Von Hippel-Lindau Disease (VHL): A Rare Radiological Case Report

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Abstract

Von Hippel-Lindau disease (VHL) is a rare autosomal dominant syndrome caused by mutation in the VHL tumor suppression gene located on chromosome 3. The presented case was a 13 years male patient who initially presented to our hospital with chief complaints of Weakness in b/l lower limbs, Low backache, Right-sided flank pain. On Physical examination there was a lump in right lumbar region– which was firm on palpation. On imaging and histopathology examination the patient was found to have multiple simple pancreatic cysts, malignant renal lesion, retialangioma and spinal hemangioblastoma. So a diagnosis of VHL was made. Regular follow-up with imaging (ultrasound, CT, MRI) are necessary to follow the previous lesions and detect any newly-developed VHL-associate tumors. The Importance of screening is emphasized because the lesions in VHL disease are treatable.

Keywords: Von Hippel-Lindau Disease, Hemangioblastoma, Retialangioma

Introduction

Von Hippel-Lindau disease (VHL) is a rare autosomal dominant syndrome caused by mutation in the VHL tumor suppression gene located on chromosome 3.[1] There is a strong predisposition for tumor development in various organs like pancreatic neuroendocrine tumors, pancreatic cysts (incidence of 35% to 70% of patients with VHL), cerebellar and spinal hemangioblastomas (incidence 60–80%), clear cell renal cell carcinoma (RCC) in 24–45% of patients, ovarian cysts, and pheochromocytoma.[2–4] Historically, the diagnosis of VHL is made based on the presence of a VHL-associated tumor (retinal or cerebellar hemangioblastoma, pheochromocytoma, or RCC) in a patient with positive family history or 2 tumors in patients without pertinent family history.[4] There is a strong family history in most of the patients. However, about 20% of patients may have de novo mutation.[5] Here, we present a young patient with multiple simple pancreatic cysts, malignant renal lesion, retialangioma and spinal hemangioblastoma suggestive of a rare sporadic case of VHL.

Case Report

The presented case was a 13 years male patient who initially presented to our hospital with chief complaints of Weakness in b/l lower limbs, Low backache, Right-sided flank pain. On Physical examination there was a lump in right lumbar region– which was firm on palpation. There was no family history for any genetic disorder. He neither had any history of visual or auditory disturbances nor had any past history of hypertension. There was no evidence of gait disturbance.

USG Abdomen showed large heterogenous solid mass lesion with internal necrotic / cystic areas and vascularity in solid part of the lesion. Also there were multiple simple pancreatic cysts of varying sizes throughout pancreas as on USG. CECT abdomen was performed which showed well defined heterogenously enhancing solid mass lesion with central non-enhancing necrotic areas, arising from upper and mid pole of right kidney and multiple non enhancing cysts of varying sizes throughout Pancreas [Figure 1]. The Contrast enhanced CT Images found homogenously enhancing spinal canal lesion at D10 - D11 Level. MRI Spine T2 Weighted MRI images sagittal section showed relatively defined isointense lesion with internal flow voids in spinal cord at D10-D11 level with long segment hydrosyrinx proximal to the lesion. The lesion shows intense homogenous enhancement on post contrast T1W image confirming its intramedullary location [Figure 2]. On suspicion of VHL disease an Indirect ophthalmoscopy was done which showed right retinal angioma. USG guided FNAC of renal mass was done and histopathological report proved it to be a malignant renal mass. On conglomeration of the above findings, the patient was found to have multiple...
Simple pancreatic cysts, malignant renal lesion, retialangioma and spinal hemangiblastoma. Hence the case was diagnosed to be VHL.

Discussion

The prevalence of VHL has been estimated to be between 1:35,000-1:40,000. The clinical diagnostic criteria for VHL is proposed as:

a. For those with a family history of retinal or central nervous system hemangiblastoma (Hb), only one hemangiblastoma (Hb) or visceral lesion (renal tumours, pancreatic cysts or tumours, pheochromocytoma, papillary cystadenomas of the epididymis) is required to diagnose VHL.

b. For isolated cases without a clear family history, two or more hemangiblastoma (Hb) or one hemangiblastoma (Hb) and a visceral manifestation is required for the diagnosis of VHL.

Central nervous system hemangiblastomas commonly involve cerebellum, spine and medulla. Medullary hemangiblastomas (MHb) occur in about 5% of VHL patients. They are found in postrema of the medulla and may lead to syringobulbia. Unusual sites of hemangiblastomas in VHL include the anterior lobe of the pituitary, pituitary stalk, hypothalamus, optic nerve, corpus callosum, wall of the third ventricle, temporal horn of the lateral ventricles, frontal and temporal lobe and meninges. Spinal hemangiblastomas (SHb) occur in 13-59% cases. The best imaging technique available for hemangiblastomas is contrast enhanced MRI employing a gadolinium chelate. Routine screening of the CNS in VHL should include, pre and post contrast T1 weighted images of the brain and spinal cord, with thin sections through the posterior fossa and spinal cord and surface coil images of the entire spinal cord. Central nervous system hemangiblastomas commonly contain cystic areas with a solid mural nodule. Small (10 mm or less) hemangiblastomas are mostly isointense on T1-weighted images and hyperintense on T2-weighted images showing homogeneous post contrast enhancement. Small hemangiblastomas are located at the surface of the spinal cord while larger ones tend to be hypointense or show mixed signal intensity on T1-weighted images and appear heterogeneous on T2-weighted images. These lesions show heterogeneous post contrast enhancement. A hemangiblastoma larger than 24 mm is invariably accompanied by vascular flow voids. The solid and contrast-enhancing portions give low signal on diffusion weighted imaging (DWI) with resultant increase in the apparent diffusion coefficient (ADC). These findings indicate rich vascular spaces of the hemangiblastomas which is not seen in the other tumours. DWI may be useful for distinguishing hemangiblastomas from other enhancing cerebellar tumours. Renal cysts are present in 59-63% of individuals with VHL. Renal cell carcinoma (RCC) develops in 24-45% of VHL patients. Renal involvement in VHL is multicentric and bilateral in at least 75% of patients. Microscopic solid tumorlets have been identified within the renal parenchyma of patients with VHL. Some of these may develop into macroscopic tumours. Solid tumours have been observed to grow at a mean rate of 1.6 cm/year which is somewhat faster than those observed in sporadic renal cell carcinoma. Retinal hemangiblastomas (RHb) is seen in 45-59% of patients with VHL. They have been called “retinal angiomas” and “retinal hamangiomas” but hemangiblastoma is the preferred term since they are histologically identical to lesions found in the CNS. In adrenal
gland involvement, pheochromocytomas tend to occur as a principle manifestation in some families with VHL. Only about 7-18% of all patients with VHL have pheochromocytomas.[8,13] Hepatic hemangioblastoma, pulmonary hemangioblastomas, omental cysts, skeletal hemangiomas, ovarian cysts and angiomas, medullary and papillary carcinoma of the thyroid, pituitary adenoma, dermal hemangiomas and pigmented nevi have also been reported to occur with VHL.[9]

The renal lesions can be of any type varying from simple cysts, hyperplastic cysts, cysts containing clear cell carcinoma or solid tumors.[13] The full pathologic spectrum may occur in a single kidney. Tumors can arise from a precursor cystic lesion or it can be completely de novo.[14] Thus there is a serious need of serial imaging to detect any malignant transformation of the previously benign cysts. US is useful in distinguishing need of serial imaging to detect any malignant transformation of the previously benign cysts. US is useful in distinguishing.

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4. In spite of the availability of genetic testing imaging plays a key role in the identification of abnormalities, in the screening of asymptomatic gene carriers and in their long-term surveillance. Regular follow-up with imaging (ultrasound, CT, MRI) are also necessary to follow the previous lesions and detect any newly-developed VHL-associate tumors. Importance of screening lies in the fact that the lesions in VHL disease are treatable. Early detection helps to adopt the more conservative form of therapy and prolongs quality of life of the patient.

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