# Progressive Spinal and Cerebellar Multifocal Hemangioblastoma in Von Lindau Disease: Case Report and Literature Review

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## Abstract

Although cerebellar hemangioblastoma is histologically benign, it can exhibit malignant clinical behavior during long-term follow-up. This report presents the case of a 51-year-old male with von Hippel-Lindau (VHL) disease, characterized by multifocal hemangioblastomas in the spine and cerebellum, as well as multiple cystic lesions in the kidneys and pancreas. The patient underwent nine surgeries for recurrent cerebellar hemangioblastomas and received cranial radiotherapy for multiple intracranial masses. Additionally, he was diagnosed with and treated for renal cell carcinoma arising from a renal cyst. This case highlights the potential for cerebellar hemangioblastoma recurrence and malignant progression of associated lesions in VHL disease, even after complete resection.

**Keywords:** Multifocal hemangioblastoma; Von Hippel-Lindau; Multiple cystic; Renal cell carcinoma; Malignant.

## Introduction

Cerebellar hemangioblastoma is a highly vascular benign tumor, accounting for approximately 3% of all intracranial tumors[1]. Around 16-69% of cerebellar hemangioblastomas are associated with von Hippel-Lindau (VHL) disease, a dominantly inherited condition with over 90% penetrance[2]. VHL leads to multiple lesions in the central nervous system, eyes, kidneys, pancreas, and other organs. Despite complete resection of cerebellar hemangioblastomas, de novo lesions may develop in VHL patients after many years[3]. We report the case of a VHL patient with multifocal hemangioblastomas in the spine and cerebellum, who underwent over nine surgeries and radiotherapy for recurrent tumors, along with the development of renal cell carcinoma from initial lesions.

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## Case Report

A 51-year-old male was admitted with a 3-month history of lower limb pain and weakness. His family history revealed that his father and sister had died from von Hippel-Lindau (VHL) disease. The patient was diagnosed with cerebellar hemangioblastoma and renal cysts 19 years ago and had undergone nine surgeries to remove cerebellar hemangioblastomas, as well as radiosurgery to treat intracranial masses. After his last surgery 12 years ago, he began experiencing difficulty in speaking and walking. Clinical examination, imaging, and subsequent biopsy revealed retinal hemangioblastoma, renal cell carcinoma, and multiple pancreatic cysts. These lesions were managed medically and closely monitored. Four years ago, the patient developed worsening headaches, dizziness, and nausea. A CT scan revealed a large hypointense mass at the site of one of the initial tumors. A brain MRI showed an abnormal signal-enhancing mass in the left cerebellar hemisphere, at the site of a previously resected hemangioblastoma (Figure 1). Multiple tumors displayed heterogeneous signal enhancement and abnormal shapes. The patient was urgently admitted, and a VP shunt surgery was performed, which alleviated his headaches.

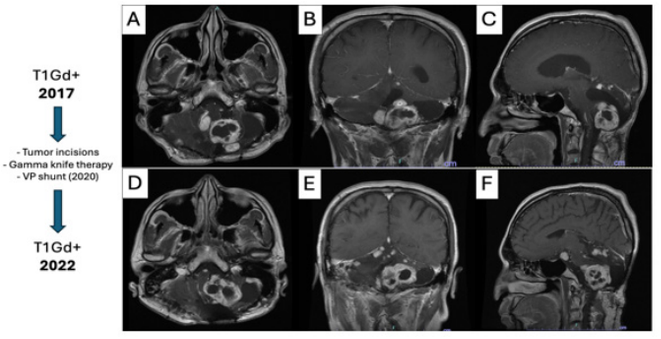


*Figure 1. Brain MRI with contrast injections from 2017 (A, B, C) to 2022 (D, E, F):*

The patient was diagnosed with cerebellar hemangioblastoma in 1992 and subsequently underwent nine tumor resection surgeries combined with intracranial gamma knife therapy. Due to the uncontrolled progression of the tumor, a VP shunt was placed in 2020 to alleviate acute symptoms. Brain MRI images with gadolinium contrast on axial (A, D), coronal (B, E), and sagittal planes (C, F) show a progression in the number and size of the tumors over time. The cerebellar mass is seen occupying nearly the entire cerebellum and exerting pressure on the brainstem.

This time, the patient was admitted due to weakness in both lower limbs. Neurological examination revealed difficulty in speaking and walking, with an ataxic gait, pain in the left anterior thigh, and muscle strength rated IP3.3, QF3.2, TA4.2, EHL2.0, FHL4.3. Babinski test was negative. Spinal MRI revealed an intramedullary tumor at L3-4, measuring 37 mm, with dilation of surrounding spinal veins (Figure 2). The tumor had a homogeneous signal on T1-weighted images and increased signal on T2-weighted images, with hypointense areas inside. Additionally, multiple other tumors were detected at L2-3. Brain MRI with contrast showed signal-enhancing lesions in the cerebellum, including a cyst occupying the left cerebellar hemisphere, and multiple other lesions. Abdominal MRI revealed multiple renal tumors that had not significantly changed in size compared to seven years earlier, as well as multiple pancreatic cysts (Figure 2).

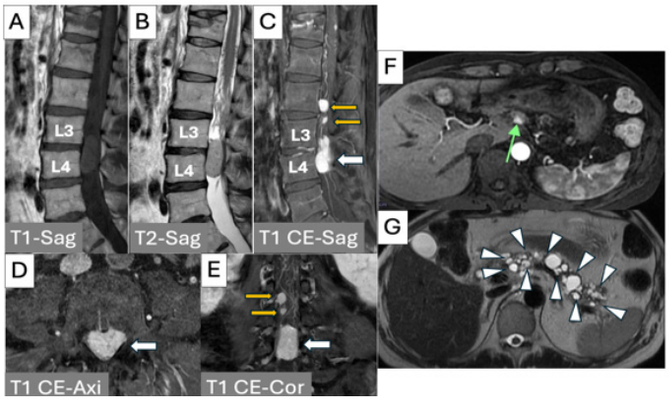


*Figure 2. MRI of the Spine (A, B, C, D, E) and Abdomen (F, G):*

Figure 2. MRI of the Spine (A, B, C, D, E) and Abdomen (F, G): Sagittal T1-weighted MRI (A) and T2-weighted MRI (B) show an intramedullary tumor at the L3-4 vertebrae level, measuring 37 mm, with surrounding spinal vein dilation. Enhanced contrast MRI after gadolinium injection reveals the tumor's extent (C) and additional masses at the L2-3 level (D, E). Abdominal MRI demonstrates a contrast-enhancing nodule (blue arrow) approximately 8 mm in size in the pancreatic body, consistent with a neuroendocrine tumor (F). Numerous cysts are observed in the head and tail of the pancreas (white arrowheads) (G).

The patient was diagnosed with lumbar spinal hemangioblastoma and underwent tumor resection surgery. A posterior laminectomy from L2 to L5 was performed, and intraoperative fluoroscopy confirmed the tumor's location (Figure 3). The tumor was completely resected, and hemostasis was achieved. The dura mater was closed, and intraoperative neurophysiological monitoring (MEP, SSEP) showed no abnormalities.

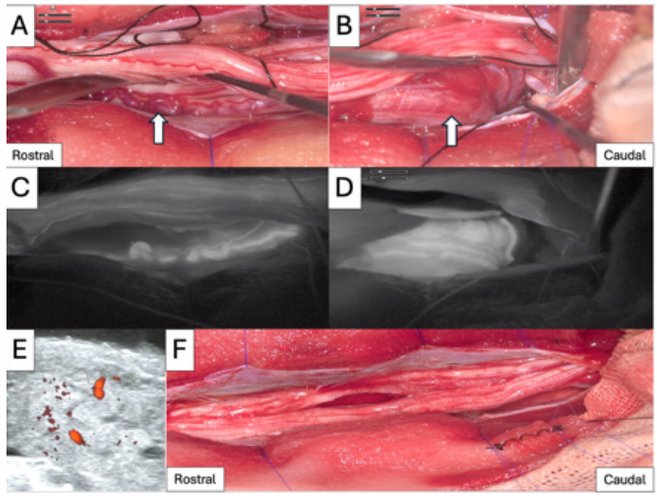


*Figure 3. Intraoperative Imaging of Hemangioblastoma in the L3-4 Level (A-F):*

Intraoperative fluoroscopy images confirm the precise location of the hemangioblastoma (white arrows) during surgery (A, B). Additional fluoroscopic (C, D) and vascular ultrasound imaging (E) further delineate the tumor's position. The hemangioblastoma is shown to be completely resected (F).

Histopathological examination confirmed hemangioblastoma (Figure 4). For the multiple intracranial lesions, the patient continued whole-brain radiotherapy. The multiple abdominal cystic lesions (in the kidneys and pancreas) were closely monitored through periodic radiological evaluations.

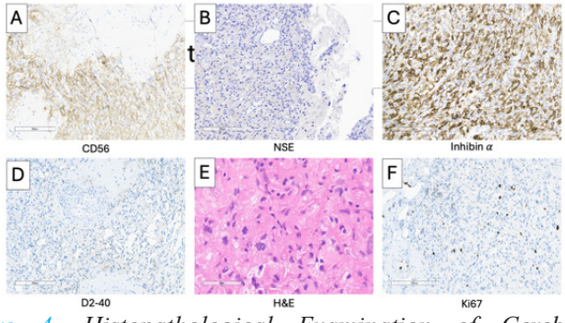


*Figure 4. Histopathological Examination of Cerebellar Hemangioblastoma (A-E):*

Figure 4. Histopathological Examination of Cerebellar Hemangioblastoma (A-E):

Pathological images demonstrate cerebellar hemangioblastoma staining positive for CD56 (A), NSE (B), inhibin α (C), and D2-40 (D). Hematoxylin and eosin (H&E) staining (E) shows typical hemangioblastoma histology. The Ki67 index is noted to be above 5%, indicating the proliferative activity of the tumor (F).

## Discussion

Hemangioblastomas account for approximately 2% of intracranial neoplasms and 2–10% of primary spinal cord neoplasms[1,4]. Although histologically benign[2,3], they often exhibit unpredictable growth and progression, especially in patients with von Hippel-Lindau (VHL) disease. VHL is an autosomal dominant disorder caused by mutations in the VHL gene on chromosome 3p [2, 5]. This disease is associated with the development of multiple tumors in the central nervous system and abdominal organs, including the kidneys, adrenal glands, and pancreas.

Hemangioblastomas may occur sporadically but are often associated with VHL. Approximately 72% of VHL patients have at least one cerebellar hemangioblastoma, and over 40% of these patients will develop spinal hemangioblastomas [6]. Cerebellar hemangioblastomas occur in 60-80% of VHL cases, while spinal hemangioblastomas are linked to VHL in 40-59% of cases [7].

Regarding the natural history of VHL, a study by Wanebo et al. [8] showed that hemangioblastomas associated with VHL have two growth phases: a rapid growth phase followed by a quiescent phase. After the rapid growth phase, tumors may enter a prolonged quiescent stage, sometimes lasting more than two and a half years. However, even after complete surgical resection, tumors may continue to recur, as seen in this patient, where cerebellar hemangioblastomas continued to grow and recur after years of follow-up.Despite advances in microsurgical and radiosurgical techniques, treating recurrent hemangioblastomas, especially those with extensive involvement of the brain and spinal cord, remains a significant challenge. The optimal management for hemangioblastomas is still complete surgical resection, but for cases with extensive lesions, treatment decisions become more complex.

Koh et al. [9] reported that whole-brain radiotherapy could achieve good tumor control rates for patients with intracranial or spinal hemangioblastomas after incomplete tumor resection. In this case, the patient also underwent whole-brain radiotherapy after primary tumor resection, but unfortunately, the tumors continued to recur and became challenging to control.

Regarding renal involvement, this case highlights the progression of small renal cysts into renal cell carcinoma, a natural course of VHL disease [3]. Long-term follow-up over 12 years showed that VHL patients tend to experience severe progression and recurrence, necessitating long-term monitoring and treatment planning.

From this clinical case, we draw two important lessons: (1) Continuous and close follow-up is necessary to detect the recurrence of primary tumors after a patient has been diagnosed and treated for cerebellar hemangioblastoma associated with VHL; (2) The frequency and duration of follow-up should be carefully considered when detecting cystic lesions in abdominal organs, as these lesions, though seemingly benign, may progress to malignancy after a long period.

## Conclusion

The progression and recurrence of central nervous system hemangioblastomas associated with VHL disease can occur even after treating primary lesions. Surgery is the treatment of choice for most hemangioblastomas. However, there is currently no definitive cure for this condition. Managing VHL patients requires screening for lesions in potential sites, lifelong close monitoring of central nervous system hemangioblastomas and other VHL-related lesions, and coordinated care across specialties to provide optimal treatment plans for each patient.

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