ISSN 2394–806X
IJHRMLP, Vol: 01 No: 01 January, 2015
Printed in India

CASE REPORT

Von Hippel-Lindau disease: Imaging findings: A single case report

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Accepted (Revised): December 16, 2014

ABSTRACT

Von Hippel Lindau disease is an autosomal dominant multisystem/multitumoral cancer disease diagnosed by clinical, radiologic and genetic findings. Its prevalence has been estimated to be of one per 36000 inhabitants. The disease is characterized by abnormal vascular proliferation and development of a variety of benign and malignant tumors in multiple organ systems.

***Keywords**: Von Hippel-Lindau disease, diagnostic imaging; Magnetic resonance imaging.*

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INTRODUCTION

Von Hippel-Lindau disease is caused by mutation in VHL tumour suppressor gene localized on chromosome 3p25[1]. Hallmarks of the condition include retinal angiomas, hemangioblastomas of the cerebellum and the spinal cord, renal cell carcinoma and cysts, and pheochromocytomas. The disease is named after Eugen von Hippel and Arvid Lindau[2].

In this article, we report imaging findings in a case of VHL disease who presented to us for routine Ultrasound. This case highlights the importance of suspecting possibility of VHL in patients with multiple pancreatic cysts.

CASE REPORT

A thirty-five years old man, who presented with vomiting and dizziness, was admitted to our hospital for further examination. On routine Ultrasound we noted the presence of multiple pancreatic cysts. On further enquiry he admitted to having difficulty walking, standing or moving in a coordinated manner which were symptoms referable to the cerebellum. He also had persistent headache and dizziness. He however denied any family history of malignancy or early death. Based on symptoms referable to the cerebellum and strong clinical suspicion he underwent CT scanning in our department.

RADIOLOGICAL FINDINGS

On NECT, a fairly well defined mixed solid-cysticlesion with internal and perilesional hypodensity suggestive of

intratumoural and peritumoural cysts was noted in the right cerebellar hemisphere. Mild perilesional edema, compression of the fourth ventricle and upstream hydrocephalus was noted. There was no calcification or hemorrhage within the lesion. Intense fairly homogenous enhancement of the solid component of the tumour was noted on post contrast study, without enhancement of the walls of the peritumoural cyst.The decision to do an MRI for complete evaluation of the brain and spinal cord was made. CEMR study of brain and spine revealed a solid lesion with intraand peritumoural cystsin the right cerebellar hemisphere with moderate perilesional edema. The solid component appears so intense on T1 and T2WI. The intratumoural cyst appears mildly T1 hyperintense and does not suppress completely on FLAIR suggesting high protein content. The peritumoural cystic component suppresses on FLAIR and is T1 hypointense. There is moderate perilesional edema. Cyst formation in HGBLs is a result of vascular leakage from tumour vessels and not tumour liquefaction or active secretion.Few flow voids due to enlarged vessels are seen predominantly in the periphery of the lesion. In addition the ipsilateral transverse and sigmoid sinuses and the IJV were dilated, possibly from high flow from the lesion. There was mass effect in the form of mild herniation of the cerebellar tonsils through the foramen magnum, contralateral displacement of the vermis and compression of the fourth ventricle with resultant upstream hydrocephalus and interstitial edema in the periventricular region. There was no diffusion restriction through the lesion. MR spectroscopy through the solid enhancing component of the lesion showed elevated Choline peaks with depression of NAA and creatine peaks with Cho: NAA ratio of 2.5. Similar spectroscopic picture was also obtained in the peritumoural region. On post contrast study, there was intense enhancement of the solid component of the lesion without enhancement of walls of the peritumoral cysts. In addition a T2 isointense and T1 hypointense subependymal nodule onecm caudal to the fourth ventricle was noted which showed intense post contrast enhancement.Multiple T2 hyperintense cysts were noted involving the cervical and dorsal cord with a T2 isointense intramedullary lesion in dorsal sub pial location at the level of D3 vertebral body. There was extensive perilesional edema. The solid T2 isointense intramedullary lesion showedintense post contrast enhancement with no enhancement of the cysts.

DISCUSSION

The VHL gene was identified in 1993 by Latif *et al.* by positional cloning[3]. The responsible gene, located on the chromosome 3p25-26 has high penetrance but delayed or variable expressionandmay cause widely different clinical manifestations.

The clinical manifestation of the disease is reportedin 14 different organs with 40 differentlesions. These include retinal and CNS hemangio blastomas, endolymphatic sac tumours, renalcell carcinomas and cysts, pancreatic tumours andcysts[4], pheochromocytomas, and epididymal cystadenomas[5,6].

The most common CNS tumour ishemangioblastoma and occurs in 40% of patients[7]. Symptoms often begin in the second to third decadesof life. Patients may present with neurologic symptoms such as headache, ataxia, and blindness or they may be asymptomatic.

VHL- associated hemangioblastomas demonstrate a 'saltatory' growth pattern characterized by quiescent periods (approx two years). Nearly half of all patients develop de novo lesions after the initial diagnosis of VHL. The median life expectancy is 49 years. Usually morbidity and mortality areassociated with frequent surgeries. Renal cell carcinomas are the cause of death in 30-50% of the patients[8].

The family history is positive in 80% cases while the other 20% of the cases are due to mutation de novo.

THE DIAGNOSTIC CRITERIA FOR VHL IN SPORADIC CASES ARE

- More than one haemangioblastoma in the CNS,
- One CNS haemangioblastoma and visceral manifestations of VHL

Molecular genetic testing allows the identification of a deletion or significant mutation that confirms the diagnosis of VHL disease[9].Two VHL phenotypes are recognized and distinguished by the presence or absence of pheochromocytoma[10].

Type I VHL: includes patients with low risk of VHL.

Type II VHL: includes patients with high risk of VHL.

- Type 2A (low risk of renal cell carcinoma)

- Type 2B (high risk of renal cell carcinoma)

- Type 2C (familial pheochromocytoma, no hemangioblastoma or renal cell carcinoma)

FIGURES

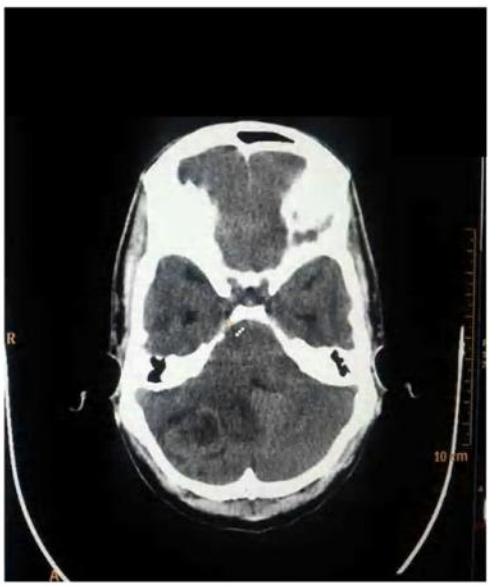

Figure I Axial NECT showing a fairly well defined predominantly solid mass with internal and peritumoral hypodensity and perilesional edema. The solid component appears isodense to grey matter.

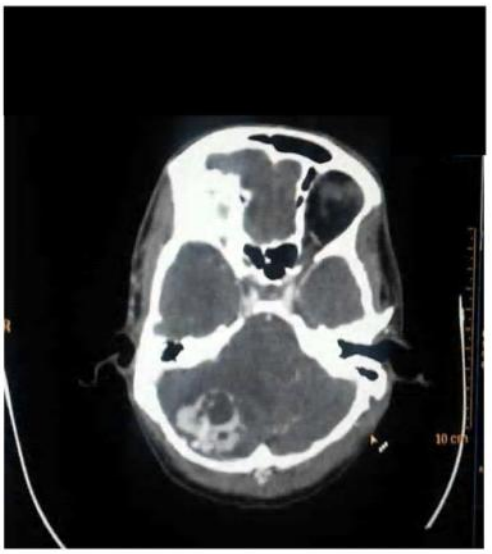

Figure 2 Axial CECT showing homogenous enhancement of the solid part of the lesion with lack of enhancement of the internal necrotic part and walls of the peritumoral cyst. The wall of peritumoral cyst is formed by compressed gliotic brain.

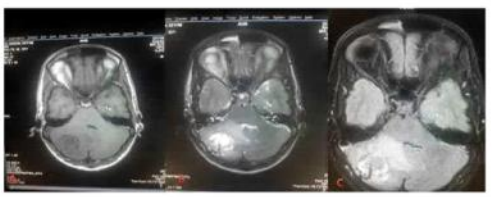

Figure 3 (A-C) T1, T2 and FLAIR weighted images showing solid lesion with intra and peritumoral cyst in the right cerebellar hemisphere. The solid component appears isointense to grey matter on T1, T2 & FLAIR images. The intra tumoural cyst appears mildly T1 hyperintense and does not suppress completely on FLAIR. The peritumoral cystic component suppresses on FLAIR. There is moderate perilesional edema. Few flow voids due to enlarged vessels are seen predominantly in the periphery of the lesion.

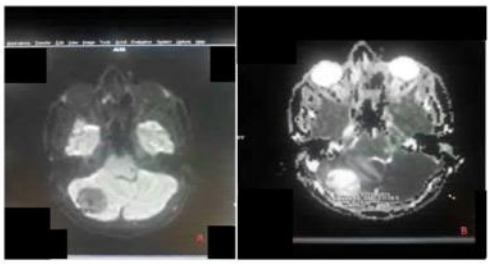

Figure 4 (A and B) DW imaging and ADC mapping showing lack of diffusion restriction.

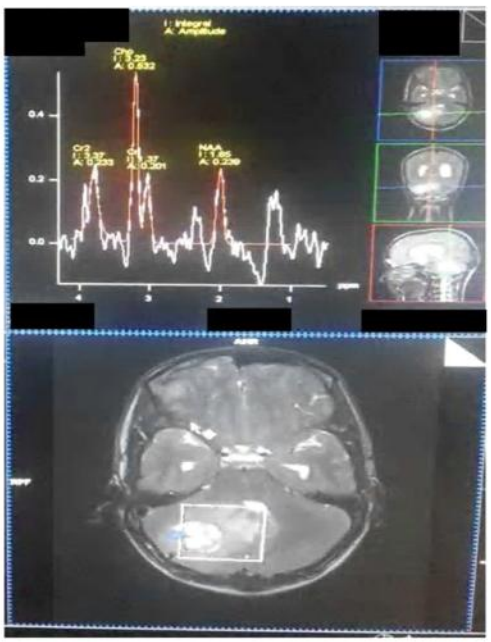

Figure 5 MR Spectroscopy the solid enhancing component of the lesion showed elevated Choline peaks with depression of NAA and creatine peaks with Cho: NAA ratio of 2.5. Similar spectroscopic picture was also obtained in the peritumoral region.

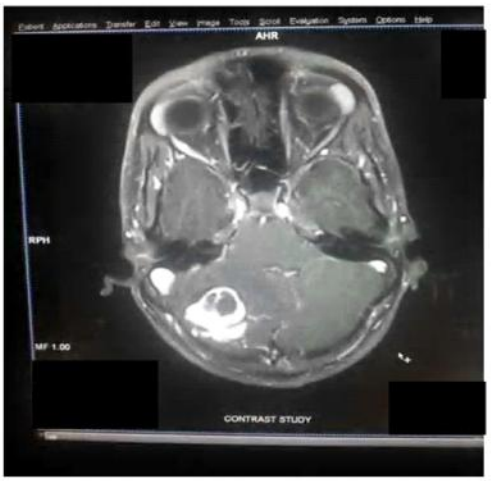

Figure 6 Axial post contrast MR showing intense enhancement of the solid component of the lesion without enhancement of the walls of the peritumoral cysts.

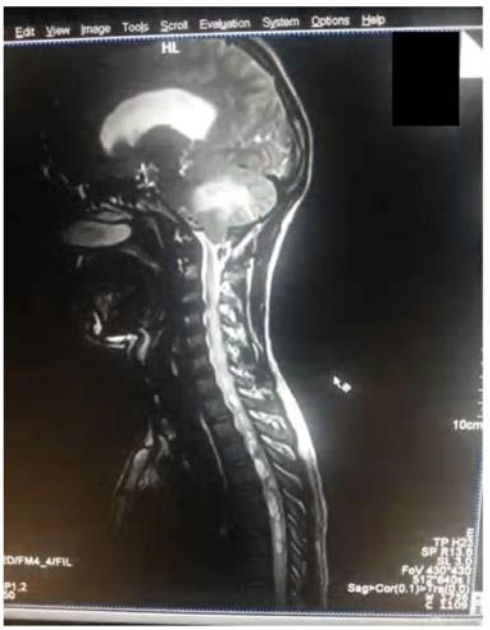

Figure 7 Multiple T2 hyperintense cysts were noted involving the cervical and dorsal cord with a T2 isointense

intramedullary lesion in dorsal sub pial location at the level of D3 vertebral body. There was extensive perilesional edema. The solid T2 isointense intramedullary lesion showed intense post contrast enhancement with no enhancement of the cysts.

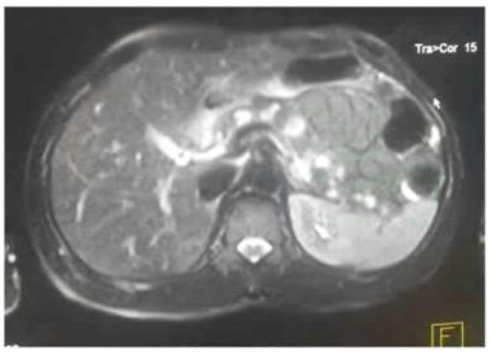

Figure 8 T2 weighted axial image of upper abdomen showing multiple intrapancreatic cysts of varying sizes.

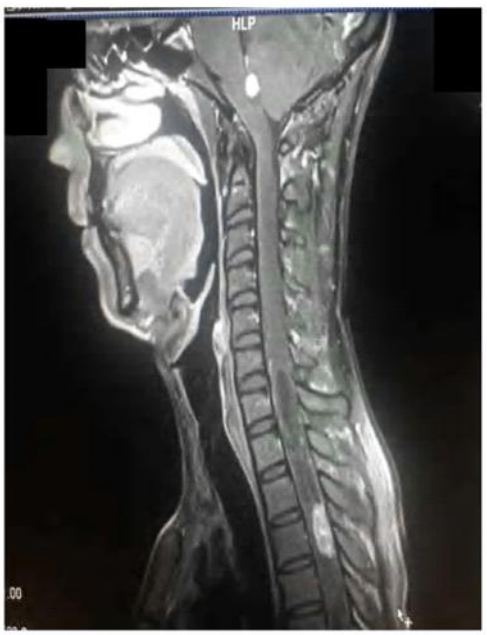

Figure 9 Saggittal post contrast T1-FS images showing enhancing subependymal nodule caudal to the fourth ventricle along with enhancing dorsal sub pial intra medullary lesion. These nodules are seen to abut pial surface. There is absence of enhancement in the cysts.

CONCLUSION

Early diagnosis, genetic consultation, adequate screening and correct therapeutic management are essential for patients with VHL syndrome. Being familiar with its imaging manifestations will be essential for making a correct diagnosis and providing guidance for further investigations. Imaging plays a key role in the identification of abnormalities and in the subsequent follow up of lesions. It is also important in the screening of individuals who are not yet symptomatic.

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