

Von Hippel Lindau Syndrome presenting with abnormal uterine bleeding: A Case Report and Review of Literature

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Abstract: Von Hippel Lindau syndrome is a scarcely reported disease, which is multi-system familial tumor syndrome. It follows autosomal dominant type of inheritance pattern. VHL syndrome is usually characterized by presence of hemangioblastoma in various places like CNS and retina. Other manifestations in VHL syndrome are renal cell carcinoma, pancreatic benign cyst and solid tumor, epididymal tumor, cystic lesion of ovary and other viscera, neuro endocrine tumor of pancreas etc. In this article we present a case of VHL syndrome, which came to us with primary complain of menorrhagia and dyspareunia. On further enquiry, patient gave history of multiple episodes of headache and dyspepsia. Radiological investigations showed multiple cysts in pancreas, kidney and ovary. By method of EUS, biopsy of pancreatic cyst was taken which came benign. We report this case of VHL, which presented to us with primary complain of abnormal uterine bleeding, a very rare presentation of this rare disease.

Keywords: VHL- Von Hippel Lindau; Hemangioblastoma; Cyst.

INTRODUCTION

Rare familial tumor syndrome, VHL has very low incidence in community. (2-3cases/100000 population) [1]. This syndrome is characterized by cystic lesion of various viscera and benign tumor of multiple organ system. These lesions very rarely have potential for malignant transformation. Detail history of patient and radiological finding, support the diagnosis. First symptom is usually neurological or ocular as other systemic involvement has late presentation. In this report, we present a case of VHL which presented with menorrhagia and other non specific symptoms due to multiple visceral cysts and we have tried to summarize its manifestation's, clinical features and treatment.

CASE REPORT

A 24 year female came to our OPD with history of heavy menstrual bleeding, pain abdomen, painful sexual intercourse and multiple episodes of headache. Pain was associated with vomiting. No past history of DM, HTN, COPD, TB, sweating, blurring of vision, hearing impairment and any surgery. Her family history was significant for maternal demise from renal cell carcinoma and also her sister had h/o head surgery. On abdominal examination, there was distention with a non tender abdominal mass of 3x4 cm size more over in epigastrium and umbilical region with well defined margins. Per vaginal examination was normal.

On GPE, vitals were in normal limits. Pallor, icterus, cyanosis, clubbing, edema, lymphadenopathy

were absent with no postural hypotension. Routine blood investigations were in normal range.

On examination of eye, her best corrected visual acuity was 6/6 in both eyes. Fundus was grossly normal. Intra ocular pressure was in normal limits. On CVS, CNS and respiratory system examination, no significant abnormality was detected.

S. Calcium, S. Phosphorus, parathyroid hormone, alkaline phosphatase, CA125, CA19-9, 24 hour urinary metanephrines and nor metanephrines were in normal limits.

On USG, simple cyst was present near right ovary in broad ligament. USG abdomen also showed left renal mass, which was s/o Angiomyolipoma.

Further imaging finding showed this disease to be extensive. Triple phase CECT abdomen showed multiple heterogeneously enhancing soft tissue density mass lesions predominantly in neck and head of pancreas. Fat planes with adjacent structures were maintained. ? Pancreatic islet cell tumor

A heterogeneously enhancing soft tissue density mass lesion of size 17x15 mm was seen in middle pole of left kidney. ? RCC

Multiple cysts were seen in whole of pancreas. Multiple cysts were in right kidney. On EUS, multiple large cysts in pancreas with bulky head were seen.

FNAC was taken, which was s/o benign cystic lesion of pancreas.

Magnetic resonance imaging of the abdomen showed major replacement of the pancreas with a multiple cystic lesion and cystic lesion in right kidney also.

On MRI brain, multiple bright signal intensity seen at cervico medullary junction and both cerebellar hemispheres surrounded by edema causing effacement

of 4th ventricle leading to dilatation of 3rd and lateral ventricle. MRI of circle of willis showed no significant abnormality. After taking consultation from endocrine, gastroenterology, ophthalmology, neurosurgery and urology departments, the follow up of patient was planned.

Non specific symptoms were treated conservatively and patient was advised for regular follow up.

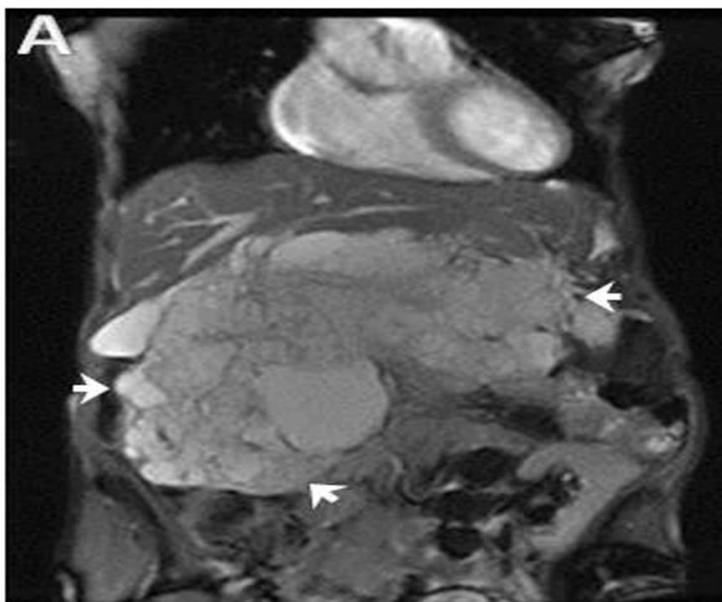


Fig.1 MRI of abdomen; Arrow head: multiple pancreatic cysts



Fig.2 MRI revealed multiple hypochoic cystic lesions at pancreas and right kidney

DISCUSSION

Hippel and Lindau independently described it[2]. It is rare disease caused by mutation or deletion of VHL gene, present on chromosome 3p25 [3]. VHL syndrome mainly cause benign and neo plastic lesions

of CNS and various organ. Patient of VHL syndrome may found to have 1) CNS and retinal hemangioblastoma, 2) cystic, benign or neo plastic lesion of pancreas, 3) cystic lesion of kidney and ovary,

4) epididymal tumor, 5) tumor of inner ear and retinal angioma etc.

Melmon was gave diagnostic criteria for it with Rosen, which are as follow:

- 1) Elucidation of mutation in VHL gene;
- 2) Any manifestation with known family history
- 3) CNS hemangiomas >1
- 4) Visceral manifestations with CNS hemangioblastoma.

Retinal hemangioblastomas are the first manifestation in approximately half of VHL cases[4]. Pancreatic involvement seen in 16% to 29% cases of VHL. Hemangioblastoma of CNS present as ataxia, weakness, headache. These lesions are usually benign and treatment is surgical excision. Nearly 10% of VHL cases have endolymphatic sac tumors, which are also benign and may cause vertigo, tinnitus, hearing loss and deafness. Retinal involvement of VHL normally follows benign course but have potential for serious complication like macular exudation, retinal traction, retinal detachment, glaucoma, vitreous hemorrhage etc. Flurorescein Angiography should be diagnostic modality. For treatment various options like argon laser, cryotherapy, anti VEGF therapy, photodynamic therapy, parsplana vitrectomy can be tried[5].

Multiple and calcified pancreatic cyst or serous cystadenoma are most frequent finding of pancreatic involvement. Patient usually have nonspecific complains like abdominal pain, distention, dyspepsia etc. Pancreatic lesion can be present as any of three forms; a) cystic, b) solid (ductal adenocarcinoma, neuro endocrine tumor], or c) combine [serous cyst adenoma][6].

Pancreatic lesions also have potential for malignant changes but very rarely. Hammel et al. concluded on the basis of his study on VHL syndrome that <1cm diameter cyst can be followed but larger must be resected in view of being metastatic[7]. Treatment modality of pancreatic pathology has various controversies but if suspicion of malignancy is there, choice of t/t must be surgery followed by lifelong replacement of pancreatic exo and endocrine functions.

For renal tumors, partial nephrectomy or radio frequency ablation may be tried. Pheochromocytoma, paragangliomas, hepatic hemangioma and adenoma are some other rare clinical entities associated with VHL syndrome.

Role of imaging in VHL is for; 1) identify lesions, 2) differentiate benign and malignant lesions, 3) as a tool to see any transformation of lesion from its baseline features. MRI if preferred imaging tool for diagnosis and followup. Complications related to cerebellar hemangiomas and metastatic renal cell carcinoma, these are two major cause of patient demise in VHL syndrome[8].

CONCLUSION

VHL is a lifelong and inheritable clinical entity. After finding of VHL patient, his or her family members should undergo clinical, radiological and molecular screening and patient should undergo annual screening. Due to potential of being metastatic, option of surgical treatment should also keep in mind. Due to wide and multiple presentation and recurrence, treatment strategy is found very complex. The border between conservative and surgical procedure must be defined well. A prompt diagnosis of systemic manifestation and appropriate treatment is effective in VHL syndrome.

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