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Case Report

Dual manifestations: spinal and cerebellar hemangioblastomas indicative of von Hippel-Lindau syndrome ☆

Nurhuda Hendra Setyawan, MD, M.Sc[a,*], *Rachmat Andi Hartanto, MD*[b], *Rusdy Ghazali Malueka, MD, Ph.D*[c], *Ery Kus Dwianingsih, MD, Ph.D*[d], *Dito Pondra Dharma, MD*[a]

[a] *Department of Radiology, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada/Dr Sardjito General Hospital, Yogyakarta, Indonesia*
[b] *Department of Surgery, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada/Dr Sardjito General Hospital, Yogyakarta, Indonesia*
[c] *Department of Neurology, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada/Dr Sardjito General Hospital, Yogyakarta, Indonesia*
[d] *Department of Pathological Anatomy, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada/Dr Sardjito General Hospital, Yogyakarta, Indonesia*

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ABSTRACT

Hemangioblastomas are rare, benign, and highly vascular tumors of the central nervous system, often associated with von Hippel-Lindau (VHL) syndrome, an autosomal dominant disorder characterized by multiple tumors. We present a case of a 32-year-old male with progressive headaches, visual disturbances, and motor deficits, who was diagnosed with multiple hemangioblastomas in the cervical-thoracic spinal cord and bilateral cerebellum through MRI. Surgical resection and histopathological biopsy confirmed the diagnosis. This case highlights the critical role of MRI in diagnosing and managing VHL-associated hemangioblastomas and underscores the importance of regular imaging for early detection and intervention of new or recurring tumors, optimizing patient outcomes.

Abbreviations: BCR, Bulbocavernosus Reflex; CN, Cranial Nerve; CNS, Central Nervous System; DAP, Deep Anal Pressure; GCS, Glasgow Coma Scale; HIF, Hypoxia-Inducible Factor; MRI, Magnetic Resonance Imaging; NLP, No Light Perception; SRS, Stereotactic Radiosurgery; VAC, Voluntary Anal Contraction; VHL, von Hippel-Lindau.

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* Corresponding author.
E-mail address: nurhuda.hendra.s@ugm.ac.id (N.H. Setyawan).

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Introduction

Hemangioblastomas are relatively uncommon benign, highly vascular tumors, constituting about 2% of all brain tumors and 2%-10% of all spinal cord tumors. The incidence of central nervous system (CNS) hemangioblastomas is estimated to be less than 1 per 1,000,000 individuals per year, with a slight male predominance (1.5-2 times more frequent in men). These tumors are most commonly diagnosed in adults between the third and fifth decades of life, but they can occur at any age, including childhood in cases associated with von Hippel-Lindau (VHL) syndrome [1]. von Hippel-Lindau syndrome is an autosomal dominant disorder characterized by the development of multiple benign and malignant tumors in various organs, including the retina, kidneys, adrenal glands, and pancreas. The presence of both spinal and cerebellar hemangioblastomas in a single patient strongly suggests the possibility of VHL syndrome. The majority of hemangioblastomas arise sporadically, but approximately 25% of cases are associated with VHL syndrome. Patients with VHL typically develop their first tumors by the age of 30, with CNS hemangioblastomas being one of the earliest manifestations. In VHL patients, retinal hemangioblastomas are also common and can present in childhood [2].

Diagnosing hemangioblastomas involves a combination of clinical evaluation, imaging studies, and genetic testing, particularly in patients with suspected VHL syndrome. Imaging studies are crucial for the accurate diagnosis and localization of hemangioblastomas. Magnetic resonance imaging (MRI) is the preferred modality due to its superior soft-tissue contrast and ability to delineate the tumor and associated cystic components. Hemangioblastomas typically appear as well-circumscribed, contrast-enhancing lesions on MRI, often with a prominent cystic component and a solid, vascular nodule [3,4].

Given the complexity and variability in presentation, the presence of both spinal and cerebellar hemangioblastomas in a single patient presents a unique diagnostic challenge. Such dual manifestations are not only indicative of the underlying genetic syndrome but also underscore the necessity for a comprehensive diagnostic approach. This case report details a patient with both spinal and cerebellar hemangioblastomas, providing insight into the diagnostic process and highlighting the importance of considering von Hippel-Lindau syndrome in similar clinical scenarios.

Case report

A 32-year-old male presented to a tertiary referral hospital with complaints of headaches and difficulty swallowing. The patient reported that approximately 9 months prior, he began experiencing mild to moderate intensity headaches. These initial symptoms were accompanied by progressively blurred vision. Six months before admission, the patient noted worsening headaches in intensity, accompanied by the onset of weakness in the right extremities, leading to difficulty walking. At that time, the patient sought consultation at the outpatient neurology and ophthalmology clinics.

Approximately 5 months before hospitalization, the patient could only perceive light (presence of light). Two months before admission, the patient experienced persistent headaches, during which he completely lost his vision. One day before admission, the patient reported difficulty swallowing, increasing generalized weakness, and a loss of appetite. The patient also began exhibiting rambling speech when attempting to communicate and complained of severe headaches. The patient did not report a history of seizures, vomiting, or loss of consciousness. However, weakness in the extremities and visual disturbances persisted. The patient also noted an inability to lift or move his shoulders.

Upon admission to the hospital, the patient's physical examination revealed the following findings. The head examination showed pupils measuring 3 mm in the left eye and 5 mm in the right eye, with no direct or indirect light reflex observed in either eye. The visual acuity in both eyes was no light perception (NLP). Cranial nerve examination revealed bilateral impairment of the optic nerve (CN II), impairment of the left oculomotor nerve (CN III), and impairments of the glossopharyngeal (CN IX), vagus (CN X), accessory (CN XI), and hypoglossal (CN XII) nerves. There was no nuchal rigidity noted in the neck. Chest and abdominal examination revealed no abnomalities.

The neurological examination revealed significant asymmetries in motor strength and a lack of sensory evaluation. In the upper extremities, motor strength was graded at 3 out of 5 on the right side across the C5 to T1 dermatomes, whereas the left side exhibited a stronger motor response with a grade of 4 out of 5 in the same regions. Similarly, in the lower extremities, motor strength was assessed at 3 out of 5 on the right side from L1 to S1, compared to 4 out of 5 on the left side. Sensory examination for both pin prick and light touch sensations in the C2 to S2 dermatomes was unable to be evaluated on either side. Reflex testing showed the absence of clonus. Deep anal pressure (DAP), bulbocavernosus reflex (BCR), and voluntary anal contraction (VAC) were all positive, indicating intact sacral reflexes. Physiological reflexes were normal, graded at +3 in all extremities. Pathological reflexes were positive in all 4 extremities, suggesting the presence of abnormal reflex activity.

The patient underwent a cervicothoracic MRI with intravenous Gadolinium contrast (Fig. 1). The examination revealed multiple intramedullary pathological lesions extending from the foramen magnum to the upper thoracic segments. These lesions predominantly comprised cystic components with some eccentric nodular solid areas. Postcontrast images showed vivid enhancement of these nodular areas, indicating their highly vascular nature. Several focal hypointense areas on T2-weighted imaging suggested focal flow voids, which are indicative of hemangioblastomas. The surrounding spinal cord appeared enlarged with extensive syrinx formation.

The spinal MRI also vaguely suggested the presence of an intracranial mass in the posterior fossa, leading to a subsequent MRI of the brain with intravenous Gadolinium contrast (Fig. 2). This examination revealed multiple intra-axial lesions in both the right and left cerebellar hemispheres. The

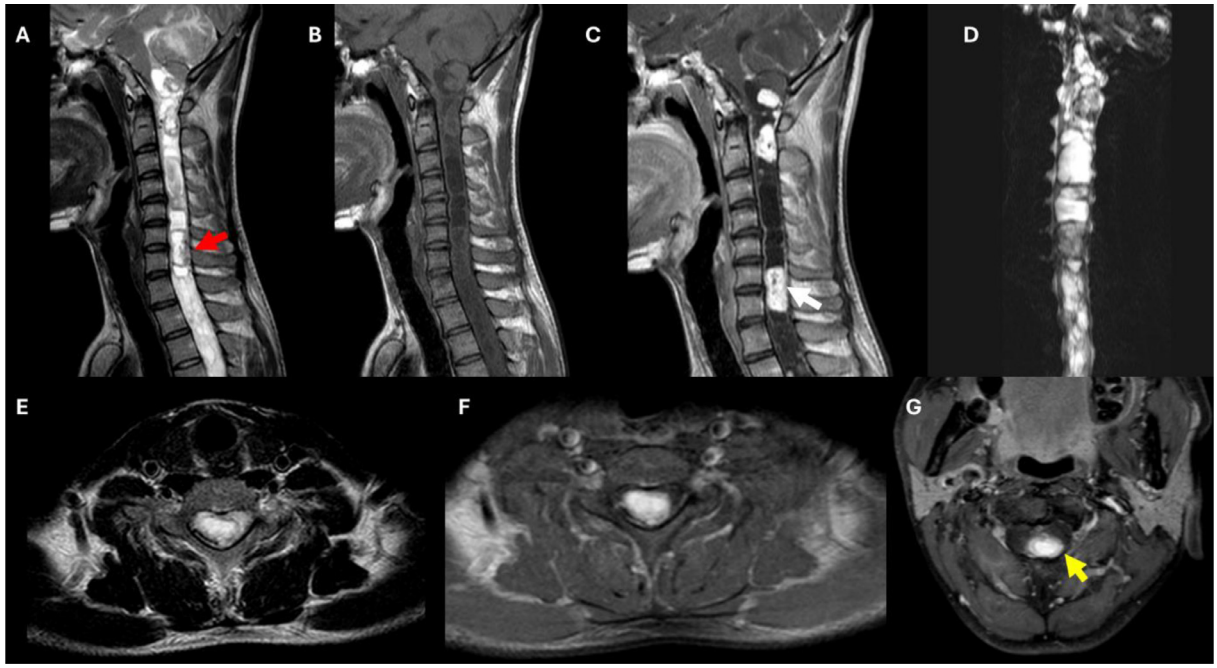

Fig. 1 – MRI of the cervical and thoracic spine demonstrating multiple spinal lesions highly suggestive of hemangioblastomas. (A) Sagittal T2-weighted image highlighting the hyperintense cystic component of the suspected lesion. The surrounding spinal cord appears enlarged, resembling a syrinx. The red arrow indicates the focal flow void within the lesion. (B) Sagittal T1-weighted image showing a well-circumscribed, intramedullary lesion extending from the C2 level to the upper thoracic segment. (C) Sagittal postcontrast T1-weighted image illustrating the vivid enhancement of the nodular component of the suspected spinal lesions (white arrow). (D) Coronal STIR (short tau inversion recovery) myelogram showing multiple hyperintense lesions throughout the cervical and upper thoracic spine, consistent with lesions that enlarge the spinal cord. (E) Axial T2-weighted image at the C6-C7 level demonstrating the hyperintense intramedullary cystic component. (F) Axial postcontrast T1-weighted image at the C6-C7 level showing the nodular vivid enhancement of the suspected lesion. (G) Axial postcontrast T1-weighted image at the C2-C3 level showing the eccentric enhancement pattern typically seen in hemangioblastomas (yellow arrow).

largest lesion, located in the left cerebellar hemisphere, exhibited a predominantly solid component, with a rounded shape, well-defined borders, and intense enhancement postcontrast administration. Additionally, multiple serpentine flow-voids were observed around the lesion, indicating vascular enlargement. The lesion caused perifocal edema, narrowing the fourth ventricle and leading to obstructive hydrocephalus. A similar lesion was also noted in the right cerebellar hemisphere. The morphology of these lesions and their enhancement patterns, similar to the spinal MRI findings, suggest that these lesions are part of the same disease entity, likely multiple hemangioblastomas.

The patient subsequently underwent a suboccipital craniotomy for tumor removal (Fig. 3). The patient was positioned prone, and a craniotomy was performed in the occipital region. Upon exposure, the cerebellar cortex was visualized, and a transvermian corticotomy was planned to access the tumor for biopsy. A corticotomy was made approximately 1 cm from the cerebellar cortex, revealing a well-encapsulated, highly vascular tumor that bled easily. Circumferential devascularization of the tumor was attempted, but complete resection was not feasible due to its firm adhesion to the tentorial surface, which resulted in significant hemorrhage. Consequently, a biopsy was taken, and hemostasis was achieved postbiopsy.

The tissue removed during the suboccipital craniotomy was sent to the anatomical pathology department. Examination revealed a benign vascular tumor with a well-demarcated lobular architecture. The tumor consisted of numerous thin-walled vessels, as shown in Fig. 4, which is consistent with the diagnosis of hemangioblastoma.

Discussion

Hemangioblastomas are strongly associated with von Hippel-Lindau syndrome, an autosomal dominant disorder caused by mutations in the VHL tumor suppressor gene located on chromosome 3p25-26. The pathogenesis of hemangioblastomas in VHL syndrome involves the loss of function of the VHL protein, which plays a critical role in cellular processes such as oxygen sensing, angiogenesis, and tumor suppression. Loss of VHL function leads to increased activity of hypoxia-inducible factors (HIFs), which promote the expression of genes involved in angiogenesis, contributing to the development of highly vascular tumors like hemangioblastomas [5].

VHL syndrome predisposes individuals to the development of multiple benign and malignant tumors, including heman-

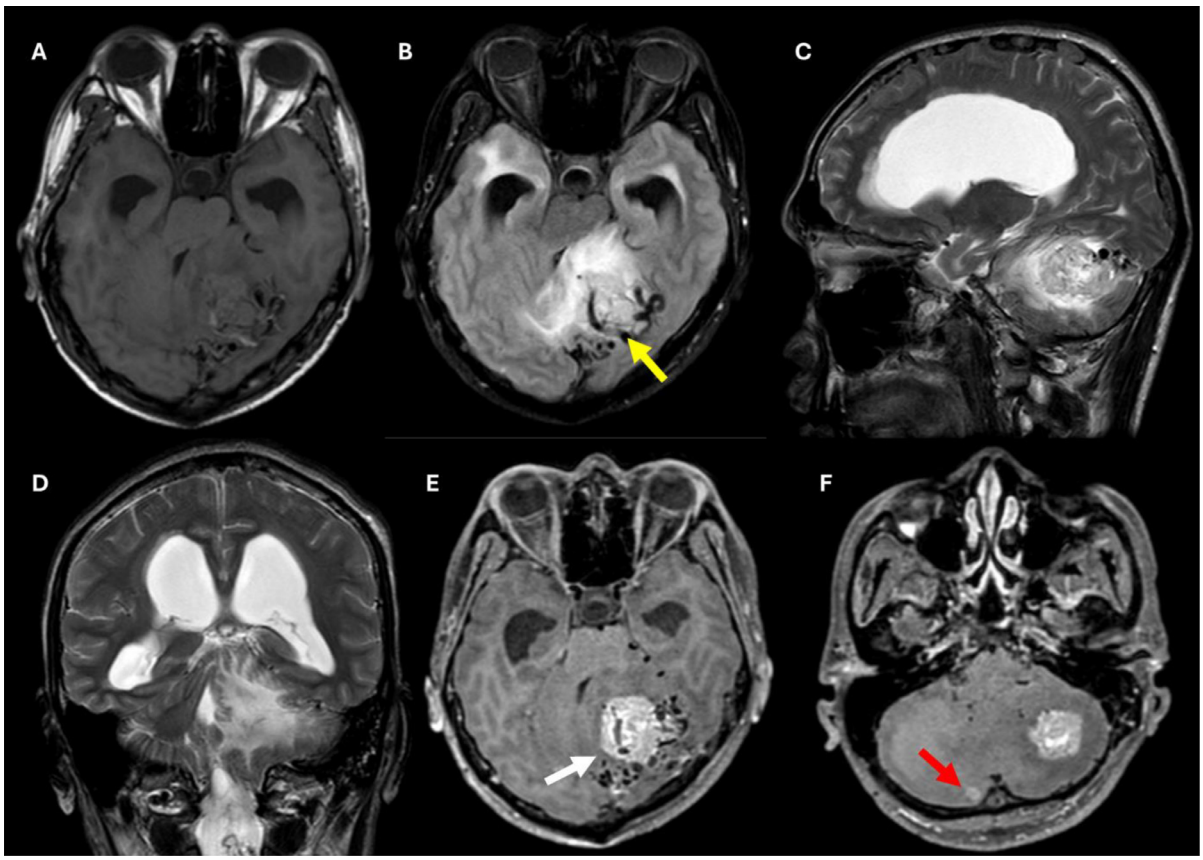

Fig. 2 – MRI of the brain demonstrating multiple cerebellar lesions highly suggestive of hemangioblastomas. (A) Axial T1-weighted image showing an intra-axial hypointense lesion in the left cerebellar hemisphere. (B) Axial T2-FLAIR image highlighting the hyperintense components of the cerebellar lesion with enlarged vessels appearing as flow voids (yellow arrow), and surrounding edema. (C) Sagittal T2-weighted image showing the location and extent of the lesion in the cerebellum, which is compressing the fourth ventricle. (D) Coronal T2-weighted image revealing hydrocephalus with periventricular edema, secondary to the mass effect from the cerebellar lesions. (E) Axial T1-weighted postcontrast image showing vivid enhancement of a large lesion in the left cerebellum (white arrow), indicating its highly vascular nature. (F) Axial T1-weighted postcontrast image at a lower level than (E), showing a smaller enhancing lesion in the right cerebellar hemisphere (red arrow).

gioblastomas, renal cell carcinoma, pheochromocytomas, and pancreatic cysts. The occurrence of hemangioblastomas in patients with VHL syndrome is significant. Approximately 25% of hemangioblastomas are associated with VHL syndrome, and up to 60% of individuals with VHL syndrome will develop hemangioblastomas during their lifetime [6]. These tumors can manifest in various parts of the central nervous system, including the cerebellum, spinal cord, and brainstem, with cerebellar hemangioblastomas being the most common. In patients with VHL, hemangioblastomas are often multiple and can present at an earlier age compared to sporadic cases [3].

Imaging plays a crucial role in the diagnosis, characterization, surgical planning, and postsurgical monitoring of hemangioblastomas. These highly vascular tumors, which can occur sporadically or as part of von Hippel-Lindau syndrome, require precise imaging to guide clinical decision-making and management strategies. MRI is the preferred modality for the diagnosis of hemangioblastomas due to its superior soft-tissue contrast, which allows for detailed visualization of both the solid and cystic components of these tumors. Hemangioblastomas typically appear as well-circumscribed, contrast-enhancing lesions with a prominent cystic component and a solid, vascular nodule [7]. The use of T1-weighted postcontrast images is particularly valuable in highlighting the vivid enhancement of the nodular components, indicative of the tumor's high vascularity. T2-weighted and FLAIR sequences can further delineate cystic areas and surrounding edema, providing a comprehensive view of the tumor's impact on adjacent structures. The presence of flow voids on MRI, indicative of high vascularity, is a distinguishing feature of hemangioblastomas [8].

High-resolution MRI provides a detailed map of the tumor's size, location, and relationship with critical neurovascular structures. This information is vital for planning the surgical approach, determining the extent of resection, and minimizing risks to surrounding healthy tissue. Preoperative angiography may also be performed to assess the tumor's blood supply and to plan for potential presurgical emboliza-

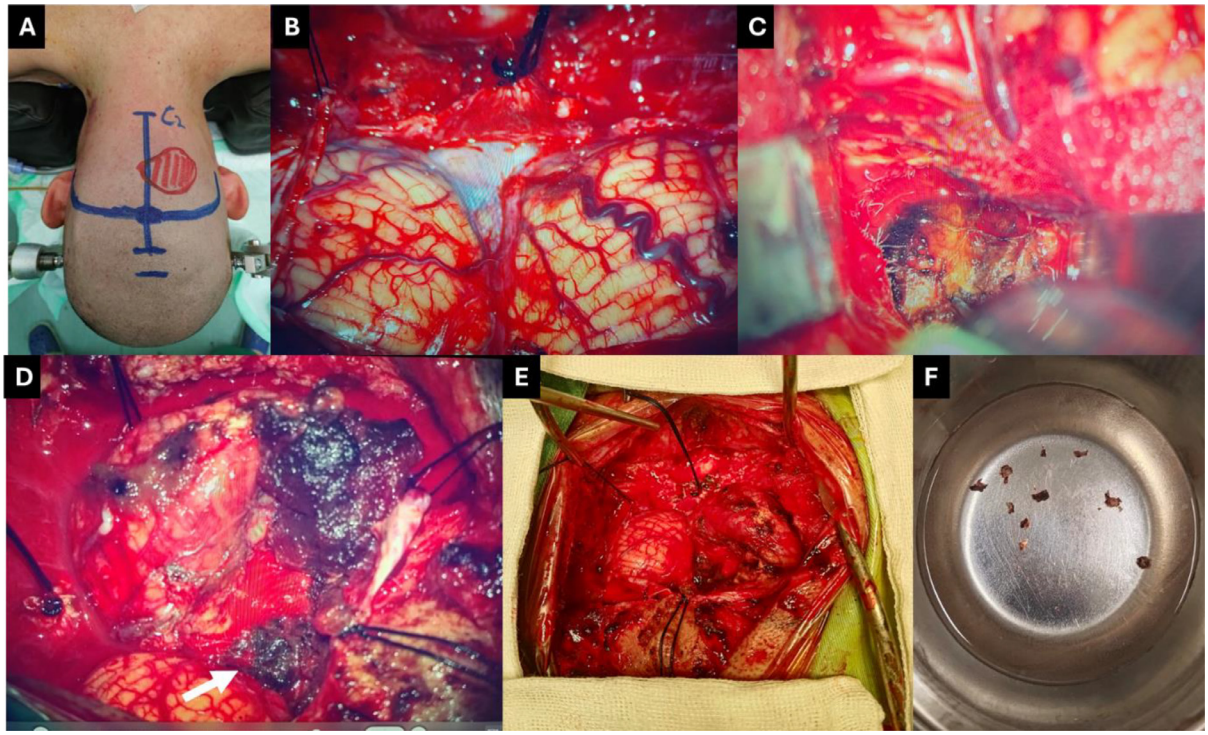

Fig. 3 – Intraoperative images of the suboccipital craniotomy for tumor removal. (A) The patient positioned in the prone position, with markings indicating the planned surgical site. (B) Postdurotomy, revealing the underlying structures. (C) Visualization of the cerebellar cortex following dual opening. (D) Post-transvermian corticotomy, white arrow shows the hypervascular, encapsulated tumor at a depth of 1 cm. (E) Surgical field post-tumor biopsy and hemostasis control. (F) Tumor samples obtained postbiopsy.

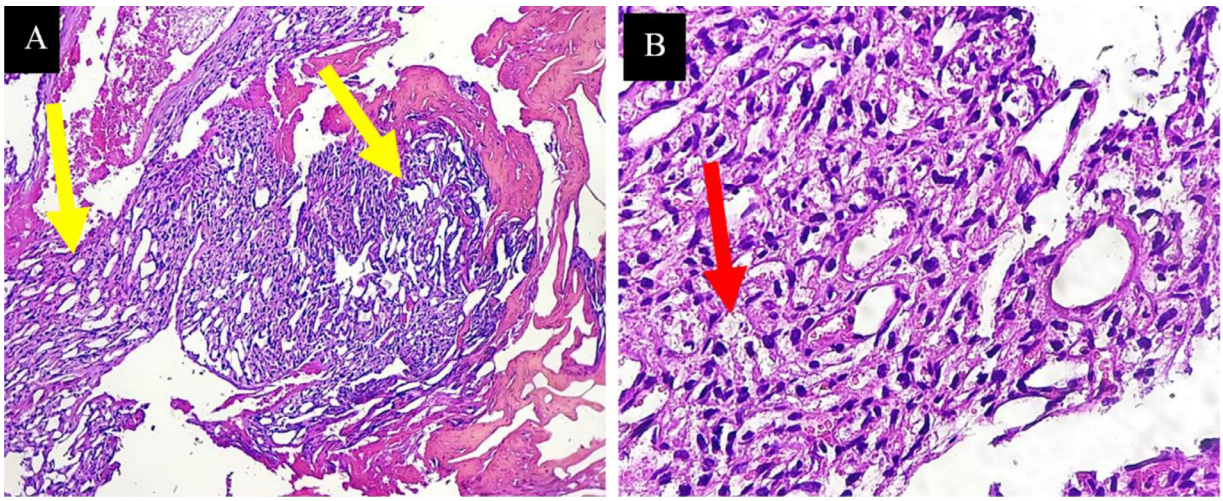

Fig. 4 – Morphological features of hemangioblastoma using hematoxylin-eosin staining are depicted. (A) The hemangioblastoma demonstrates noninfiltrative growth with variable lobularity. Yellow arrows show neoplastic stromal cells arranged amidst numerous small vessels and shows evidence of red blood cell leakage. (B) The stromal component exhibits mild nuclear pleomorphism, degenerative atypia, clear foamy cytoplasm with lipid-filled vacuoles, and a few hyaline globules (red arrow).

tion, which can reduce intraoperative blood loss. Intraoperative MRI and neuronavigation systems, which use preoperative imaging data, enhance surgical precision and safety [4].

The management of multiple hemangioblastomas in VHL syndrome involves a multidisciplinary approach, including surgical resection, stereotactic radiosurgery (SRS), and pharmacotherapy with agents like belzutifan. Surgical resection is typically used for symptomatic tumors, while SRS is effective for small to medium-sized lesions not suitable for surgery [1]. Belzutifan, a HIF-2α inhibitor, has shown promise in reducing tumor size and perilesional edema [9]. Postsurgical imaging is critical for evaluating the success of tumor resection and for monitoring potential recurrence. MRI is the modality of choice for postoperative evaluation due to its ability to detect residual tumor tissue, postoperative changes, and early signs of recurrence. Contrast-enhanced MRI can distinguish between postsurgical scar tissue and residual or recurrent tumor based on enhancement patterns [10]. Regular follow-up imaging is necessary, especially in patients with VHL syndrome, to monitor for new tumor development in other CNS locations or in other organs affected by the syndrome.

Hemangioblastomas, especially within the central nervous system, can present diagnostic challenges due to their imaging similarities with other neoplastic lesions, such as metastases, pilocytic astrocytomas, medulloblastoma, and ependymoma. Metastatic lesions often exhibit a “ring-enhancing” pattern and are more likely to be multiple and located at the gray-white matter junction, unlike the typical posterior fossa location of hemangioblastomas. Metastases may also show a higher likelihood of being associated with significant surrounding edema [11]. Pilocytic astrocytomas are more common in a younger demographic and often exhibit a less vascular appearance compared to hemangioblastomas. The absence of flow voids, which are indicative of high vascularity, helps distinguish pilocytic astrocytomas from hemangioblastomas [12]. Medulloblastomas are typically located in the midline cerebellar vermis, whereas hemangioblastomas are more often found in the cerebellar hemispheres. Medulloblastomas are more common in children, while hemangioblastomas are frequently diagnosed in adults. The presence of significant peritumoral edema and restricted diffusion is more characteristic of medulloblastomas [13,14]. Ependymomas commonly extend from the fourth ventricle into adjacent cisterns, which can help differentiate them from hemangioblastomas. Additionally, ependymomas can exhibit calcifications and hemorrhage, which are less common in hemangioblastomas [14,15].

Our patient presented with multiple hemangioblastomas in the cervical to thoracic spinal cord and intracranial lesions in the bilateral cerebellum. While the spinal hemangioblastomas were consistent with literature, featuring cystic components and vividly enhancing mural nodules, the cerebellar hemangioblastomas in this patient were atypical, lacking prominent cystic areas. Hemangioblastomas typically present as predominantly cystic lesions with an enhancing mural nodule. However, in the early stages, some hemangioblastomas can appear as solid lesions. Over time, these solid lesions often develop a cystic component surrounding the solid nodule. Several studies and reviews support this observation. For example, hemangioblastomas are often described as cystic lesions with an avidly enhancing mural nodule in approximately 75% of cases. Purely solid enhancing lesions are less common, accounting for about 10% of cases, and lesions with multiple cystic areas make up about 15% [3]. The development of the cystic component is believed to result from fluid leakage from the dilated vasculature within the hemangioblastoma. This hypothesis is supported by imaging findings that often show flow voids, indicative of high vascularity, around the lesion. These flow voids are thought to contribute to the leakage of fluid, leading to the formation of the cystic component [8].

Conclusions

In this case report, the comprehensive use of radiological techniques was crucial in diagnosing and managing multiple hemangioblastomas in a patient with von Hippel-Lindau syndrome. MRI, the preferred imaging modality due to its superior soft-tissue contrast, effectively identified the well-circumscribed, contrast-enhancing lesions characteristic of hemangioblastomas. The presence of flow voids, indicative of high vascularity, and the delineation of cystic and solid components were key radiological findings that guided the clinical diagnosis and surgical planning. This case underscores the pivotal role of radiological imaging in the diagnosis, treatment planning, and long-term follow-up of hemangioblastomas, highlighting its value in optimizing patient outcomes through precise and detailed visualization of tumor characteristics. Regular imaging follow-ups remain imperative in managing this chronic condition, enabling early detection and intervention for new or recurring tumors.

Patient consent

Written informed consent for the publication of this report was obtained from the patient.

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