathology affecting the nucleus tractus solitarius in the brainstem.

Ondine's curse is a well-described phenomenon of central sleep apnea. Patients are asymptomatic when awake but when asleep may become apneic. Maximal edema in the nervous system occurs 48–72 h postoperatively. Some advocate leaving patients intubated for this period of time, but at the very least, patients should be monitored closely in the immediate postoperative period [3, 5, 6]. Patient 4 demonstrated these findings, and patient 3 developed aspiration pneumonia 2 weeks after surgery.

Twenty-five percent of the patients with hemangioblastomas have von Hippel-Lindau disease. Von Hippel Lindau disease is an autosomal-dominant neurocutaneous syndrome that is linked to a genetic defect on the short arm of chromosome 3 (3p25–3p26). This area on the tip of the chromosome is thought to encode for a tumor suppressor gene [1]. The vHL protein is involved in transcription elongation and regulation of hypoxia-induced factors such as vascular endothelial growth factor. Tumors' characteristic of the von Hippel Lindau include: hemangioblastomas of the central nervous system, retinal hemangioblastomas, renal cell carcinoma, pheochromocytoma, islet cell tumors of the pancreas, and cysts of the pancreas, liver, kidney, and epididymis. The hemangioblastoma itself may cause erythropoetin elevation and an abnormally elevated hematocrit as a result. Von Hippel Lindau is a clinical diagnosis made by multiple central nervous systems hemangioblastomas, a central lesion with a peripheral lesion, e.g., in the viscera, and finally a characteristic tumor as mentioned above combined with a first degree relative that is affected [2].

Several groups who have presented a series of hemangioblastomas advocate baseline screening for all patients for the von Hippel-Lindau syndrome. Any patient with a hemangioblastoma should receive detailed imaging of the entire neuraxis for additional tumors, abdominal ultrasound, a detailed ophthalmologic exam, a genetics consult, and an investigation of family history for relatives with blindness and early death from brain tumor [2, 4]. A blood test is currently available to screen for the vhl gene (http://www.vhl.org). Patients in whom von Hippel Lindau is diagnosed should receive annual surveillance for CNS, retinal, and visceral lesions. Seventy-five percent of hemangioblastomas are isolated. If the initial screen for von Hippel Lindau is negative and a gross total resection is achieved, extraordinary follow up is not recommended.

Conclusions

Hemangioblastomas of the cervicomedullary junction present a surgical challenge. This series shows that it is possible to safely resect these hemangioblastomas. The tumor should be treated as a vascular malformation during its resection. All patients should have a basic screening for von Hippel-Lindau disease to identify other CNS tumors and prevent morbidity from other organ systems. Perioperatively, a high index of suspicion should be held for neurogenic hypertension and Ondine's curse.

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