Original Article

The Impact of Preoperative Endovascular Embolization on Surgical Outcome of Cerebellar Cystic Hemangioblastoma

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ABSTRACT

Background: Cystic hemangioblastoma (HB) account for 1.5-2.5% of all intracranial and 7-12% of posterior fossa tumors. The treatment of choice is total resection though their hypervascularity and location present a formidable challenge. Preoperative embolization may have a role in these cases. Objective: We present a single center experience with twelve cases of intracranial cystic hemangioblastomas. Six retrospective cases and another six cases in a prospective study design of preoperative embolization. The study presents a preliminary experience with poly –vinyl alcohol copolymer for hemangioblastoma vessel embolization before surgical resection. Patients and Methods: This study included all patients of intracranial hemangioblastoma admitted in our department over a period of 5 years, from January 2010 through January 2015. Results: There were a total of twelve patients (nine males and three females). Six cases received preoperative artery embolization. The other six cases underwent surgical resection without preoperative embolization. Complete obliteration of tumor blush at the control angiogram was achieved in five out of six patients while near total obliteration was achieved in one patient. In the embolized group, complete resection was achieved in all the patients. All the six patients were free of serious complication after the surgery. There were no postoperative hemorrhage, neither permanent morbidity nor mortality in this group. Conclusion: Preoperative embolization of cystic HB provides a safe, short and clear surgery for the neurosurgeons and faster rehabilitation for the patients.

INTRODUCTION

Surgical excision of hyper vascular cranial tumors can be daunting and is associated with excessive blood loss. The need to decrease intraoperative tumoral hemorrhage has refined the neuroendovascular techniques for preoperative embolization of tumors. Since these techniques were first described in the early 1970s, the field has matured rapidly, with advances in micro catheter technology and improvements in the design of embolisates. They include an understanding of neurovascular anatomy and of the natural history and behavior of tumors. 1 Tumor embolization means interruption of blood supply to a tumor. The goal of preoperative embolization is to decrease intraoperative blood loss. Embolization-induced tumor ischemia often softens a tumor, thereby facilitating its resection. So, tumor resection then becomes safer and more complete. 2 Intracranial hemangioblastoma (HB) are benign and highly vascular neoplasms mainly located in the posterior fossa of the central nervous system. Cushing and Bailey coined the term ‘Hemangioblastomas’ to describe tumors arising from the endothelial cells of the central nervous system. They account for 1.5-2.5% of all intracranial and 7-12% of posterior fossa tumors. 3 The treatment of choice for tumors containing mural nodules such as hemangioblastoma is total resection though their hypervascularity and location present a formidable challenge. As this lesion usually originated in the posterior cranial fossa and is highly vascular tumor with excessive arterial bleeding occasionally occurs in the narrow operative field. So, it is hard to perform total resection. If successful preoperative embolization of hemangioblastoma is performed, it will facilitate surgery and total resection can be done. 4

PATIENTS AND METHODS

A total of twelve patients with cystic cerebellar HB underwent complete surgical resection in our department of Neurosurgery between January 2010 and January 2015. Of them, six cases received preoperative transarterial embolization, including four males and two females, and their ages ranged from 9 to 58 years. Another Six cases underwent surgical resection without
preoperative embolization, including five males and one female, and their ages ranged from 22 to 61 years. Inclusion criteria were as follows: patients were diagnosed with cystic cerebellar HB and underwent surgical resection in our department. Exclusion criteria were patients with HB located outside cerebellar hemispheres and in solid tumors.

**Preoperative embolization:**

Embolorization material: For embolization, we used Excelsoir SL 10 and 10/18 (Stryker, USA), Transend 10 soft tip (Stryker, USA), different sizes Polyvinyl alcohol (PVA, 150-500 um).

Embolorization process: Patients were maintained under general anesthesia. A cerebral angiography was performed to investigate the tumor feeding arteries and venous drainage. Using the road-mapping technique, microcatheter was advanced to tumor end of feeding artery. Super selective angiography was performed to avoid the involvement of blood vessels in normal tissue. Then, according to the vascular diameter, blood flow velocity, blood circulation time and tumor staining, embolization was proceeded with different sizes of PVA particle diluted in contrast material (1 bottle +30 ml non ionic contrast material) starting with smaller and finishing with larger particles until total obliteration of the tumor blush.

Surgical Staff: Preoperative embolization was conducted by the second author. Tumor resection was leaded by first author and with the assistance of experienced team.

A comparison of the patients’ age, gender, rate of complications and clinical effects, surgical time, amount of intraoperative blood loss and blood transfusion were done between the two groups.

**RESULTS**

This study has been conducted on twelve patients with cystic hemangioblastoma at our Neurosurgical Department. The study included both retrospective evaluation of cases operated without embolization and a prospective evaluation of newly operated cases after preoperative endovascular embolization from January 2010 through January 2015. Six cases received preoperative arterial embolization, including four males and two females, and their ages ranged from 9 to 58 years. The other six cases underwent surgical resection without preoperative embolization, including five males and one female, and their ages ranged from 22 to 61 years.

The patients had full general and neurological examination. Also full laboratory investigations were done with special consideration for the coagulation profile. CT and MRI Brain with contrast were done in all the cases. CT Brain Angiography was done in some cases as MRI Brain with contrast was not conclusive. Digital Subtraction Angiography (DSA) was done in all the cases as a primary procedure before endovascular treatment decision. Male distribution was predominant in this age group. The main presentation was headache and blurring of vision in most cases. The patients presented with headache 90%, neck pain 70%, dizziness 60%, blurred vision 90%, vomiting 60% and/or loss of balance in 50% of patients.

**Patients with embolization:**

The study presents a preliminary experience with polyvinyl alcohol copolymer for hemangioblastoma vessel embolization before surgical resection. Diagnostic imaging revealed a posterior fossa cystic mass with a nodular component. Angiography demonstrated a significant vascular blush with arteriovenous shunting that was a characteristic of hemangioblastoma. Tumor vessels originating off the posterior inferior cerebellar artery were embolized in five cases and originating from anterior inferior cerebellar artery in one case. Fig. (1).

![Fig. 1 a-d: a: Axial post contrast MRI shows an intensely enhancing right cerebellar HB. b: Coronal post contrast MRI shows intensely enhancing right cerebellar HB. c: The vertebral artery injection shows the dense vascularity of a hemangioblastoma. d: The deep arterial supply is obliterated with super selective PVA embolization.](image-url)
Surgical resection:
In embolized group, complete resection was achieved in all the patients. There was no adjacent brain tissue damage. The mean operation time was 4.5 hours, average intraoperative blood loss was 450 ml (range 300-700 ml), and average amount of blood transfusion was 400 ml. Blood transfusion was not needed in one patient. All the six patients were free of serious complication after the surgery. There were no postoperative hemorrhage, neither permanent morbidity nor mortality in this group.

In the control group, complete resection was achieved in five patients. Near total resection of the tumor was achieved in one patient with excessive bleeding and masking of the surgical planes. Also, adjacent tissue contusion with excessive use of cauterization occurred. The mean operation time was 6.5 hours, average intraoperative blood loss was 1000 ml (range 600-1800 ml), and average amount of blood transfusion was 900 ml. one patient had postoperative hemorrhage at the tumor bed that needed surgical evacuation. Only one patient had ataxia at hospital discharge that improved on follow up. There was no mortality in this group. Table (1)

Table 1: Shows comparison of both groups.

<table>
<thead>
<tr>
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<th>HB with preoperative embolization</th>
<th>HB without preoperative embolization</th>
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<tbody>
<tr>
<td>Mean operation time</td>
<td>4.5 Hours</td>
<td>6.5 Hours</td>
</tr>
<tr>
<td>Average intraoperative blood loss</td>
<td>450 ml</td>
<td>1000 ml</td>
</tr>
<tr>
<td>Average amount of blood transfusion</td>
<td>400 ml</td>
<td>900 ml</td>
</tr>
<tr>
<td>Post operative complications</td>
<td>No</td>
<td>one patient with ataxia</td>
</tr>
<tr>
<td>Postoperative hemorrhage</td>
<td>No</td>
<td>One case</td>
</tr>
<tr>
<td>Surgical resection</td>
<td>Complete in all cases</td>
<td>Complete in five cases and subtotal in one case</td>
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Preoperative embolization resulted in complete obliteration of all tumor vessels, transforming a highly vascular tumor into an avascular mass. Safe and uneventful surgical resections were performed the next day. Fig. (2)

Follow up was done clinically and radiologically by brain CT and MRI (pre and post contrast) after 3 months to evaluate the possibility of recurrence and the extent of excision.

**DISCUSSION**

Preoperative embolization is used to devascularize the tumor bed by filling intratumoral vascularization as deep as possible into the precapillary level to initiate tumor necrosis, decrease blood loss during surgery and thus make it easier and possibly, more radical. Hemangioblastoma is a benign and highly vascular tumor. Complete surgical resection of highly vascular tumor such as hemangioblastoma may be challenging due to excessive bleeding. Preoperative embolization of these lesions may decrease the intraoperative blood loss and facilitate excision. They report three cases of cerebellar hemangioblastoma that were embolized using Onyx. Selective internal, external carotid and vertebral angiograms are followed by selective catheterizations of feeding arteries to analyze arterial supply of the tumor.

Fig. 2 a-e: a: Axial post contrast MRI shows an intensely enhancing left cystic cerebellar HB. b: Coronal post contrast MRI shows an intensely enhancing left cystic cerebellar HB. c&d: The vertebral artery injection shows the dense vascularity of a hemangioblastoma. e&f: The deep arterial supply is obliterated with PVA embolization.
Complex vascular anatomy of the skull base requires meticulous digital subtraction angiograms to reveal dangerous anastomosis from external carotid artery branches to internal carotid or vertebral arteries. 8

This technique was first employed by Brooks in 1930 for the treatment of carotid-cavernous fistula. Embolization facilitates tumor resection by limiting blood loss, and causing ischemic necrosis of the lesion. Preoperative embolization of cranial hemangioblastomas is used to facilitate surgical resection of these lesions. Several embolic agents have been used for decreasing the arterial supply to the lesion with adequate capillary bed penetration. 1,9

Hemangioblastoma constitute 2% of craniospinal tumors. 7 It occurs mostly within the cerebellar hemispheres and rarely at the vermis, cerebellopontine angle, or brain stem. Most of these lesions are sporadic, but in approximately 20% are associated with von Hippel-Lindau (VHL) disease. VHL disease is transmitted in an autosomal dominant fashion. The tumors are hypervascular, which makes their resection exceedingly difficult, particularly in eloquent areas. Severe intraoperative hemorrhage is a significant contributor to the morbidity and mortality rates associated with the resection of hemangioblastoma. Before microsurgical techniques, morbidity and mortality rates approached 50%. 10 There was no morbidity or mortality in our series.

The ideal embolic agent should be permanent, easily used, and should not encumber tumor resection. Embolic materials are divided into three categories: mechanical devices, particles, and liquid agents. Mechanical devices, such as balloons or coils, are able to occlude large feeders but they lack the ability to penetrate the tumor bed. Particles, such as polyvinyl alcohol have also been used. Despite smaller particles have the advantage of better tumor bed penetration; their use also carries a higher risk of inadvertent non-target embolization. Polyvinyl alcohol PVA is the most common particulate agent used. It can be used for all tumors, including those that were associated with high blood flow and arteriovenous shunting. 9,10 We use PVA for embolization of our embolized cases.

Takeuchi et al reported their series of hemangioblastoma treated with preoperative embolization using primarily particles and concluded that preoperative embolization is useful to reduce operative complications when 80% or more of tumor could be embolized. Three patients had temporary neurological complications as a result of the embolization. 11 There was no morbidity or mortality in our series.

Terada et al. 12 noted disappearance of tumor flow voids after embolization with Gelfoam or PVA. Most tumors showed a decrease in the level of contrast enhancement. Bendszus et al. 13 found that more completely embolized tumors showed less contrast enhancement on post embolization MRI. This coincide with our cases that showed less contrast enhancement on post embolization MRI.

Wakhloo et al. 14, however, reported diminished enhancement on contrast MRI in only 2 of 14 patients after embolization with 150- to 300-lm particulates. They theorized that this disappointing radiographic result reflected proximal occlusion of the feeding arteries by larger particulates.

Grand et al. 15 described only a minimal decrease in tumor enhancement after embolization and attributed this discrepancy to vasospasm of the embolized vessels. Therefore, smaller particulates may allow embolization of more distal capillaries to increase tumor necrosis after embolization. PVA allow more distal capillaries embolization that caused tumor necrosis in our series.

The optimal timing for preoperative embolization is controversial. Some authors recommend surgical resection one to five days after embolization, whereas others advocate waiting one to two weeks. With time, embolization-induced necrosis shrinks and softens the tumor, thereby facilitating surgical resection. Compared with more proximal occlusion, delivering micro emboli directly into the tumor maximizes this necrotic effect. The potential for recanalization of embolized vessels and collateral development increases if surgical resection is significantly delayed (more than one week). 16,17,18

In contrast, Kai et al. 19 retrospectively reviewed forty five patients with meningiomas embolized with cellulose porous beads. Resectability was greatest in tumors excised seven to nine days after embolization. However, the greatest benefit is derived from embolization if surgical resection is performed within a few days of embolization. 17,20 We operated our cases three to five days after embolization.

The blood supply, on angiography is typically via the posterior inferior cerebellar artery (PICA) and, less commonly, via the anterior inferior cerebellar artery (AICA) or branches of the superior cerebellar artery (SCA) branches. Dural branches of the vertebral artery, such as the posterior meningeal artery, may supply superficial lesions. The criteria for embolizing hemangioblastoma include large tumors with well-defined arterial feeders that are not readily accessible surgically and the lesion is larger than three cm. 21

Tampieri et al. 22 treated two patients with large hemangioblastoma, one spinal and one involving the posterior fossa, with preoperative embolization. Both lesions were then resected with blood loss of less than 100 mL.

Eskridge et al. 4 treated nine patients with craniospinal hemangioblastoma with PVA embolise and got no permanent complications. One patient developed malignant posterior fossa edema associated with hydrocephalus after treatment. They advocated perioperative steroids, intensive care unit observation, and surgical resection within 48 to 72 hours because of the potential for recanalization of feeding arteries after embolization with PVA. We found that embolization facilitated tumor manipulation and surgical resection in our embolized cases more than cases without embolization.
Conway et al. described four of forty patients with hemangioblastoma who underwent preoperative embolization. These investigators recommended reserving embolization for tumors with large surgically inaccessible feeders.

Eskridge et al. reported that one patient experienced worsening of hydrocephalus after embolization, requiring emergency craniotomy and surgical resection. Cornelius et al. reported different clinical outcome of preoperative particulate embolization between spinal and cerebellar hemangioblastoma. Although the outcome of embolization in spinal hemangioblastoma was favorable, that of all cerebellar hemangioblastoma (three patients) was not. This result might be due to smaller capillary size of cerebellar hemangioblastoma causing venous congestion and subsequent rupture.

Preoperative embolization of larger tumors may be performed without additional neurologic deficit even if the tumor is fed by more than one pedicle. However, there have been reports of worsening of preexisting hydrocephalus within two hours of embolization. There was no mortality or morbidity in our cases.

Liquid embolic agents (N-butyl cyano acrylate) (NBCA) and Onyx have the best combination of durability and penetration, being able to devascularize the tumor reaching its core. The major disadvantage associated with NBCA embolization is that the glue polymerizes very rapidly when it contacts an ionic solution such as blood. It increases the risk of gluing the micro catheter in place.

Onyx is a non-adhesive liquid embolic agent (ethylene-vinyl alcohol) dissolved in an organic solvent, dimethyl sulfoxide. With Onyx, fewer arterial feeders require catheterization because of the diffusion properties of the agent. It allows deep penetration of the tumor capillary bed, which often results in artery-to-artery embolization of tumor feeders. Another major advantage of this agent in tumor embolization was that reflux along the infusion catheter could be tolerated without requiring removal of the catheter.

We use PVA in our embolized cases.

A nineteen patients presenting with symptoms of vertigo and or headaches were diagnosed with HB based on preoperative magnetic resonance imaging and cerebral angiographic findings. Embolization had a favorable outcome in all the patients. No permanent neurological complications were observed after preoperative embolization using NBCA. The authors recommend NBCA as an embolization material for large cerebellar HBS.

Unlike NBCA, Onyx can be injected much more slowly, on the order of minutes. The injection can even be discontinuous, thereby allowing angiographic assessment of the embolization and improving the control of embolic delivery. Another advantage of Onyx is its excellent surgical handling properties. Because the tantalum is black, in the operating room, the embolized vessels are easy to see. Onyx includes its radio-opacity, durability, and availability in commercial formulations and the relatively modest inflammatory reaction that it generates.

Given the advantageous features of PVA, the need for fewer arterial catheterization, excellent tumor penetration, and low complication profile, we believe that its use may actually be effective and safe compared with other agents.

Direct puncture embolization overcomes many of the limitations of endovascular embolization but its safety and feasibility for intracranial tumors is unknown. They reported a 48-year-old man who was diagnosed with a large cerebellar hemangioblastoma after presenting with headaches and gait ataxia. After the skull burr hall was performed in a standard fashion, Onyx was injected through the catheter, resulting in 75% tumor devascularization without evidence of complications. The patient was taken directly to surgery where a gross total resection of the hemangioblastoma was achieved with an acceptable operative blood loss. At his 2 year follow-up, the patient was neurologically intact without neuroimaging evidence of residual tumor. We had no cases with direct puncture of the tumor.

Clinical data from eleven patients with solid hemangioblastomas in the dorsal medulla oblongata who were treated with endovascular embolization followed by micro neurosurgery were analyzed retrospectively. They conclude that preoperative endovascular embolization is a safe and effective adjunct treatment. Employing this treatment, solid hemangioblastomas in the dorsal medulla oblongata can be safely and completely resected.

In our cases of preoperative embolization, marvelous decrease in blood loss was noticed in most of cases. Short operative time was reported. Clear surgical field, well demarcated line of cleavage and good devascularization were noticed in comparison with the other cases without preoperative embolization. Tumor dissection and debulking were very good in 90% of cases. Total excision was achieved in most cases and documented in early postoperative CT brain with contrast. This coincides with the results of Sakamoto et al. 2014. They conclude that presurgical embolization using NBCA made tumor removal safe and reduced bleeding volume in posterior fossa HB.

**CONCLUSION**

Preoperative embolization of brain tumors is an adjuvant treatment before surgery. Preoperative embolization plays a vital role in the management of hyper vascular tumors, such as hemangioblastomas. As it decreases blood loss, shortens operative time, leads to less manipulation to normal brain tissues and facilitates total excision. Recent advances in micro catheter technology and micro embolisates have improved the safety of preoperative embolization, which has become a requisite tool for the neurosurgical team and represents a significant improvement in patient care. Preoperative embolization of cystic HB provides a safe,
short and clear surgery for the neurosurgeons and faster rehabilitation for the patients.

Approval was provided by the Ethical Committee Faculty of Medicine, Tanta University, Egypt.

Disclosure:
The authors have no personal, financial or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES


