

Multifocal Haemangioblastoma Associated With Erythrocytosis A Case Report And Review Of The Related Literature

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Abstract : A 22 year old woman with a solid haemangioblastoma in the posterior fossa, cervicomedullary junction and spinal cord is reported. Preoperative magnetic resonans imaging (MRI) provided precise indications of the anatomical location and radiological features of the tumor that facilitated its partial removal by microsurgery. Laboratory investigations showed associated erythrocytosis of the haemangioblastoma. The patient was treated

with conventional radiation therapy after attempts at surgical resection failed. Twenty- one months after the operation and twenty months after radiation therapy, the patient was neurologically normal.

Key Words : Erythrocytosis, Haemangioblastoma, Radiation therapy

INTRODUCTION

Haemangioblastomas of the central nervous system (CNS) are histologically benign vascular tumors that arise most commonly in the posterior fossa and spinal cord. Haemangioblastomas account for only 1 to 2.5 % of all intracranial neoplasms, 7 % to 12 % of posterior fossa tumors, and 1.6 to 5.8 % of spinal cord tumors (7,15,16,18,21,22,24). They are frequently multiple and cystic if the tumor localizes in the cerebellum. The type that involves the midline structures of the brain stem and spinal cord is usually solid.

Haemangioblastoma may occur either as an isolated lesion or as part of a systemic autosomally dominant, multisystem disease complex, the von Hippel Lindau (VHL) syndrome (4,16,18,19,21).

This report concerns a case of haemangioblastoma of the posterior fossa, cervicomedullary junction and spinal cord associated with erythrocytosis.

CASE REPORT

A 22-year-old woman was admitted with headache, vomiting, ataxia and progressive motor weakness of 2 months' duration. On admission there was quadriparesis, gait and stance ataxia.

Radiological signs: In the sagittal plane, a contrast T1-weighted magnetic resonance image revealed an enhancing round mass in the caudal portion of the fourth ventricle, a mixed, low signal intensity mass in the cervicomedullary junction, and an enhancing round mass in the spinal cord (thoracal-4)(Fig.1). Vertebral angiogram showed well-demarcated vascularization in the posterior fossa and cervicomedullary junction fed by small branches of the left posterior inferior cerebellar artery, the anterior spinal artery, the left anterior inferior cerebellar artery, superior cerebellar artery, and an early venous filling of the dilated draining vein on the dorsocaudal side of the tumor (Figs. 2A and 2B).

Laboratory findings: Abdominal ultrasonography was normal. Blood white cell and platelet count was

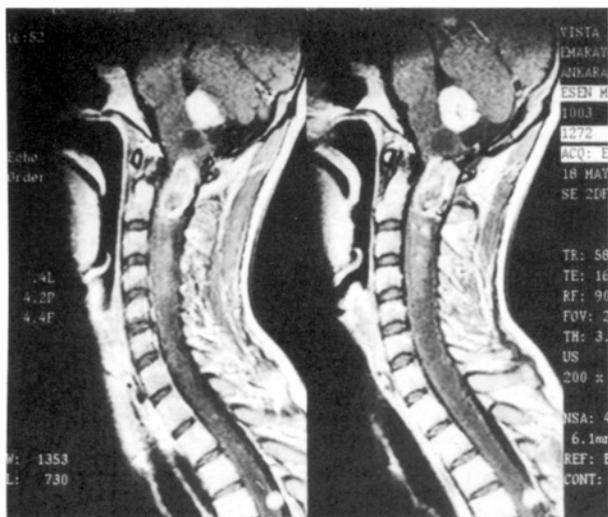


Fig. 1 : Figure 1: Preoperative T1 - weighted magnetic resonance imaging scan. postcontrast sagittal image showing a round, solid well-demarcated, well-enhanced mass in the caudal portion of the fourth ventricle and spinal cord (Thoracic-4), and a mixed, low signal intensity mass in the cervicomedullary junction.

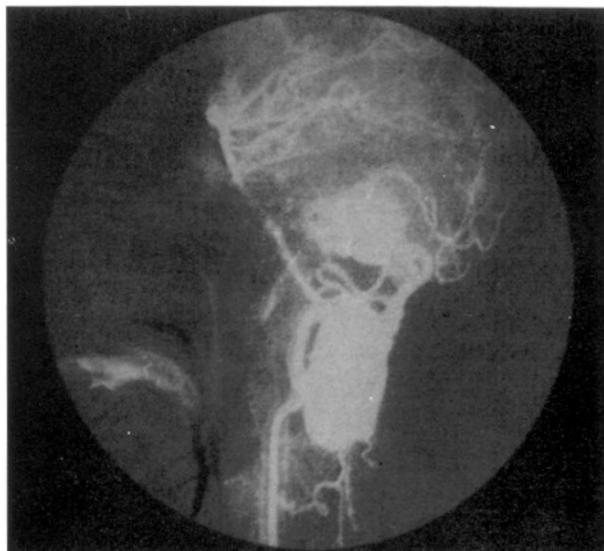


Fig. 2B : Vertebral angiogram showing an early venous filling of the dilated draining vein on the dorsocaudal side of the tumor.

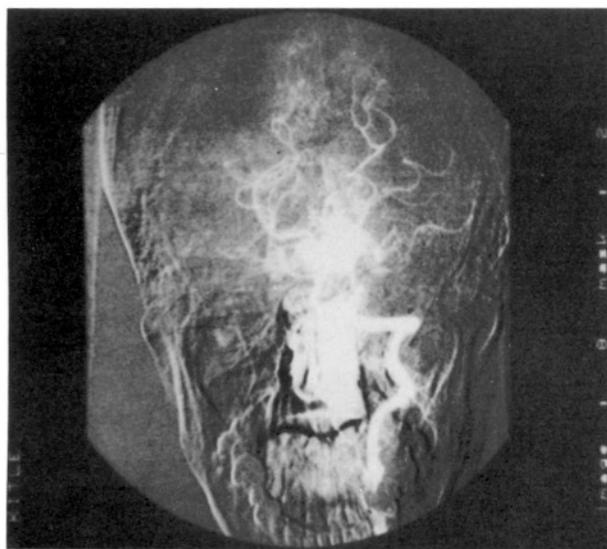


Fig. 2A : Vertebral angiogram in the late arterial phase showing well-demarcated vascularization in the posterior fossa and cervicomedullary junction.

normal, but the red cell volume was increased, and plasma volume was normal.

Operation: Under general anaesthesia; in the sitting position, a suboccipital craniectomy combined with laminectomy of the cervical - 1 and cervical - 2 was performed. Then the dura was opened. Under the operating microscope; a well - demarcated,

reddish vascular, solid mass was demonstrated in the cervicomedullary junction. Lateral retraction of both cerebellar tonsils and a small incision at the caudal end of the vermis disclosed the fourth ventricle. Dissection around the circumference of the tumor commenced with bipolar coagulation forceps and microscissors along the dorsal surface, where the tumor was relatively well demarcated in the cleavage plane and richly fed, mostly by fine and thick arterial branches. In spite of it's distinct cleavage with normal tissue, we did not try to remove it totally, because of the close relationship of the upper cervical nerves with dorsal surface of the tumor. This relationship with nearby neural structures and the high vascularity of the tumor constrained us to conservative surgery. Accordingly the tumor could only be partially excised. The dura was left open and considerable decompression was achieved. The postoperative course was uneventful. All of her complaints, except motor weakness, improved. Histopathological examination confirmed the diagnosis of haemangioblastoma (Fig.3). Radiation therapy was given one month after the operation (more than 5000cGy over 5 weeks).

A control neurological examination 21 months after the operation revealed that motor weakness had reduced and the patient was living a normal life.

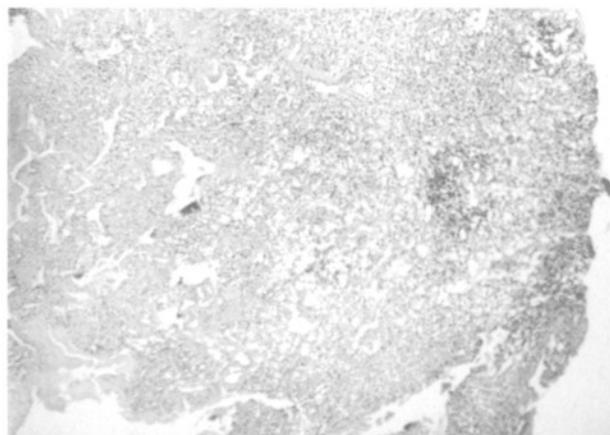


Fig. 3: Histopathological examination demonstrated abundant thin-walled vascular channels intersected by enlarged vacuolated stromal cells (Hematoxylin and eosin, X 100).

DISCUSSION

In 1926, Lindau (13) described a cystic tumor of the cerebellum associated with retinal angiomas and tumours of the kidney. Cushing and Bailey (6) called this CNS tumor "haemangioblastoma", emphasizing its neoplastic nature. This is an unfortunate name because it suggests an aggressive anaplastic neoplasm whereas the tumor has a benign nature with low a mitotic rate and little cellular pleomorphism. Microscopically, the mural nodule and solid tumor are composed of thin-walled vessels and capillaries. These endothelial cells are separated by fat-laden stromal cells.

Von hippel-Lindau disease is an autosomal dominant disorder of incomplete penetrance, characterized by (14, 18, 19, 21,22):

- 1) haemangioblastoma of the retina (retinal angiomas),
- 2) haemangioblastoma of the cerebellum (Lindau tumor), medulla, and spinal cord, as in our case,
- 3) angioma of the kidney,liver, and epididymis,
- 4) renal cell carcinoma,
- 5) pheochromocytoma,
- 6) cysts of the pancreas, kidney, and epididymis,
- 7) erythrocytosis, as in our case,

Haemangioblastoma is the only CNS tumor to be associated with erythrocytosis. It has been reported in 9 to 50% of cases of posterior fossa and supratentorial

haemangioblastoma but not with purely spinal lesions. There is erythrocytosis with no associated splenomegaly or increase in white cell or platelet count. The red cell volume increases, but the plasma volume remains normal. The red cell life span is within the normal range. There is no evidence of accelerated red cell destruction in the liver or spleen. The rate of red cell synthesis is increased, and the red cell turnover is increased proportionally. The bone marrow may show erythroid hyperplasia. Erythrocytosis in patients with haemangioblastoma is believed to be due to the unregulated secretion of erythropoietin or an erythropoietin-like substance, by the neoplastic tissue. Erythropoietin is known to promote the differentiation, proliferation, and maturation of red cell precursors in the bone marrow. Erythropoietin levels are increased in patients with anemia, renal artery stenosis, renal cyst, and renal neoplasm. Thus erythrocytosis in a patient with VHL complex may be due to a renal lesion or a nervous system haemangioblastoma. The erythrocytosis induced by haemangioblastoma may improve after total excision of the tumor or irradiation. It may reappear with recurrence of the tumor. Ultrastructural studies of certain haemangioblastomas have shown granules thought to represent intracellular erythropoietin, but positive proof of their identity is lacking (2,4,8,10,14,18,21,22,25,28). In our case, abdominal ultrasonography and white cell and platelet count were normal. But, the red cell volume was increased.

Other preoperative investigations consist of angiography, computed tomography (CT) and MRI. Angiography is particularly useful in patients with haemangioblastoma. On vertebral angiography four different vascular patterns may be observed: (7) a vascular mural nodule within an avascular cyst, (15) a doughnut ring of abnormal vessels surrounding an avascular space representing an intratumoral cyst, (16) a large, solid vascular mass,(18) multiple small, widely-separated vascular nodules and a late-appearing homogeneous stain may identify the neoplasm and allow accurate localization of the tumor nodule. Dilated arteries and early filling veins may be seen. Angrography results are rarely normal with this tumor (1,11,22). In our case, angiography revealed a network of small vessels and a late-appearing homogeneous stain, dilated arteries and early filling veins.

CT and MRI reveal a tumor with density (isodense or isointense) similar to that of brain. Intravenous injection of contrast material results in intense homogeneous enhancement. The tumor is not calcified and there is little surrounding edema. In 90% of patients it is associated with a cyst. MRI scans have been shown to provide preoperative information indispensable for successful treatment. The diagnosis of spinal cord lesions has been significantly improved by the introduction of MR - imaging with the addition of paramagnetic contrast medium. It can reveal the location and characteristics of a deep-stated tumor close to bony structures, such as intramedullary haemangioblastoma of the brain stem. In the presented case, T1 -weighted MRI provided the most comprehensible and reliable diagnostic evidence of such a tumor (4,5,18,19,26). Preoperative MRI clearly demonstrated that the well -demarcated hypervascular tumors were located in the caudal portion of the fourth ventricle, cervicomedullary junction, and thoracic-4 and had no surrounding edema.

Haemangioblastomas can be cured by complete surgical excision, making surgery the treatment of choice (7,9,11,12,20,26). However, the highly vascular nature of these lesions and their frequent proximity to vital structures in the brain stem and upper cervical spinal cord can preclude complete excision, as in our case. Since the advent of microsurgical techniques, total removal of haemangioblastomas of the brain stem, cervicomedullary junction and upper cervical spinal cord have become feasible (11,15,20,22). The operations, however, have an uncertain outcome for the patient's survival and residual functional disabilities. The difficulties encountered in operating on solid brain stem, cervicomedullary junction and upper cervical spinal cord haemangioblastomas of the medulla oblongata arise from the following: (1) The solid highly vascular tumor is fed by deep-stated arteries and drained through the superficial dilated vein. (2) "En bloc" total removal is desirable even for benign tumours in order to control bleeding from the tumor itself and to prolong survival (11,22,27). (3) Surrounding brain parenchyma involves the respiratory and vasomotor areas, sensorimotor tracts in extremities, and nuclei of the cranial nerves. The tumor had good cleavage in our case. But, we did not try to remove it totally. Under the operating microscope, we could identify the rootlets of upper cervical nerves upon the dorsal surface of the tumor. Lateral retraction of both cerebellar tonsils and a

small incision at the caudal end of the vermis revealed the tumor extending to the brain stem. This relationship with nearby neural structures and the high vascularity of the tumor constrained us to conservative surgery. Accordingly tumor could only be partially excised. There is relatively little information in the literature regarding the efficacy of radiation therapy in the management of haemangiomas, but reports (3,17,23) indicate that long-term control of these lesions may be achieved in patients with subtotal excision who undergo high-dose radiation therapy postoperatively. Smally et al. (23) reported (27) haemangioblastoma patients treated between 1963 and 1983. Of those patients with gross residual tumor after surgery, 12 received a dose of less than 5000cGy. Local control was achieved in 57 % of the higher dose group versus 33% in the lower dose group. Page et al. (17) reported that stereotactic radiosurgical ablation should be considered in patients with recurrent and multifocal haemangioblastoma.

Our case with a gross residual tumor after surgery received a dose of more than 5000 cGy. 21 months after the operation, the patient was neurologically normal.

CONCLUSION

This is the only central nervous system tumor to be associated with polycythaemia (erythrocytosis) which occurs in 10-20% of posterior fossa haemangioblastoma due to secretion of an erythropoietic substance by the tumor. CT provides the best screening modality, particularly for cystic tumours. The tumor nodule is isodense with cerebellum on non-enhanced scan and highly hyperdense after i.v. contrast injection. MRI provides accurate anatomical information on the lesions, especially those of the brain stem and spinal cord. On T1 images the solid components of the tumor are of similar intensity to the cerebellum. Cystic components are hypointense due to their prolonged relaxation times. On T2 images the solid components are usually hyperintense with respect to the cerebellum, often of similar intensity to the surrounding edema. Angiography may demonstrate the rich vascularity of the mural nodule. The majority of posterior fossa haemangioblastomas are satisfactorily treated by operation. Postoperative morbidity of solid

haemangioblastomas with attachments to the midline of the IV ventricle floor and medulla oblongata are extremely hazardous because of the eloquent location. In this situation, radiation therapy may be an alternative to surgery (in brain stem and multifocal haemangioblastomas) as in our case. In the present case, the clinical symptoms were relieved. Although the postoperative follow-up was only 21 months, the long-term survey of the patient will be evaluated with MRI.

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