Case Report

A Rare Case of Von Hippel Lindau (VHL) Disease

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ABSTRACT

Von Hippel-Lindau disease is a rare autosomal dominantly inherited multisystem genetic condition involving the abnormal growth of blood vessels in some parts of the body which are particularly rich in blood vessels. It is caused by a flaw in one gene, the VHL gene on the short arm of chromosome 3 which regulates cell growth. The spectrum of clinical manifestations of the disease is broad and includes retinal and central nervous system hemangioblastomas, endolymphatic sac tumors, renal cysts / tumors, pancreatic cysts / tumors, adrenal tumors and epididymal cystadenomas. The various manifestations can be demonstrated with imaging modalities such as ultrasonography, computed tomography, magnetic resonance imaging, and nuclear medicine. We hereby report a rare case of VHL with imaging features and approach to the diagnosis of VHL.

Keywords: *Von Hippel-Lindau disease, autosomal dominant disease.*

INTRODUCTION

Von Hippel Lindau (VHL) disease is characterized by the abnormal growth of tumors in certain parts of the body. We are presenting a case who had such tumors in various parts of body.

Casehistory: A 25 year old male patient presented to our hospital with a history of chronic headache since 2 months. Patient had similar episodes of headache along with blurring of vision 3 years back and he visited a government hospital where he was diagnosed to have retinal hemangiomas in right eye and was investigated further. Patient underwent CT Brain and USG abdomen which were normal then. Patient was operated for the retinal hemangiomas. Now patient presented with similar complaints of headache 2 months ago for which he consulted an ophthalmologist and found to have multiple retinal haemangiomas in both eyes. Patient was referred to our hospital for further evaluation.

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ON GENERAL EXAMINATION:

Patient was irritable but responding to oral commands. There were no neurological deficits. CVS, RS and Abdomen examination was normal. Patient was investigated with CT brain (Plain and Contrast) which showed a well defined intra axial cystic lesion measuring 6x5 cms with enhancing mural nodule measuring 8 mm in the left cerebellum and fourth ventricle was compressed, causing

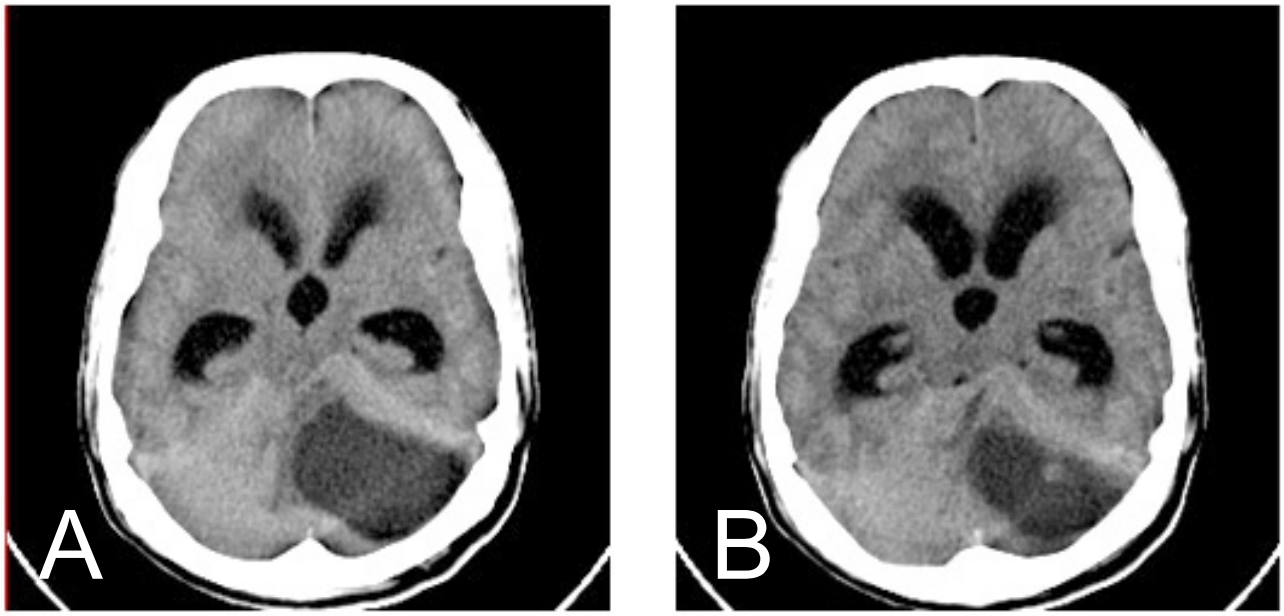

Figure 1: NECT AXIAL IMAGES- OF BRAIN showing intra axial cystic lesion with a mural nodule in the left cerebellum with hydrocephalus.

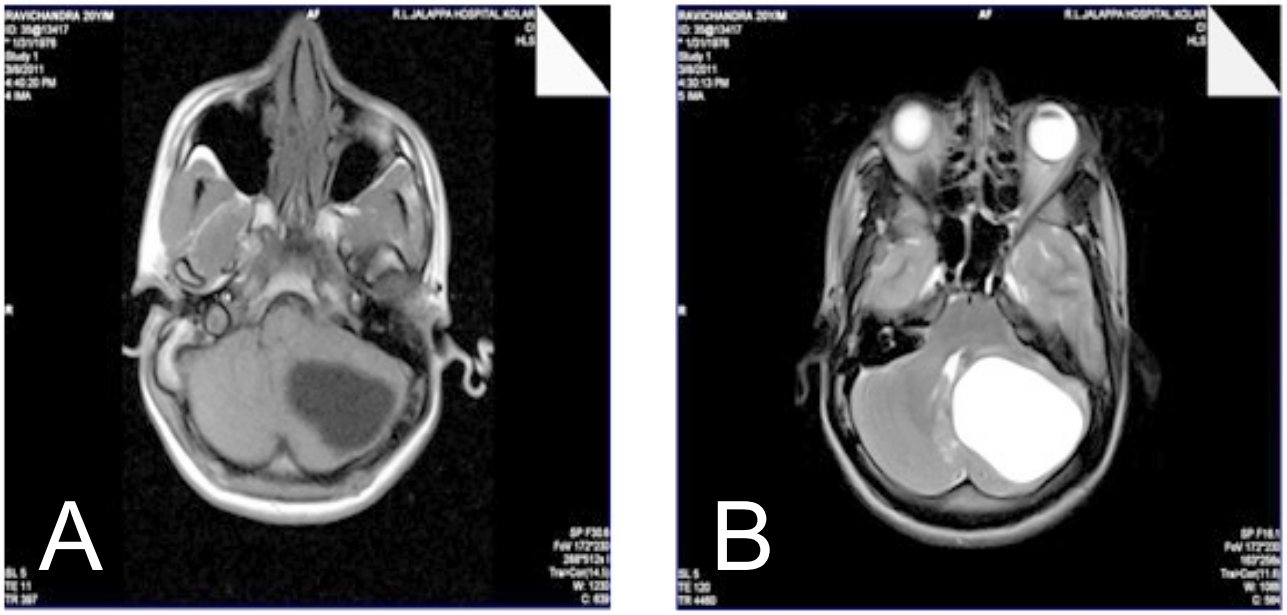

Figure 2: AXIAL MRI IMAGES- OF BRAIN A -TI WEIGHTED shows a hypointense space occupying lesion in left cerebellum. B -T2 WEIGHTED shows a hyperintense mass in left cerebellum.

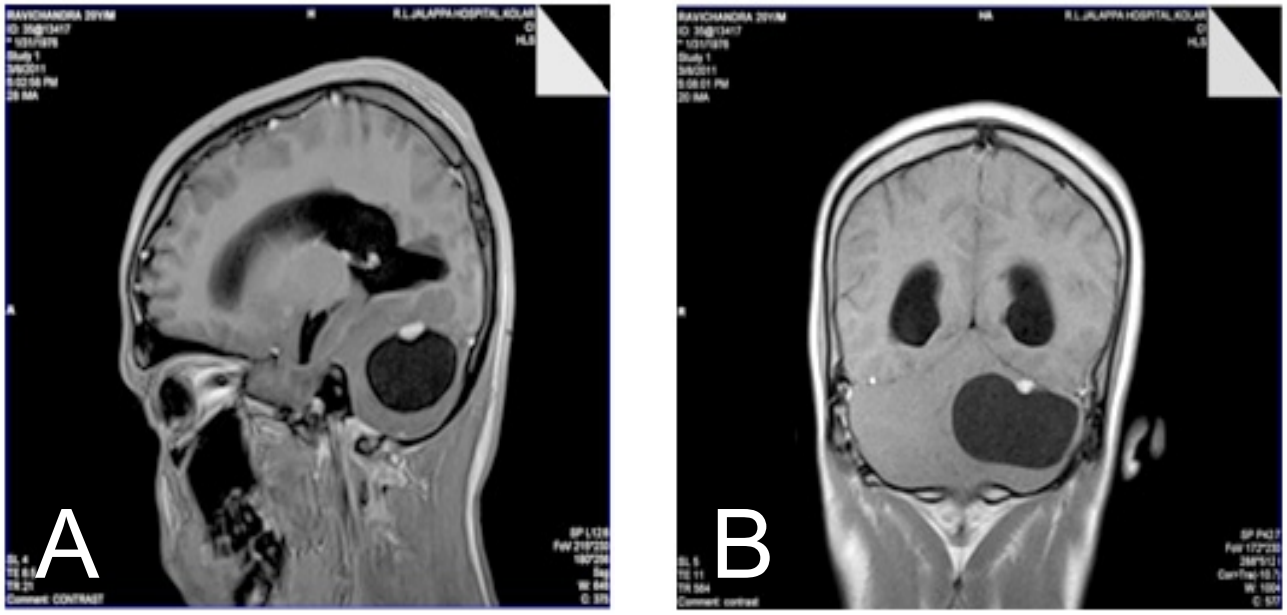

Figure 3: TI WEIGHTED CONTRAST SAG & CORONAL BRAIN MRI IMAGES- shows a enhancing mural nodule along upper margin of the cystic mass.

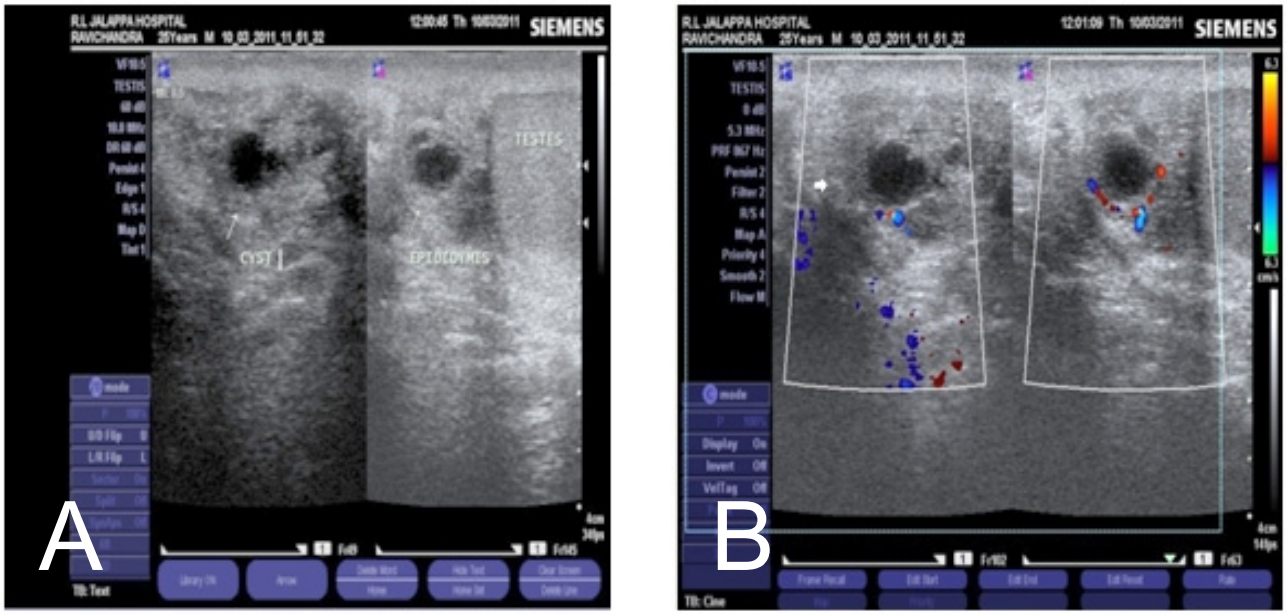

Figure 4: Scrotal ultrasound showing bilateral bulky epididymis containing multiple small cysts.

hydrocephalus. (Fig 1)

MRI Brain (Plain and contrast) was done which confirmed a large cystic lesion with an intensely enhancing mural nodule involving the left cerebellar hemisphere. Mural nodule is seen along the roof of the cyst abuting the lateral aspect of tentorium. (Fig 2 and 3).

A diagnosis of left cerebellar haemangioblastoma was done. SCREENING of whole spine was done which showed no obvious enhancing or similar lesions.

USG abdomen was normal, especially pancreas and kidneys.

Scrotal ultrasound showed bilateral bulky epididymis containing multiple small cysts. (Fig 4) Testis was normal.

DISCUSSION

VHL is a heritable, autosomal dominant, neoplastic disorder that predisposes to development of specific types of benign and malignant tumors. The estimated prevalence of VHL disease is 1 in 35,000 to 1 in 40,000.[1] Reports of the syndrome began in the 1860s, with ophthalmologists describing retinal angiomas that caused blindness and were sometimes associated with identical lesions in the cerebellum. In 1894, Treacher Collins was the first to recognize the angiomatous nature of the retinal tumors in a family.[2] By 1904, Eugen von Hippel, a German ophthalmologist, published descriptions of retinal angiomas in members of a small number of families spanning several generations.[3] In 1926, Arvid Lindau, a Swedish pathologist, published a report recognizing that retinal angiomas, cerebellar hemangioblastomas, and renal and pancreatic cysts were part of a familial syndrome.[4] Melmon and Rosen's study of a large kindred and literature review in 1964 established the diagnostic criteria of VHL including renal cancer.[5] Link age of the VHL gene (VHL) to the short arm of chromosome 3 was reported in 1988.[6] Finally, Latif and colleagues at the National Cancer Institute identified the VHL tumor suppressor gene by positional cloning in 1993.[7]

Individuals with VHL syndrome may be at risk for development of CNS hemangioblastomas, retinal angiomas, endolymphatic sac tumors, clear-cell renal carcinomas, pheochromocytomas, pancreatic neuroendocrine tumors, epididymal cystadenomas in men, and cystadenomas on the broad ligament in women.[9, 10]

VHL syndrome is diagnosed in a patient with / without a family history (Table 1), a geneticist and a physician informed about VHL manifestations should be consulted to coordinate the various tests (Table 2) needed to completely evaluate the proband. Next, a plan should be initiated to work with the proband and offer contact information for counselling and screening of at-risk family members who choose informed testing for VHL. The aim is to diagnose symptomatic and asymptomatic affected individuals among at-risk family members, allowing earlier detection and opportunities for improved treatment outcomes. For patients known to carry the disorder or for at-risk family members, a number of clinical screening regimens have been proposed, ranging from ophthalmologic examination to laboratory tests and various imaging techniques

Table 1: Diagnostic approaches to von Hippel-Lindau syndrome (VHL)

With a family history of VHL	Without a family history of VHL
Genetic testing: test for same VHL gene mutation as in affected biologic relative(s). Clinical diagnosis (when genetic testing marker/VHL mutation is unavailable): One or more of the following: CNS hemangioblastoma / Renal cell carcinoma, clear-cell, multifocal / Pheochromocytoma / Retinal angiomas / Pancreatic neuroendocrine tumor / Pancreatic cysts and/or cystadenomas / Endolymphatic sac tumor / Epididymal or broad ligament cystadenomas	Genetic testing: may be negative if VHL mutation occurred post zygotic (eg, VHL mosaicism) Clinical diagnosis (when genetic testing marker/VHL mutation is unavailable): Either or both of the following: CNS hemangioblastoma / Retinal angiomas If only one of the above is present, then also one of the following: Renal cell carcinoma, clear-cell Pheochromocytoma / Pancreatic cysts an neuroendocrine tumor / Endolymphatic tumor / Epididymal or broad ligan cystadenomas.

Table 2: Suggested screening guidelines for manifestations of (VHL) : Adapted from Glenn et al

Exam/test	Age and frequency
Ophthalmoscopy	From infancy; every 6–12 months
Fluorescein angioscopy	If needed (not routine)
Catecholamines and metanephrine levels	From 2 years; annually and if symptomatic
Enhanced MRI of brain/spine	From 11 years; every 1–2 years and if symptomatic
IF SYMPTOMS:	From 18 years, earlier if indicated;
Abdominal CT with and without contrast	every 1-2 years
Abdominal ultrasonography	Annually from 8 to 18 years, earlier If indicat ed
MRI and CT/IACs, audiology, neurology	Any age when hearing loss, tinnitus, Or vertigo

hydrocephalus. (Fig 1)

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