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A RARE CASE OF VON HIPPEL-LINDAU DISEASE WITH MULTI-ORGAN TUMORS - ROLE OF RADIOLOGICAL IMAGING

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ABSTRACT

von Hippel-Lindau disease is an autosomal dominant inherited disease with a wide spectrum of manifestation which causes benign and malignant tumors in multiple systems. We present a case of von Hippel-Lindau disease (VHL) who initially presented with retinal hemangioblastomas, but after 10 years had tumors in multiple organs,and few benign conditions. This signifies the importance of annual screening for detection and monitoring of conditions which can lead to timely surgical intervention and improve morbidity and mortality for patients. Radiological imaging plays a crucial role in diagnosing, monitoring, and screening for various manifestations and along with newer surgical techniques have contributed to significant reduction in morbidity and mortality of VHL patients. It is important to have a multidisciplinary team approach in screening for VHL disease.

Introduction

We present a case of von Hippel-Lindau disease (VHL) who initially presented with gradual loss of vision in both eyes and was diagnosed with bilateral retinal hemangioblastomas and VHL. Then the patient remained asymptomatic for other conditions and was not undergoing annual screening. He then presented 10 years with neurological complaints of headache and dizziness but now had tumors in multiple organs and few benign conditions. von Hippel-Lindau disease is an inherited disease caused due to inactivation of a tumor suppression gene on chromosome

3p25.5. It has a wide spectrum of manifestation involving multiple organs. Pancreatic cysts, cerebellar hemangioblastoma, renal cysts, retinal hemangioblastoma, renal cell carcinoma, spinal cord hemangioblastoma, pheochromocytoma, and pancreatic neuroendocrine tumor are the most frequent symptoms. Diagnostic criteria is: a) > one CNS hemangioblastoma, b) one CNS hemangioblastoma and visceral manifestation of VHL disease, c) any manifestation and a known family history of VHL (1).

Case report

A 39-year-old male patient who was a known case of von Hippel-Lindau disease presented to our institution with complaints of headache and dizziness for 10 months. He had a past history of gradual loss of vision in both eyes 11 years ago when he was diagnosed to have retinal angiomas in both eyes with secondary retinal detachment and had undergone endolaser membrane peeling and silicon injection in 2012 at an outside institution. Gradually the vision loss progressed into total blindness. Patient had been diagnosed with VHL and had undergone MRI brain, MRI spine, and USG abdomen and pelvis for screening for other associated conditions but all the studies were normal. Now the patient underwent MRI brain and spine, plain and with gadolinium contrast enhancement. On MRI brain, bilateral cerebellum showed few well defined solid lesions appearing heterogeneously hyperintense on T2WI, showing multiple small hyperintense foci on T1WI and showed moderate post contrast enhancement (Figure 1a, 1b, 1c). They showed multiple hemorrhagic and calcific foci on SWI sequences, with hemorrhagic foci showing blooming on Magnitude and appearing bright on Phase images while Calcific foci showing blooming on Magnitude with signal drop on phase images (Figure 1d, 1e). Surrounding edema was seen. These lesions were causing mass effect on adjoining 4th ventricle and dorsal aspect of medulla with obstructive hydrocephalus in both lateral and third ventricles (Figure 1f). Subcentimeteric nodular enhancing lesions in bilateral cerebellar hemispheres (Figure 1g,h). These lesions were suggestive of multiple cerebellar hemangioblastomas. Multiple variable sized enhancing lesions (both peripheral and central) (Figure 1h) were noted in posterior segments of both eyeballs- likely to be retinal hemangioblastomas. MRI spine showed an intramedullary well defined solid- cystic lesion of size 18 x 5 mm is noted at the level of D4-D5. The solid lesion was hyperintense on T2 showing post contrast enhancement and the cystic component is isointense on T2WI (Figure 2a, 2c). Cord edema and cord widening was seen at D3 to D6 level. Small nodular enhancing lesions at level C5 and C6 level (Figure 2b, 2c, 2d). These lesions were suggestive of multiple spinal hemangioblastomas. Screening Ultrasonography (USG) of abdomen and pelvis was done which revealed a Bosniak IV complex cystic lesion in left kidney (Figure 3a) - possibility of renal cell carcinoma. Multiple anechoic simple cysts were seen in both kidneys. Screening USG scrotum revealed an epididymal cyst on the left side (Figure 3b). VP shunting was done for the patient for symptomatic relief. The patient showed signs of improvement and was discharged with advice for workup and treatment for other conditions. However the patient's condition worsened after a few months and the patient passed away following brief period loss of loss of consciousness, likely due to neurologic complications.

Discussion

von Hippel-Lindau disease is an autosomal dominant inherited disease with a wide spectrum of manifestation which causes benign and malignant tumors in multiple systems. The spectrum of clinical manifestations includes endolymphatic sac tumors, CNS and retinal hemangioblastomas,

pancreatic cysts and tumors, renal cysts and tumors, pheochromocytomas, and epididymal cystadenomas. Earliest and most common lesions in VHL disease are retinal hemangioblastomas. These are reported in about 50% of VHL patients with half being bilateral and are usually diagnosed after the age of 10 years. By the time these lesions are picked up on contrast MRI are significantly enhancing areas there is already profound vision loss and hence screening is done with direct and indirect ophthalmoscopy/ fluorescein angiography (2). CNS hemangioblastomas are another common manifestation and occur at typical sites which are cerebellum, spinal cord, and medulla (2,3,4). Presenting symptoms of cerebellar lesions include vertigo, headache, and ninth cranial nerve palsy, while spinal cord hemangioblastoma presents with focal spinal pain, however they may present late with hydrocephalus or spinal cord compression (4). Hemangioblastomas promptly enhance with contrast and can be solid, cystic, hemorrhagic, or mixed. Renal cysts and renal cell carcinoma (RCC) occur, with RCC being bilateral in 75% (2). Periodic screening is vital because they have poor prognosis and metastasizes widely if left untreated. Nephron sparing surgeries such as enucleation are done and may prevent metastasis (5)**.** Pancreatic presentation may include simple pancreatic cysts (50%–91%) (6), serous microcystic adenomas (12%) (6), and rarely adenocarcinomas. Bilateral Papillary cystadenomas of the epididymis are pathognomonic of VHL, as it is usually present unilaterally in general population. Common cause of death is renal cell carcinomas, and neurologic complications from cerebellar hemangioblastomas (7,8). Different imaging modalities like ultrasonography, magnetic resonance and imaging, and computed tomography, and nuclear medicine are used to demonstrate the various manifestations. Although there is availability of genetic testing, as the manifestations of the syndrome are protean, imaging is crucial to the detection of abnormalities and subsequent monitoring of lesions. As the lesions in VHL are treatable, regular screening is vital because early detection enables conservative therapy, which improves a patient's quality of life. Radiological imaging plays a crucial role in diagnosing, monitoring, and screening for various manifestations and along with newer surgical techniques have contributed to significant reduction in morbidity and mortality of VHL patients. It is important to have a multidisciplinary team approach in screening for VHL disease; the team has ophthalmologists, radiologists, neurologists, urologists, and gastroenterologists, and is led by a geneticist.

Conclusion

von Hippel-Lindau disease is a rare autosomal dominant inherited disease having a wide spectrum of manifestation which causes benign and malignant tumors in multiple systems. Regular screening and long-term surveillance are crucial because VHL lesions can be treated, and early diagnosis enables conservative treatment that improves a patient's quality of life. Radiological imaging plays a crucial role in diagnosing, monitoring, and screening for various manifestations and along with newer surgical techniques have contributed to significant reduction in morbidity and mortality of VHL patients.

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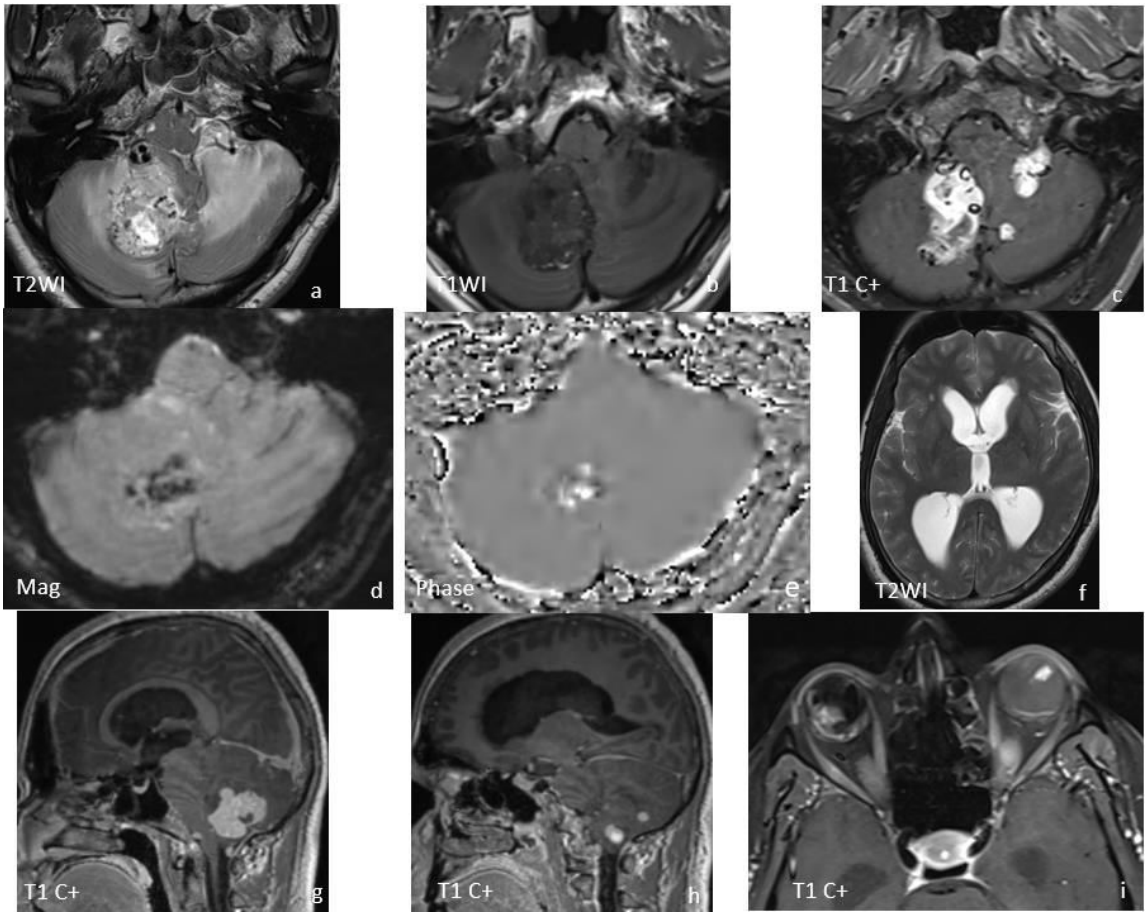

Figure 1. CNS and retinal hemangioblastoma. (a, b, c) MRI brain shows well defined solid lesion in bilateral cerebellar hemispheres appearing heterogeneously hyperintense on T2WI with surrounding edema and showing multiple small hyperintense foci on T1WI showing moderate heterogeneous post contrast enhancement. **(d, e)** multiple hemorrhagic and calcific foci on SWI sequences. **(f)** Obstructive hydrocephalus. **(g, h)** Subcentimeter nodular enhancing lesions in bilateral cerebellar hemisphere. **(i)** Retinal hemangioblastomas seen as multiple enhancing lesions seen in posterior segments of both eyeballs

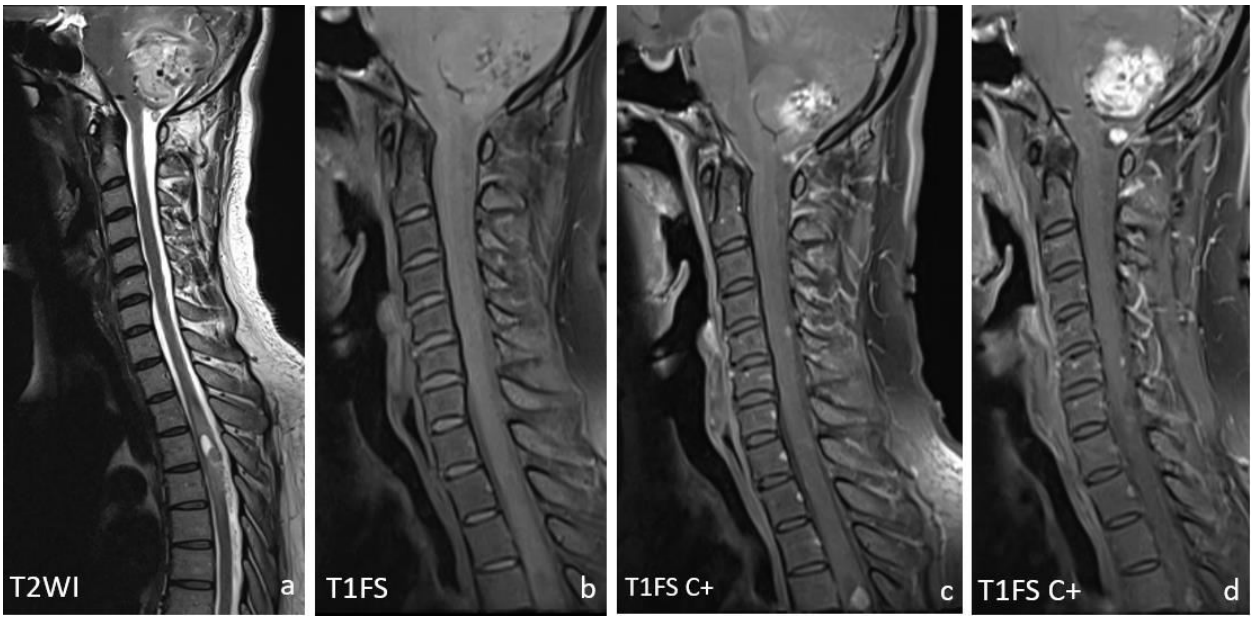

Figure 2. Spinal hemangioblastomas. (a, c) MRI spine shows an intramedullary well defined solid- cystic lesion at the level of D4-D5. The solid lesion was hyperintense on T2 showing post contrast enhancement and the cystic component is isointense on T2WI. Cord edema and cord widening was seen at D3 to D6 level. **(b, c, d)** Small nodular enhancing lesions at level C5 and C6 level.

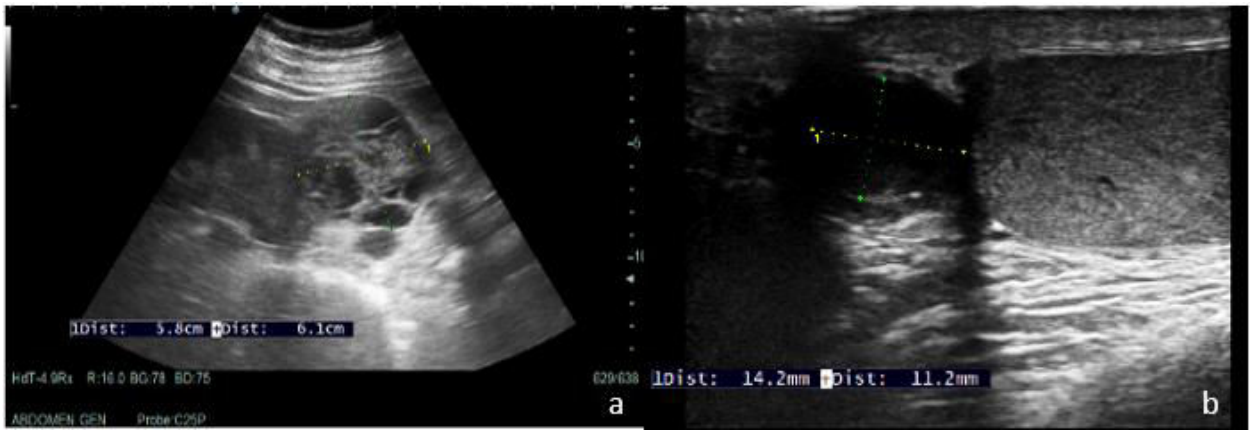

Figure 3 (a). Ultrasonography of the abdomen shows Bosniak IV cyst in left kidney - likely renal cell carcinoma. **(b)** Ultrasonography of scrotum shows left epididymal cyst.