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A rare case of von Hippel Lindau disease

Kanika Deora
kanikadeora@gmail.com
Kasturba Medical College, Manipal, Karnataka

Dr. Girish Mennon
kanikadeora1@gmail.com
Kasturba Medical College, Manipal, Karnataka

ABSTRACT

Von Hippel Lindau disease is a rare disease characterized by the formation of tumors, which may be cancerous or non-cancerous and fluid-filled sacs in different parts of the body like kidney, pancreas, genital tract. The incidence of the disease is estimated to be 1 in 36,000 individuals. VHL is a tumor suppressor gene, mutations in this gene lead to abnormal growth of cells forming tumors, cysts that are characteristic of Von Hippel Landau disease. Non-cancerous tumors called hemangioblastomas, which are growth made up of abnormally formed blood vessels are characteristic of this disease, which if develop in the brain, spinal cord causes headache, vomiting, weakness, ataxia and in the retina causes retinal hemangioma. People are also at risk of developing renal cell carcinoma, pheochromocytoma, and tumors in the inner ear. Being a multisystem disease, diagnosis is made by doing genetic testing, ultrasound abdomen, radiological examination like CT, MRI of various organs and treatment is by doing surgery which can be minimally invasive and laser surgery, chemotherapy, immunotherapy. We report a case of Von Hippel Lindau Disease. A 27-year-old lady presented with headache, 3-4 episodes of vomiting which was non-bilious, non-projectile in nature. She had one episode of generalized tonic-clonic seizure which was associated with rolling of eyes and frothing of mouth. USG abdomen revealed asymmetric pancreatic cyst, mass lesion in the superior pole of left kidney suggestive of renal cell carcinoma, as her father also died due to renal cell carcinoma. Radiology reports showed a well-defined cystic lesion in the left cerebellar hemisphere suggestive of cerebellar hemangioblastoma for which craniectomy was done. The patient was put on tablets Pan, Luperitin, Oxevion, Dexona and was advised to review to urology, neurosurgery department if any new onset deficits.

Keywords— *Von Hippel Lindau disease, Hemangioblastoma*

1. INTRODUCTION

VonHippel Lindau disease is an Autosomal dominant, cancer- predisposition syndrome with a mutation in the VHL tumor suppression gene on chromosome 3[1]. Patients are prone to develop cysts and tumors in various organs [2]. Cerebellar and spinal hemangioblastoma (seen in 60-80%) is the most commonly reported cysts and tumors) [4] followed by Pancreatic cysts, Pancreatic neuroendocrine tumours (seen in 35% to 70% of patients with VHL) [2, 3], Clear Cell Carcinoma (RCC) IN 24-45% of patients, ovarian cysts and pheochromocytoma. Inactivation of the VHL tumor suppressor protein and loss of function of the VHL protein, elongin B,C (VBC) complex results in dysfunction of the ubiquitination of Hypoxia –Inducible Factors (HIF) and other proteins for VBC complex leading to failure of degradation of HIF, thus development of highly vascular tumours. [5]
Clinical Criteria for the diagnosis of VHL Disease:

- Patients with a family history of developing HB in the CNS or RA, RCC, Pheochromocytoma or pancreatic tumors or cysts, or epididymal cystadenoma.
- Patients without a family history of VHL disease, but who develop HB or RA in combination with other tumors, such as RCC, Pheochromocytoma , pancreatic tumours or cysts, or epididymal cystadenoma.
- After diagnosis genetic testing to find out the mutation in the VHL gene should be done in order to help family members who are at risk to define their status.

2. CASE REPORT

A 27 old lady presented to Medicine OPD complaining of 3-4 episodes of vomiting, non-bilious, non- a projectile type of vomiting, associated with headache holocranial type. She is also compliant of 1 episode of generalized tonic-clonic seizures. She also complaint of difficulty in walking and swaying to either sides. There was no history of tingling, numbness, loss of sensation, no history of any trauma. She gave the history of Renal Cell carcinoma in the father . On examination sign of cerebellar involvement in the form of nystagmus , hypotonia, gait ataxia, pendular knee jerk, rebound phenomenon was present. CT brain revealed homogenous , intra- axial , hypodense lesion in right and left cerebellar hemisphere suggesting hemangioblastoma, figure 1 (a), (b), (c) CT abdomen showed a large heterogeneously enhancing lesion in the inferior pole of both kidneys suggesting

renal cell carcinoma, multiple pancreatic cysts. In the context of radiological findings and with a family history of renal cell carcinoma , diagnosis of Von- hippel lindau disease was made. Cerebella hemangioblastoma and craniectomy was done as he was symptomatic. For asymptomatic pancreatic cysts, renal mass <3 cm she was asked for follow up . Genetic testing was done which showed mutaton in the VHL gene and she was given genetic counseling.

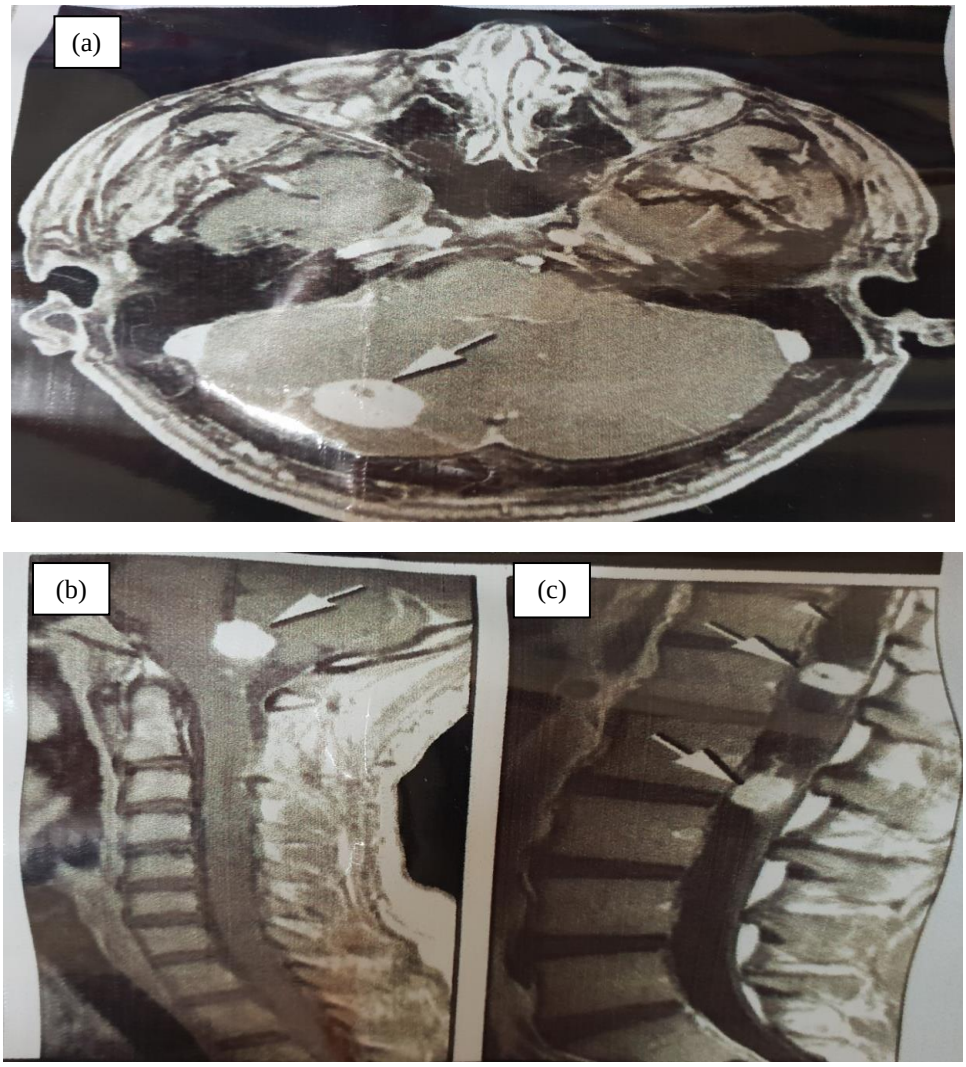

Fig. 1: (a) CT brain revealed homogenous, intra- axial, (b) (c): hypodense lesion in right and left cerebellar hemisphere suggesting hemangioblastoma

3. DISCUSSION

The presented case showed several VHL associated tumours . Hemangioblastoma of CNS is seen in childhood to <10 years, early teen until the age of 30 years [6]. The mean age of presentation of cerebellar hemangioblastoma is 30 years (11-78). The expansion of tumor in intracranial space causes symptoms which can be best treated by surgical resection. Gamma knife surgery can be the substitute if surgical resection is not possible. Bilateral renal involvement is also a common finding in VHL disease. 25-50% of VHL patients have RCC [7] and is been reported as a major cause of mortality [8]. Multiple cysts can develop in the kidney, but usually, do not compromise renal function. A nephron-sparing surgery is the recommended management for multiple renal cysts [7] instead of radical nephrectomy Tumour with a diameter of <3 cm are carefully observed and with a diameter of >3 cm enucleation , partial nephrectomy , Percutaneous radiofrequency ablation or cryosurgery can also be tried. Pancreatic cysts or cystadenoma are generally asymptomatic , benign characteristically seen as multiple cysts in the pancreas on imaging and rarely transform into malignant tumors [9]. Recently, various clinical trials have been conducted with the use of anti-angiogenic therapies to stop the formation or growth of vascular tumors in VHL disease. Drugs inhibiting VEGF-receptor kinase are showing excellent response by partially controlling the disease and making it stable [9, 10]. With the advancement in the surgical field and various non- surgical methods , curable rates are becoming high.

4. CONCLUSION

Von Hippel Lindau disease causes multisystem damage. The average life expectancy reported is 49 years. The patient should be constantly checked for tumours and cysts that develop at various sites in the lifetime, regular follow-ups play an important role to tackle this disease. The patient should be offered genetic counselling, anti-angiogenic drugs, care by a well trained specialist to improve the prognosis.

5. REFERENCES

[1] Keutgen XM, Hammel P, Choyke PL, et al. Evaluation and management of pancreatic lesions in patients with von Hippel-Lindau disease. Nat Rev Clin Oncol. 2016; 13(9):537–49.

[2] Sharma A, Mukewar S, Vege SS. Clinical profile of pancreatic cystic lesions in von Hippel-Lindau disease: A series of 48 patients seen at a tertiary institution. Pancreas. 2017; 46(7):948–52.
[3] Ayloo S, Molinari M. Pancreatic manifestations in von Hippel-Lindau disease: A case report. Int J Surg Case Rep. 2016; 21:70–72.
[4] Bhuyan M, Dutta D, Baishya BK, Hussain Z. Cerebellospinalhemangioblastoma with bilateral pheochromocytoma and hepatic cyst: A rare entity. Asian J Neurosurg. 2016; 11(3):311.
[5] Kaelin WG Jr. Molecular basis of the VHL hereditary cancer syndrome. Nat Rev Cancer 2002; 2:673–82
[6] Taro Shuin, Ichiro Yamasaki, Kenji Tamura, Heiwa Okuda, MutsuoFurihata and Shingo Ashida, Von Hippel–Lindau Disease: Molecular Pathological Basis, Clinical Criteria, Genetic Testing, Clinical Features of Tumors and Treatment; Jpn J Clin Oncol 2006;36(6)337– 343.
[7] Junaid M, Ur Rashid M, Afsheen A, et al. Von Hippel-Lindau syndrome and surveillance: A five year follow up case report. J Ayub Med Coll Abbottabad. 2015; 27(4):930–32.
[8] Safo A-OF, Pambuccian SE. Pancreatic manifestations of von Hippel-Lindau disease. Arch Pathol Lab Med. 2010; 134(7):1080–83.
[9] Michaelson MD, Redman BG, Hudes GR, Wilding G, Rini BI, George DJ et al. Phase 2 trials of SU11248 show antitumor activity in second-line therapy for patients with metastatic renal cell carcinoma (RCC). 2005 ASCO Annual Meeting, May 13–17, 2005, Orlando, FL.
[10] Rini B, Rixe O, Bukowski R, Michaelson MD, Wilding G, Hudes G, et al. AG-013736, a multi-target tyrosine kinase receptor inhibitor, demonstrates anti-tumour activity in a phase 2 study of cytokine-refractory, metastatic renal cell cancer (RCC). 2005 ASCO Annual Meeting, May 13–17, 2005, Orlando, FL.

