# Sciatic Nerve Schwannoma in a Patient With Von Hippel-Lindau Syndrome: Case Report and Literature Review

## Von Hippel-Lindau Sendromlu Bir hastada Siyatik Sinir Schwannomu: Olgu Sunumu ve Literatürün Gözden Geçirilmesi

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**Abstract:** Radiological examinations of a 21-year-old man with headache and gait abnormality revealed hemangioblastomas in both cerebellar hemispheres and in the cervical spinal cord. There were also other findings consistent with the diagnosis of von Hippel-Lindau syndrome (VHLS), but no retinal hemangioblastomas were detected. The patient underwent bilateral suboccipital craniectomy for removal of the cerebellar tumors. Three months after this surgery, a C6 laminectomy was performed and the cervical hemangioblastoma was also totally excised. In the immediate postoperative period, the patient developed motor weakness and radiating pain in his right leg. Physical examination and a computerized tomography scan revealed a well-circumscribed solid mass in his right posterior thigh, which was thought to be sciatic nerve tumor. A third operation was done to totally excise this mass. Histological examination identified the neoplasm as a schwannoma. Although we considered the presence of a sciatic nerve schwannoma in this patient to be coincidental, we believe that maintaining a high index of suspicion for clinically silent peripheral nerve sheath tumors in individuals with VHLS may reveal that these masses are yet another manifestation of this syndrome. Already more than 30 lesions characteristic of this condition have been described to date. This is the first reported case of VHLS accompanied by a peripheral nerve sheath tumor.

**Key words:** Hemangioblastoma, peripheral nerve schwannoma, von Hippel-Lindau syndrome

**Özet:** Baş ağrısı ve yürüme güçlüğü olan 21 yaşındaki bir erkek hastada radyolojik incelemeler sonucu her iki serebellar hemisferde ve servikal spinal kordda hemanjioblastomlar saptandı. Retinal hemanjioblastom hariç, von Hippel-Lindau sendromunun (VHLS) diğer bulguları da mevcuttu. Bilateral suboccipital kraniotomi yapılarak serebellar tümörler çıkarıldı. Üç ay sonra, C6 laminektomi yapılarak servikal yerleşimli hemanjioblastomda tam olarak çıkarıldı. Hastada postoperatif erken dönemde sağ bacağa yayılan ağrı ve güçsüzlük gelişti. Fizik muayene ve bilgisayarlı tomografide, sağ uyluk arkasında, siyatik sinir tümörü olduğu düşünülen iyi sınırlı bir kitle saptandı. Üçüncü bir operasyonla kitle tam olarak çıkarıldı. Histolojik incelemede kitlenin schwannoma olduğu saptandı. Her ne kadar bu hastadaki siyatik sinir schwannom varlığının rastlantısal olduğu düşünülse de, VHLS mevcut kişilerde, klinik olarak sessiz periferik sinir kılıfı tümörlerinin olabileceğinin akılda tutulmasının, bu sendromun yeni bir şeklini ortaya çıkarabileceğini düşünüyoruz. Çünkü bugüne kadar, bu sendromun 30' dan fazla farklı klinik durumu tanımlanmıştır. Bu olgu VHLS ile birlikte olan ilk periferik sinir tümör olgusudur.

**Anahtar kelimeler:** Hemanjioblastoma, periferik sinir schwannomu, von Hippel-Lindau sendromu

## INTRODUCTION

Hemangioblastomas are uncommon neoplasms that represent only 1.5% to 2.5% of all intracranial tumors (4,7,19,22,25). Although one report has documented subarachnoid spread of hemangioblastoma in two patients (17), these vascular neoplasms are almost always histologically benign, and usually arise in the posterior cranial fossa (7,20,22). Hemangioblastomas typically arise in the third through fifth decades of life, and there is a slight predominance in males (7,22). There is a strong association between hemangioblastoma and von Hippel-Lindau syndrome (VHLS), an autosomal dominant disorder with partial penetrance that is characterized by cerebellar, spinal cord and retinal hemangioblastomas.

Approximately 20% of all hemangioblastomas occur in association with VHLS (7,20,25). Individuals with this syndrome are at risk of developing a variety of lesions, including cysts or tumors of the kidney, pancreas, liver, adrenal gland and epididymis, in addition to pheochromocytoma (2,4,5,7,9,10,12,13,20-23,24). In this report, we present the case of a VHLS patient who had hemangioblastomas in the cerebellum and spinal cord, cysts in both kidneys and in the pancreas, erythrocytosis and schwannoma. Our literature search indicated that this is the first report of a peripheral nerve sheath tumor in a patient with VHLS.

## CASE REPORT

A 21-year-old man was admitted to our center with severe headache and gait disturbance of 2 weeks' duration. Physical examination revealed bilateral papilledema, mild disorientation, ataxia, dysmetria, intention tremor and stance-dysequilibrium. The patient's white blood cell count, platelet count and plasma volume were normal, but his packed cell volume and blood hemoglobin concentration were both markedly elevated. These findings indicated significant erythrocytosis. Urinalysis and renal function

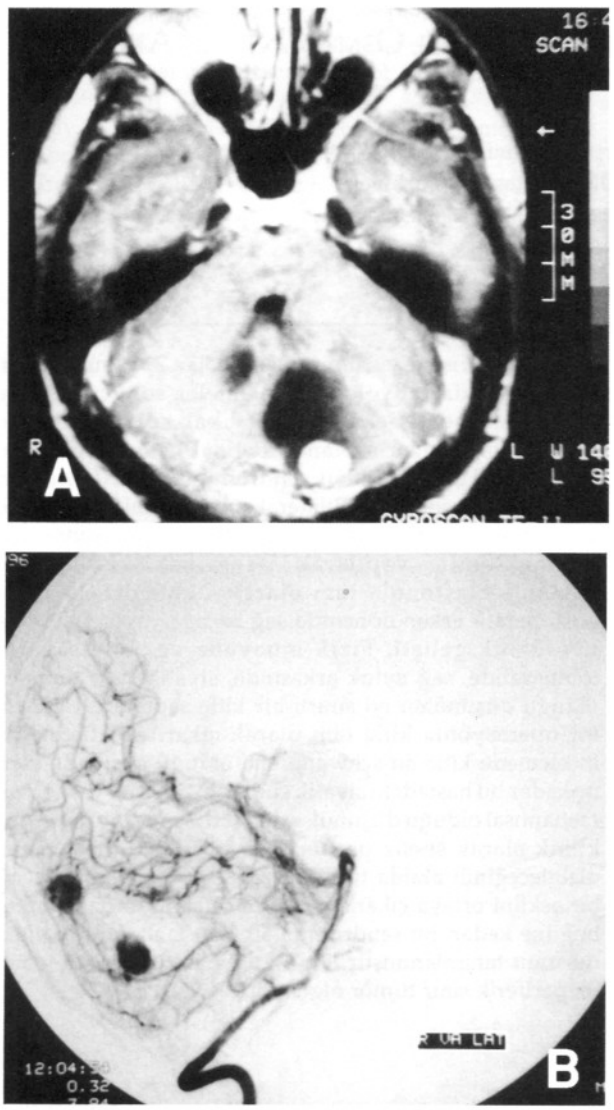


Figure 1: Radiologic results prior to the first operation: A gadolinium-enhanced T1- weighted MR image (axial image) (A) and right vertebral angiography (lateral view) (B), reveal findings typical of cerebellar hemangioblastoma. In addition, a T-1 weighted MR image (sagittal plane) shows syringobulbia and a multilocular syrinx (C). There was no communication between the syringobulbia and the fourth ventricle.

were normal. Contrast-enhanced computerized tomography (CT) scans demonstrated two cystic lesions with hyperdense mural nodules in the cerebellum, as well as a separate, noncystic, hyperdense nodule. There was no enhancement at the cyst margins. Magnetic resonance imaging (MRI) demonstrated smooth and sharply defined cyst borders. The mural nodules were isointense on T1-weighted images, and were hyperintense on T2-weighted images. Intravenous administration of gadolinium led to intense enhancement of the mural nodules. We also noted longitudinal syringobulbia and syringomyelia. Vertebral angiography showed that two of the nodules were highly vascular (Figure 1-A,B,C).

When the patient developed depressed mental status, we immediately performed bilateral suboccipital craniectomy. At surgery, we noted that the cyst fluid was xanthochromic. We removed both mural nodules. Duraplasty involved the use of a surgical membrane constructed of expanded polytetrafluoroethylene (Gore-Tex, W.L. Gore & Associates, Arizona, USA). The patient's postoperative course was uneventful. Histological analysis of the removed tissue was consistent with hemangioblastoma, as indicated by numerous endothelium-lined vascular channels and stromal cells that appeared foamy because of their lipid contents. The finding of this tumor type in association with cystic lesions, erythrocytosis and the family history of VHLS led to a presumptive diagnosis of VHLS. The patient's mother and brother had both undergone surgery for hemangioblastoma 10 years and 2 years earlier, respectively.

Two months after his first surgery, the patient was readmitted for further evaluation. Cervical MRI revealed another contrast-enhanced, globular, sharply demarcated mass in the spinal cord at the level of C6. There was no sign of the previously noted syringobulbia, but the syringomyelic cavity that had been found during the initial work-up was still present. Vertebral angiography revealed well-defined vascularization of the lesion at C6 (Figure 2-A,B). Testing indicated that the erythrocytosis had resolved. Abdominal ultrasonography and CT

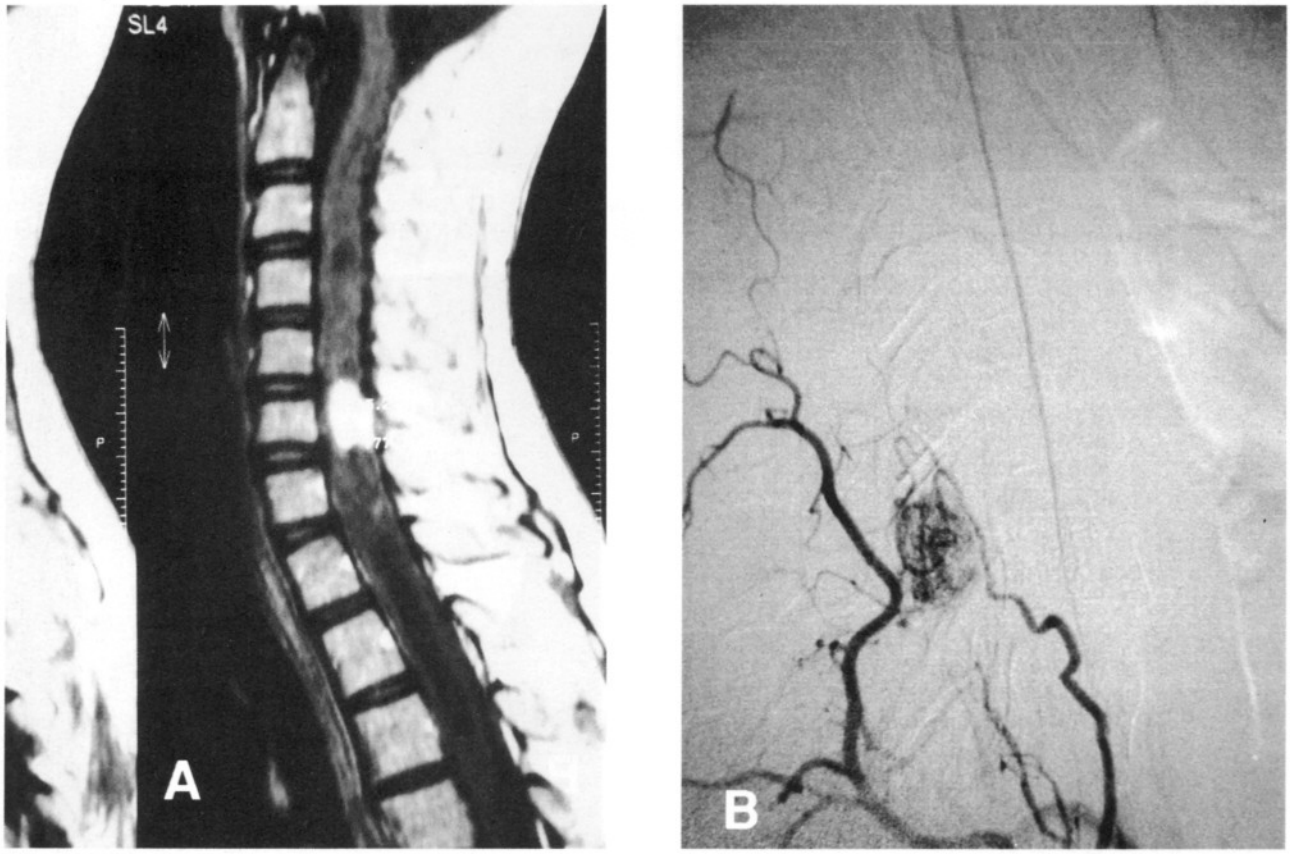


Figure 2: Preoperative radiologic findings pertaining to the cervical tumor: A gadolinium-enhanced T1-weighted MR image (midsagittal plane) (A) and spinal cord angiography (lateral view) (B) demonstrate an intensely enhanced lesion at the level of C6. The tumor was fed by the thyrocervical trunk.

revealed a clinically silent cyst in the pancreas and cysts in both kidneys (Figure 3-A,B). We detected no hemangiomas of the retinal capillaries on a second detailed fundoscopic examination.

A second surgery was needed to address the lesion in the cervical spinal cord. For this procedure, a C6 laminectomy was performed with the patient in the sitting position. The incision in the dura at this level exposed a tumor on the dorsal surface of the cord, and we were able to totally excise the mass. In the immediate postoperative period, the patient complained of radiating pain, motor weakness and dysesthesia in his right leg. Initially, we suspected an entrapment neuropathy brought on by the length of time he was in the sitting position during surgery. Physical examination revealed a painful swelling in his right posterior thigh and hypoalgesia in the right L5 and S1 dermatomes. His motor power on plantar flexion was scored as 4 on the manual muscle test. CT revealed a solid and well-circumscribed tumor on the right sciatic nerve, with surrounding hyperdense areas that were thought to represent focal hemorrhage. Contrast injection caused enhancement at the tumor periphery (Figure 4-A,B).

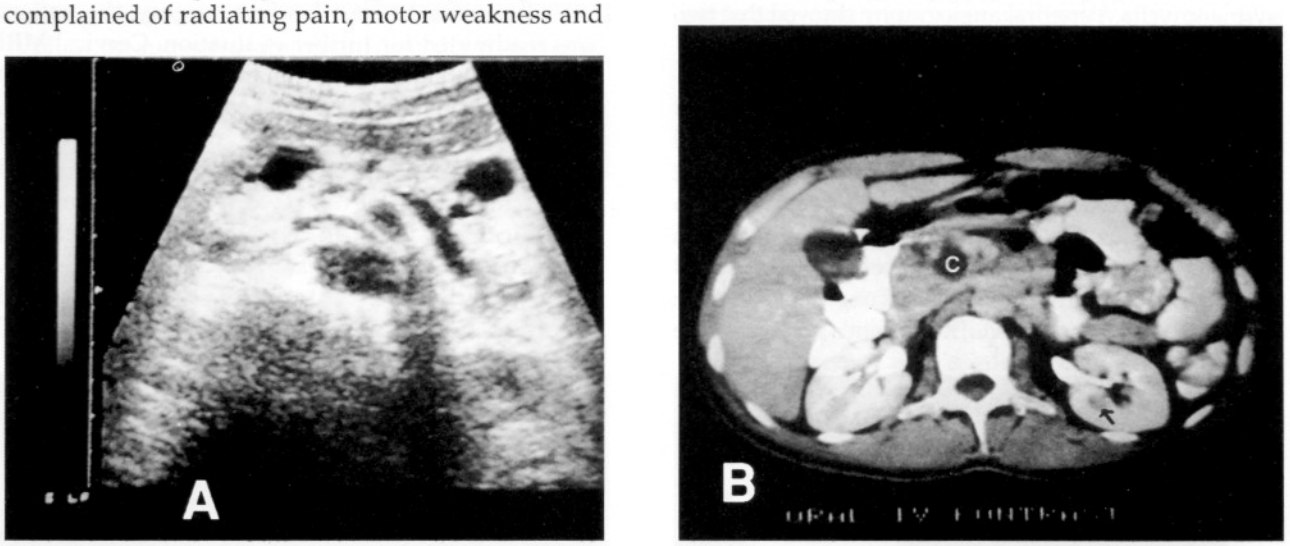


Figure 3: A) Abdominal ultrasonography reveals a cyst in the pancreas. B) CT scans of the abdomen demonstrate cysts in the pancreas (c) and the left kidney (arrow). The cysts did not enhance with either intravenous or oral contrast.

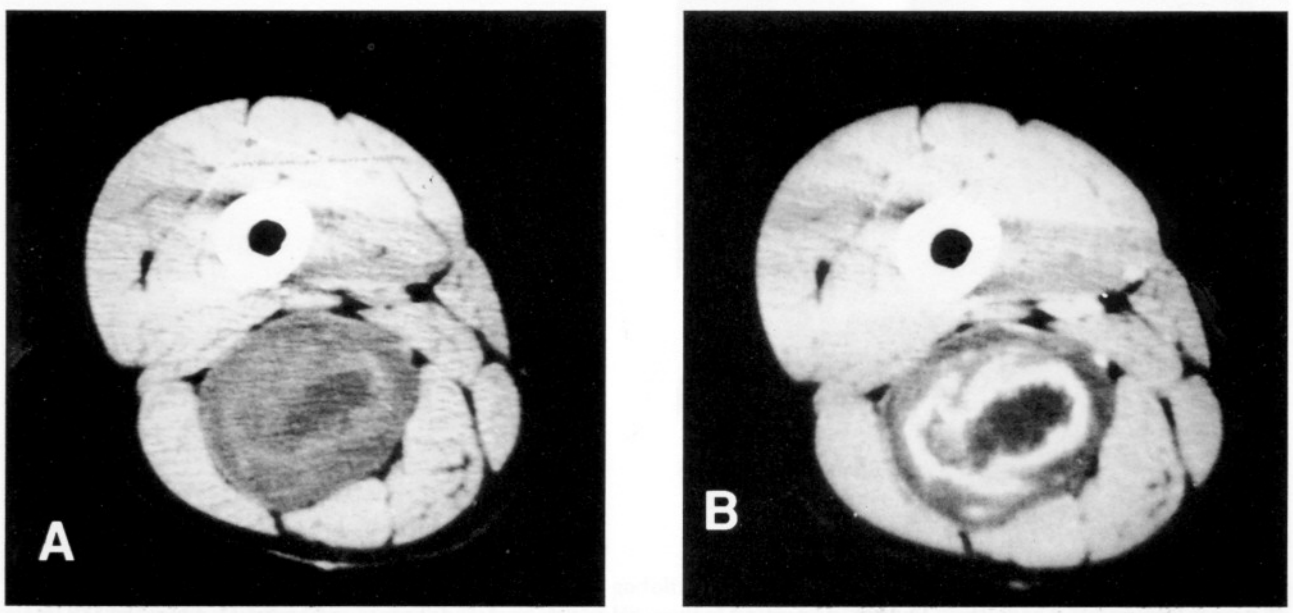


Figure 4: A CT scan (axial view) of the right thigh without (A) and with contrast (B). Intravenous injection of contrast material caused enhancement at the periphery of the tumor.

The patient's third surgery revealed a well-demarcated, encapsulated, solid mass. We separated the tumor capsule from the surrounding nerve fascicles, and then severed the fascicles running into the tumor immediately proximal and distal to the mass to achieve total excision. In the early postoperative period, the patient's pain was relieved but his muscle weakness and hypoalgesia persisted.

Grossly, the excised tissue was an encapsulated tan-yellow mass. Histological examination confirmed it was a schwannoma (Figure 5), a neoplasm that is distinguished from other nerve sheath tumors by its composition of Schwann cells only. There were no perineural cells or fibroblasts, nor were there nerve fibers running through the tumor. The Schwann cells were arranged in alternating hypercellular palisading regions (Antoni A) and hypocellular loosely meshed regions (Antoni B).

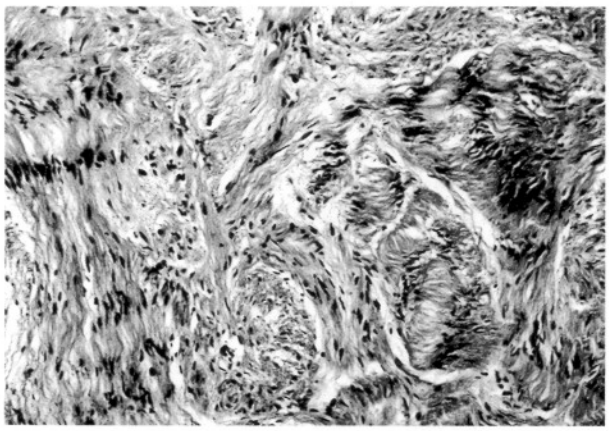

Figure 5: The light microscopic appearance of the schwannoma shows hypercellular palisading regions (Antoni A). There are narrow elongated bipolar cells with small amounts of cytoplasm (hematoxylin and eosin x 200).

## DISCUSSION

Hemangioblastomas typically arise either sporadically or as a component of VHLS (28). The retinal and cerebellar forms are the most common. Patients with cerebellar hemangioblastomas tend to develop symptoms in the third through fifth decade of life (7,20,21,25). Sporadic cases of hemangioblastoma tend to be seen in patients who are in their forties, whereas VHLS cases generally present earlier. In familial VHLS, the mean age at onset of symptoms is 30 years, the range being 3 to 83 years (1,22). Our patient was 21 years old.

One interesting feature of hemangioblastoma is that it is the only central nervous system tumor known to be associated with erythrocytosis (15,16,22,28). This is thought to occur through secretion of erythropoietin or an erythropoietin-like substance by the neoplastic tissue. Ultrastructural studies of some hemangioblastomas have identified distinctive granules that are considered to represent intracellular erythropoietin (5,7,16,24). It has also been demonstrated that the systemic effects of this type of activity disappear after tumor excision (15,26). Erythrocytosis has been reported in 9 and 50 cases of posterior fossa and supratentorial hemangioblastoma, respectively, but has never been observed in association with purely spinal lesions (22). Prior to his first operation, our patient exhibited erythrocytosis in the absence of splenomegaly or any elevation in his white cell or platelet counts. Testing done before the second operation showed that the patient's erythrocytosis had resolved, even though his other lesions had not been treated. We deduced that the erythrocytosis in this case was likely caused by the mature hemangioblastomas that were removed from the posterior fossa.

The development of multiple small hemangioblastomas in the cerebellar hemispheres and cervical spinal cord in patients with VHLS can pose problems regarding treatment. Some of these lesions may represent recurrence, whereas others are immature tumors. Although hemangioblastomas are considered benign, they recur in up to 25% of cases, and recurrence is more common in familial disease (8). Several factors are known to be correlated with tumor recurrence, including younger age (less than 30 years at time of diagnosis), VHLS, and multicentric hemangioblastoma of the central nervous system at presentation (1,8). Patients who undergo repeated surgeries often have adhesions that present difficulty for the surgeon. At the initial operation, since it is known that the hemangioblastoma recurrence rate is very high, and particularly in multicentric cases, it is best to prepare the patient for the likelihood of subsequent reexploration and to ensure that the surgical site is approached with this in mind. Reexploration is extremely difficult in cases where adhesions have formed due to inadequate dural closure in a previous procedure. In both operations, we used Gore-Tex surgical membrane as opposed to autogenous material because Gore-Tex tends to remain inert, and has proven beneficial in terms of preventing adhesions (6,27). We believe that use of this synthetic material should always be considered in patients with immature and/or multifocal

hemangioblastomas, with a view to preventing neural tissue adhesions at the site of repair.

Hemangioblastomas account for 1.5% to 2.5% of all spinal cord neoplasms, and an estimated 60% of these tumors are intramedullary (4,18,19,22). They tend to arise in the cervical or thoracic region, and more than half are accompanied by syringomyelia (4,22). The development of syringomyelia in these cases is considered similar to the development of a cyst□within a cerebellar hemangioblastoma. In our case, the patient's cervical tumor was extramedullary, and was situated in the dorsal half of the spinal cord. Initially, the patient's large syrinx extended superiorly from the tumor to the medulla without communicating with the fourth ventricle, and extended inferiorly to the end of the thoracic segment of the spinal cord. Prior to the second operation, we noted that the extent of the syrinx superior to the tumor had markedly diminished, but that the size of the lower section remained unchanged. In these cases, syringomyelia occurs as a result of transudation from capillaries, but we also believe that obstruction of the central canal probably plays an important role, especially in patients with extramedullary tumors.

Patients with VHLS invariably have multicentric hemangioblastoma (2,28). Although a wide variety of lesions have been described in this syndrome, the vast majority of tumors occur in the retina and the posterior fossa. The literature also documents many visceral lesions associated with VHLS, including renal cell carcinoma (13,19) pheochromocytoma (12), adrenal hemangioblastoma (5), pancreatic carcinoma (10), epididymal tumor (9) and cysts in the pancreas, kidney (2,13) and liver (23). Hemangioblastoma associated with primary hyperparathyroidism, and optic nerve hemangioblastoma have also been observed (11,14). This type of tumor very rarely affects peripheral nerves (3).

To date, there are no reports in the literature of VHLS associated with peripheral nerve sheath tumors. We believe that our finding of a sciatic nerve schwannoma in this patient was incidental, and that this neoplasm was distinct and not a component of VHLS. However, this case highlights the fact that clinically silent peripheral nerve sheath tumors do arise as a separate clinical manifestation in patients with VHLS. Already more than 30 lesions characteristic of this condition have been described. We wish to emphasize that the neurosurgeon should be alert to the possibility of a link with peripheral nerve sheath tumors, as future discoveries of this nature may expand the broad spectrum of lesions associated with VHLS.

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