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Imaging Manifestations of Von Hippel Lindau Disease

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Abstract

Introduction and importance: Von Hippel-Lindau (VHL) disease is a rare genetic condition inherited in an autosomal dominant manner. It was first described independently by Von Hippel in 1911 and Lindau in 1926. The disease affects approximately 1 in every 36,000 live births. VHL is known for causing both benign and malignant tumors, along with cysts in various organs. Early and accurate diagnosis is crucial for effective prognosis and management.

Case presentation: In this study, we present a case of a 48-year-old man diagnosed with VHL disease, characterized by multiple lesions in the central nervous system (CNS), retina, and renal cortex. He underwent surgical treatment and showed significant improvement, with notable alleviation of his signs and symptoms observed at a 3-month follow-up.

Discussion: VHL disease involves the development of both benign and malignant tumors, as well as cysts in several organs. It is inherited in an autosomal dominant manner with nearly complete penetrance across generations. Surgical intervention is typically used to manage CNS lesions. Regular follow-up appointments are essential for monitoring the condition.

Conclusions : VHL disease is highly complex, requiring diagnosis and genetic testing for both patients and their family members. Close monitoring of carriers of the mutated gene is essential to achieve early diagnosis and effective treatment of malignancies. The significant expenses associated with diagnostic tests and surgical treatments pose a substantial challenge. Therefore, government support and financial assistance are crucial aspects to address in managing this condition.

Keywords: Case report, Von Hippel-Lindau disease, Hemangioblastoma, MRI, Resection, CNS

Introduction

Von Hippel-Lindau (VHL) disease is a rare genetic condition inherited in an autosomal dominant manner [1]. Von Hippel first described it in 1911 [2], and Lindau independently in 1926 [3]. The prevalence of VHL is estimated to be approximately 1 in every 36,000 live births [4]. The disease is associated with mutations in both alleles of the VHL gene located on chromosome 3p [5]. It is characterized by the development of various

benign and malignant tumors, as well as cysts in multiple organs. Common manifestations include retinal and central nervous system hemangioblastomas, clear cell renal cell carcinomas (RCC), pheochromocytomas, pancreatic neuroendocrine tumors, and endolymphatic sac tumors (ELSTs) [6]. VHL significantly impacts patients and their families due to its diverse symptoms and increased healthcare needs.

Here, we present a case study of a 48-year-old man diagnosed with VHL disease, who presented with multiple CNS lesions, retinal lesions, and renal cortical cysts. He underwent surgical treatment, and this case report follows the SCARE guidelines [7].

Case description

A 48-year-old man presented to the Emergency Department with complaints of abnormal gait, visual disturbances, ascites, bilateral pedal edema, and weakness in both lower limbs. He had a Glasgow Coma Scale score of 15/15 and was fully oriented. Neurological examination revealed reduced power (4/5) in all limbs and decreased tone in the lower limbs. Laboratory tests showed polycythemia. There was no significant family or personal history of genetic diseases, chronic conditions, or substance abuse. Differential diagnoses such as stroke, cerebellar dysfunction, and substance abuse were ruled out. The rest of his physical examination was unremarkable.

MRI scans of the brain and spine revealed a cerebellar hemangioblastoma (Figure 1) and cervical spinal hemangioblastomas at the C3/C4 levels (Figure 2), respectively. Fundoscopy detected a left retinal angioma. Contrast-enhanced MRI of the abdomen identified a malignant lesion in segment VII of the liver (Figure 3) and bilateral renal cortical cysts (Figure 4). A liver biopsy confirmed capillary liver hemangioblastoma. Genetic testing was not performed due to its unavailability.

Based on these clinical and radiological findings, a diagnosis of Von Hippel-Lindau (VHL) disease was established. The patient underwent midline suboccipital craniectomy for resection of the brain hemangioblastoma via a transfollial approach. Embolization was performed for the spinal hemangioblastoma. The liver mass was surgically resected in two stages. Regular follow-up was planned for the retinal angioma and renal cortical cysts. Laser photocoagulation would be considered if the retinal lesion showed progression.

At a 3-month follow-up in the outpatient setting, the patient showed significant improvement with marked alleviation of his signs and symptoms.

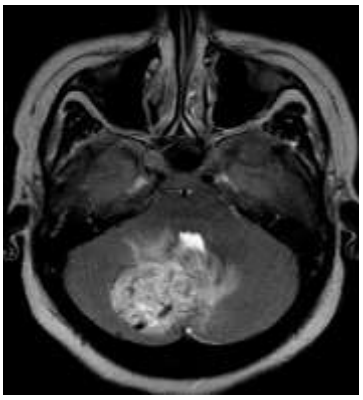

Fig 1: Axial T2W MRI shows a well-defined hyperintense mass with flow signal void is demonstrated in the right cerebellar hemisphere. The mass is isointense with flow voids and linear hyperintense signal of blood components. The mass shows dense contrast enhancement. The fourth ventricle was displaced anteriorly with signs of obstructive hydrocephalus.

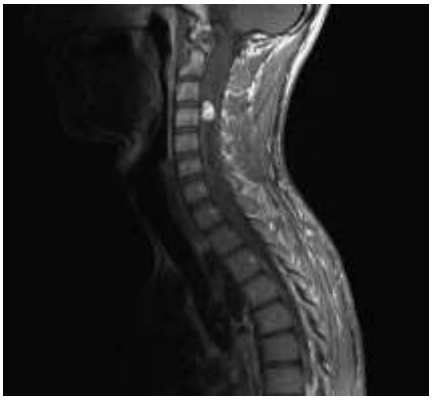

Fig 2: MRI spine reveals an enhancing intramedullary lesion in the cervical spine associated with syringomyelia.

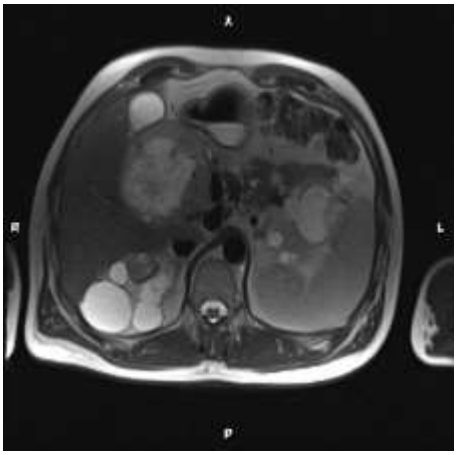

Fig 3: A high T2W mass in segment VII of the liver also shows early peripheral nodular enhancement with centripetal extension suspected for hemangioma

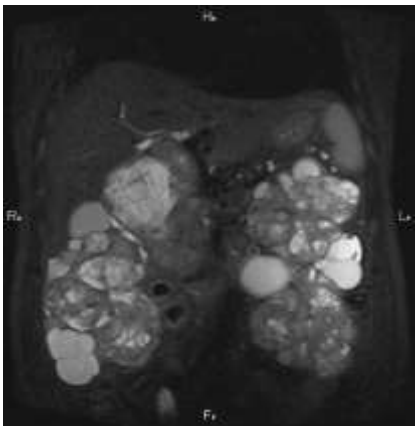

Fig: 4 Coronal T2W MRI shows both kidneys are enlarged and contain multiple varying p-sized cystic lesions. Some cysts show thick irregular enhancing walls or eccentric enhancing solid components

Discussion

VHL disease is characterized by the development of various benign and malignant tumors, as well as cysts in multiple organs, and is inherited in an autosomal dominant pattern with nearly complete penetrance. Current clinical diagnostic criteria encompass several manifestations including CNS hemangioblastomas (including retinal hemangioblastomas), endolymphatic sac tumors (ELST), renal cell carcinomas (RCC), pheochromocytomas, paragangliomas, and neuroendocrine neoplasms [8].

Diagnosis of VHL is confirmed when individuals exhibit specific symptoms in combination with genetic or family history factors:

- At least two CNS hemangioblastomas
- At least one CNS hemangioblastoma and another manifestation listed above
- At least one of the manifestations listed above, along with a pathogenic mutation in the VHL gene or a first-degree relative with VHL.

Recent advances in genetic testing, such as DNA sequencing and semi quantitative Southern blotting, can identify VHL mutations in nearly 100% of cases [9]. However, due to the lack of availability of genetic testing in our setting, it was not performed.

CNS hemangioblastomas are a predominant manifestation of VHL disease, affecting up to 72% of patients. These tumors commonly occur in the cerebellum (16–69%), brainstem (5–22%), spinal cord (13–53%), cauda equina (11%), or supratentorial region (1–7%) [10]. They often present in the second or third decade of life and, despite being benign, can cause significant morbidity and mortality due to their mass effect on CNS structures [8]. Contrast-enhanced magnetic resonance imaging is the gold standard for detecting and monitoring CNS hemangioblastomas [11].

Microsurgical resection is typically the preferred treatment, and in most cases, these tumors can be safely and completely removed [12]. Preoperative embolization to reduce intraoperative bleeding is occasionally performed but carries additional risks [13]. In our patient's case, both cerebellar and spinal hemangioblastomas were managed with midline suboccipital craniectomy and spinal hemangioblastoma embolization.

Retinal hemangioblastomas are also common in VHL patients, occurring in approximately 49%–62% of cases [8]. Treatment options include laser photocoagulation and cryotherapy. Our patient's small retinal angioma is currently under regular surveillance, with plans for laser photocoagulation if it shows signs of enlargement.

Renal cell carcinomas (RCC) or renal cysts are rarely the initial symptoms of VHL, occurring less than 7% of the time. Large RCCs may present with typical symptoms of renal masses such as flank pain, hematuria, or a palpable mass. Simple renal cysts are usually asymptomatic, but complex cysts can develop into solid RCC tumors. Despite the presence of multiple renal cysts, renal function can often be preserved in VHL patients [8]. In our case, the renal cortical cysts were simple in nature, requiring no surgical intervention and instead necessitating regular monitoring.

Prenatal and preimplantation genetic testing should be offered for pregnancies at risk of Von Hippel-Lindau (VHL) disease (where either parent has a known VHL illness or mutation) [14]. Referral to a genetic counselor is recommended to ensure accurate interpretation of test results. Regular monitoring and early detection are crucial in minimizing the impact of VHL symptoms. Factors such as tobacco use and exposure to environmental pollutants can increase the risk of kidney cancer. Individuals with adrenal or pancreatic lesions should avoid contact sports [15].

Conclusions

VHL disease is highly complex, necessitating diagnosis and genetic testing for both patients and their families, as well as close monitoring of gene carriers to facilitate early detection and effective treatment of malignancies. The considerable costs associated with diagnostic procedures and surgical therapies pose significant challenges. Management of individuals with VHL syndrome should involve specialized care provided by trained professionals at genetic facilities, with additional psychological support from psychologists and involvement in familial support groups being essential. Government support and financial assistance are crucial factors to consider in addressing the needs of these patients.

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