Case Report

Fluorodeoxyglucose positron emission tomography-computed tomography scan in von Hippel-Lindau syndrome: A case report and review of literature

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ABSTRACT

Von Hippel-Lindau (VHL) syndrome is a hereditary autosomal dominant disorder caused by defective tumor suppression gene at 3p25-p26. The gene for VHL disease is found on chromosome 3, and is inherited in a dominant fashion. The VHL gene is a tumor suppressor gene. This means that its role in a normal cell is to stop the uncontrolled growth and proliferation. It is characterized by abnormal growth of blood vessels. It strikes the eyes, central nervous system, kidneys, endocrine glands, etc. It predisposes the patient to retinal angiomas, central nervous system hemangioblastoma, renal cell carcinoma (RCC), pheochromocytomas, islet cell tumor of the pancreas, endolymphatic sac tumors, renal, pancreatic, epididymal cysts. We present a case of familial VHL syndrome whose Fluorine 18-fluorodeoxyglucose positron emission tomography-computed tomography scan was truly positive for adrenal pheochromocytoma but was falsely negative for RCC. Review of literature related to this entity is made.

Keywords: Fluorine 18-fluorodeoxyglucose positron emission tomography-computed tomography scan, pheochromocytoma, renal cell carcinoma, von Hippel-Lindau syndrome

INTRODUCTION

Von Hippel-Lindau (VHL) syndrome may present with ocular symptoms related to retinal detachment, uveitis, glaucoma or retinal hemorrhage. Headache, ataxia, variable neurodeficit may occur as a result of affection of the nervous system. Pheochromocytoma may present as hypertension, incidental mass. Islet cell tumors of the pancreas may cause gastrointestinal tract or metabolic upset, depending on the type. Pancreatic cysts and islet cell tumors may be the only manifestations of VHL, and these may precede any other manifestation of the disease by several years. Rarely, pancreatic masses may cause bile duct obstruction. Renal cysts are seldom clinically significant; however, in VHL disease they have an appreciable rate of malignant transformation. Renal cell carcinoma (RCC) is the leading cause of death in patients with VHL disease, with a prevalence as high as 75%. The average age at which patients with VHL disease develop RCC is 44 years. These facts reinforce the importance of obtaining renal imaging studies on a regular basis.

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CASE REPORT

A 22-year-old gentleman with family history of RCC presented with hypertension. Sonography revealed right suprarenal mass. The echotexture of both the kidneys was normal. The urinary vanilyl mandelic acid was elevated. Iodine 131-metaiodobenzyl guanidine (MIBG) scan (not shown here) was normal. Fluorine 18-fluorodeoxyglucose positron emission tomography-computed tomography (F18-FDG PET-CT) scan revealed hypermetabolic right adrenal mass suggestive of pheochromocytoma [Figure 1]. There were no hypermetabolic renal cortical or pancreatic lesions. Subsequent high resolution computer tomography of the kidneys revealed multiple hypervascular cortical based lesions in the right kidney [Figure 2]. The pancreas was replaced by multiple cysts. Per operative needle aspiration from pancreas did not show malignant cells. Partial nephrectomy was done. Histology of the renal lesion showed clear cell carcinoma [Figure 3].

DISCUSSION

VHL disease was first described at the beginning of the 20th century by Eugen von Hippel and Arvid Lindau. RCC occurs

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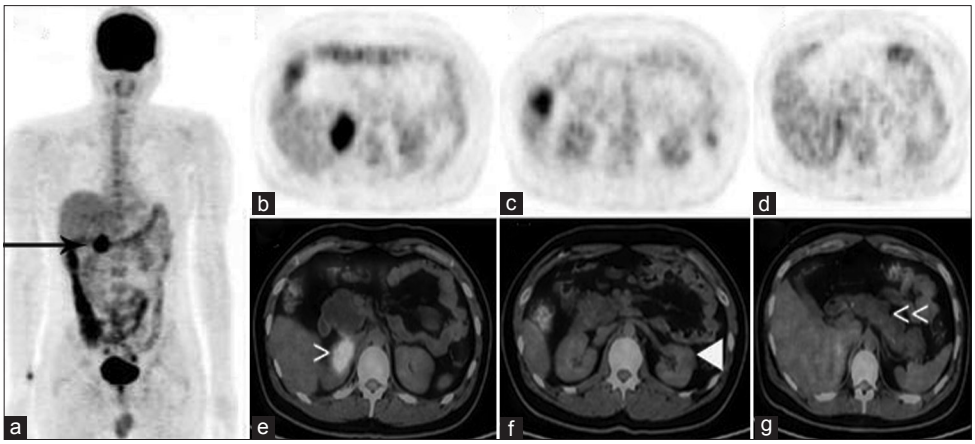

Figure 1: Maximum intensity projection image (a) shows avid FDG uptake in the right suprarenal region; (e) fusion image; shows localization to the right adrenal gland (>); another section; (f) shows ametabolic lesion in the lateral cortex of left kidney; (g) the entire pancreas; shows ametabolic cystic degeneration (<<)

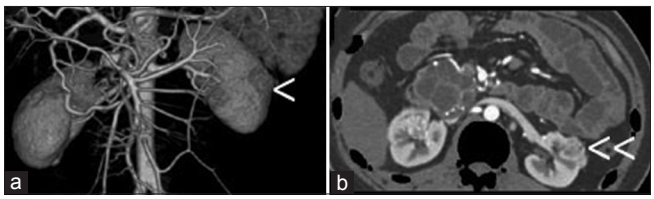

Figure 2: Three dimensional reconstructed image (a) shows lesions in the left kidney (<), these were hypervascular; (b) in the arterial phase (<<)

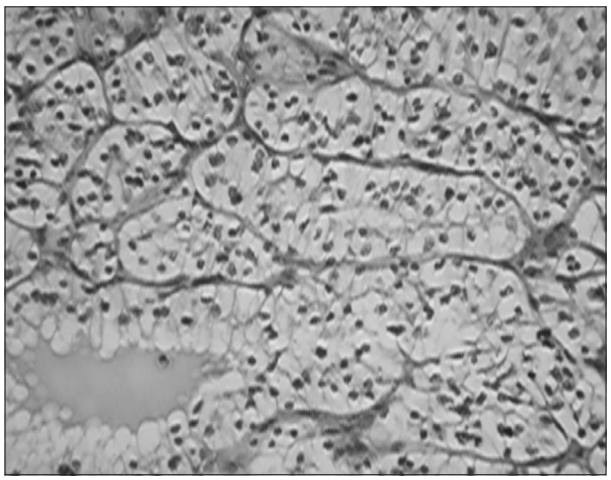

Figure 3: Histology revealed clear cell carcinoma of the kidney

in 36% of patients of VHL disease.[1] RCC may also be associated with pheochromocytoma as part of the VHL syndrome.[2] A synchronous tumor occurs in contralateral kidney in about 2% of patients. Multifocal lesions in the same kidney occur more frequently. The presented case had multiple foci of clear cell carcinoma in right kidney. Only 6% to 10% patients with RCC present with classical triad of hematuria, flank pain and a palpable lump. In recent years more than 50% of RCC are diagnosed incidentally.[3,4] Fever may be the only presenting symptom in some patients. Hepatic dysfunction in absence of liver metastasis in cases of RCC is called as Stouffers syndrome.[5] 25% of patients present because of symptoms related to metastases to the bones and brain.[6] It is important to diagnose this tumor early in the disease because the 5 year survival falls to 5% to 10% with spread to the bones, lungs, brain, adrenal and liver.[7] FDG PET-CT has shown high sensitivity in RCC in one study.[8] However, majority of studies have shown limited sensitivity of FDG PET-CT in primary evaluation of RCC and high sensitivity to evaluate metastasis and restaging.[9,10] The overall sensitivity and specificity of FDG PET-CT has been shown to be 60% and 100% respectively in RCC.[11] In the presented case FDG PET-CT did not show hypermetabolic activity within the renal parenchymal lesions. These were related to clear cell carcinoma on histology. Carbon11-Acetate has also shown variable sensitivity in RCC.[12,13] Clear cell carcinoma of kidney over expresses carbonic anhydrase IX receptors. Recent phase one study has demonstrated potential value of Iodine124-G250 chimeric antibody in assessment of clear cell renal carcinoma with a sensitivity of 94% and negative predictive value of 90%.[14]

With the detection of renal tumors at an earlier stage, partial nephrectomy and nephron-sparing surgery have evolved as effective alternatives to radical nephrectomy. Many a times more than one parenchymal-sparing operation either partial nephrectomy or enucleation, i.e., removal of a malignant lesion with a 0.5 cm rim of normal tissue may be required.[15] The presented case underwent partial nephrectomy.

Pheochromocytomas are tumors of sympathetic chromaffin tissue of adrenal medulla. The tumor occurs in 10-20% patients with VHL disease.[16] VHL can be subdivided into type 1 (low risk of phaeochromocytoma) and type 2 (high risk of phaeochromocytoma). Type 1 disease is associated with large deletions and mutations resulting in a truncated VHL protein, thereby conferring a lower risk for phaeochromocytoma. Type 2 is subdivided into type 2A (low risk of RCC), type 2B (high risk of RCC) and type 2C (phaeochromocytoma only).[17]

Pheochromocytomas are known to be hypermetabolic on FDG PET-CT scan as in the presented case.[18] Iodine-123 MIBG has been reported to diagnose multiple pheochromocytomas in VHL disease presenting initially with retinal angiomatosis.[19]

The pancreatic cysts seen in the presented case were ametabolic. Although different histologic types of cystic pancreatic neoplasms have been reported in the literature, serous cystadenomas, mucinous cystic neoplasms, and intraductal papillary mucinous neoplasms account for 90% of all primary cystic pancreatic neoplasms. Serous cysadenomas are usually benign and mucin secreting tumors have malignant potential. Cysts in pancreas may be unilocular, multilocular, with or without solid component. Multiple cysts usually follow pancreatitis. VHL disease is also associated with multiple cysts that are usually true epithelial cysts. Other causes of true epithelial cysts being autosomal dominant polycystic kidney disease and cystic fibrosis. Per operative needle aspiration from the pancreatic cysts in the presented case did not reveal malignant cells.[20,21]

Somatostatin receptors have been demonstrated in RCC.[22] 68Ga-DOTA-NOC (68Ga-labelled [1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid]-1-Nal3-octreotide) holds promise for evaluation of such lesions in future. The molecule has already been used to demonstrate somatostatin receptors in cerebellar lesion in VHL disease.[23]

CONCLUSION

VHL syndrome may present with a combination of various organ involvement. Presented case had affection of the kidney, adrenal and pancreas. FDG PET-CT has its limitations in identifying all the lesions hence a combined imaging strategy is suitable in evaluation of such a case.

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REFERENCES

1. Levine E, Collins DL, Horton WA, Schimke RN. CT screening of the abdomen in von Hippel-Lindau disease. AJR Am J Roentgenol 1982;139:505-10.
2. Patard JJ, Shvarts O, Lam JS, Pantuck AJ, Kim HL, Ficarra V, *et al.* Safety and efficacy of partial nephrectomy for all T1 tumors based on an international multicenter experience. J Urol 2004;171:2181-5.
3. Levine E. Renal cell carcinoma: Clinical aspects, imaging diagnosis, and staging. Semin Roentgenol 1995;30:128-48.
4. Smith SJ, Bosniak MA, Megibow AJ, Hulnick DH, Horii SC, Raghavendra BN. Renal cell carcinoma: Earlier discovery and increased detection. Radiology 1989;170:699-703.
5. Holland JM. Proceedings: Cancer of the kidney – Natural history and staging. Cancer 1973;32:1030-42.
6. Hock LM, Lynch J, Balaji KC. Increasing incidence of all stages of kidney cancer in the last 2 decades in the United States: An analysis of surveillance, epidemiology and end results program data. J Urol 2002;167:57-60.
7. Thrasher JB, Paulson DF. Prognostic factors in renal cancer. Urol Clin North Am 1993;20:247-62.
8. Ramdave S, Thomas GW, Berlangieri SU, Bolton DM, Davis I, Danguy HT, *et al.* Clinical role of F-18 fluorodeoxyglucose positron emission tomography for detection and management of renal cell carcinoma. J Urol 2001;166:825-30.
9. Martínez de Llano SR, Delgado-Bolton RC, Jiménez-Vicioso A, Pérez-Castejón MJ, Carreras Delgado JL, Ramos E, *et al.* Meta-analysis of the diagnostic performance of 18F-FDG PET in renal cell carcinoma. Rev Esp Med Nucl 2007;26:19-29.
10. Kumar R, Shandal V, Shamim SA, Jeph S, Singh H, Malhotra A. Role of FDG PET-CT in recurrent renal cell carcinoma. Nucl Med Commun 2010;31:844-50.
11. Cheow HK, Joseph JA, Balan KK. Large renal cell carcinoma isometabolic with normal liver on F-18 FDG PET scan. Clin Nucl Med 2004;29:488-90.
12. Oyama N, Okazawa H, Kusukawa N, Kaneda T, Miwa Y, Akino H, *et al.* 11C-Acetate PET imaging for renal cell carcinoma. Eur J Nucl Med Mol Imaging 2009;36:422-7.
13. Shreve P, Chiao PC, Humes HD, Schwaiger M, Gross MD. Carbon-11-acetate PET imaging in renal disease. J Nucl Med 1995;36:1595-601.
14. Divgi CR, Pandit-Taskar N, Jungbluth AA, Reuter VE, Gönen M, Ruan S, *et al.* Preoperative characterisation of clear-cell renal carcinoma using iodine-124-labelled antibody chimeric G250 (124I-cG250) and PET in patients with renal masses: A phase I trial. Lancet Oncol 2007;8:304-10.
15. Hes FJ, Slootweg PJ, van Vroonhoven TJ, Hené RJ, Feldberg MA, Zewald RA, *et al.* Management of renal cell carcinoma in von Hippel-Lindau disease. Eur J Clin Invest 1999;29:68-75.
16. Lenders JW, Eisenhofer G, Mannelli M, Pacak K. Phaeochromocytoma. Lancet 2005;366:665-75.
17. Richards FM, Webster AR, McMahon R, Woodward ER, Rose S, Maher ER. Molecular genetic analysis of von Hippel-Lindau disease. J Intern Med 1998;243:527-33.
18. Taïeb D, Sebag F, Barlier A, Tessonnier L, Palazzo FF, Morange I, *et al.* 18F-FDG avidity of pheochromocytomas and paragangliomas: A new molecular imaging signature? J Nucl Med 2009;50:711-7.
19. Thoren KL, Balingit AG, Billingsley J. Multiple pheochromocytomas in a patient with blurred vision. Clin Nucl Med 2008;33:597-601.
20. Fernández-del Castillo C, Warshaw AL. Cystic tumors of the pancreas. Surg Clin North Am 1995;75:1001-16.
21. Buetow PC, Rao P, Thompson LD. From the Archives of the AFIP. Mucinous cystic neoplasms of the pancreas: Radiologic-pathologic correlation. Radiographics 1998;18:433-49.
22. Reubi JC, Kvols L. Somatostatin receptors in human renal cell carcinomas. Cancer Res 1992;52:6074-8.
23. Ambrosini V, Campana D, Allegri V, Opocher G, Fanti S. 68Ga-DOTA-NOC PET/CT detects somatostatin receptors expression in von hippel-lindau cerebellar disease. Clin Nucl Med 2011;36:64-5.

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