Unusual Diagnosis of Von Hippel Lindau Syndrome on PET/CT – Case Report and Brief Review of Literature

Case Report

Maria M. D'Souza, Rajnish Sharma, Madhavi Tripathi, Abhinav Jaimini, Dinesh Singh, Anupam Mondal

Division of PET Imaging, MIRC, Institute of Nuclear Medicine and Allied Sciences, Brig. SK Majumdar Marg, Delhi, India

(Received 16 November 2009, Accepted 3 December 2009)

ABSTRACT

We report an unusual case of a young male with cerebellar hemangioblastoma treated previously for medullary carcinoma of thyroid, whose PET/CT scans revealed a constellation of findings that suggested the rare Von Hippel Lindau syndrome. The diagnosis was clinched by confirming the findings on whole body contrast enhanced computed tomography (CECT) and contrast enhanced magnetic resonance imaging (CEMR). The report highlights the need to carefully evaluate subtle findings on PET/CT that could be missed or misinterpreted as other diagnoses. It also adds to the existing literature of two cases with Von Hippel Lindau syndrome and medullary carcinoma of thyroid.

Key words: Von Hippel Lindau syndrome, Medullary carcinoma, PET/CT

Iran J Nucl Med 2009;17(2):50-54

Corresponding author: Dr. Maria M D'Souza, Division of PET Imaging, MIRC, Institute of Nuclear Medicine and Allied Sciences, Delhi – 110054, India
E-mail: maria.md@rediffmail.com

INTRODUCTION

A detailed evaluation of PET/CT findings, however subtle, in every oncology patient, may at times, unexpectedly lead to the identification of unusual features, which when interpreted in the proper clinical context, can facilitate the diagnosis of rare disorders or syndromes. We report here, a rare, clinically unsuspected case of Von Hippel Lindau (VHL) syndrome in a patient with a past history of medullary carcinoma thyroid, wherein the diagnosis was made on PET/CT and confirmed by subsequent ancillary investigations.

CASE REPORT

A 39 year old man operated for left cerebellar hemangioblastoma underwent ^{18}FDG -PET/CT scan after completion of radiotherapy to rule out residual and/or metastatic disease. Several years previously, he had been diagnosed to have medullary carcinoma of thyroid, for which he underwent total thyroidectomy and lymphnode dissection. The PET/CT scan was done 60 minutes after injection of 370MBq ^{18}FDG, with a whole body Full Ring PET/CT camera (Discovery STE16-GE, USA). The scan revealed a photopenic defect in the left cerebellar hemisphere corresponding to the craniotomy site (Fig 1A) with multiple small, mildly photopenic defects in the posterior fossa (Fig 1B). In addition, a focus of low grade uptake in the cervical cord (Fig 2A), a nodule with intense FDG uptake in the right lung, bilateral renal masses with low grade uptake and multiple pancreatic and renal cysts (Fig 3A) were observed.

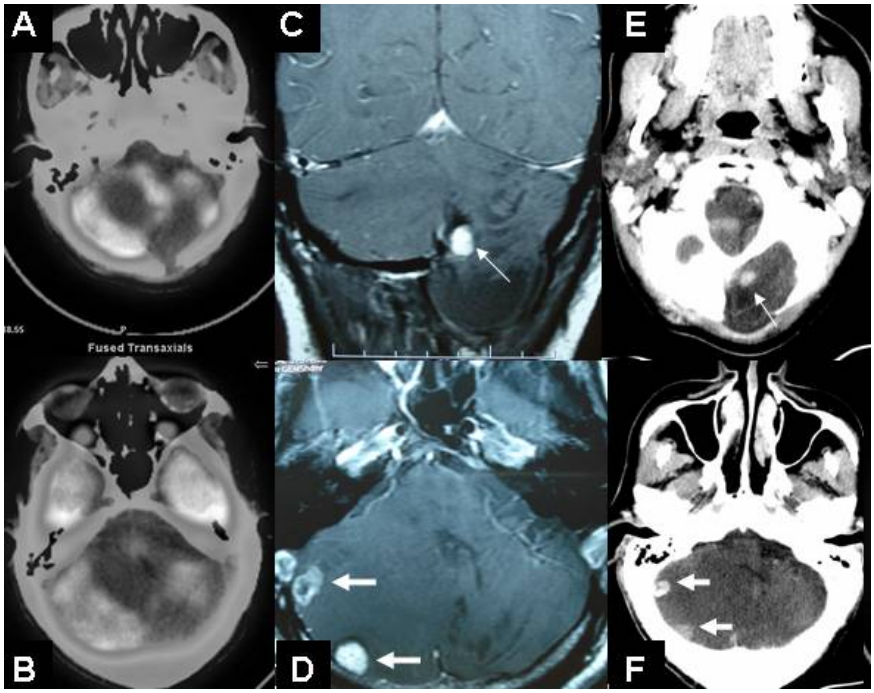

Figure 1. Axial PET/CT fusion image showing a photopenic defect in the left cerebellar hemisphere (A) seen on coronal CEMR (C) and axial CECT images (E) as a residual tumor with solid enhancing mural nodule (thin arrows) and cystic component herniating through the calvarial defect. Multiple mildly photopenic defects on PET/CT fusion image (B) seen as small intensely enhancing masses abutting on the pia mater (thick arrows) with surrounding edema in right cerebellar hemisphere on axial CEMR (D) and CECT (F).

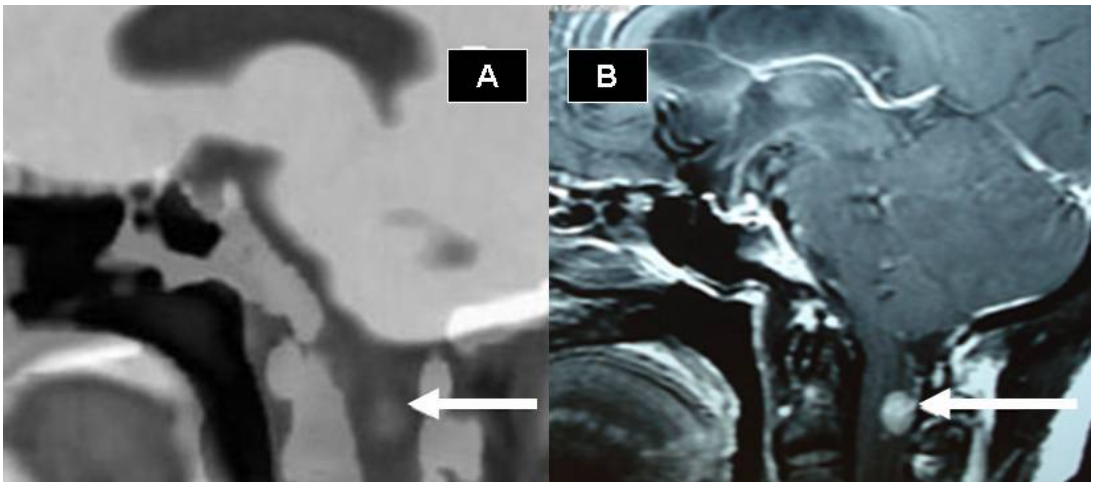

Figure 2. Focus of low grade ^{18}FDG uptake on sagittal PET/CT fusion image of cervical cord (A) seen on CEMR as an enhancing nodule (B).

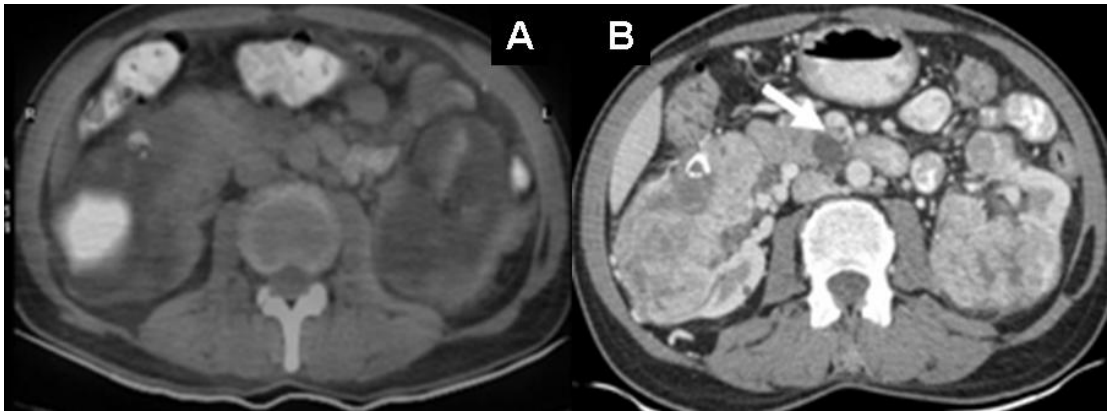

Figure 3. Low grade FDG uptake noted in bilateral renal masses on PET/CT fusion image (A) well seen on axial CECT abdomen (B), with calcification in right renal mass and multiple cysts in both kidneys and head of pancreas (thick arrow).

Based on these findings, the initial impression was residual tumour with multiple metastases to the brain, spinal cord, lung, and kidneys. However, correlating the clinical profile of a male with cerebellar hemangioblastoma and subtle PET/CT findings of multiple renal and pancreatic cysts, an alternate diagnosis of Von Hippel Lindau syndrome (VHL) was proposed.

Therefore, the patient underwent whole body contrast enhanced CT (CECT) at the same session, followed by contrast enhanced MRI (CEMR) of the brain and spine. The residual tumour was visible as a solid enhancing mural nodule with associated cystic component herniating through the post-operative calvarial defect on CEMR (Fig.1C) and CECT (Fig.1E). Multiple smaller but intensely enhancing masses abutting the pia mater in the posterior fossa were detected on CEMR (Fig.1D) and CECT (Fig.1F) suggesting multiple

hemangioblastomas. An intensely enhancing intradural nodule was noted in the cervical cord on CEMR (Fig.2B) and CECT. The metastatic pulmonary nodule, bilateral renal masses, renal and pancreatic cysts were well delineated on CECT (Fig.3B). Putting these findings together, the diagnosis of VHL syndrome was confirmed.

DISCUSSION

Von Hippel Lindau disease is a rare disorder characterised by multiple hemangioblastomas in the central nervous system and retina. In addition, other neoplastic lesions such as endolymphatic sac tumors, renal cell carcinoma, pancreatic cysts and tumors, pheochromocytoma, and epididymal cystadenomas, are sometimes present (1). The condition has been traditionally categorised as one of the neurocutaneous syndromes (phakomatosis) and is transmitted as an autosomal dominant disorder. The prevalence of VHL has been estimated to be between 1:35,000-1:40,000 (2, 3).

Melmon and Rosen proposed criteria for VHL several decades back (4), whereby clinical diagnosis is made on the basis of a family history of retinal or CNS hemangioblastoma, and either the presence of a hemangioblastoma or visceral lesion (renal tumors, pancreatic cysts or tumors, pheochromocytoma, papillary cystadenomas of the epididymis) (5). In the absence of clear family history, two or more hemangioblastomas or one hemangioblastoma and a visceral manifestation is required to confirm diagnosis (2) as in the index case.

Cerebellar hemangioblastomas are found in 44-72% of cases of VHL (1). They may be seen as photopenic areas on PET/CT owing to their low malignant potential. Spinal hemangioblastomas which can occur in 13-59% cases (5, 6) may be present throughout the cord, along nerve roots or cauda equina. They may be intramedullary, extramedullary or partially intra and extramedullary as in the index case. Renal cysts are encountered in 59-63% of patients, with renal cell carcinoma occurring in a large number of cases (1). Pancreatic and epididymal cysts are also frequent in these patients (7). Although only about 7-18% of all patients with VHL have pheochromocytomas (5), the prevalence can be very high among selected families. Four classic VHL disease phenotypes have been described based on the likelihood of pheochromocytoma or renal cell carcinoma (8). In the index case, the diagnosis of VHL was confirmed based on the recognition of a link between the patient's clinical profile and the subtle findings on PET/CT. This highlights the necessity of having a good background skill of interpreting not only the pattern of radio-trace uptake, but also the anatomical delineation of lesions on the CT component. But for this, the index case would have been assumed to have multiple metastases of the primary tumour rather than VHL.

Detailed literature review shows that medullary carcinoma is not part of the VHL syndrome. However, two cases of medullary thyroid carcinoma developing in patients with VHL germline mutations have been reported (9), based on which it was suggested that a VHL mutation could be the second hit required to initiate development of medullary carcinoma in people with a genetic predisposition. However such a link can be neither proved nor disproved in the index case. This also highlights the need to follow patients with VHL for the development of tumours not currently recognised as part of the syndrome.

CONCLUSION

This case report highlights the diagnosis of a rare disorder that was made by astute examination of the clinical profile with careful correlation of the PET and CT scans in PET/CT.

REFERENCES

1. Choyke PL, Glenn GM, Walther MM, Patronas NJ, Linehan WM, Zbar B et al. von Hippel-Lindau disease: genetic, clinical, and imaging features. Radiology. 1995;194(3):629-642.
2. Maher ER, Iselius L, Yates JR, Littler M, Benjamin C, Harris R et al. von Hippel Lindau disease: a genetic study. J Med Genet 1991;28(7): 443-447.
3. Neumann HP, Wiestler OD. Clustering of features of von Hippel-Lindau syndrome: evidence for a complex genetic locus. Lancet. 1991;337(8749):1052-1054.
4. Melmon KL, Rosen SW. Lindau's disease. Review of the literature and study of a large kindred. Am J Med. 1964;36:595-617.
5. Maher ER, Yates JR, Harries R, Benjamin C, Harris R, Moore AT et al. Clinical features and natural history of von Hippel-Lindau disease. Q J Med. 1990;77(283):1151-1163.
6. Filling-Katz MR, Choyke PL, Oldfield E, Charnas L, Patronas NJ, Glenn GM et al. Central nervous system involvement in Von Hippel-Lindau disease. Neurology. 1991;41(1):41-46.
7. Seizinger BR, Smith DI, Filling-Katz MR, Neumann H, Green JS, Choyke PL et al. Genetic flanking markers refine diagnostic criteria and provide insights into the genetics of Von Hippel Lindau disease. Proc Natl Acad Sci U S A. 1991;88(7):2864-2868.
8. Zbar B, Kishida T, Chen F, Schmidt L, Maher ER, Richards FM et al. Germline mutations in the Von Hippel-Lindau disease (VHL) gene in families from North America, Europe, and Japan. Hum Mutat. 1996;8(4):348-357.
9. Koch CA, Brouwers FM, Vortmeyer AO, Tannapfel A, Libutti SK, Zhuang Z et al**.** Somatic VHL gene alterations in MEN2-associated medullary thyroid carcinoma. BMC Cancer 2006; 6:131.