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A RARE CASE OF VON HIPPEL LINDAU SYNDROME PRESENTING AS HYPERTENSIVE URGENCY.

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Abstract

Von Hippel-Lindau (VHL) syndrome is a rare, autosomal dominant hereditary disorder characterized by the development of multiple benign and malignant tumours across various organ systems, including the central nervous system, retina, adrenal glands, kidneys, and pancreas. Early diagnosis is often challenging due to its variable presentation and age-dependent penetrance. We present a case of a 21-year-old male who presented with hypertensive urgency, along with a history of childhood retinal surgery and a positive family history suggestive of a hereditary syndrome. Laboratory investigations revealed elevated plasma and urinary metanephrines, and subsequent imaging using contrast-enhanced CT and DOTANOC PET-CT scans identified somatostatin receptor-expressing lesions in the right adrenal gland, pancreatic head, and prevertebral region. The patient underwent successful right adrenalectomy following preoperative alpha-blockade, with significant clinical improvement. Based on the clinical, biochemical, radiological findings, and family history, a diagnosis of VHL syndrome was established. This case highlights the importance of considering VHL syndrome in young patients presenting with secondary hypertension and syndromic features. Timely recognition, genetic evaluation, and surveillance are crucial in reducing morbidity associated with this multisystem disorder.

Keywords: Von Hippel-Lindau syndrome, Pheochromocytoma, Secondary hypertension, Pancreatic neuroendocrine tumour, DOTANOC PET-CT, Adrenalectomy, Hereditary cancer syndrome

INTRODUCTION

Von Hippel-Lindau (VHL) disease is a rare, autosomal dominant hereditary cancer syndrome with an estimated incidence of 1 in 36,000 live births and a penetrance of over 90% by the age of 65 years (Maher et al., 1990). The condition results from a germline mutation in the VHL tumour suppressor gene located on chromosome 3p25-26. The VHL gene plays a critical role in regulating hypoxia-inducible factors, and its loss of function leads to abnormal angiogenesis and tumour development (Kaelin, 2002). VHL disease is characterized by a predisposition to develop a wide spectrum of benign and malignant neoplasms, including retinal hemangioblastomas, central nervous system hemangioblastomas (commonly in the cerebellum, spinal cord, and brainstem), renal cell carcinomas (clear cell type), pancreatic neuroendocrine tumours, endolymphatic sac tumours, pheochromocytomas, and cystadenomas of the epididymis or broad ligament (Lonser et al., 2003).

Clinical manifestations vary depending on the specific organ involvement and can occur at different stages in life, often making diagnosis challenging, especially in the absence of a known family history. Pheochromocytomas, although less common than renal or CNS lesions, are significant due to their potential to cause life-threatening cardiovascular complications. In VHL patients, pheochromocytomas are typically bilateral and may present in adolescence or early adulthood with symptoms such as hypertension, headache, palpitations, and diaphoresis (Walther et al., 1999). Given the multisystem nature of the disease, a multidisciplinary approach is essential in both diagnosis and management.

Early identification and surveillance protocols have shown to significantly reduce morbidity and mortality associated with VHL by allowing timely interventions. Genetic testing and family screening play a crucial role in early detection, especially in asymptomatic carriers. This case illustrates a rare presentation of VHL syndrome in a young adult who presented with hypertensive urgency secondary to pheochromocytoma, emphasizing the importance of considering genetic tumour syndromes in young patients with suggestive clinical features.

Case Presentation

Patient information

A 21-year-old male presented to the emergency department with complaints of persistent headache and intermittent abdominal pain for the past three months. There was no associated vomiting, visual disturbance, or convulsions. However, the patient reported episodes of palpitations and excessive sweating during this period. On clinical examination, he was found to have a significantly elevated blood pressure of 190/110 mmHg, indicating hypertensive urgency.

Past Medical History

The patient had a notable ophthalmological history, having undergone retinal detachment surgery in childhood. Medical records revealed that this surgery was performed in 2006 for a diagnosed case of retinoblastoma. There was no known previous history of hypertension, diabetes, or cardiovascular disease. Family history was positive for similar retinal and abdominal disorders, though detailed pedigree analysis was pending at the time of presentation.

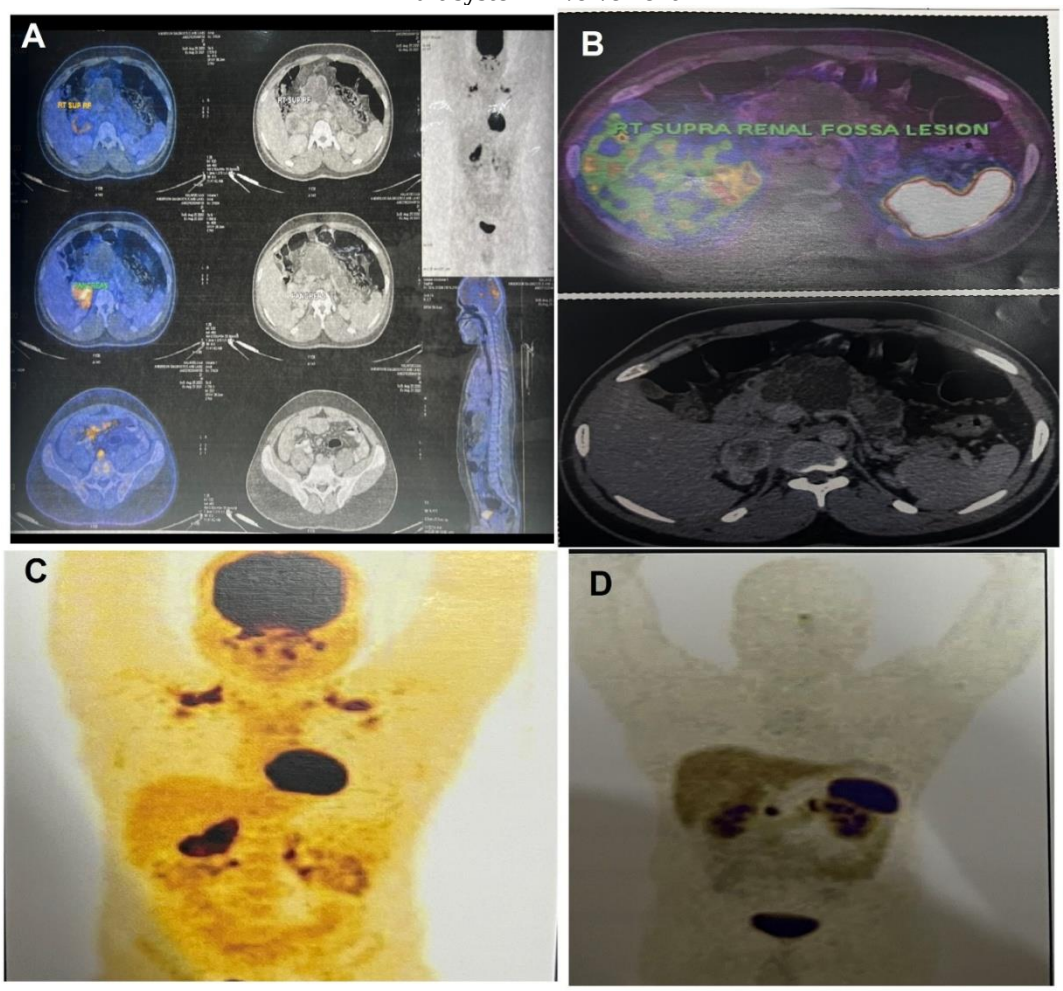
Initial Workup

In view of his young age and the sudden onset of severe hypertension, the patient was evaluated for secondary causes of hypertension. Initial biochemical investigations showed significantly elevated plasma free metanephrines (180 pg/mL) and urinary fractionated metanephrines (2100 mcg/24 hours), pointing toward a catecholamine-secreting tumour, most likely pheochromocytoma.

Radiological Evaluation

Imaging studies were conducted to localize the source of catecholamine secretion. A contrast-enhanced CT scan of the abdomen revealed a mass in the right adrenal gland. Further whole-body evaluation with DOTANOC PET-CT showed somatostatin receptor (SSTR)–expressing lesions in multiple sites: the pancreatic head/uncinate process, the right suprarenal fossa, and the prevertebral region at L5-S1 level. These findings were suggestive of multifocal lesions commonly associated with a syndromic condition.

Figure 1: Functional and Structural Imaging Findings in Von Hippel-Lindau Syndrome: Evidence of Multisystem Involvement



Surgical Management

Following adequate preoperative preparation with alpha-blockade to prevent intraoperative hypertensive crises, the patient underwent right adrenalectomy. The surgery was uneventful, and the patient remained hemodynamically stable in the postoperative period. His symptoms of headache and abdominal discomfort significantly improved following surgery.

Diagnosis and Follow-up

Given the presence of pheochromocytoma, pancreatic and prevertebral lesions, a prior history of retinal tumour, and a positive family background, the diagnosis of Von Hippel-Lindau (VHL) syndrome was considered and confirmed. The patient was advised regular follow-up with surveillance imaging and clinical screening for other possible VHL-associated lesions.

DISCUSSION

Von Hippel-Lindau (VHL) syndrome is a rare but clinically significant hereditary tumour syndrome that predisposes individuals to develop multiple neoplasms involving the central nervous system, retina, kidneys, adrenal glands, pancreas, and reproductive organs. This case of a young adult male presenting with hypertensive urgency led to the discovery of a right adrenal pheochromocytoma and other visceral lesions, ultimately confirming a diagnosis of VHL syndrome. His prior history of retinal surgery for presumed retinoblastoma and a positive family history further supported the syndromic nature of the presentation.

Pheochromocytomas are catecholamine-producing tumours that are well-recognized manifestations of VHL syndrome, though they occur in only 10–20% of affected individuals, usually at a younger age than sporadic

cases. Unlike sporadic pheochromocytomas, those in VHL are often bilateral and may be asymptomatic, necessitating active surveillance in known cases and family members (Neumann et al., 1993). In our case, the patient's symptoms of headache and abdominal pain were attributed to excessive catecholamine release, and biochemical evaluation confirmed elevated plasma and urinary metanephrines.

This clinical profile aligns with other published reports. A retrospective study by Walther et al. (1999) analysed VHL-associated pheochromocytomas and highlighted their tendency to present early and bilaterally, often detected incidentally or during screening of at-risk individuals. Furthermore, imaging in our case revealed somatostatin receptor–positive lesions in the pancreas and retroperitoneum, suggestive of neuroendocrine tumours, another hallmark of VHL. In line with findings from Maher et al. (1990), pancreatic involvement in VHL can range from benign cysts to neuroendocrine tumours with metastatic potential, making timely imaging crucial for prognosis.

The diagnostic criteria for VHL, originally outlined by Melmon and Rosen (1964), emphasize the presence of at least one hemangioblastoma or visceral tumour in patients with a positive family history, or multiple such lesions in the absence of one. Our patient satisfied these criteria, presenting with both retinal and adrenal involvement, as well as suggestive family history. Genetic confirmation is the gold standard for diagnosis; however, clinical criteria remain vital, especially in resource-limited settings.

Early identification of VHL is critical because of the progressive and multisystemic nature of the disease. Patients benefit from a multidisciplinary management strategy involving endocrinology, oncology, ophthalmology, and genetics. Guidelines suggest routine screening of at-risk individuals through annual plasma metanephrines, abdominal imaging, and ophthalmological exams starting in early childhood for known mutation carriers (Lonser et al., 2003).

CONCLUSION

The present case study emphasizes the importance of considering VHL syndrome in young patients with secondary hypertension and associated visceral or retinal findings. Delayed diagnosis can lead to avoidable complications, whereas timely intervention allows for curative or life-prolonging treatments. Surgical resection of pheochromocytoma, as performed in our patient, remains the primary treatment and usually results in resolution of hypertension and catecholamine-related symptoms.

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