CASE REPORT

Contiguous haemangioblastomas of the brain and spine in a patient of Von Hippel-Lindau disease

Asifur Rahman, Saif Ul Hoque, Paawan Bahadur Bhandari, Shamsul Alam

Department of Neurosurgery,
Bangabandhu Sheikh Mujib
Medical University, Dhaka,
Bangladesh

Correspondence to

Dr Asifur Rahman,
bijoun14@yahoo.com

SUMMARY

Von Hippel-Lindau (VHL) disease is an inherited, autosomal-dominant syndrome caused by heterozygous germline mutations in the VHL gene, and predisposing to the development of benign and malignant tumours and cysts in multiple organ systems involving eyes, kidneys, pancreas, liver and central nervous system. The responsible tumour suppressor gene for VHL disease is in chromosome 3p25. We are presenting a case of a patient with both cerebellar as well as spinal haemangioblastoma in addition to polycystic pancreas. We operated on both the spinal and the cerebellar haemangioblastomas and the patient had made a very good recovery. We present this case for its rarity along with the literature review.

BACKGROUND

Von Hippel-Lindau (VHL) disease, an autosomal-dominant hereditary disease, having the responsible tumour suppressor gene in chromosome 3p25, characterised by neoplasms arising in multiple organs including eyes, kidneys, pancreas, liver and central nervous system (CNS). Spinal haemangioblastomas are intradural intramedullary tumours and most are found at the level of the cervical and dorsal vertebrae.¹ Very few literatures have mentioned the contiguous presence of haemangioblastomas both in the brain as well as the spinal cord. Many authors have mentioned asymptomatic pancreatic cysts in their study of VHL patients.² Microsurgical excision of these lesions remains the mainstay of treatment, as supported by some.^{3, 4} Our patient had presented with a single haemangioblastoma in the posterior cranial fossa as well as two similar lesions in the spinal cord. She also has multiple cystic lesions in the pancreas, thus fulfilling the diagnostic criteria of VHL disease. The haemangioblastomas had been successfully operated. For these reasons, we feel this case deserves to be reported.

CASE PRESENTATION

A 27-year-old woman presented with occasional occipital headache of moderate severity, pain in the mid-dorsal region and progressive weakness of both lower limbs for duration of 6 months. Radiation of the back pain had a band-like distribution from the anterior chest wall down to the umbilicus. She had no bladder or bowel dysfunction.

On examination, she had bilateral secondary optic atrophy. Muscle power of all groups in both lower limbs was 4/5 with a sensory level at D6. All

the deep tendon reflexes were brisk with bilateral plantar extensors. She also had bilateral ankle and patellar clonus.

INVESTIGATIONS

Her blood workup did not reveal any evidence of polycythaemia or diabetes mellitus. Ultrasound and CT of the abdomen revealed multiple pancreatic cysts (figure 1). MRI of the dorso-lumbar spine revealed two separate lesions in the dorsal spinal cord, situated at D5 and D8/9, hypointense on both T1-weighted and T2-weighted images with homogeneous contrast uptake. There was syrinx extending from D1/2 to D7/8 level. The lesion at D8/9 had transforaminal extension into the left thoracic cavity (figure 2). CT scan of the brain revealed a cystic lesion with enhancing mural nodule (figure 3) in the posterior fossa compressing the fourth ventricle.

DIFFERENTIAL DIAGNOSIS

Haemangioblastomas, pilocytic astrocytoma of the posterior fossa, ependymoma and spinal schwannoma.

TREATMENT

She underwent surgery for removal of both the spinal as well as cranial lesions in two separate sessions. In the first stage, she was operated for the intracranial lesion. Midline suboccipital craniectomy was carried out. A cystic lesion was encountered which was punctured and the contents sucked out. The mural nodule was identified, which appeared reddish and vascular. It was meticulously dissected free from the surrounding structures and the feeders were coagulated. The nodule was then removed in a piecemeal fashion. The capsule was then excised as far as possible. A week later, she underwent surgery for both the spinal lesions in a single session. Standard laminectomies were carried out at both levels to expose the pathologies. The lesions were removed completely in piecemeal fashion. The lesion was at D8/D9 level had an extracanalicular extension, being well separated from the nerve root. This lesion was also cherry red in colour, encapsulated, having good cleavage margins, quite vascular and partially suckable. As before, the mass was also removed in a piecemeal fashion.

OUTCOME AND FOLLOW-UP

The histopathology reports of all surgically resected lesions confirmed the diagnosis of haemangioblastoma (figure 4).

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Figure 1 Contrast-enhanced CT scan of the abdomen showing multiple cysts in the pancreas (arrows).

Her postoperative recovery in both instances was uneventful. An immediate postoperative CT scan revealed a patent fourth ventricle, with a small residual haematoma in the tumour bed (figure 5). There were no further deterioration of existing or development of any new neurological deficits, and she was relieved of her occipital headache.

On her follow-up 1.5 years after the surgeries, she was doing fine clinically.

DISCUSSION

Haemangioblastomas constitute $0.9 \pm 2.1\%$ of CNS neoplasms and occur sporadically or as a manifestation of VHL disease, an autosomal-dominant hereditary disease characterised by neoplasms arising in multiple organs including eyes, kidneys, pancreas, liver and CNS. The responsible tumour suppressor gene for VHL disease was recently identified from chromosome 3p25, and inactivating germline mutations of this gene, VHL, were found in the majority of VHL disease patients.¹ Therefore, a chromosomal study is required in such patients not only to

establish a diagnosis but also for counselling. The disease is inherited in an autosomal-dominant pattern, and hence all family members require screening. We intended to carry out a thorough genetic workup in our patient. But they had declined.

The Melmon and Rosen diagnostic criteria for VHL disease require the presence of only one retinal or CNS haemangioblastoma or one visceral lesion (renal tumour, pheochromocytoma, pancreatic cyst or tumour, or papillary cystadenoma of the epididymis) if there is a family history of VHL disease. In the absence of a relevant family history, two or more CNS haemangioblastomas or one CNS haemangioblastoma and one visceral lesion—excluding (1) unilateral papillary cystadenoma of the epididymis and renal cysts, which are frequent findings in the general population and (2) papillary cystadenoma of the broad ligament—are required to make the diagnosis. About 20% of patients fall into the latter category. Diagnosis is made on these clinical criteria. However, the presence of pathogenic germline mutations in the VHL gene is the most specific way to confirm or exclude the disease and is particularly useful when the family

Figure 2 Contrast-enhanced MRI of the dorsal spine showing lesions (white arrows) with syringomyelia (black arrows). The lower lesion has extended into the thoracic cavity (grey arrow).

Figure 3 CT scan of the brain showing cyst in the posterior fossa (white arrow) with an enhancing mural nodule (black arrow).

history is negative or when a young patient presents with a single CNS haemangioblastoma or isolated renal cell carcinoma and no other manifestation.³ In the presence of multiple cystic lesions in the pancreas with minimal or absent clinical symptoms, a diagnosis of VHL syndrome must always be considered.² The clinical history, image findings and histopathology reports of the case in discussion all pointed towards a diagnosis of VHL disease, in accordance with the Melmon and Rosen diagnostic criteria.

One of the problems of all these studies is that the pancreatic cysts were generally asymptomatic or associated with only mild symptoms, such as minor abdominal discomfort with tension in the upper abdomen, or unspecific nausea. Episodes of serious clinical manifestations, such as pancreatitis or diabetes, seem to be relatively rare.² Similarly, our patient had no features of pancreatitis or diabetes, hence her pancreatic cysts may be deemed asymptomatic. The abdominal symptom with which she had initially presented can be attributed to the dorsal spinal lesions, as evidenced by its remission following surgery.

There are at least three phenotypic expressions of VHL disease, on the basis of which the following classification has been proposed:

- ▶ Type 1: Haemangioblastoma of the retina or CNS, kidney tumours or cysts or pancreatic cysts in the absence of pheochromocytoma. This is the most frequent form.
- ▶ Type 2: VHL disease with pheochromocytoma.

Haemangioblastoma of the CNS or retina is the most commonly detected pathology (60%) of cases, while kidney tumours develop in 40% of cases, pheochromocytoma in 18%, and pancreatic involvement ranges from 16% to 29% of cases in the various patient samples described in the literature.⁵ By the above mentioned criteria, the patient in discussion falls under type 1.

Spinal haemangioblastomas are intradural intramedullary tumours and most are found at the level of the cervical and dorsal vertebrae. They can occur throughout the spine from the

cervical to the lumbosacral areas affecting the spinal cord, nerve roots, conus medullaris and cauda equina and filum terminale.¹ These are rare tumours accounting for less than 2% of all spinal cord tumours and 7% of haemangioblastomas. They most commonly present with symptoms of spinal cord compression, radicular pain or symptoms related to an associated syrinx. Rarely, spinal cord haemangioblastoma can present with sub-arachnoid haemorrhage. They are intramedullary tumours and are said to arise most commonly in the posterior columns of the spinal cord, or extend from the pia on the posterior surface of the cord into the posterior columns.⁶ Our patient had presented with not one but two separate haemangioblastomas in the dorsal spine. The lower lesion had a transforaminal extension into the thoracic cavity; a similar case has been reported by Purandare and Misra⁷ where a patient had presented with thoracic intraspinal haemangioblastoma presenting as a posterior mediastinal mass.

In treating cases of spinal haemangioblastomas, the use of laminectomy, laminotomy and laminoplasty have been advocated by authors with good results. Branczerowski *et al* have observed that laminotomy techniques help to prevent damage to the crucial posterior stabilisers of the spine. In contrast to conventional spinal canal approaches, preservation of the majority of posterior structures leaves muscle attachments on the spinous processes and laminae completely intact.⁸ We have carried out laminectomies in both the spinal lesions in our case and post-operatively the patient recovered well.

Although documented growth on serial MRIs and the need for pathological diagnosis have been suggested as indications for surgery in otherwise asymptomatic patients, Harati *et al* in their series showed that a potentially larger group of asymptomatic patients with spinal haemangioblastomas associated with VHL disease would benefit from microsurgical resection. Long-term results of the surgical management of spinal haemangioblastomas are generally favourable. Their results suggested staging and early treatment for spinal haemangioblastomas larger than

Figure 4 Histology slides showing a cerebellar (A) and spinal (B) haemangioblastoma.

Figure 5 Postoperative CT scan of brain showing a patent fourth ventricle (black arrow) with a small haematoma in the tumour bed (white arrow).

55 mm, especially in patients with VHL disease. Small spinal haemangioblastomas may be followed up.² The case in discussion indeed had symptomatic spinal lesions, warranting surgical resection.

Angiography has been used by many surgeons in resection of CNS haemangioblastomas, both preoperatively and intraoperatively. Hovarth *et al* have described a case of cerebellar haemangioblastoma being supplied by the posterior cerebellar artery. They have used Onyx 18 for the arterial embolisation. As a result, the tumour was found to be completely avascular intraoperatively.⁹ Others have discussed nine cases of haemangioblastoma involving either the cerebellum or the spinal cord that were embolised preoperatively. In each case the feeding artery was selectively catheterised with a microcatheter and the hypervascular tumour nidus was devascularised with polyvinyl alcohol particles.¹⁰ Some authors have advocated temporary arterial occlusion intraoperatively in these cases. This may be achieved by aneurysm clip placement with concurrent neuromonitoring at the tumour edge to differentiate arteries supplying the tumour from those supplying the healthy spinal cord. Arteries that were assumed not to supply important regions of the cord were divided at the tumour surface provided there was no change in evoked potentials after 4 min of occlusion.¹¹

Glasker *et al*¹² have shown that the power doppler flow sonography may be a sensitive intraoperative tool to guide the surgical approach and resection and provides reliable resection control in surgery of CNS haemangioblastoma.

Our centre lacks the necessary facilities required for preoperative or intraoperative angiogram. Careful and meticulous microsurgical resection was carried out without any injury to adjacent vital neurovascular structures, which is evident by the good postoperative outcome.

During surgery of haemangioblastomas, discrimination of the arterialised draining veins from the feeding arteries may be difficult, so Ueba *et al* have used indocyanine green videography to differentiate them. The tumour was successfully resected, and postoperative indocyanine green videography showed total removal of the tumour as a signal-negative region.¹³ Unfortunately, we currently do not have this facility at our centre.

In describing the optimal surgical approach, some authors recommended the suboccipital ipsilateral approach, modified far-lateral approach, suboccipital midline approach and suboccipital supracerebellar approach for treating posterior fossa haemangioblastomas. Tumours can be identified intraoperatively by microscopy. They usually appear as superficial racemose haemangiomas appearing bright or dark red. The authors maintained the principle that the feeding arteries should be divided in

advance and the draining veins should be ligated last.⁴ Although preoperative embolisations have been advocated by some, a recent study found this unnecessary to achieve complete tumour resection. Microsurgical resection remains the gold standard for spinal haemangioblastomas that are clearly symptomatic or have developed radiographic progression in size, spinal cord oedema or syrinx.²

In their collective review of 275 patients with VHL syndrome, malignant pancreatic tumours were found in only 8 patients, 6 of whom had malignant islet cell tumours and 2 of whom had adenocarcinomas. In the absence of complications or evidence of tumours, pancreatic cysts should be managed conservatively with regular follow-up.¹⁴

There are many reports in the literature of patients bearing multiple haemangioblastomas separately in the brain and spine.^{3 15–18} Only recently, a paper has reported on a pregnant lady bearing haemangioblastomas both in the brain and in the spine along with pancreatic cystadenoma. She also underwent laparotomy for the pancreatic lesion.¹⁹

Following surgery, during her hospital stay, our patient had not developed any features of raised intracranial pressure suggesting the development of hydrocephalus. As such, we planned to follow her up.

Learning points

- ▶ Our case had presented to us mainly with pancreatic cysts and spinal lesions. The posterior fossa tumour had been diagnosed with further imaging. A diagnosis of Von Hippel-Lindau (VHL) disease was done on this basis.
- ▶ Given the advent of improved imaging and advanced microsurgical techniques, we were able to almost completely resect all the lesions. The patient had made a satisfactory recovery and her preoperative symptoms improved dramatically.
- ▶ A proper preoperative workup is essential in diagnosing VHL disease cases, this includes the lesions causing clinical symptoms as well as those that have not yet caused any clinical manifestation.
- ▶ Regarding surgery, complete removal of surgically accessible lesions is the goal.
- ▶ Patient counselling is of paramount importance as the disease is inherited in an autosomal-dominant pattern and this would aid us screen the family members as well, necessitating further interventions wherever deemed necessary to ensure patient well-being.

Competing interests None.

Patient consent Obtained.

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