A Case of Von Hippel Lindau Disease

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Introduction

A young recruit presented with weakness of right lower limb, which was diagnosed as a case of Von Hippel Lindau (VHL) disease. It is a rare disease which causes central nervous system and other visceral neoplasm/ cysts.

Case Report

A 24 year old recruit presented with complaints of weakness of the right lower limb of one month duration. After neurological evaluation, a clinical impression of compressive myelopathy at cervical vertebral levels C6-7 was made. Magnetic resonance imaging (MRI) of cervico-dorsal spine and brain was done which revealed a mass in the left cerebellar hemisphere with predominant cystic component along with a peripheral nodule which showed significant contrast enhancement on intravenous gadolinium administration (Fig. 1). MRI of spine showed enhancing intramedullary mass

Fig. 1 : Cerebellar hemangioblastomas. T1 weighted post contrast MRI images show hypointense cystic lesion in cerebellar hemisphere with eccentric enhancing nodule.

lesions at C2-3, D1-2 and D9-10 vertebral levels. Lesions varied in size from 5 - 13mm. These lesions were hypo to isointense on T1 and hyperintense on T2 weighted images with intense contrast enhancement. The associated syringohydromyelic changes of spinal cord were seen in cervical and dorsal regions (Fig. 2). Based on the MRI findings a provisional diagnosis of cerebellar and spinal haemangioblastomas was made.

In view of known occurrence of multiple hemangioblastomas in VHL disease, patient was further investigated radiologically. An ultrasound of abdomen revealed multiple simple cortical cysts in both kidneys, the

Fig. 2 : Spinal haemangioblastomas T1 weighted post contrast sagittal images show enhancing intramedullary masses at CV2-3,DV1-2 and DV9-10 vertebral levels. Syringohydromyelic changes of spinal cord were seen in cervical and dorsal regions.

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Fig. 3 : Renal cysts. Coronal T2 weighted MRI images showing bilateral multiple renal cysts of varying sizes.

liver, pancreas, spleen and adrenals were normal. MRI abdomen with half-Fourier acquisition single-shot turbo spin-echo (HASTE) sequence was done, which showed multiple cortical cysts in both kidneys measuring 3-13 mm in diameter (Fig. 3). In view of the imaging findings, a diagnosis of VHL disease was established. There was no history of familial involvement. The diagnosis was further substantiated by fundoscopic findings which revealed multiple angiomas in the right eye, for which laser cauterization was done.

Discussion

Von Hippel Lindau disease is a rare autosomal dominant disorder which causes retinal hemangioblastomas, hemangioblastomas of the central nervous system, endolymphatic sac tumours, renal cell carcinomas, pancreatic cysts and tumours, pheochromocytomas and epididymal cyst adenomas. This case shows that in a patient with central nervous system (CNS) hemangioblastoma, one should rule out VHL by suitable investigations. The cranio-spinal lesions in this patient were eccentric as well as centrally located and had intense homogeneous enhancement. Mild to moderate peritumoral oedema was also present. Flow voids were seen in cerebrospinal fluid (CSF) space indicating arteriovenous shunting which is common due to the high vascularity of these lesions. Renal lesions were further evaluated by MRI using HASTE sequences where lesions with high water content show high signal intensity while the signal in background tissue is suppressed. This results in better delineation of cystic lesions and its internal contents. Maximum intensity projection (MIP) reconstruction of these images gave excellent overview of size and distribution of renal cysts.

VHL disease has been recognized for almost 70 years and recent developments in the genetics and imaging of VHL have significantly improved our understanding of

the disease and its natural history. The prevalence of VHL has been estimated to be between 1:35,000-1:40,000 [1,2]. The VHL gene was localized to the short arm of (3p25-26) chromosome in the late 80s and early 90s by researchers at the National Cancer Institute [3]. The mean ages (and ranges) of diagnosis of retinal hemangioblastoma (RHb), cerebellar hemangioblastoma (CHb), and renal cell carcinoma are 25 years (1-67), 30 years (11-78), and 37 years (16-67), respectively [4]. The clinical diagnostic criteria for VHL were proposed by Melmon and Rosen in 1964 [5]. If a family history of retinal or central nervous system hemangioblastoma (Hb) exists, only one Hb or visceral lesion (renal tumours, pancreatic cysts or tumours, pheochromocytoma, papillary cystadenomas of the epididymis) is required to make the diagnosis of VHL [4]. For isolated cases without a clear family history, two or more Hb or one Hb and a visceral manifestation is required.

Central nervous system hemangioblastomas commonly involve cerebellum, spine and medulla. CHb associated with VHL occurs at a younger age, is often multiple and has a worse prognosis than sporadic CHb, which occurs in 44-72% of VHL patients, making it one of the most common manifestations of the disease. Medullary hemangioblastomas (MHb) occur in about 5% of VHL patients [4, 6]. They are found in postrema of the medulla and may lead to syringobulbia. Unusual sites of hemangioblastomas 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 [4].

Spinal hemangioblastomas (SHb) occur in 13-59% cases. Unlike CHb where only a minority are associated with VHL, SHb is associated with VHL in 80% of all cases. SHb can be intramedullary, partially intra and extramedullary or exclusively extramedullary. Extensive replacement ("hemangioblastomatosis of the cord") of the spinal cord and brainstem has also been reported in VHL [7]. The best imaging technique available for hemangioblastomas 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. CHb commonly contain cystic areas with a solid mural nodule. Small (10 mm or less) hemangioblastomas are mostly isointense on T1-weighted images and hyperintense on T2-weighted images showing homogeneous post contrast enhancement. Small hemangioblastomas 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 hemangioblastoma larger than 24 mm is invariably accompanied by vascular flow voids [8]. 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 hemangioblastomas which is not seen in the other tumours. DWI may be useful for distinguishing hemangioblastomas from other enhancing cerebellar tumours [9].

Renal cysts are present in 59-63% of individuals with VHL. Renal cell carcinoma (RCC) develops in 24-45% of VHL patients [1,4]. Renal involvement in VHL is multicentric and bilateral in at least 75% of patients [9]. 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 1.6cm/year which is somewhat faster than those observed in sporadic renal cell carcinoma [10].

Retinal hemangioblastomas (RHb) is seen in 45-59% of patients with VHL [2,4]. They have been called "retinal angiomas" and "retinal haemangiomas" but hemangioblastoma is the preferred term since they are histologically identical to lesions found in the CNS.

Lesions associated with VHL

The pancreatic lesions associated with VHL include pancreatic cysts, serous microcystic adenomas and adenocarcinomas. The pancreatic cyst is the most common of these lesions. 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 [4,10]. 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 [5].

Majority of the symptoms in CNS involvement are due to mass effect produced by the cystic component of the tumour. These tumours often have multiple periods of tumours growth separated by periods of arrested growth, and many untreated tumours may remain static for several years. In patients where multiple CNS hemangioblastomas are present, diagnosis of Von Hippel Lindau disease should be considered and a search for cysts and tumours in other organs must be made.

Conflicts of Interest

None identified

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Answers to MCQs

1. (c)	2. (c)	3. (b)	4. (b)	5. (a)
6. (b)	7. (a)	8. (c)	9. (c)	10. (d)
11. (b)	12. (d)	13. (c)	14. (d)	15. (c)