Posterior Fossa Giant Solid Hemangioblastomas

Submitted for MCh Neurosurgery

By

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Sept 2012

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Programme : MCh Neurosurgery

Month & year of submission : September, 2012

CERTIFICATE

This is to certify that the thesis entitled “Posterior Fossa Giant Solid Hemangioblastomas” is a bonafide work of Dr. Adesh Shrivastava and was conducted in the Department of Neurosurgery, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram (SCTIMST), under my guidance and supervision.

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DECLARATION

This thesis titled "Posterior Fossa Giant Solid Hemangioblastomas" is a consolidated report based on a bonafide study of the period from January 2010 to June 2012, done by me under the Department of Neurosurgery, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram.

This thesis is submitted to SCTIMST in partial fulfillment of rules and regulations of MCh Neurosurgery examination.

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ACKNOWLEDGEMENT

The guidance of **Dr. Suresh Nair**, Professor and Head of the Department of Neurosurgery, has been invaluable and I am extremely grateful and indebted for his contributions and suggestions, which were of invaluable help during the entire work. He will always be a constant source of inspiration to me.

I owe a deep sense of gratitude to **Dr. Girish Menon** for his invaluable advice, encouragement and guidance, without which this work would not have been possible.

The critical remarks, suggestions of **Dr. Gopalakrishnan C. V**, helped me in achieving a high standard of work.

I am deeply indebted to **Dr. Mathew Abraham**, **Dr. Easwer H. V**, **Dr. Krishnakumar K, Dr. George Vilanilam, Dr. Jayanand Sudhir** and thank them for their constant encouragement and support.

Last but not the least, I owe a deep sense of gratitude to all my patients without whom this work would not have been possible.

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INTRODUCTION

Hemangioblastomas are benign tumors of central nervous system, and constitute 1.5-2.5 % of all brain tumors and 7-12 % of all infratentorial tumors in adults (1). Hemangioblastomas are most commonly associated with von Hipple-Lindau syndrome which associated with 3p chromosomal mutation (2, 3). In these cases they are present in multiple locations in and outside the central nervous system (4, 5). Sporadic solitary hemangioblastomas, although rare, are known to be confined to the posterior cranial fossa (5, 6). With respect to their content, hemangioblastomas can be cystic, solid or mixed type (5). Those solitary hemangioblastomas occurring in the brain stem and spinal cord are prevalently of a solid type, even though solid lesions can also be present in cerebellar hemispheres (1). As the name indicates, hemangioblastomas possess highly vascularized nodules. These tumors are treated by complete excision, making surgery the primary treatment of choice. However, their highly vascular nature and their frequent proximity to vital structures in the brain stem and upper cervical spinal cord preclude complete excision, especially of tumors exceeding a resectable size (6).

The type and size of the tumor also determines the appropriate method of treatment. Whereas cystic tumors provide a relatively less difficult dissection, solid tumors are often a challenge due to the minimal safe manipulation space available in the posterior fossa. Similarly, whereas small tumors in resectable locations can be completely excised, those in vitally eloquent brain areas may require primary radiosurgery(5). Large tumors require a staged combination treatment strategy, where all three modalities, i. e., interventional embolization, surgery and radiosurgery, can prove beneficial (4). Preoperative embolization of hemangioblastomas of the posterior fossa minimizes surgical morbidity and mortality by reducing the vascularity of the tumors, and thus prevents intraoperative bleeding disasters (5,6). Two aspects must be considered when treating these vascular tumors: a) the prevention of spontaneous bleeding (which can be achieved by complete embolization, whenever possible), and b) the elimination of the space occupying process from the posterior cranial

fossa (via surgery or radiosurgical shrinking), both aimed at maximally preserving the functional integrity of eloquent brain structures (4). Thus the modern treatment concept of hemangioblastomas includes a staged strategy, where the tumors are first embolized, and then removed surgically soon after. However, even super-selective embolization of large hemangioblastomas in or near the brainstem is not without infarction hazards, which may not only eventually compromize caudal cranial nerve function, but also become life threatening. Thus preoperative embolization of large tumors that draw their vascularity from the posterior circulation is not always possible; moreover, there are numerous innominate minor feeders that simply cannot be embolized. Surgical resection is nevertheless indicated, because of the space occupying nature of the lesions, before bleeding or decompensation of the brain stem can occur (4).

GIANT HEMANGIOBLASTOMAS

All these issues get compounded as the solid tumor size increases. The term giant hemangioblastomas has been used only rarely in the literature. Zhou et al in 2005 reported a series of thirty three patients with brainstem hemangioblastomas of which twenty nine were solid. They categorised their tumors as five small (<3cm), nineteen large (3.1 to 4cm) and nine giant (>4cm) hemangioblastomas (5). Similarly in 2009, Rachinger et al from Germany, reported their experience with 17 consecutive cases of solid hemangioblasomas where they also labelled case of size more than 4cm as 'Giant'.

Here we present eight cases of giant solid hemangioblastomas and discuss the management issues associated with them.

REVIEW OF LITERATURE

History and Introduction

In 1928, Cushing and Bailey introduced the term hemangioblastoma. It refers to a benign vascular neoplasm that arises almost exclusively in the central nervous system (7). Cerebellar hemangioblastomas are frequently referred to as Lindau tumors because Swedish pathologist Arvid Vilhelm Lindau first described them in 1926 (8, 9). Hemangioblastomas are grade I benign tumours which have been classified under the category of meningeal tumors in the fourth edition of WHO classification of CNS tumors, 2007 with an uncertain origin(10). They are defined as slow growing , highly vascular tumour of adults, occurring in the cerebellum, brain stem or spinal cord; histologically comprised of stromal cells and small blood vessels; occurring in sporadic forms and in association with von Hippel-Lindau (VHL) syndrome (10).

Epidemiology

Hemangioblastomas are rare tumors and according to various studies they account for 1.5% – 2.5% of intracranial tumors (11). Majority of the central nervous system hemangioblastomas are located in the posterior cranial fossa accounting for 7% - 10% of posterior fossa tumors (12). Constans et al in 1986 reported that Hemangioblastoma is the most common primary adult intraaxial posterior fossa tumor on the basis of 40 personal cases of infratentorial hemangioblastomas and a review of 36 series from the literature for a total number of 1023 patients (13). Hemangioblastomas can occur sporadically but in about 20% to 30% cases, it is associated with von Hippel-Lindau (VHL) disease (14). The disease usually occurs in the adults, but VHL syndrome associated tumors may present in

significantly younger patients than do sporadic tumors (15). Usually no sex predilection has been observed and these tumors are said to occur with equal frequency in males and in females (10).

Hemangioblastomas can occur in both solid and cystic forms with variable amount of solid component (16). Relative incidences of these morphological variants varies according to the location and cystic tumors mostly occur in the cerebellar hemispheres, while solid tumors mostly occur in the brain stem, cerebellar vermis and spinal cord (12).

The second most common location of hemangioblastomas is the spinal cord (17-20), where the frequency ranges from 2-3% of primary spinal cord neoplasms to 7-11% of spinal cord tumors. This tumor's occurrence in other locations, such as the supratentorial compartment (21-23), the optic nerve (24), the peripheral nerves (25), or the soft tissues of extremities (26) is extremely rare.

Etiopathogenesis

The genetic basis of hemangioblastomas is very much evident considering their presence in various clinical syndromes, and with Von Hippel-Lindau syndrome in particular. The genetic hallmark of hemangioblastomas is the loss of function of the von Hippel-Lindau (VHL) tumor suppressor protein (27).

Genetics of hemangioblastomas:

Sequencing of constitutional DNA from patients with haemangioblastoma reveals VHL mutations in a proportion of cases, as a recent study identified 5 germline mutations among patients from 16 families (28). Among 14 haemangioblastoma patients without evidence of a family history or additional clinical manifestations of VHL syndrome, 2 germline mutations

in the VHL gene were identified (29). While biallelic inactivation of the VHL gene is a frequent occurrence in familial cases, it is not common in sporadic tumours. Studies on sporadic tumours, including somatic mutation analyses, assessment of allelic loss, and hypermethylation studies have revealed loss or inactivation of the VHL gene area only in approximately 20% to 50% of the cases (30, 31). One study using comparative genomic hybridization indicated that multiple chromosomal aberrations, including those on 3p and elsewhere, are observed in sporadic tumours (21). Loss of heterozygosity studies demonstrate allelic imbalance at chromosome 6q in the majority of cases, with a reported minimally deleted region at 6q23-24 (32).

The von Hippel-Lindau disease (VHL):

VHL disease is a syndrome of multisystem neoplastic disorders characterized by hemangioblastomas of the cerebellum, retina, brainstem and spinal cord, along with renal cysts/tumors, epididymal cysts, and pancreatic endocrine tumors and cysts among others (33, 34). The disease has an incidence of 1 in 35,000 live births and it has been estimated that 30% of patients with hemangioblastomas are actually suffering from VHL disease (35). Multiple authors have reported a wide range for incidence of hemangioblastomas in various locations in the central nervous system : Cerebellum – 44 to 80%, retinal – 41 to 59%, brainstem – 10 to 25% and spinal cord – 10 to 50% (34, 36, 37). The disease has an autosomal dominant inheritance with around 95% penetrance by the end of sixth decade of life (38). The VHL gene has been mapped to the short arm of chromosome 3 at the allelic location 25, and functions as a tumor suppressor gene, thus requiring biallelic inactivation for tumor development (35). As compared to sporadic cases, hemangioblastomas in VHL disease occur on an average a decade earlier.

Friedrich in 2005 classified VHL disease into four subtypes (39):

Type I: may have manifestations of VHL except pheochromocytoma

Type II: pheochromocytoma is characteristic

Type IIA: have low risk of renal cell carcinoma and neuroendocrine pancreatic tumor

Type IIB: higher risk of cell carcinoma and neuroendocrine pancreatic tumor

Type IIC: risk of pheochromocytoma only with risk of hemangioblastoma or renal cell carcinoma

The spectrum of clinical manifestations of the disease is broad. About 40 different lesions in 14 different organs have been described (40). These include retinal and central nervous system (CNS) hemangioblastomas, endolymphatic sac tumors, renal cysts and tumors, pancreatic cysts and tumors, pheochromocytomas, and epididymal cystadenomas.

Histogenesis of hemangioblastomas:

The histogenesis of haemangioblastoma is uncertain. Tissue microdissection, combined with deletion analysis of the VHL gene locus, have identified the stromal and not the vascular cells as neoplastic (30, 41). More controversial, however, has been the identification of the nature of the stromal cell. A series of immunohistochemical studies has been performed to elucidate the origin of the stromal cell resulting in identification of markers that are consistently, frequently or only occasionally immunoreactive with the stromal cells. Neural cell adhesion molecule (NCAM/ CD56) is consistently immunoreactive (42, 43). Positive immunoreactivity for S-100 protein is frequently but not always observed (44, 45). Factor XIIIa has been reported to be expressed by haemangioblastoma stromal cells (45, 46), while other studies found it exclusively expressed by the reactive vascular component (47, 48). Similarly, factor VIII has been found in the stromal cells by some authors (46, 49, 50), whereas others report expression to be limited to vascular cells (47). GFAP positivity is

variable (42, 51) and it is unclear whether GFAP marks entrapped reactive astrocytes, stromal cells with glial differentiation or stromal cells with intracytoplasmic GFAP from phagocytic activity. It is therefore not surprising that the histogenesis of the stromal cell is controversial. Suggested origins include glial cells (52), endothelial cells (50), arachnoid cells (53), embryonic choroidplexus (54), neuroendocrine cells (55), fibrohistiocytic cells (56) cells of neuroectodermal derivation (57) or heterogeneous cell populations (47). It was noted that stromal cells of haemangioblastoma express proteins common to embryonal haemangioblast progenitor cells (58). It was further noted that one such protein, Scl, has a distribution of expression in the developing nervous system that is similar to the topographical distribution of haemangioblastoma tumours in patients.

Pathology

Hemangioblastomas on gross examination in-situ are usually cherry red in color. They may include a cyst that contains a clear or xanthochromic fluid, but solid tumors are as common as cystic ones. The tumor usually grows inside the parenchyma of the cerebellum, brain stem, or spinal cord; it is attached to the pia mater and gets its rich vascular supply from the pial vessels. The cyst walls are non-neoplastic and comprised of compressed cerebellar tissue. However, extramedullary and extradural hemangioblastomas also have been described (59). Jagannathan in 2008 on the basis of his study on eighty consecutive patients of cerebellar hemangioblastomas found that lesions are preferentially distributed in the posterior half of the cerebellum, than they are in the brainstem and spinal cord, especially in cases of VHL disease. Also he reported that 70% of cerebellar lesions are cystic (60). The cysts which are proposed to develop due to thin leaky vessel walls through which proteins

donot cross readily, can be present in three patterns (60): peritumoral, intratumoral and combined.

Hemangioblastomas donot have a true capsule but are well circumscribed. They have numerous capillary channels, lines by a single layer of endothelium, surrounded by reticulin fiblres. The cardinal feature on Microscopic examination of the specimen reveals three cell types with in a hemangioblastoma: endothelial cells, pericytes surrounded by a basement membrane and polygonal stromal cells. The stromal cells are characteristically large and vacuolated, but can reveal highly considerable cytologic variation, and abundant vascular cells. Cellular and reticular variants are distinguished on the basis of the abundance of the stromal cell component (10). Numerous thin walled vessels are apparent and are readily outlined by a reticulin stain. In accordance with the highly vascular nature of haemangioblastoma, intratumoural haemorrhage may occur. Some tumours show extensive sclerosis. In adjacent reactive tissues, particularly in cyst and syrinx walls, astrocytic gliosis and Rosenthal fibers are frequently observed. The tumour edge is generally well-demarcated, and infiltration into surrounding neural tissues rarely occurs. Mitotic figures are rare. The stromal cells represent the neoplastic component of the tumour. Their nuclei may vary in size, with occasional atypical and hyperchromatic nuclei. However, their most characteristic and distinguishing morphological feature is represented by numerous lipid-containing vacuoles, resulting in the typical ‘clear cell’ morphology of haemangioblastoma, which may resemble metastatic renal cell carcinoma. Adding to the complexity of this differential diagnosis is the fact that patients with VHL syndrome are prone to renal cell carcinoma. There are also reports of tumour-to-tumour metastasis (renal cell carcinoma metastatic to haemangioblastoma) in this setting (61). As such malignant transformation of

these tumors have never been reported. Though there have been reports of CSF seeding in post operative cases but they remain benign.

Silver et al in 1952 did a clinicopathological study on 40 cases of cerebellar hemangioblastomas and recognized three patterns on histology (62):

Juvenile Hemangioblastomas: Composed of thin walled capillaries and dilated vessels which are tightly packed.

Transitional Hemangioblastomas: composed of thin walled capillaries and dilated vessels intermingled with stromal cells, some of which are lipid laden.

Clear Cell Hemangioblastomas: These are neoplasms made up almost entirely of sheets of xanthoma cells with a rich vascular stroma.

Immunohistochemistry:

The stromal and capillary endothelial cells differ significantly in their expression patterns. Stromal cells lack endothelial cell markers, such as von Willebrand factor and CD34, and do not express endothelium-associated adhesion molecules such as CD31 (PECAM) (63, 64). Unlike endothelial cells, stromal cells variably express neuron-specific enolase, neural cell adhesion molecule, S-100, CD56 and ezrin (42, 63, 65). Vimentin is the major intermediate filament expressed by stromal cells. Stromal cells express a variety of molecules, including CXCR4 (27, 66) aquaporin 1 (67), several carbonic anhydrase isoenzymes (68), as well as EGFR (56), but do not usually express glial fibrillary acidic protein(64). Vascular endothelial growth factor (VEGF), a prime regulator of physiological and pathological angiogenesis, is

highly expressed in stromal cells (69), with corresponding endothelial expression of its receptors VEGFR-1 and -2 (70), and the endothelial cell receptor Tie-1 (71). The endothelial cells of haemangioblastomas also express receptors for other angiogenic growth factors, including platelet-derived growth factors (72). Immunohistochemistry is useful to distinguish haemangioblastoma from renal cell carcinoma. Renal cell carcinoma is positive for epithelial markers, such as EMA, while haemangioblastomas are negative. Additional potentially useful markers include the D2-40 antibody (73) and inhibin A (74), which are positive in haemangioblastoma but generally negative in renal cell carcinoma. CD10 staining, in contrast, shows the opposite results (75).

Electron microscopy:

Ultrastructurally, the most prominent feature of the stromal cells is an abundant electron-lucent cytoplasm containing lipid droplets. Some studies have demonstrated electron-dense bodies, reminiscent of Weibel-Palade bodies, and small granules, reminiscent of neuroendocrine granules.

Proliferation:

Proliferation rates tend to be low, in the range of 0–2%, as measured by the MIB-1 antibody (76).

Clinical features

The clinical presentation of hemangioblastomas usually depends on the anatomical location and growth patterns. Cerebellar lesions may present with signs of cerebellar dysfunction, such as ataxia and discoordination, or with symptoms of increased intracranial pressure due to associated hydrocephalus. These are produced by mass effect of the expanding cyst associated with the tumor. Only in the purely solid type does the actual tumor mass itself

cause pressure effect and in such cases the solid component grows to considerable size before presentation. Often the cyst may expand at a much faster rate than the tumor itself, so that the imaging of the symptomatic patient reveals a large cystic tumor with only a small nodular solid component. Hemangioblastomas usually have a saltatory growth patterns with spurts of growth between periods of quisence. Overall growth rate remains slow which is why they usually present in adults. And eventually it is observed that intracranial hemangioblastomas present with a long history of minor neurological symptoms that, in most cases, are followed by a sudden exacerbation, which may necessitate immediate neurosurgical intervention (36).

Clinical manifestations of mass effect:

In a study by Wanebo et al in 2003 on 231 patients of von Hippel-Lindau disease with 650 hemangioblastomas, they found that 72% of symptomatic tumors were associated with cysts and in most instances the cyst was larger than the tumor associated with it. They also reported that almost all symptom producing spinal hemangioblastomas had associated syringomyelia. It was also concluded that sign and symptoms develop as a result of rate of cyst growth and its volume (36).

Rachinger et al in 2009 retrospectively analysed 17 consecutive patients with 23 solid hemangioblastomas in the posterior fossa and spinal cord. Their observation was that despite frequent localization in functionally important areas such as brainstem and CPA, rather unsystematic clinical symptoms such as vertigo and headache were the main symptoms, except for spinal cord lesions, presenting with progressive quadriparesis. Except for one patient presenting with vestibular nerve irritation, no distinct cranial nerve symptoms were found. One patient, suffering from a haemangioblastoma within the

medulla oblongata, presented in a comatose state due to an acute haemorrhage. Otherwise distinct neurological deficits were rare for intracranial locations (77).

Jagannathan in his series of 80 patients of cerebellar hemangioblastomas in 2008 found that presenting symptoms were consisted with a mass in the posterior fossa and included the following: headache (75%), gait difficulties (55%), dysmetria (29%), hydrocephalus (28%), nausea/vomiting (28%), nystagmus (13%), dysarthria (9%), and/or dysphagia (8%)(60).

The symptom profile in 160 patients of VHL disease with 214 posterior fossa hemangioblastomas, reported by Wanebo et al in 2003 was as follows (36). Patients with cerebellar lesions presented with gait ataxia (64%), dysmetria (64%), headaches (12%), diplopia (8%), vertigo (8%), and/ or emesis (8%). Those with brainstem lesions presented with hypesthesia (55%), gait ataxia (22%), dysphagia (22%), hyperreflexia (22%), headaches (11%), and/or dysmetria (11%).The appearance of symptoms was related to the volume of the mass effect of the lesion. As expected, a serial increase in the size of a hemangioblastoma was observed in cerebellar and brainstem lesions, as patients progressed from being asymptomatic to symptomatic ($p < 0.0001$ & $p < 0.01$, for the cerebellum, & brainstem, respectively; unpaired t-test).

<u>Hemangioblastomas and hemorrhage:</u>

Hemangioblastoma is rarely documented as a cause of apoplexy due to intracerebral hemorrhage (lobar or cerebellar), however some cases indicate that if cases of intracerebral hemorrhage are carefully examined, abnormal vessels consistent with hemangioblastoms may be found with surprising frequency even though the CT and /or angiography were negative (78). Glasker et al in 2005 reviewed a clinical database of 277 patients with central nervous system hemangioblastomas for the incidence of spontaneous or perioperative

hemorrhage. They concluded that the overall incidence of hemorrhage in patients with hemangioblastoma is low. An important indicator for the probability of hemorrhage is tumor size, as spontaneous or postoperative hemorrhage occurred exclusively in extraordinarily large tumors. Hemangioblastomas smaller than 1.5 cm (the vast majority of these tumors) harbor virtually no risk of spontaneous hemorrhage. Furthermore, they observed severe postoperative hemorrhage in two extraordinarily large solid hemangioblastomas (4 and 5 cm) (79). In 2006 Lee et al reported a case of cerebellar hemangioblastoma in a 69 year male where the diagnosis was delayed by four year after presentation with spontaneous cerebellar hemorrhage. Conversly, Young et al in 2010 reported a case of 49 year old male who had undergone radiosurgical treatment of cerebellar hemangioblastomas. Follow up imaging showed reduction in tumor size and contrast enhancement and the tumor was labelled as controlled. But the patient suffered a delayed cerebellar hemorrhage which was fatal (80). De San Pedro et al in 2010 did a literature review on massive hemorrhage due to hemangioblastomas and found 45 reported cases. In all the intracranial cases the hemorrhage was parenchymal and subarachnoid hemorrhage was reported only in spinal hemangioblastomas. They also illustrated a case of purely tetraventricular bleed in a case of cervicomedullar hemangioblastoma and claimed it to be the first such case (81). In 1999 Guzman et al repoted a case of cerebellar hemangioblastoma with a coexistent arterial aneurysm on the feeding artery of the tumor is reported. The patient presented with an acute onset of headache, loss of consciousness, and left-sided hemiparesis due to a posterior fossa hemorrhage found adjacent to a hemangioblastoma. Four-vessel angiography revealed an aneurysm on the anterior inferior cerebellar artery (AICA), which was the main feeding vessel of the hemangioblastoma (82).

Other manifestations:

Apart from the usual expected manifestations in a case of any posterior fossa space occupying lesion, infratentorial intracranial hemangioblastomas have anecdotal reports of uncommon presentations. Song and Lonser in 2008 presented a report on four cases of posterior fossa hemangioblastomas that presented with features of pathological satiety and atypical anorexia. All the four lesions were localized to the obex region (83).

Similarly in the Rachinger series of 2009, one patient with hemangioblastoma localized to the CP angle, the presentation was with features of vestibular nerve irritation (77).

Imaging and diagnostic workup

The diagnostic workup of suspected hemangioblastomas must include, in addition to history, physical, and thorough neurological examination, complete neural axis imaging and abdominal CT scan or ultrasound. The goal of these additional tests is to reveal associated lesions that may be a part of VHL disease complex (84).

Lee et al in their landmark paper on Magnetic Resonance Imaging of posterior fossa hemangioblastomas have traditionally described them into four types. Type 1 (5% of posterior fossa HBs) is a simple cyst without a macroscopic nodule. Type 2 is a cyst with a mural nodule (60%). Type 3, or solid tumors (26%), and type 4, or solid tumors with small internal cysts (9%), are also seen in the cerebellum and predominate in the spinal cord (85).
Skull Radiographs show no specific findings suggest hemangioblastomas and are of no diagnostic value.

Computerised Tomography Scan (CT Scan):

CT scan is no more considered a preferable investigation because of poor sensitivity (especially for lesions with small nodules) and is ordered only if there is a contraindication for Magnetic Resonance Imaging, as in cases of in-situ ferromagnetic materials like stainless steel clips, orthopaedic implants or non-MRI safe pacemakers (86). None the less, CT scan is often used, especially for follow-ups. On CT scans, the tumor appears well circumscribed, solid, or cystic, with a mural nodule. Usually, the nodule is smaller than the cyst. This feature helps in differentiating it from cystic astrocytoma, which tends to have a larger nodule. The cyst is hypoattenuating on CT scans (87-90). In precontrast studies, the nodule is isoattenuating relative to the surrounding brain tissue, but it is hyperattenuating in occasional cases. After the administration of contrast material, the attenuation is equivalent or higher than that of the straight sinus, and the nodule enhances homogeneously. Commonly, the nodule abuts a pial surface. Multiplanar CT and MRI help in identifying the subpial localization. Generally, the cyst wall does not enhance, but occasionally, it can appear as a paper-thin line of enhancement that represents a combination of compressed cerebellar tissue and gliosis. Occasionally, the edge of the tentorium can be misinterpreted as an enhancing rim, with differentiation made by using coronal sections.

CT shows all the clinically significant features of hemangioblastoma, along with secondary features such as hydrocephalus and edema. False-negative results are found in patients with small nodules (< 5 mm) that can be obscured by posterior fossa artifacts; therefore, CT is not a sensitive screening procedure. False-positive results are rare. Metastases and cystic astrocytoma can appear similar. A diagnostic pitfall is the hemangioblastoma with a small central lucency, which can be interpreted as a necrotic metastasis. In this case, the ringlike enhancement of the necrotic nodule is thick and irregular (87).

Magnetic resonance Imaging (MRI):

MRI with gadolinium enhancement is the best study for screening, with the highest sensitivity and specificity compared with CT and nonenhanced MRI. Large studies are necessary to achieve a high degree of confidence; however, the advantages are obvious (91-94).

Intracranial hemangioblastomas can manifest as 3 morphologic patterns based on the macroscopic pathology. These are well correlated with the MRI findings and include the following (85, 95).

- Cyst with a small mural nodule
- Solid mass with a central cystic component
- Solid tumor without a cystic component

A cyst with a small mural nodule is the most common presentation. Cystic fluid surrounding the nodule is hyperintense on T1-weighted images and hyperintense on T2-weighted images. Characteristics of the fluid vary slightly related to protein content. The mural nodule is isointense on T1-weighted images and demonstrates high signal on T2-weighted images. After the administration of gadolinium-based contrast medium, the nodule shows prominent enhancement and the cyst does not enhance (95).

Solid masses with a central cyst behave similarly; therefore, the different morphologic patterns have been postulated to be part of the natural history of a solid tumor that develops a cystic component around or within it (96, 97).

Solid hemangioblastomas occur less frequently than the other patterns. The lesion is isointense or hypointense on T1-weighted images and hyperintense on T2-weighted images. Transition from a solid tumor to a classic cystic tumor with a small mural nodule has been reported. Occasionally, signal in solid tumor components can be heterogeneous on T1-weighted images, with areas of increased signal within the solid portion. These regions may represent lipid in the stromal cells or methemoglobin from hemorrhage (91). Commonly (60-69%), hemangioblastomas have associated internal or peripheral serpentine signal voids, which represent dilated afferent and efferent vessels (98). Therefore, the presence of a peripheral cyst with a mural nodule surrounded by signal voids is characteristic of hemangioblastoma (85). Pathologic dilated vessels can be demonstrated as hyperintense structures on flow-enhanced gadolinium studies. MRI with intravenous contrast enhancement shows enhancing nodules well because of their vascularity (95). False-negative results can be seen with small lesions (< 5 mm) and with delayed imaging because of the early enhancement of the lesions. False-positive findings are rare, and most false-positive findings lead to an inadequate diagnosis. For solid and multiple enhancing lesions, metastases are the most important differential diagnosis; supratentorial lesions are more common in metastases. The visualization of associated abnormal vessels helps in differentiating hemangioblastomas from other cystic lesions.

Angiography

For many years, angiography was the primary diagnostic modality and still is a preoperative requisite in many patients. Infratentorial hemangioblastomas are evaluated by using vertebral angiography, which provides a selective opacification of both vertebral arteries by arterial femoral catheterization. Subtraction and magnification are necessary (99).

Angiography is superior to CT in defining the vascular nodule and in characterizing occult and multiple lesions. The relationship of the nodule with the cyst is not demonstrated as well on angiograms as on MRI or CT scans (99).

Angiography provides detection, exact localization, and definition of the vascularity of tumors in the vertebrobasilar system. Findings are specific, and the diagnosis can be made with confidence. Nodules usually stain intensely with either a homogeneous or mottled appearance (see the images below). The tumor has irregular vessels. The largest tumors are associated with 1 or more enlarged feeding arteries and draining veins and can demonstrate arteriovenous shunting. When a cyst is present, it can be seen as an avascular area producing vascular displacement (96, 99).

Imaging of the neck with injection of each vertebral artery should be routine in patients with von Hippel-Landau (VHL) complex or a posterior fossa hemangioblastoma. The blood supply is usually received through the pia mater; however, external carotid angiography provides valuable preoperative information in selected patients in whom a hemangioblastoma is superficial and abuts the dura (which is usually supplied by meningeal branches of the carotid system).

Preferred examination:

Contrast-enhanced MRI is considered to be the best method for screening patients with von Hippel-Lindau (VHL) and to be the first evaluation used in symptomatic patients. However, preoperative angiography remains important for defining feeding vessels and aiding in embolization (85, 91).

Prior to MRI, contrast-enhanced CT scanning was performed frequently; however, beam-hardening artifacts produced by the petrous and vertebral bone limited its use.

MRI is superior to nonenhanced CT in the detection of vascular components of the tumor (91, 100). Contrast-enhanced CT has the same sensitivity as nonenhanced MRI; however, it is inferior to contrast-enhanced MRI (91).Contrast-enhanced MRI permits the identification of small tumor nodules. In addition, MRI is helpful in separating cystic and solid components of the tumor from edema. Patients with VHL should be screened, and follow-up studies should be performed at 6 months.

The sensitivity of MRI increases with the use of gadolinium-based contrast material. Angiography is better in the detection of small (< 1 cm) vascular tumor components, and it is better for showing the vascular nature, supply, and drainage of tumors, compared with CT (99). However, CT and MRI depict tumor cysts better (92).

Use of a gadolinium-based contrast agent is mandatory in the evaluation of hemangioblastomas because it increases the sensitivity for small, solid lesions (93, 99). When the diagnosis of hemangioblastoma is established, a careful evaluation for other small enhancing lesions should be performed because of the multiple lesions seen in some patients. The presence of multiple lesions has an important impact on the prognosis(101).

Management strategies

Indications for treatment:

Studies by Wanebo et al in 2003 and Ammerman et al in 2006, delineate the long-term natural history of CNS hemangioblastomas in patients with VHL disease and demonstrate several important features that guide their management (36, 102). Specifically, a saltatory growth pattern is

associated with hemangioblastomas, which is characterized by quiescent periods that are interspersed with periods of growth, with quiescent periods lasting an average of over 2 years (mean: 25 months). Despite growth of tumors in nearly all patients, 41% of patients became symptomatic over long-term follow-up (mean follow-up of 12.4 years). Of the patients that did become symptomatic, 45% of symptom-producing tumors were not evident on initial radiographic studies (102).

Owing to the characteristic hemangioblastoma saltatory growth pattern, and until other presymptomatic factors that can predict symptom formation can be identified, these tumors are ideally resected after the development of early signs or symptoms. Based on long-term surveillance data from patients with VHL, if radiographic progression was only used as an indication for hemangioblastoma resection, patients with VHL-associated hemangioblastomas would undergo an average of four additional unneeded operations over a 10-year period. This would expose these patients to operative risk for tumors that would not have become symptomatic (102).

Wanebo et al in 2003 and Ammerman et al in 2006 analysed to determine tumor characteristics that will predict symptom formation has revealed that larger tumors and more rapid growth rates of a tumor and an associated cyst may be associated with symptom development. Moreover, previous data demonstrate that peritumoral edema preceeds cyst formation with hemangioblastomas (103). The sequence of edema and cyst development and the association of size and growth rates with symptom development can guide patient education and follow-up in asymptomatic patients. As per Ammerman's work in 2006, tumor size >246 mm (7.9 mm in diameter) and tumors growing by >0.07 mm/ month were predictors of symptom development and indications for treatment. Pavesi suggested that surgery should be carried out in patients with solid or cystic lesions growing rapidly even if the patient is asymptomatic (104).

<u>Embolization</u>

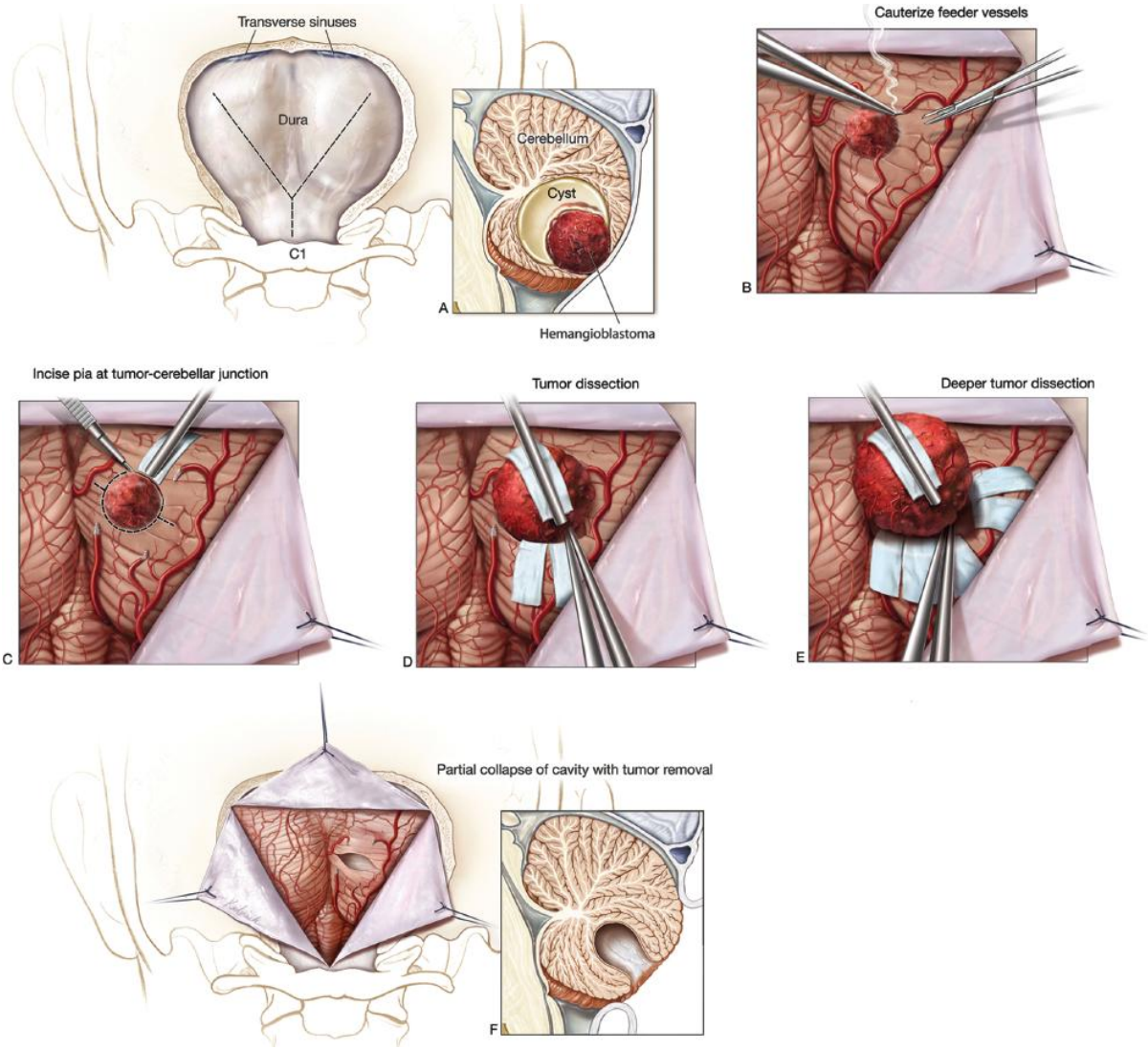
Preoperative embolization of hemangioblastomas has been suggested to reduce blood loss and to be convenient for total removal of tumors (particularly for lesions within the eloquent area (105-107). Takeuchi reported the treatment of three large hemangioblastomas with presurgical embolization. The complications associated with embolization included nausea, transient nystagmus, and slight facial palsy. The author advocated that complete embolization could reduce surgical complications (108). However, severe adverse outcomes associated with embolization have been reported. Connelius noted that preoperative embolization of three cerebellar hemangioblastomas were complicated by fatal intratumoral hemorrhage (109). Considering the substantial risk for peri-procedure morbidity, Rachinger chose to carry out the surgery on solid hemangioblastomas without embolization (77).

Operative Technique

Solid hemangioblastomas remain a great challenge for most neurosurgeons (particularly large hemangioblastomas). The feeding arteries often arise from the ventral or ventrolateral sides of the tumors, with large draining veins crossing the tumor surface. Several steps should be followed. First, removal of solid hemangioblastomas should adhere to the principle of dissection of arteriovenous malformations. That is, identification and elimination of feeding arteries should be done first, followed by dissection of the tumor and occlusion of draining veins (110, 111). Second, rigorous microsurgery should emphasize en bloc removal; attempts at “piecemeal” removal lead to inordinate, uncontrollable bleeding because hemangioblastoma vasculature is devoid of contractile elements. Third, devascularization should be done gradually; with diminishing blood supply, the lesion shrinks, and careful manipulation of the tumor from side-to-side allows coagulation and section of each succeeding feeding vessel. Premature obliteration of venous drainage can

lead to disastrous intraoperative swelling and hemorrhage, bearing in mind that usually, there is a distinct cleavage plane between the tumor and brain tissue. As per most authors, the plane of cleavage could be found in all primary hemangioblastomas cases. It is very difficult to deal with the patients with recurrent hemangioblastomas for the plane of cleavage is hard to be found. Minimizing compression or traction over parenchyma by rotating or retracting the tumor as far as possible is important because the surrounding brain parenchyma may involve eloquent areas. In the future, preoperative fiber-tracking will become common in imaging preoperatively, as well as careful monitoring during surgery. In such a way, the limits of the resection of the lesion could be more appropriately assessed.

In 2008, Jagannathan et al described in detail the surgical technique for removing cerebellar hemangioblastomas and remains the standard technique (60). The following is the description of the described technique. Because cerebellar hemangioblastomas are often located in the posterior and medial portions of the cerebellum, a midline suboccipital approach is frequently used to resect these tumors. For hemangioblastomas located in the lateral, anterior, or anteromedial cerebellum, most authors have previously described a variety of approaches that provide optimum visualization and direct access to the tumors in these regions (102, 112-115). Whichever approach is used, the basic tenets of hemangioblastoma removal (as dictated by their biological features) from the surrounding cerebellar tissues are the same as the technique described here. After general anesthesia is induced, the patient is secured in 3-point skull fixation and placed prone. The head and neck are flexed and the midline incision site (from the inion to the level of the spinous process of the second cervical vertebral body) is prepared and draped. Using a high-speed drill and rongeurs, a suboccipital craniectomy is created that extends superiorly from the foramen magnum to 1 cm above the upper edge of the tumor or to the level of the inferior edge of the transverse sinus, whichever is lower. If necessary, a laminectomy of the ring of the first cervical vertebra is used to expose the lower portion of the cerebellum and/or cervicomedullary junction.



After bone removal, intraoperative ultrasonography is used to localize hyperechoic hemangioblastomas and hypoechoic cysts, and to confirm the adequacy of bone removal for optimum exposure. A Y-shaped dural incision is then made (while keeping the underlying arachnoid intact) within the bone opening. The dural edges are reflected and secured using 4-0 silk sutures through the nuchal musculature. The arachnoid is opened sharply and tacked to the dural edges with titanium vascular clips. Because these tumors can be associated with increased posterior fossa (and intracranial) pressure, several intraoperative maneuvers can be used to reduce increased posterior fossa pressure and avoid the need for ventricular drainage. These include CSF drainage from the cisterna magna after arachnoid

opening, ultrasound-guided drainage of peritumoral or intratumoral cysts by using a spinal needle, and intravenous mannitol and/or furosemide.

When the hemangioblastoma reaches the pial surface, the pia mater at the tumor–pial junction is sharply incised with a diamond knife for dissection around the superficial portion of the tumor capsule and to give access to deeper portions of the tumor. Deeper tumors that do not reach the posterior pia mater are approached through a corticectomy (parallel to the folia) to the most accessible (superficial) portion of the tumor capsule. After defining the interface between the surface of the tumor and adjacent cerebellar tissue, the hemangioblastoma is resected by dissection at the tumor–neural tissue interface by working circumferentially and proceeding to the deeper regions by creating progressively deeper layers of dissection. Care is taken to coagulate and sharply interrupt vessels individually as they enter or leave the tumor capsule. Irrigation concurrent with each use of the bipolar forceps prevents adherence of small vessels or the tumor capsule to the bipolar tips and prevents unnecessary bleeding. As the feeding arteries/arterioles are interrupted by deeper circumferential dissection, the tumor will soften, and gentle retraction of the capsule with a suction device placed on a cotton patty becomes possible. Retraction of the deep surface of the hemangioblastoma on the tumor capsule is then used to enhance exposure of the tumor–tissue interface at the deepest portion of the dissection. At all times during the resection, tumor removal is achieved with visualization of the interface between the margin of the lesion and the cerebellum.

For large tumors, 2 maneuvers can be used to reduce the lesion's mass, minimize cerebellar manipulation/retraction, and enhance the ease of removal. First, the central portion of the tumor can be coagulated using broad-tipped bipolar forceps (2 mm) and then removed in a

piecemeal manner with microscissors or ultrasonic aspiration to permit manipulation of the tumor margin and to gain access to the ventral edge of the lesion. Alternatively, the tumor can be shrunk by using bipolar coagulation of the exposed capsule with broad-tipped bipolar forceps (116). Because coagulation of the hemangioblastoma surface turns the capsule tan-white, one should generally avoid bipolar cautery of the tumor surface at the point of deepest dissection at the tumor–cerebellar interface. This permits the bright red color of the tumor to stand out distinctly from the immediately surrounding cerebellar tissue as dissection is carried deeper.

For lesions associated with peritumoral cysts, the entire cyst wall is carefully inspected after tumor removal. Any additional tumors found associated with the cyst are removed. Once the hemangioblastoma is removed, the titanium vascular clips holding the arachnoid layer open are removed and the dura mater is sutured closed. The wound is closed in layers.

Prognosis and long term outcomes

The first successful surgical removal of a medullary hemangioblastoma was already performed in 1936, long before the advent of microneurosurgery and advances in para-surgical adjuvant therapy (117). This case remained an isolated case until well into the era of microneurosurgery, since the location was considered too malignant to attempt surgical removal (1). Symon et al. (1993) stated that a complete removal was considered too hazardous in 6 cases of a series of 51 posterior fossa hemangioblastomas, and concluded that the postoperative morbidity for fourth ventricle or medulla oblongata tumors was noticeably higher than that of the cerebellar tumors (4). In 1986 Sanford and Smith reported on three isolated cases of microsurgical removal of hemangioblastomas of the posterior

cranial fossa (118). At least in one, total resection was impossible and two patients suffered from serious respiratory disturbances in the postoperative period (118).

Long-term results of hemangioblastoma management generally are favorable. Advancement of neuroimaging methods, improvements in microsurgical technique, and the addition of preoperative embolization have significantly lowered morbidity and mortality associated with hemangioblastoma surgery. Subarachnoid dissemination of hemangioblastomas is extremely rare (119), and local recurrences after complete tumor resection seem to be more frequent in patients with von Hippel-Lindau (VHL) disease, in patients diagnosed at a young age, and in patients with multiple hemangioblastomas. The results of one study found that resection of brainstem hemangioblastomas is generally a safe and effective treatment for patients with VHL disease. However, due to VHL disease–associated progression, long-term decline in functional status may occur (115). The recurrence rate varies in different surgical series but generally remains less than 25%. Recently, histological subtype was found to correlate with a probability of hemangioblastoma recurrence, with a 25% recurrence rate in cellular subtype and an 8% recurrence rate in reticular subtype (120).

AIM OF THE STUDY

This study was undertaken to indentify patients with giant solid hemangioblastomas and discuss their management issues and outcomes.

MATERIALS AND METHODS

This is a retrospective study conducted in the department of neurosurgery, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram.

All patients who were surgically treated, with the diagnosis of Posterior fossa hemangioblastomas with the solid compoment measuring 4cm or more in any dimension were retrospectively reviewed for the period of January 1991 to June 2011.

Data were collected concerning patient age, sex, clinical symptoms and signs, imaging and surgical findings.

Patient's condition and outcome were evaluated minimum at the time of discharge and at 6 months and one year after discharge, and then any time latest. The clinical outcomes were categorized according to the Glasgow Outcome Scale as favorable (good recovery and moderate disability) or unfavorable (severe disability, vegetative state, or dead) and/or Karnofsky performance status.

RESULTS

Between January 2000 and Dec 2011 a total of 73 cases of posterior fossa hemangioblastomas were treated in the department of Neurosurgery, Sree Chitra Tirunal Institute for Medical Science and Technology, Trivandrum. Of these eight cases were identified that had a solid component with a dimension of equal to or more than 40mm (4cm) and were labelled as giant solid hemangioblastomas. The records of these patients were retrospectively analysed. There were four male and four females with age ranging from 30 years to 59 years. Only one of these patients had an association with von Hippel Lindau Syndrome, suspected due to the family history. No genetic studies were done. The following is the detailed description of all the individual cases.

Table showing the patient variable of the eight cases of giant solid hemangioblastomas:

Case	Age	Sex	Presentation	Clinical Findings	Location	Lesion no and size (mm)	VHL
I	30	F	Headache, Vomiting, Gait unsteadiness	Papilloedema with cerebellar signs	Left cerebellum posterior pia based	35X25X40	Yes
II	59	M	Headache and gait unsteadiness	Papilloedema and cerebellar signs	Right cerebellum posterior pia based	52X38X48	No
III	43	M	Reduced hearing, tinnitus and gait unsteadiness	Papailloedema, SNHL and cerebellar signs	Anteromedial left cerebellum and CP angle	43X33X31	No
IV	48	M	Headache and gait unsteadiness	Papilloedema, lower cranial nerve paresis and cerebellar signs	Superior vermian and exending posteriorly	68.3X56X50.9	No
V	30	F	Headache and vomiting	Papilloedema with no localization	Dorsal medulla extending into fourth ventricle	40X33X30	No
VI	43	F	Right upper and lower limb weakness	Spastic quadriparesis	Cervicomedullary junction	28X43X31	No
VII	38	M	Headache and gait unsteadiness	Papilloedema with cerebellar signs	Vermis and left cerebellum	50X48X47	No
VIII	53	F	Headache, hearing loss, Gait unsteadiness	Papilloedema with SNHL and Cerebellar signs	Anteromedial left cerebellum and CP angle	44X38X35	No

Table showing the interventions in the eight cases of giant solid hemangioblastomas:

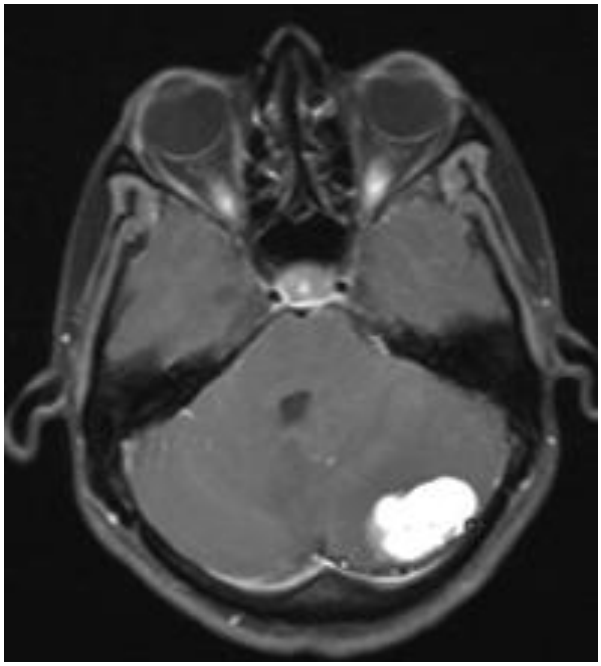
Case	CSF Diversion	Preop Emb	Intraop Glue	TCA + Hypothermia	GTR	Blood loss	Immediated postoperative complicationa
I	No	Yes	Yes	No	Yes	2 litres	None
II	No	Yes	Yes	No	Yes	7 litres	Cerebellar incoordinaion and ataxia
III	No	No	Yes	No	Yes	2 litres	Left sided vocal cord paralysis
IV	No	No	Yes	No	Yes	3 litres	Lower cranial nerve paresis
V	No	No	No	No	Yes	2 litres	Lower cranial nerve paresis requiring temporary tracheostomy
VI	Yes	No	Yes	No	Yes	1.5 litres	None
VII	Yes	No	No	No	Yes	2 litres	None
VIII	Yes	Yes	Yes	Yes	Yes	800 ml	Post op hematoma requiring resurgery

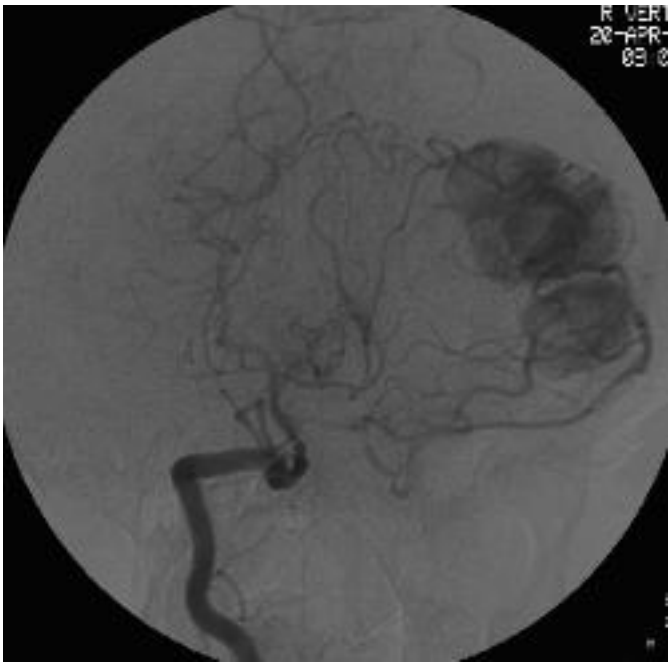
Table showing the outcomes in the eight cases of giant solid hemangioblastomas:

Case	Preop KPS	Postop KPS (short term6 wks)	Postop KPS (long term >1 yr)	Total Follow up duration	Recurrence	New permanent deficit	Full Functional Recovery at last followup	Glassgow outcome score at last followup	Surgical mortality
I	80	80	100	4 years		No	Yes	5	No
II	70	60	90	5 years	No	No	No (Persistant Ataxia)	5	No
III	80	80	100	3 years	Small asymptomatic under observation	Yes (LCN – Voice)	No	4	No
IV	70	100	100	Lost to followup	Small asymp	No	-	-	No
V	90	90	100	2 years	No	No	Yes	4	No
VI	80	90	100	2 years	No	No	Yes	5	No
VII	90	90	100	1.5 yrs	No	No	Yes	5	No
VIII	80	-	-	-	-	-	-	1	Yes

CASE I

A thirty year old lady had presented to our out patient department with history of recurrent episodes of holocranial headache over past six months. The headaches were more prominent in the morning hours and associated with nausea and vomiting which used to partially relieve the headache. She also complained of visual blurring in both eyes since the onset of headache. The lady also gave history of unsteadiness of gait since the same time duration with tendency to sway to either side while walking. No history of appendicular incoordination of ataxia. She had a positive family history of von Hippel-Lindau disease, with an affected brother, her mother and two of maternal uncles. Examination revealed presence of bilateral established papilloedema and trunkal ataxia. She had KPS of 80% and a McCormick functional grade I. A local physician had evaluated her with a computerised tomography scan of the brain which revealed an intensly enhancing mass lesion in the right cerebellar hemisphere with mass effect and obstructive hydrocephalus. A magnetic resonance imaging of the brain was done which further characterised the lesion. The left cerebellar hemisphere showed a well defined solid mass lesion, abutting the posterior pial surface with multiple flow voids within. It was isointense on T1 weighted image, heterogeneously hyperintense on T2/FLAIR with moderate perilesional vasogenic edema. Intense postcontrast enhancement was noted. Lesion was 40X25X35 mm in size. Superior transtentorial herniation causing effacement of superior cerebellar cistern and perimesencephalic cistern seen. There was compression of the fourth ventricle with prominent aqueduct and dilated third and lateral ventricles. Periventricular seepage seen. Another small dot like lesion noted in superior cerebellar hemisphere on the right side. An intradiploic hemangioma was additionally noted in the right parieto-occipital region, which was hyperintense on T2 and enhancing with contrast.





A diagnosis of left cerebellar giant solid hemagioblastoma was made. Her haemoglobin level was 15.1gm% with a packed cell volume of 45%. Screening ultrasound on the abdomen showed a large solid cystic mass in the region of the pancreas and almost completely replacing it. CT scan of the abdomen showed the entire pancrease was full of a multiloculated cystic mass with areas of calcification and moderate enhancement. Other

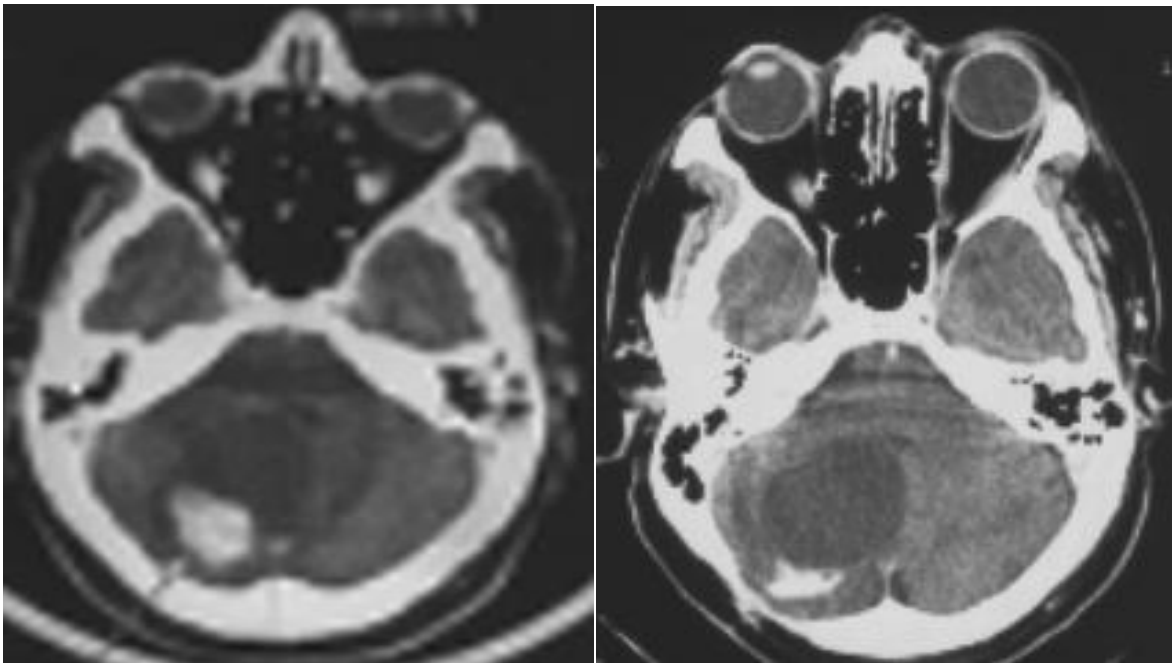
solid viscera were normal. The patient was taken up for four vessel cerebral angiogram with possible embolization if feasible. The lesion showed feeders from left AICA, PICA and SCA, with early draining veins. Only partial embolization via the AICA feeders could be done since the other feeders could not be selectively catheterised. The next day the patient was posted for surgical excision. Patient was placed prone under GA with head on MFK clamp. A lateral suoccipital craniectomy was performed. Tumor was surfacing on the pia and had an angry looking appearance. It was reddish in colour with numerous draining veins coursing over the surface. It had a good gliotic plane with the surrounding cerebellar parenchyma and a circumferential dissection could be done successfully. Total excision of the lesion was achieved with about 2 ltrs of blood loss intraoperatively. Cerebellum was lax at closure, so the patient was reversed and extubated. Postoperative scan done next day showed small operative site hematoma without significant mass effect. The ventriculomegaly had come down. Histopathological examination of the specimen was confirmatory of a hemangioblastoma. Patient was discharged uneventfully with no new deficits one week later. Upon followup at six weeks patient had complete resolution of headach with improvement in ataxia. At six months the patient was completely asymptomatic and repeat imaging did not reveal any residual lesion or hydrocephalus. Upon last follow up four years postoperatively patient was asymptomatic with full functional recovery.

CASE II

A 49 year old gentleman had presented to us in March 2007 with complaints of Headache, giddiness and gait unsteadiness since one year. For the past 5 months the patient experienced weakness of right upper and lower limbs.

He had been operated twice before in 1992 and 2001. In 1992 when evaluated for headache, vomiting and gait unsteadiness, he was diagnosed as a case of right cerebellar cystic hemangioblastoma a mural nodule. He underwent lateral suboccipital craniectomy and excision of the lesion. Postoperatively his symptoms resolved. He was operated again in 2001 for a recurrent cystic hemangioblastom with a mural nodule. He had received radiotherapy after both surgeries.

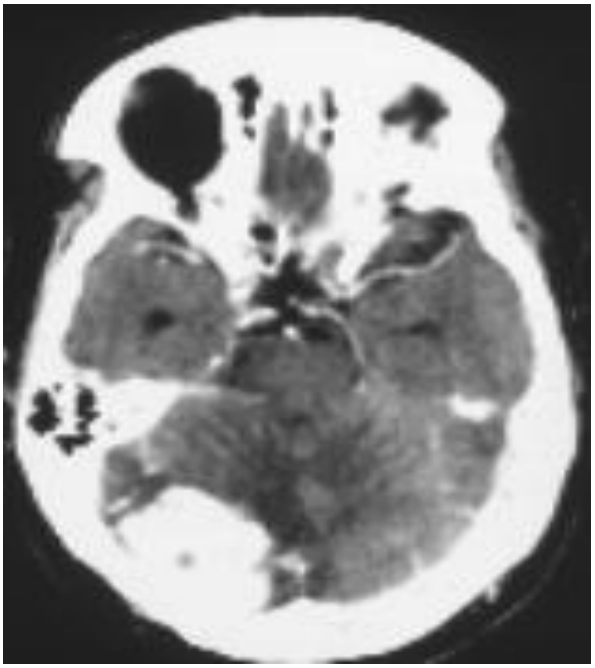
1991 2001



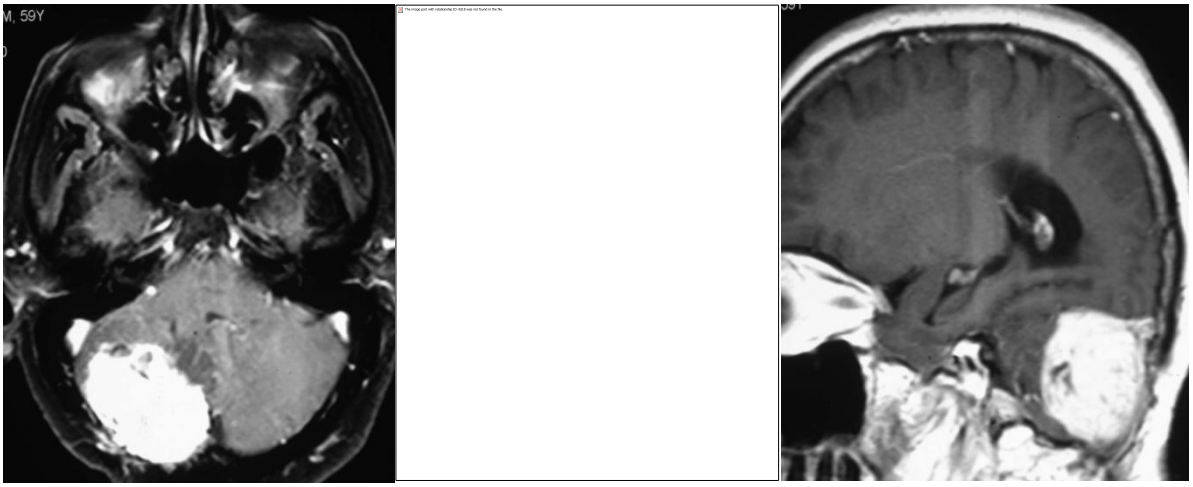
On examination the patient was conscious and alert and ambulant with support. He could carry on his activities of dialy living with assistance. He had bilateral papilloedeme. None of the cranial nerves were affected. He had sided spastic hemiparesis with power grade 4 on

MRC power charting. Right sided cerebellar signs were positive. Repeat CT brain revealed large solid recurrence at the previous operative site with intense contrast enhancement and mass effect.

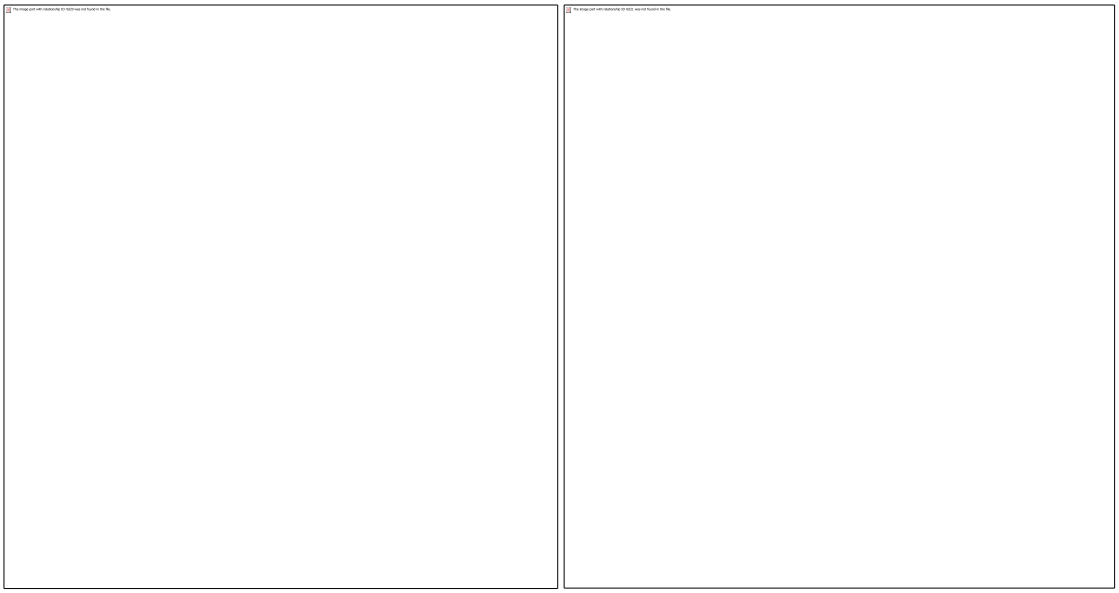
2007



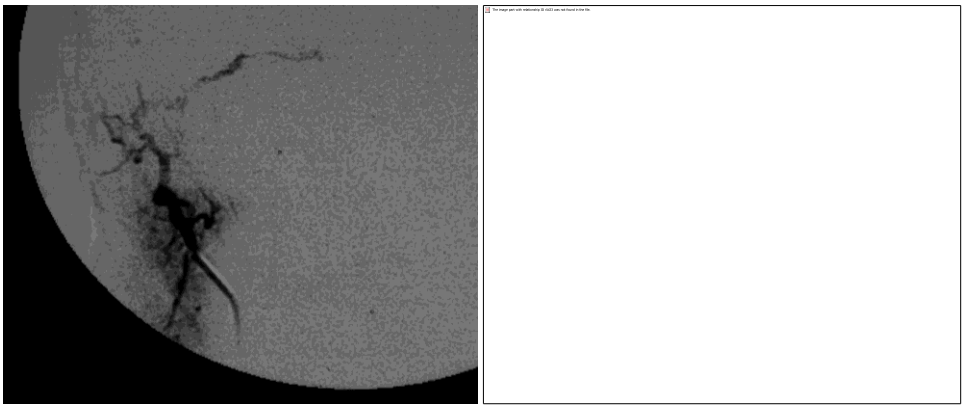
MRI of the brain showed a large solid hemangioblastoma with dimensions of 52X38X48mm. There was no associated cyst this time. Presence of perilesional edema with mass effect and ventriculomegaly was noted.



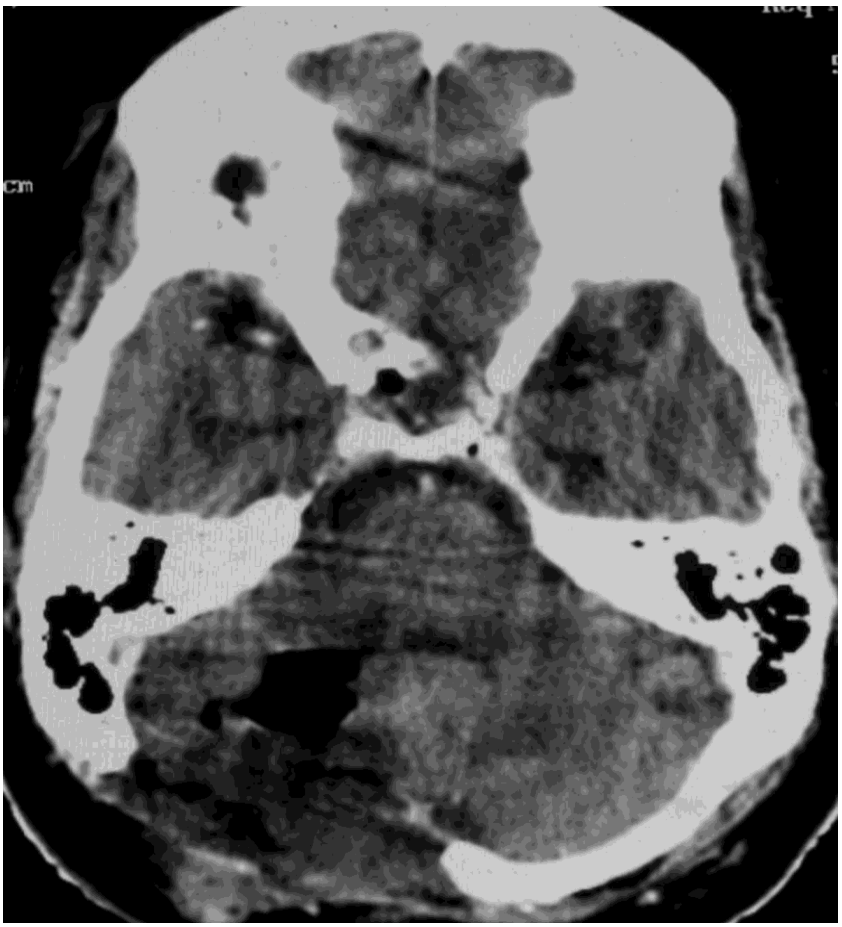
Blood haemoglobin level was 14.6gm% with a packed cell volume of 44% and a total RBC count of 4.9 million per cubic cm. Ultrasound screening of the abdomen did not reveal any abnormality. A four vessel cerebral angiogram with embolization was planned. The tumor blus was fed by muscular and dural branches of the right occipital arterh. Dural branch of the left occipital artery, multiple branches from the right superior cerebellar artery and dural and meningeal branches of the right vertebral artery. No AV shunting or early venous drainage was noted.



The occipital feeders were selectively catheterised and the tumor embolised with PVA particles to achieve good reduction in tumor blush.



Patient was taken up for surgery next day in prone position under GA with head fixed in the MFK clamp. A highly vascular lesion was encountered. Though it had a good gliotic plane with the surrounding parenchyma, it was very friable and came out in a piecemeal manner. To control bleeding during dissection of the nidus, intratumoral injection of fibrin glue and cyanoacrylate gel was done. Some brisk bleeding was also encountered from with transverse sinus as one of the veins snapped. The total intraoperative blood loss was around seven litres. He was ventilated overnite electively. Post operative scan next day did not reveal any residue, hematoma or infarct.

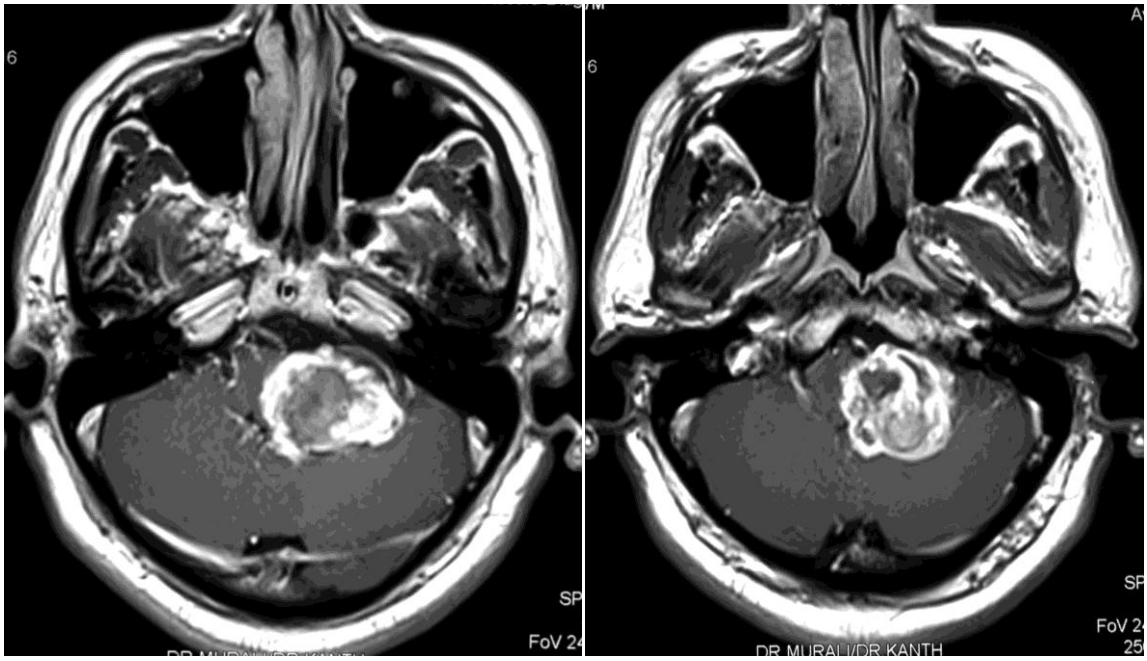


Patient did not develop any fresh neurological deficits. He was uneventfully discharged after one week. Fifteen day later he presented with operative site swelling which turned out to be a pseudomeningocele. Since it was not responding to conservative measures a

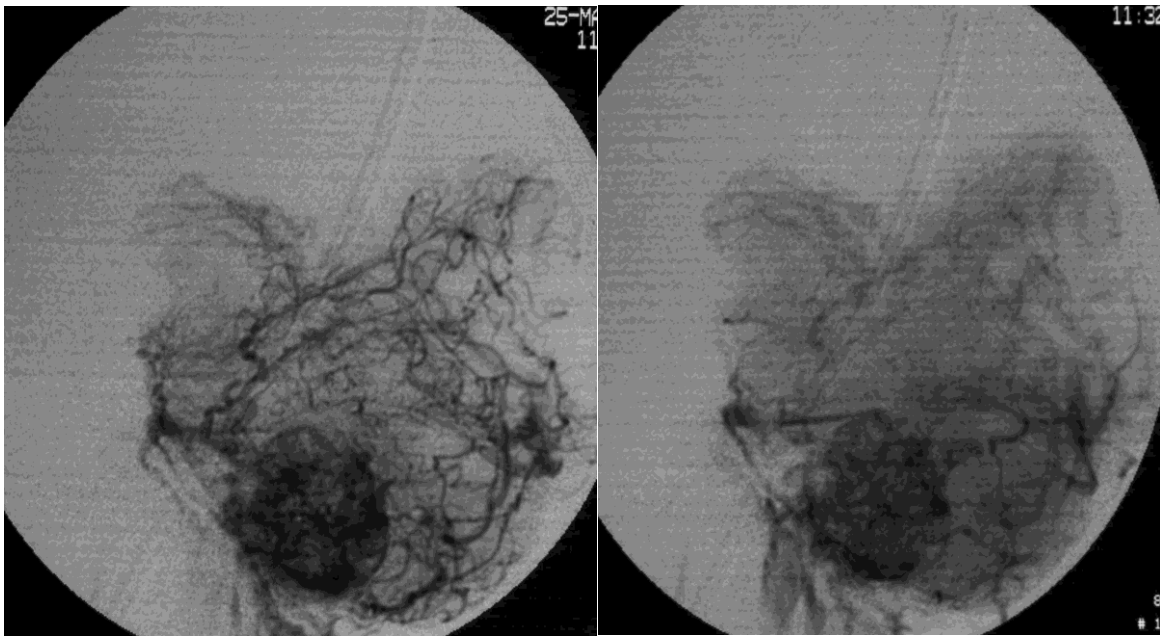
thecoperitoneal shunt was done which completely resolved the swelling. Followup at six months, one year and two years had persistent ataxic gait though, headache, giddiness and right spastic hemiparesis had resolved.

Case III

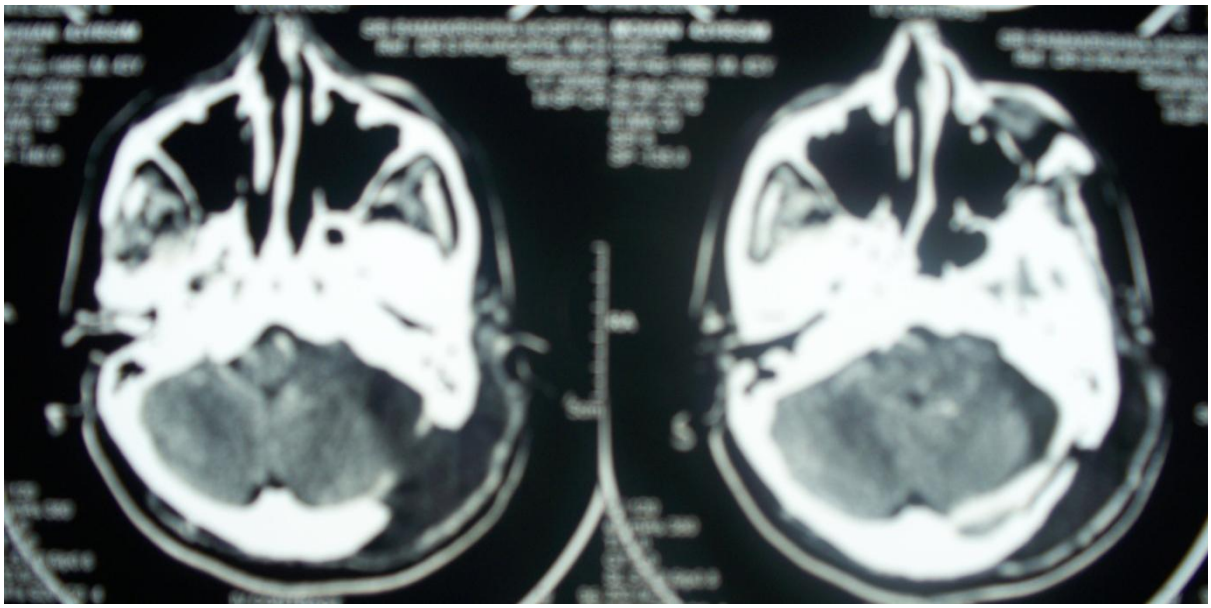
A 43 year old gentleman presented with progressive painless hearing loss in the left year over one year associated with tinnitus and gait unsteadiness since three months. The nature of hearing loss was that of conductive hearing loss with improvement in noisy surroundings and no loss of discriminative hearing capacity. Gait unsteadiness was characterised by tendency to sway to the left side while walking. There was history of mild incoordination with the use of left hand since three months. There was no history suggesting raised ICP. On examination he was conscious and alert and was able to do his daily chores independently. Fundus examination was normal. There was left conductive hearing loss. The motor and sensory examination was within the normal limits. Patient had broad based gait with left sided cerebellar signs present. CT scan of the brain revealed a well defined heterogenous peripherally enhancing lesion in the left cerebellar hemisphere. Further characterization with MRI showed a 43X33X31mm well defined lesion in the left cerebellar hemisphere based anteriomedially involving the middle and inferior cerebellar peduncle. It was hypointense on T1WI and heterogeneously hyperintense on T2/FLAIR with perilesional vasogenic edema and mass effect causing effacement of fourth ventricle. There was intense heterogeonous contrast enhancement with evidence of flow voids extending to the pial surface. No ventriculomegaly was seen.



The screening scans of the abdomen did not reveal any other pathology. He was taken up for four vessel cerebral angiogram and embolization attempt. There was evidence of tumor blush fed by the branches of left PICA and AICA. There was no evidence of AV shunting and no early draining veins. Embolization could not be done as superselective feeder catheterization could not be achieved.



Three days later he was taken up for surgical removal of the lesion. Patient was positioned in right lateral park bench position and a left retromastoid suboccipital craniectomy was done. Retrosigmoid durotomy was done and tumor was seen surfacing over the ventral left cerebellar pia. It was reddish brown, firm in consistency, very vascular with areas of hemorrhage and necrosis within its cavity. Capsule was well defined in most places. It was adherent to the arachnoid over the lower cranial nerves and PICA. Multiple tortuous vessels were running across the surface of the tumor. Feeders were mostly from PICA and AICA. Gross total excision was done. Patient was kept of elective ventilation for 48 hours under controlled hypotension as in management of arteriovenous malformations. Post operatively patient developed hoarsness of voice which on indirect laryngoscopy was attributed to left laryngeal paresis. Post operative CT scan did not reveal any residue, hematoma or infarct.

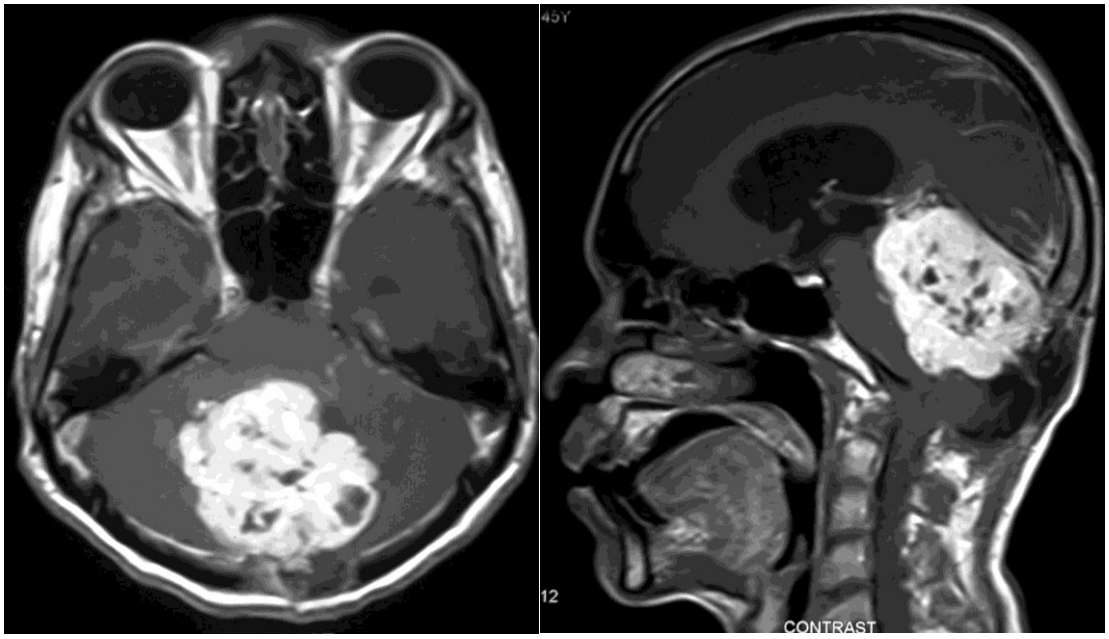


He was discharged uneventfully and was ambulant with support at discharge. At six months followup his voice and gait unsteadiness had improved and was ambulant without support. At 1 and 2 yrs followup he was doing well and performing all his activities independently. At last followup 3yrs postoperatively, an MRI was done which revealed a small recurrence in

the region of left cerebellar peduncle. He has been planned to be kept of followup with repeat scan at 6 months or earlier if he develops symptoms.

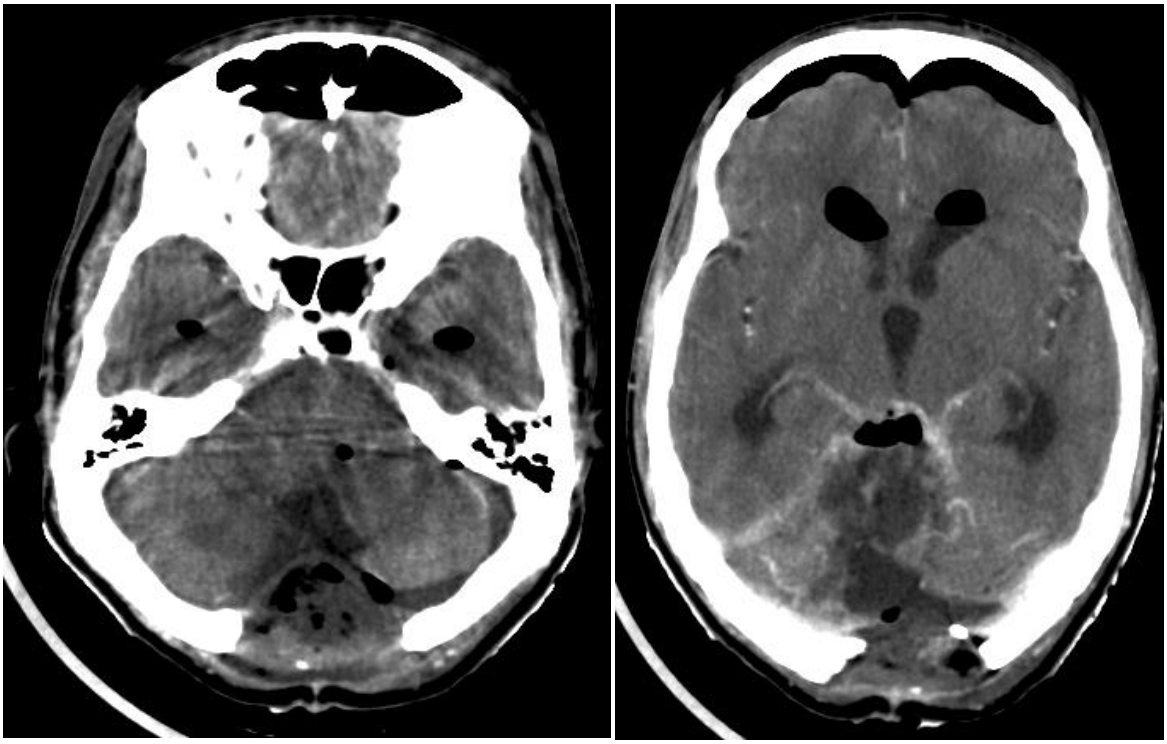
Case IV

This 45 year old right handed gentleman had initially presented to another hospital in May 2007 to another hospital with complaint of occipital headache and gait unsteadiness over two months. He was evaluated there and diagnosed as having a midline posterior fossa SOL. He was taken up for surgery and a midline suboccipital craniectomy done. But due to highly vascular lesion only biopsy was taken and closed. The biopsy was reported as inconclusive. Due to progressive symptoms one month later, biopsy was reattempted and this time reported as meningotheliomatous meningioma. Since his symptoms were progressive and there was no relief, the patient came to our centre. When seen by us, the patient had holocranial headache with worsened gait unsteadiness such that he was ambulant only with support requiring two person support to walk. There was a lax pseudomeningocele at the operative site. Patient was conscious, alert and oriented. There was bilateral papilloedema. The right gag was impaired and right palatal sensations were absent. No motor weakess. Ataxia was present and right cerebellar signs positive. Magnetic resonance imaging revealed a multilobulated well defined lesion of 68.3X56.1X50.9mm. It was hypointense on T1WI and heterogeneously hyperintense in T2/FLAIR. There was perilesional edema with mass effect causing obstructive hydrocephalus.



Patients haemoglobin value was 15.5gm% with a packed cell volume of 52% and a total RBC count of 7.25 million per cu mm. Abdominal screening did not show any solid organ pathology. Considering the biopsy report, a working diagnosis of meningiomas was made.

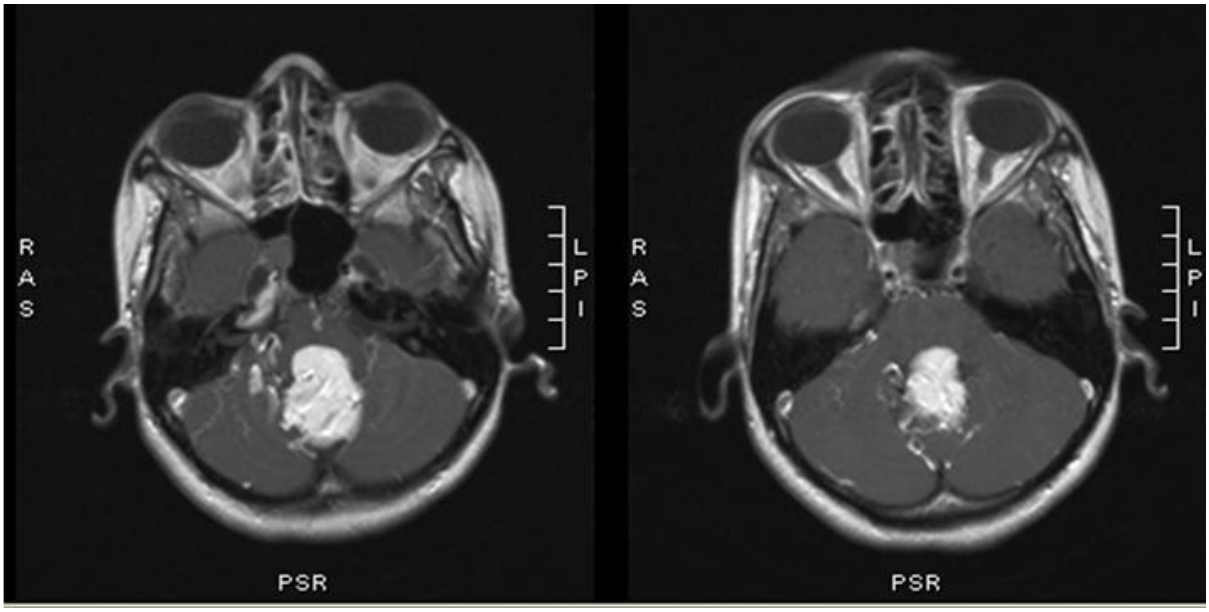
Patient was taken up for surgery and a midline suboccipital craniectomy was done. There was defect in dura of the previous surgery through which the cerebellum was prolapsing. Tumor was reddish, soft, partially amenable to CUSA, highly vascular with plane of cleavage from the adjacent cerebellum. Tumor was extending anteriorly upto the pineal region; superiorly attached to the lower leaf of tentorium by means of few vascular pedicles; inferiorly about 4-5cm from the C1 arch. Frozen biopsy of the lesion was reported as inconclusive. Total excision of the lesion could be achieved.

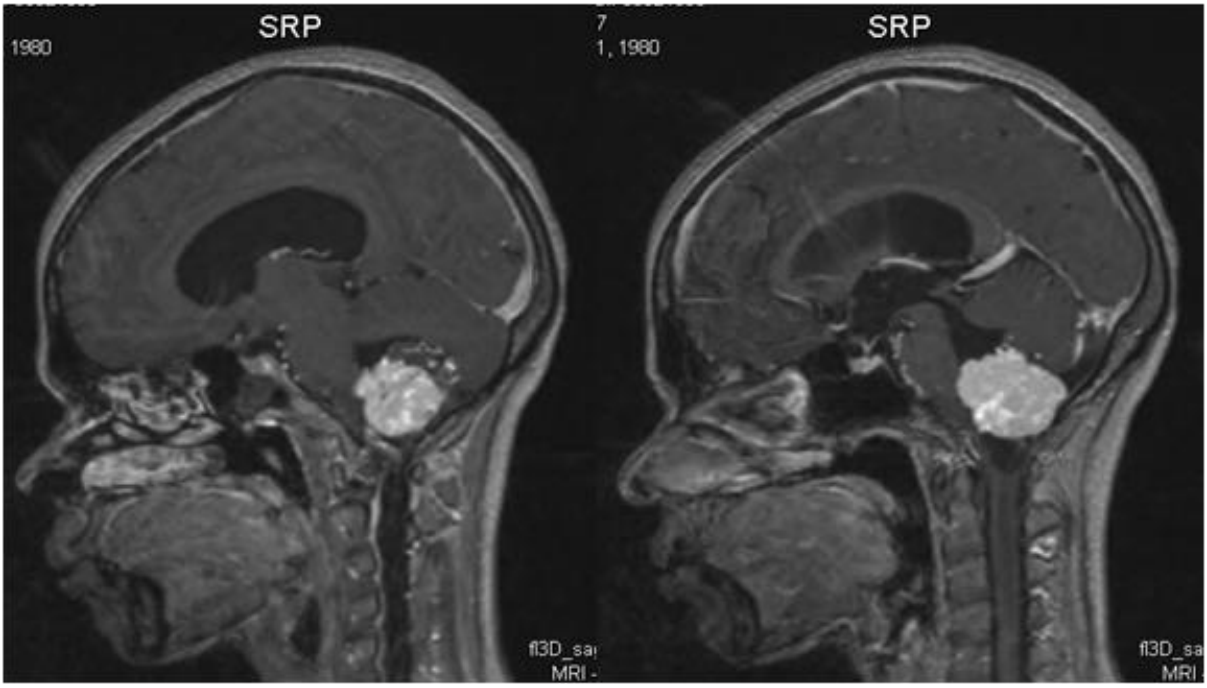


The final histopathology report of the lesion was suggestive of a hamangioblastoma. Post operatively patient had a week cough response with choking on coughing. He was discharged on RT feeds. He was lost to follow up.

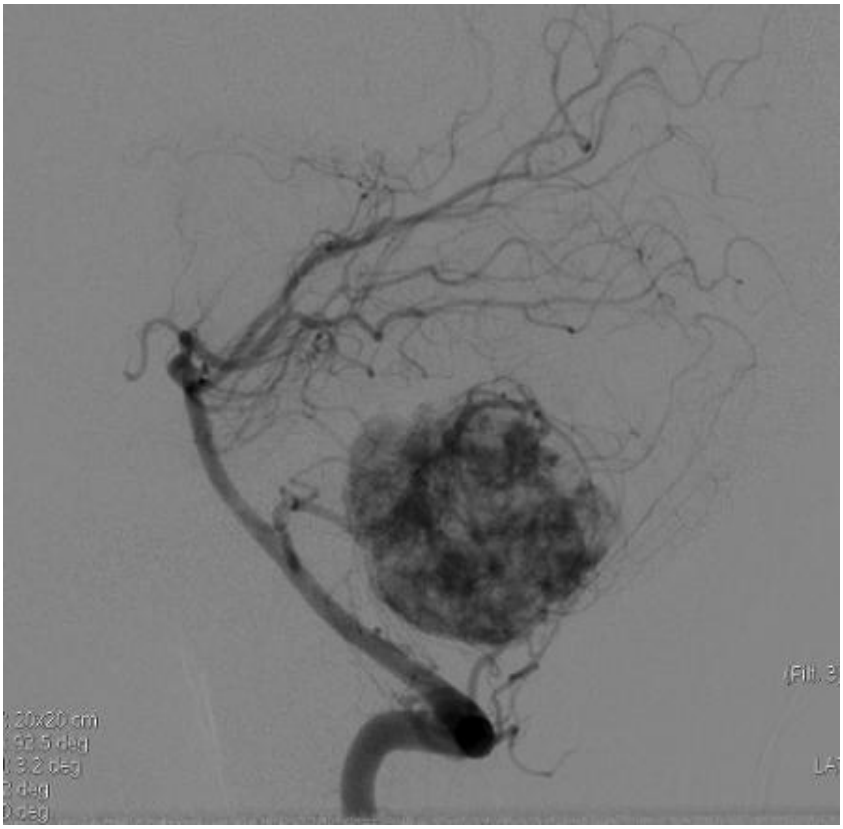
Case V

A thirty year old right handed lady presented to is in August 2010 with history of headache since two years which had become holocranial over the last 6 months and associated with early morning exacerbation and vomiting. There were no other localizing clue on history. On examination she was conscious and alert with stable vital signs. Bilateral fundi showed papilloedema. There no other cranial nerve deficits or motor or sensory findings. There were no cerebellar signs and systemic examination was unremarkable. CT scan of the brain showed an enhancing midline posterior fossa lesion with obstructive hydrocephalus. Magnetic resonance scanning done to further delineate the lesion showed a midline posterior fossa lesion seemed to be within the cavity of the fourth ventricle at the level of medulla and coming out of the foramen on magendie. The lesion was well defined and measured 40X37X35mm with intense contrast enhancement. Mass effect with obstructive hydrocephalus was evident.

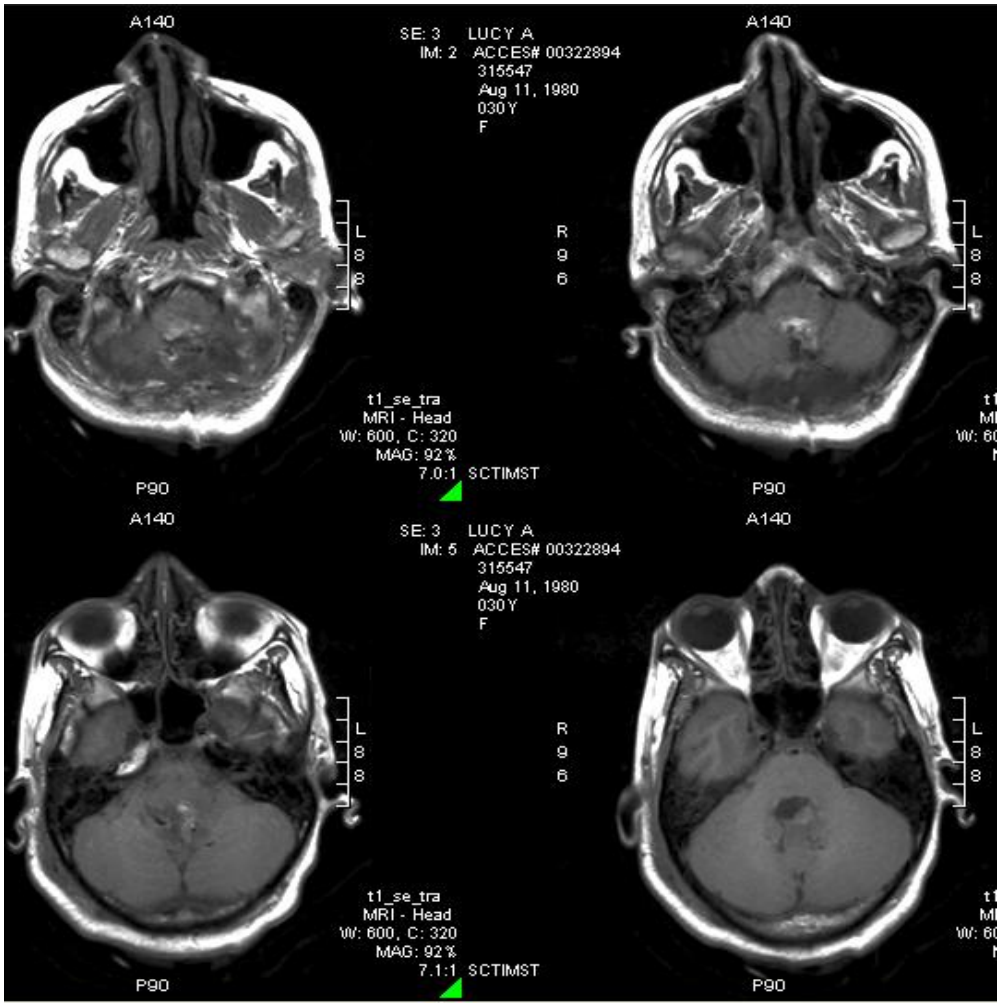




Screening imaging of the abdomen did not reveal any other pathology. A four vessel cerebral angiogram was done revealing tumor blush supplied by bilateral PICAs. The right VA and PICA were larger as compared to their left counterpart.



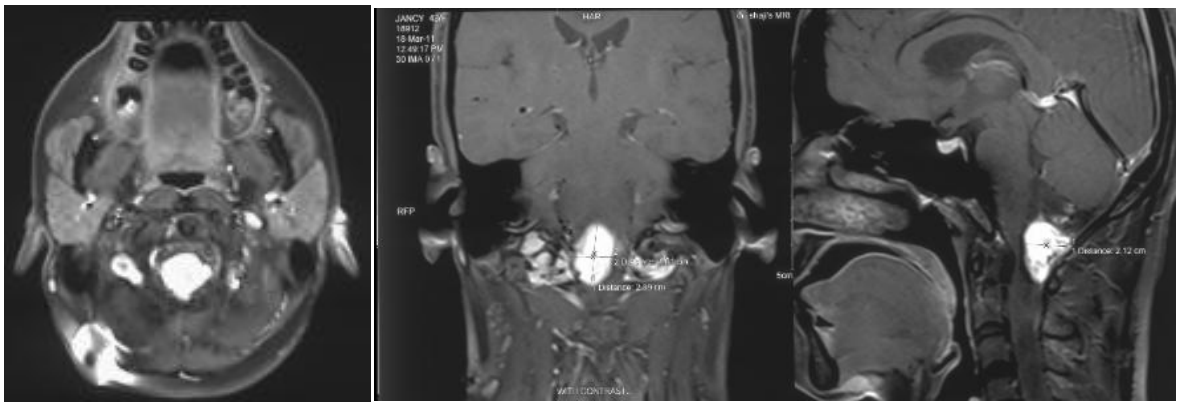
Since superselective catheterization was not achieved, embolization could not be done. It was decided that intraoperative injection of glue will be done. A midline suboccipital craniectomy was done and C1 arch excised. Upon durotomy, the tumor was seen protruding between the tonsils, coming out of the foramen of magendie. Tumor was red, fleshy, extremely vascular with multiple arterial feeders. It has a poor plane with the vermis and lower medulla. Lesion had a cyst in the upper medulla and in this region had a good plane. Brisk bleeding was encountered during dissection from the brain stem and about 2 ltrs of blood was lost intraoperatively. Post operatively the patient was kept on elective ventilation. Histopathology was reported as typical of hemangioblastoma. Postoperative scan did not show any residue, hematoma or infarct.



As paitent developed lower cranial nerve palsy, she was tracheotomised and was gradually decannulated after satisfactory return of function. She was discharged after three weeks when he had become ambulant with support and was on ryles tube feeding. Upon followup at six weeks she had started taking orally and was ambulant with minimal support. Upon followup at one and two years the patient had become ambulant without support and could carry out all her activities independently. Postoperative magnetic resonance imaging did not show any residue or recurrence.

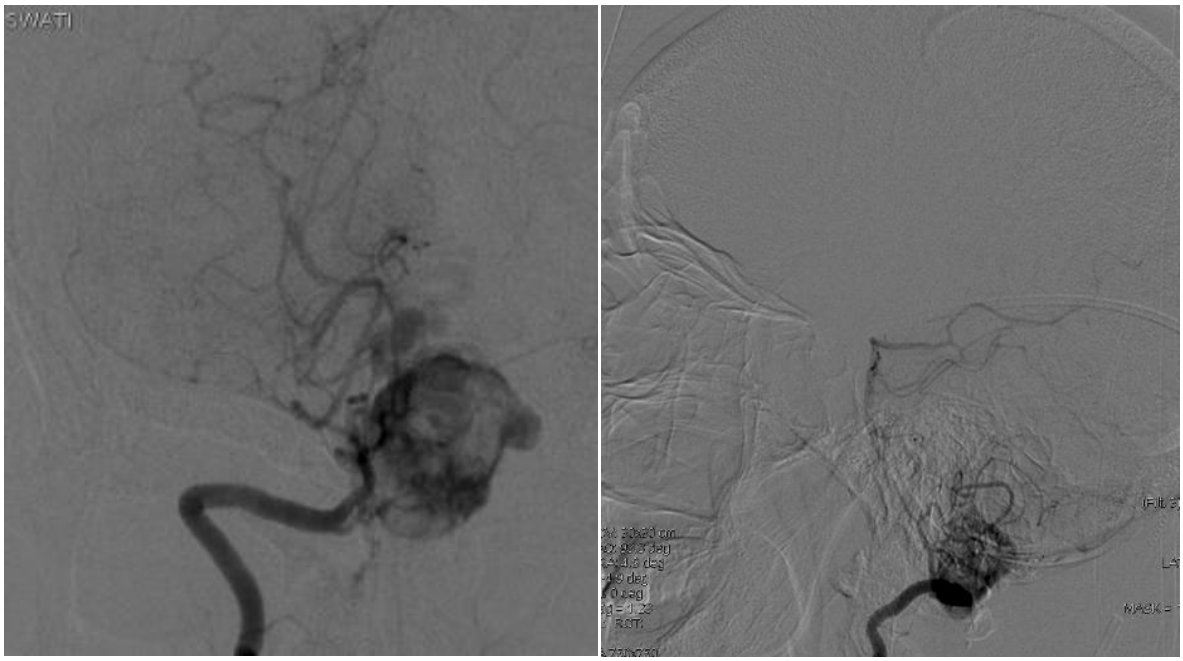
Case VI

A 43 year old lady had presented to us with a history of very gradually progressive weakness in the right upper and lower limbs over five years but rapidly progressing since last 2 months. 1 month prior she also started having holocranial headache with vomiting. She was evaluated at a local hospital where a CT scan brain was done and she was diagnosed as having a posterior fossa mass lesion with obstructive hydrocephalus. She had undergone and ventriculoperitoneal shunt surgery there with resolution of headache and vomiting. When she was received by us her major concern was the progressive weakness in the right upper and lower limbs. On examination she was conscious and alert. There were no cranial nerve dificits. Tone was increased in all four limbs (Rt>Lt) power was grade 4. All deep tendon reflexes were exaggerated and plantars were extensor. Magnetic resonance imaging was suggestive of a well defined solid lesion at the cervicomedullar junction which was hypointense on T1WI and heterogeneously hyperintense on T2/FLAIR weighted images. It had multiple flow voids with intense enhancement on administration of contrast.



It was extending down to the level of C1 arch and causing pressure over the cervicomedullary junction which would explain the patients symptoms. A four vessel digital substraction cerebral angioram was performed which showed supply form right intadural

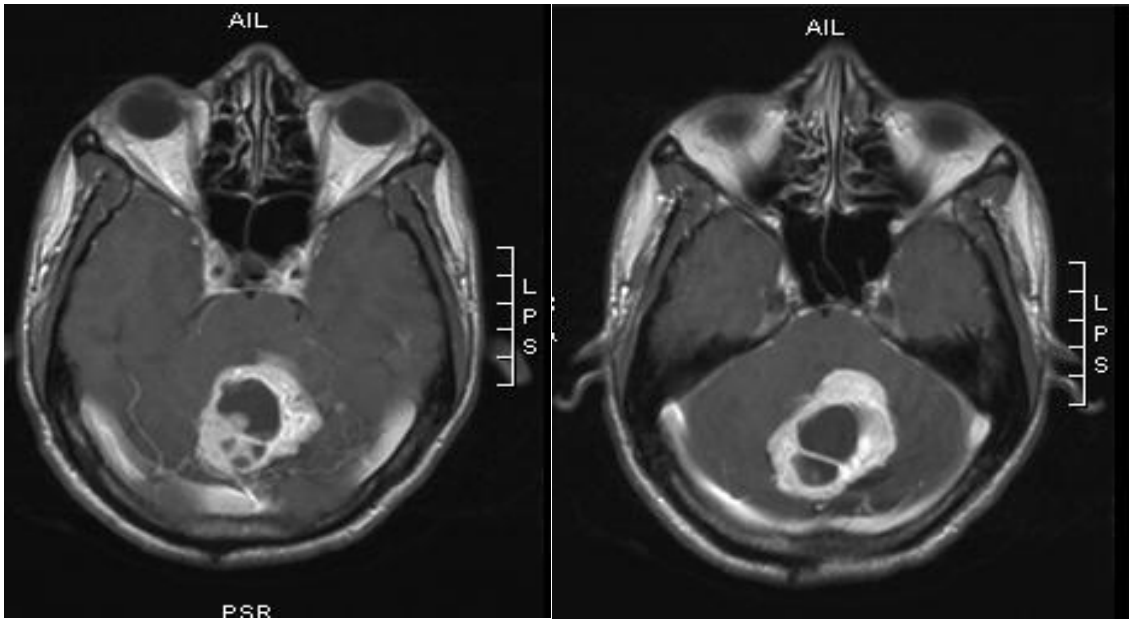
vertebral artery feeders. There was evidence of AV shunting and drainage was into the left transverse and sigmoid sinus.

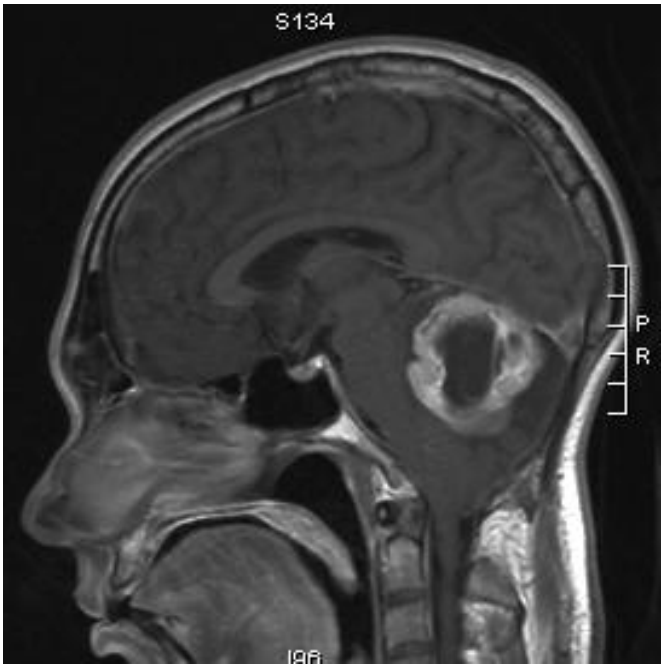


Abdominal screening was negative for solid organ pathology. Patient was taken up for midline suboccipital craniectomy and reddish, highly vascular lesion was seen at the cervicomedullary junction with multiple tortuous vessels over it. Total excision could be achieved. Post operatively patient has an uneventfull course and did not develop and new neurological deficits. Postoperative scan did not show any residue, hematoma or infarct. At six weeks followup she was doing well with reduced spasticity. At 6 months and one year review she was ambulant without support and required minimal assistance to daily activities. At last follow up 2 years post operatively patient was carrying out her daily activitied independently with no new deficits and no recurrence on imaging.

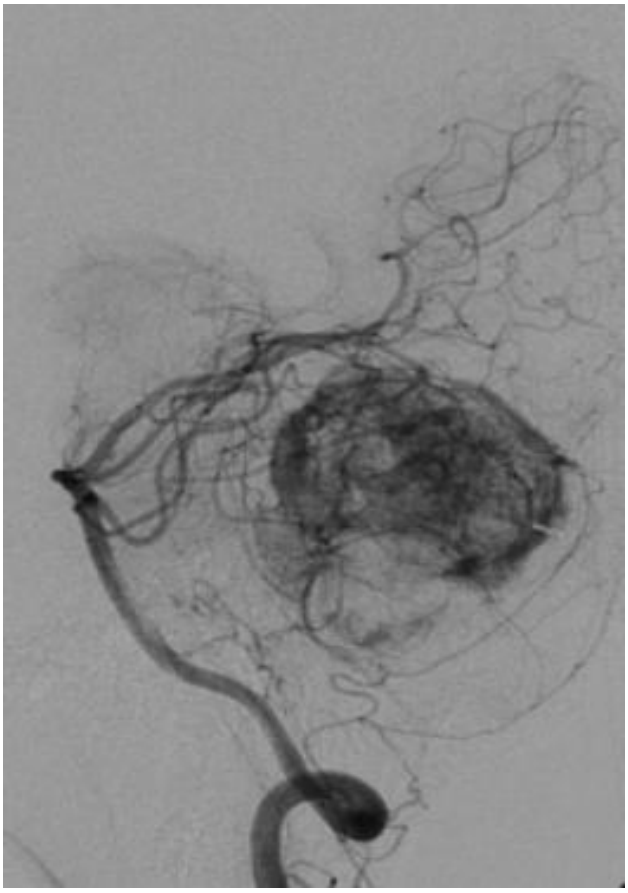
Case VII

A 25 year old man had presented to us in 1997 with clinical features of raised ICP he was evaluated at that time and found to have a left cerebellar tumor with hydrocephalus. He under CSF diversion with a ventriculoperitoneal shunt followed by midline suboccipital craniectomy and decompression. The lesion was very vascular but total excision was achieved. Histopathology report was suggestive of hemangioblastoma. Patient was discharged with no new deficits but was lost to followup. The 13 years later in 2010 at the age of 38 years, he presented to us again with history of gait insteadiness since one month and holocranial headache and vomiting since 1 week. On examination the patient was conscious and alert, stable vitals and no cranial nerve or motor/sensory deficits.Patient had mild left sided incoordination. Repeat imaging of the brain revealed large recurrent left cerebellar hemangioblastoma with typical features and cystic changes within the lesion. The lesion size was 50X48X47mm causing mass effect with effacement of the fourth ventricle.

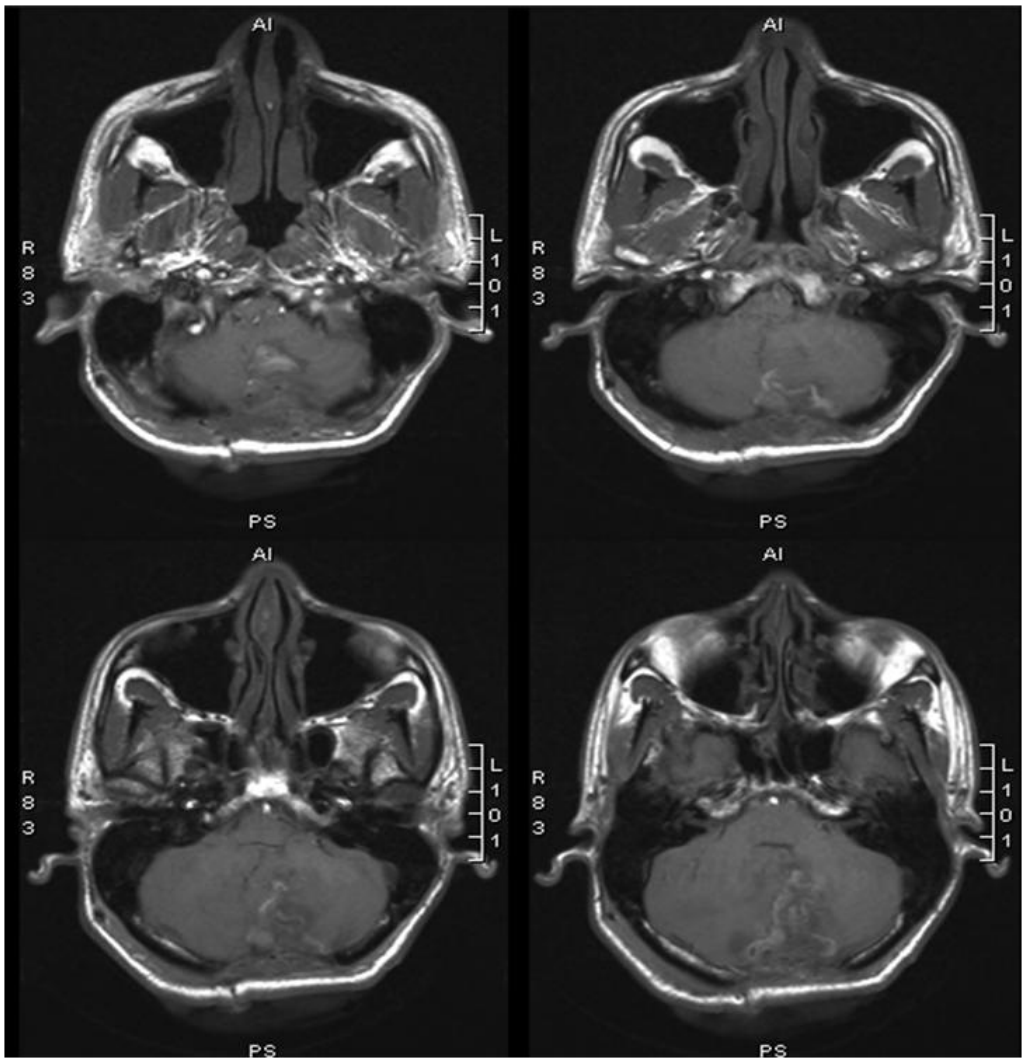




A four vessel angiogram was done which revealed supply from vermian branch of bilateral SCAs. Embolization was not feasible, hence planned direct surgery.

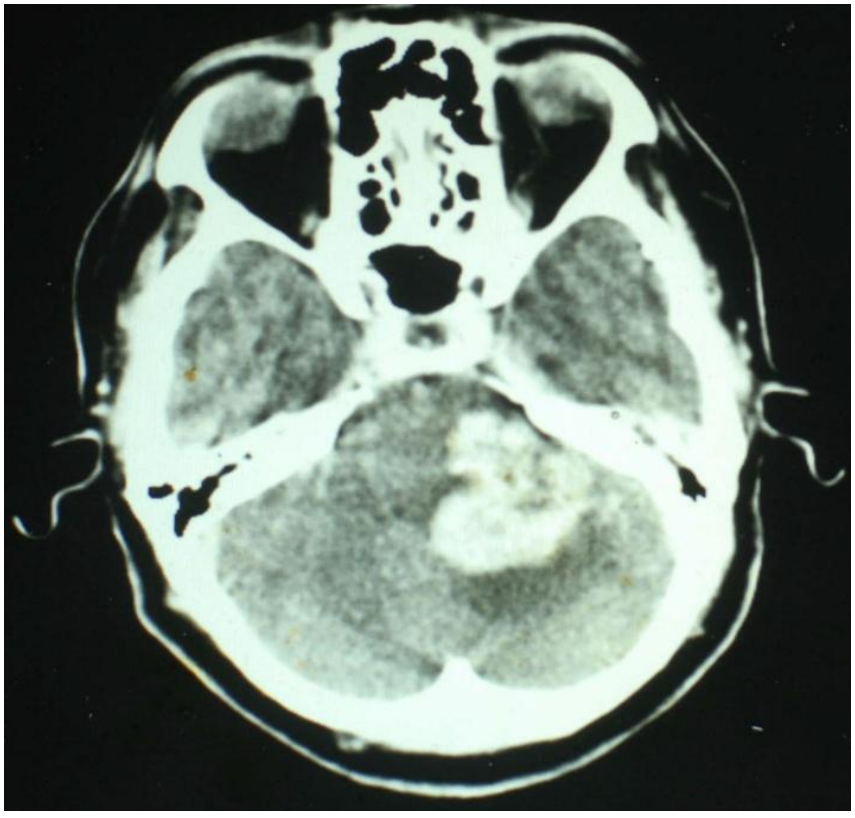


Preoperative abdominal screening showed multiple small cystic lesion in the pancreas with bilateral multiple renal cortical cysts. But the patient was asymptomatic for both. At surgery a highly vascular tumor was encountered with multiple tortuous vessels over it. It had a good gliotic plane with the cerebellar parenchyma and a total excision was achieved with a total blood loss of around 2 litres. The HPR was suggestive of hemangioblastoma. Postoperative scan did not show any residue, hematoma or infarct. The patient had an uneventful recovery and was discharged with no addition neurological deficits. At 6 weeks patient was completely symptom free and repeat scan at 6 months did not show any residue. At last follow up 1.5 yrs postop patient was doing well with no fresh complaints.

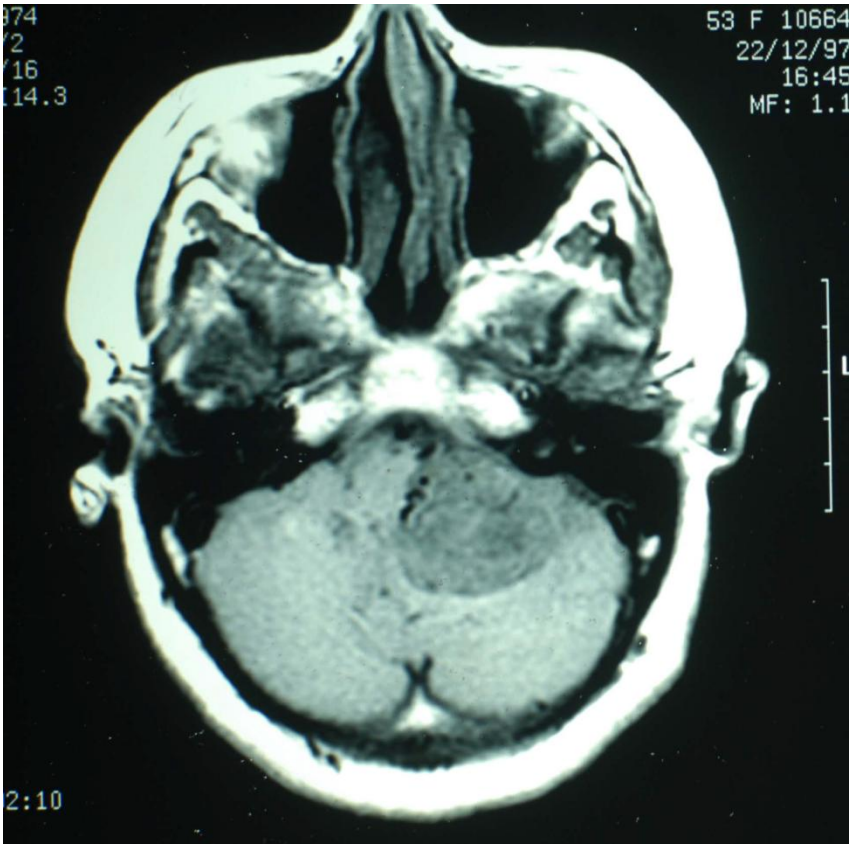


Case VIII

A 53 year old lady had presented to us in November 1998 with history of holocranial headache since one year and gait unsteadiness since 2 months. She also gave a history of reduced hearing on the left side. On examination she was conscious and alert, with stable vital signs. Fundus showed bilateral papilloedema. There was sensorineural type of hearing loss in the left year. The examination of other cranial nerves was within normal limilts. There were no motor or sensory deficits and no cerebellar signs. CT scan of the brain showed an isodense enhancing mass in the left cerebellopontine angle region with obstructive hydrocephalus.



MRI showed the lesion to be isointense on T1WI and heterogeneously hyper on T2/FLAIR imaging. Lesion was causing mass effect over the brainstem with effacement of the fourth ventricle. It had multiple flow voids with intense contrast enhancement.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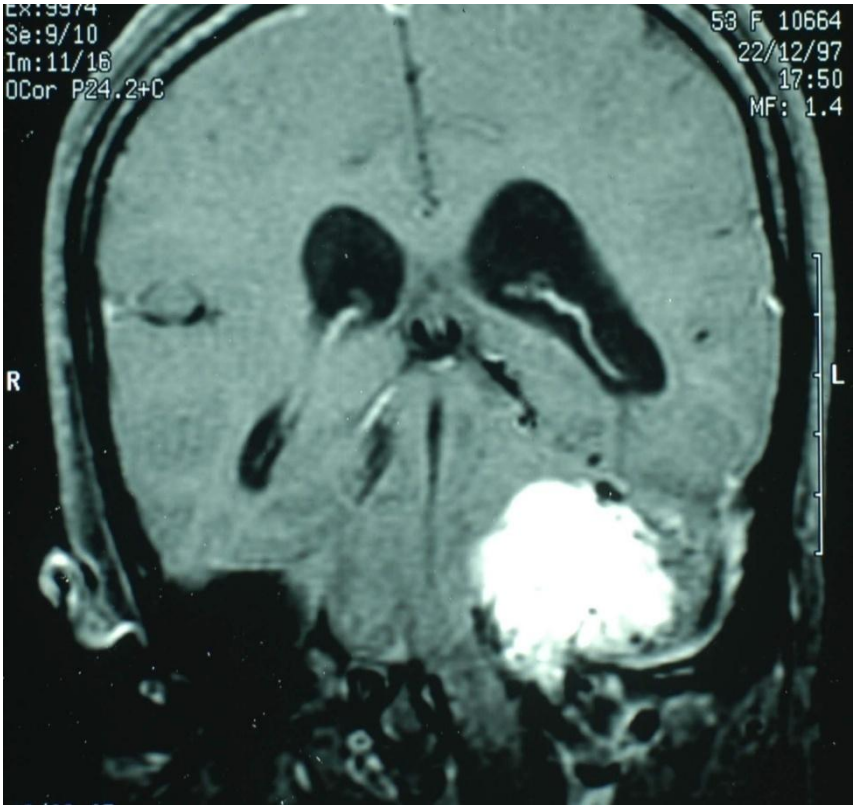
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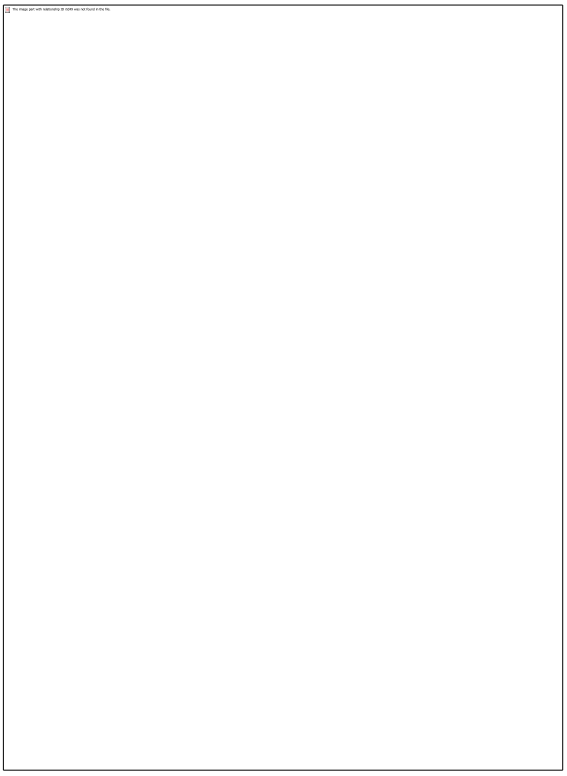
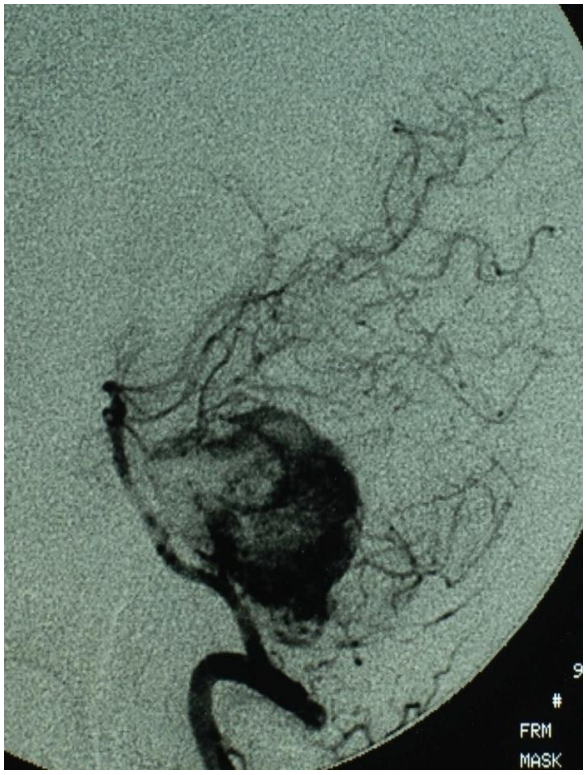
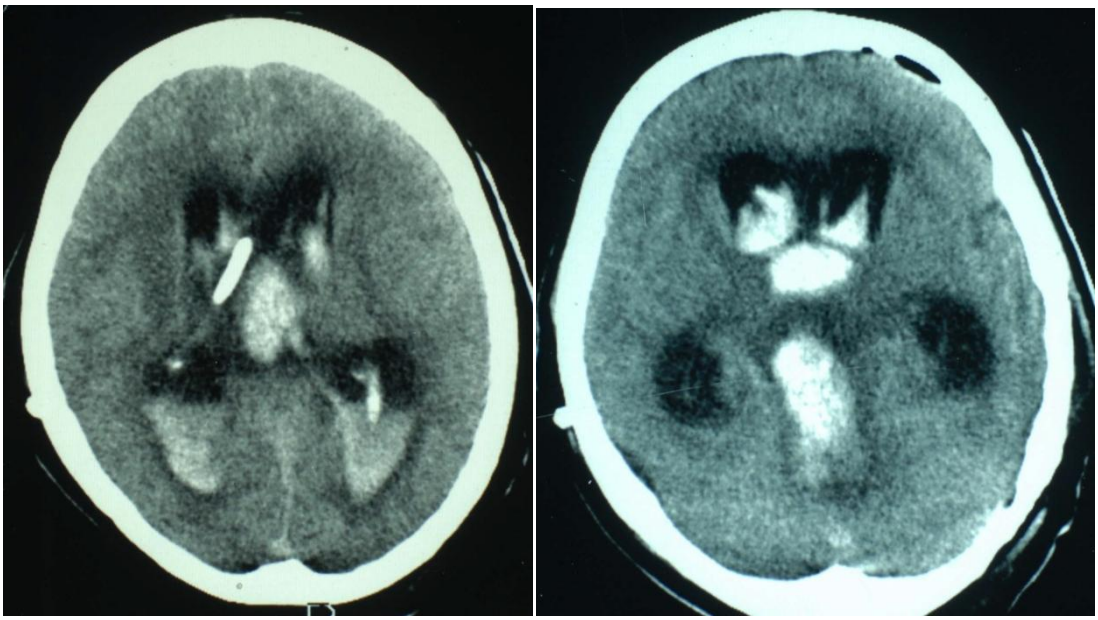
Four vessel cerebral angiogram showed tumor blush supplied by left SCA and PICA. Only partial embolization of the nidus could be done.

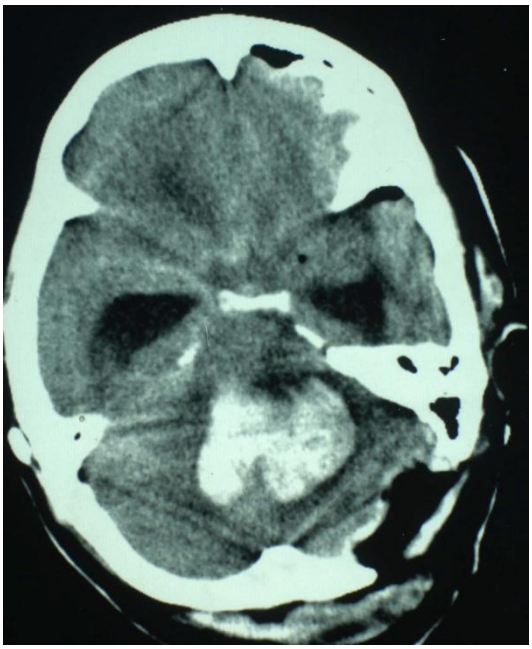




She had polycythemia with Hb value of 17.3 gm % and had undergone four sessions of phlebotomy prior to surgery. A diagnosis of left anteromedial cerebellar hemangioblastoma was made. To relieve her for raised ICP she initially underwent a ventriculoperitoneal shunt. She was then taken up for definitive surgery. A left retrosigmoid approach was used and lesion was totally excised under hypothermic cardiac arrest on a cardiopulmonary bypass. Post operatively she was electively ventilated. On ventilator she developed pupillar asymmetry for which a CT scan was done. It showed blood in both lateral ventricle and fourth ventricle with hydrocephalus. She was taken up for hematoma evacuation and a twist drill ventriculostomy was made. While she was continued on ventilation and external ventricular drainage, she had fall in blood pressure and required high ionotropic support.

She did not improve and ultimately succumbed to death on thirteenth postoperative day. The proposed cause of death was brainstem failure.





Discussion

Introduction

Solid hemangioblastomas can be labelled as “Giant” when they exceed 40mm in the maximum dimension. These tumors are distinct from smaller lesion in terms of presentation, management strategies and also the long term outcome as reported by multiple authors (5, 60, 77, 117). Such large tumors pose considerable challenge in management requiring multimodal and staged therapy, and even then the prognosis may not be as good as smaller lesions in the same locations.

Epidemiology

Hemangioblastomas are tumor of the adults, affecting both the sexes equally and so is true for giant solid types as well. In a report by Zhou et al in 2005, the authors studied 85 cases of solid hemangioblastomas among a total of 213 cases. Of these only 9 cases were of giant variety (>4cm). There was equal distribution between males and females and the average age of presentation was 45 years (5). Krishnan and Schackter in 2006 reported three cases of giant posterior fossa solid hemangioblastomas aged 68, 36 and 38 years (117). Similarly in 2009, Rachinger et al reported their experience in management of 17 consecutive cases of solid hemangioblastomas of which only one case was of giant type. The mean age of presentation in their study was 44.3 years (range 20 – 69 years)(77). In our study also, of the 73 consecutive cases of posterior fossa hemangioblastomas, only eight tumors were of the giant type. The age range was from 30 to 59 years with equal distribution among males and females. Only one patient had an associated von Hippel-Lindau disease and two cases

were of recurrent disease where the initially operated lesions were macrocystic, which had recurred as giant solid hemangioblastomas.

Clinical presentation

As is expected patients with giant lesions most commonly present with features of raised ICP and brainstem compromise manifesting as cranial nerve, cerebellar or long tract signs. Among all the previously reported cases of giant solid hemangioblastomas, none have been detected incidentally and the most common presentation has been of increased intracranial pressure (5, 60, 77, 117). Localization may be suggested by presence of lateralising cerebellar symptoms and signs, cranial nerve dificits and by presence of long tract signs. The 2005 study of Zhou et al, had features of raised ICP (headache and vomiting) as the most common feature present in more than ninety percentage of cases, followed by long tract sings and cerebellar signs. Cranial nerve deficits were the least common in their report (5). All three patient of Krishnan and Schackter in 2006 had features of raised ICP. Two patients additionally had cranial nerve deficits (117). The one patient of giant posterior fossa solid hemangioblastoma in the study of Rachinger et al 2009 had headache with vomiting with associated gait disturbance and cerebellar incoordination (77). In our study also all the eight patients had features of raised incracranial pressure at presentation. Six patients had associated complaint of gait unsteadiness with cerebellar signs on examination. Two patients with anteromedially location in the cerebellum had sensory neural hearing loss and one patient with a cervicomedullary junction tumor had spastic quadriparesis. This observation is in correlation to the patients performance status at presentation which is brought down significantly by raised ICP. Such patient will require initial CSF diversion if early tumor removal is not feasible and the pressures are high. But presence of large

posterior fossa tumor has the risk of patient developing reverse tentorial herniation. Hence an individualised decision is needed and early definitive surgery is warranted.

Imaging and tumor characteristics

As mentioned in the review of literature the imaging modality of choice for posterior fossa hemangioblastomas is a contrast enhanced magnetic resonance imaging (85, 91). Nevertheless almost all the patients had already undergone a computerised tomography scan as a screening modality for the presenting symptoms. The typical MR features of hemangioblastomas include T1 hypointense lesion with T2/FLAIR hyperintensity and an intense contrast enhancement. In all the previously mentioned studies, majority of patients had undergone both MRI and CT scan and none of the patients with giant solid tumors had CT alone though only MRI was done in a few cases (5, 60, 77, 117). In our study also all patients had undergone atleast MRI for proper lesion characterization.

Whenever a hemangioblastoma is suspected on CT/MRI, a digitally substracted angiogram is warranted (85, 91). The posterior circulation study will opacify the tumor and define the vascular anatomy about feeders and its drainage to assess the feasibility of preoperative embolization (99). All the patients of previously reported giant solid hemangioblastomas in the literature were subjected to preoperative angiographic lesion characterization (5, 60, 77, 117). In our study seven of the eight cases had undergone a four vessel cerebral angiogram when suspected of having a hemangioblastoma. Only one case was taken up for surgery without angiogram. The reason was that he had already undergone an attempt of surgical excision at another center where only biopsy was done due to high vascularity; and the histopathology was reported as a meningioma.

Role of Preoperative embolization and intraoperative glue

Preoperative embolization of hemangioblastomas of the posterior fossa minimizes surgical morbidity and mortality by reducing the vascularity of the tumors, and thus prevents intraoperative bleeding disasters (5,6). The major challenge for embolization is the ability to successfully carry out superselective catheterization of the feeders which may not be possible in about 50% of cases. However, even super-selective embolization of large hemangioblastomas in or near the brainstem is not without risks of infarction. Moreover, there are numerous innominate minor feeders that simply cannot be embolized which leads to only partial reduction in tumor blush (4). This is especially true of giant hemangioblastomas which often have multiple minor feeders in addition to prominent catheterizable feeders (117).

Of the 33 cases of solid hemangioblastomas reported by Zhou et al in 2005, twelve were embolised. Statistics on giant lesion embolization were not available. Nevertheless, in only two cases could they achieve complete occlusion, >50% in 7 cases and <50% in 3 cases (5). Of the three cases reported by Krishnan and Schackter (2006), the first patient with 40mm lesion at cervicomedullary junction developed PICA territory infarct post embolization with residual blush. The second case of a 40X50mm lesion underwent superselective catheterization but could not be embolized because test occlusion produced neurological deficits. And the third case could also not be embolised.

In our study we could perform superselective catheterization and embolization in only three of the seven cases that underwent preoperative angiogram. Of these two patients had <50% reduction in tumor blush whereas only one patient had >50% reduction. None could be completely occluded. For those in which superselective catheterization and significant occlusion was not feasible our strategy has been the use of intraoperative injection of glue into the feeding vessels. This was done in five of the eight cases and even in the case where >50% preoperative occlusion was achieved.

Surgical Treatment

The arteriovenous malformation (AVM)-like character of solid haemangioblastomas requires individually tailored approaches in order to achieve adequate surgical exposure. In contrast to cystic lesions, in which the cystic component provides sufficient exposure, solid lesions may require extended skull base approaches (77). In most solid lesions, individually tailored and varied standard procedures such as midline suboccipital or retromastoid approaches allow safe removal. For haemangioblastomas of the brainstem and cerebellar hemispheres, a suboccipital midline craniotomy with or without laminectomy of C1 is the most common surgical approach, whilst most tumours of the CPA can be operated via a suboccipitolateral, retrosigmoid craniotomy (77). Considering these lesions as arteriovenous malformations the following is the strategy followed by majority of authors (5, 60, 77, 117). Identification and elimination of the feeding arteries should be done first, followed by dissection of the tumor and occlusion of the draining veins. Premature obliteration of the venous drainage can lead to disastrous intraoperative swelling and hemorrhage, bearing in mind that the major feeding arteries often come from the ventral or ventrolateral sides of the tumors with large drainage veins crossing the surface of the tumors. Therefore, it is of utmost importance to identify the feeding arteries and not to confuse them with “red” drainage veins. With experience, it is not difficult to differentiate these veins from arteries under high-power magnification because their walls are thinner and they are less turgid than arteries of the same size. In addition, the veins tend to be larger in diameter than most feeding arteries. If the differentiation is still doubtful, the application of temporary clip will clearly indicate whether the pulsations are dampened toward or away from the tumors. The veins and arteries can also be identified by tactile sensation by gently compressing the vessels between the tips of the bipolar forceps. After identification, any feeding arteries should be coagulated as close to the margin of the tumor as possible to avoid any injury to adjacent brain and any interference to the normal brain blood supply. The feeding arteries should be completely coagulated for the length of 2 to 3 times its diameter and “half cut” of the coagulated arteries if perfect coagulation. After all superficial feeding arteries have been divided, careful and deliberate circumferential dissection around the tumor can begin. Usually

there is a distinct cleavage plane between the tumor and brain tissue. It is of importance to minimize the compression or damage on the brainstem by rotating or retracting the tumor itself as far as possible because surrounding brain parenchyma involves the respiratory and vasculomotor areas, sensorimotor tracts on extremities, and nuclei of cranial nerves. It is sometimes helpful to cauterize the tumor to control bleeding and bulging of the tumor using bipolar coagulation. After circumferential dissection and control of all feeding arteries, the tension of the tumor will be relaxed and the color of the main drainage veins will turn red to dark red. The main drainage veins are then coagulated and cut, and the tumor can be removed “en bloc”.

In addition to this we often use intraoperative injection of fibrin or cyanoacrylate glue into the tumor which makes the dissection more blood free and meticulous. We have used it in five of our patients with good results and no additional morbidity. With the use of of glue injection, ultrasonic aspiration could be done without excessive bleeding to decompress and then gain ventral access in anteromedial large lesions.

Silverberg and his colleagues (121) have advocated the use of deep hypothermia and selected circulatory arrest in the management of medullary hemangioblastomas. This method, however, is unpopular because of complicated technique and high morbidity. Rather, mild hypothermia (32-34°C), is strongly recommended for the surgical removal of large or giant lesions because it is easy and safe to conduct and can be combined with hypotension if needed. Usually, the mean arterial pressure is maintained 60 to 70 mm Hg(5). In one case we also used hypothermic cardiac arrest to intraoperatively in a staged manner for a total of 79 minutes, to facilitate dissection. In this case a femorofemoral bypass was used and blood loss was only 800ml. But unfortunately the patient developed massive intraventricular haemorrhage during re-establishment of circulation and expired on thirteenth postoperative day due to brainstem failure.

OUTCOMES

Literature is lacking in large series of patients with giant posterior fossa solid hemangioblastomas. There are only few cases of giant solid hemangioblastomas in each series and no statistical analysis pertaining to giant lesions are available separately. But it has been uniformly reported that larger the lesion size, the more the chances of post operative morbidity, both immediate and long term (5, 60, 77, 117).

In the three cases of giant solid hemangioblastomas reported by Krishnan and Schackter (2006), there was no mortality. While two patients were back to full functional recovery with totally independent survival, one patient was still in a teriary care nursing facility at 2.5 yrs but doing daily activities without assistance (Postop KPS = 70%). There has been no recurrence (117).

The one case of giant hemagnioblastoma in the series of Rachinger et al (2009) had undergone complete microsurgical resection. He had complete resolution of raised ICP and cerebellar symptoms and regained a KPS of 100% at long term followup (77).

Among the eight patients in our series four of the patients developed new neurological deficits or worsening of preoperative defecits in the immediate postoperative period (ataxia, dysmetria, dysphagia and nystagmus. In long term followup four patients had full functional recovery, regaining 100% KPS. One patient with medullary hemangioblastoma developed persistent LCN paresis with dysphonia. One patient became functionally independent but still had mild persistent ataxia at long term follow. While one patient was lost to followup, at early postoperative followup, he was doing well with no deficits. And one patient died.

Conclusions

The conlusions which were drawn with the observations in this study are:

1. Giant hemangioblastomas often require a staged multimodality therapy to achieve satisfactory and safe treatment.
2. Though preoperative embolization is very helpful in reducing the tumor vascularity and thereby intraoperative blood loss, superselective catheterization of all feeders is not always possible often leading to no or partial occlusion.
3. These lesions should be surgically dealt with like arteriovenous malformations. This holds true even for the immediate postoperative period to prevent reperfusion injury. In case intratumoral decompression is warranted for safe resection, use of intratumoral glue is helpful to reduce blood loss and facilitate dissection.
4. If a planned staged treatment strategy is followed with a meticulous microsurgical technique, the long term outcomes can be as favourable as seen in small and cystic hemangioblastomas, even in eloquent locations.

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