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Case Report

18F-FDG-PET/CT & 123I-MIBG-SPECT Imaging in Melanoma Differentiation: A Case Report

Mesharck Gariba[1] and Emma Louise Cox[2]*

[1]*Department of Life Science, University of Hull (Alumni), England, UK*

[2]*Department of Nursing, Central Bedfordshire College, England, UK*

Abstract

Case presentation: A 78-year-old male referred for diagnostic medical imaging reveals a mass of the left posterior neck which has been biopsied to confirm melanoma. An FDG-PET/CT scan, with contrast enhancement, reveals multiple lesions around the body including the pituitary, bones and the retroperitoneal region.

Discussion: The medical imaging of the mass also shows size and hypodensity of the retroperitoneal lesion which lead to additional medical imaging modality (123I-MIBG-SPECT) to identify possible paraganglioma. The results from the two medical imagining modalities were compared to understand the extent of and distinguish the melanoma and paraganglioma in the patient as well as offering explanation of incidental tracer uptake.

The recommended treatment for this patient was largely based on his fitness due to his age, as well as detailed biopsy results, alternative for treating the cancer is presented as well as the rationale behind the need for future advanced medical imaging.

Keywords: 18F-FDG-PET/CT scan; Melanoma; 123I-MIBG-SPECT scan; Biopsy

Case Presentation

The patient is a 78-year-old male presenting with a mass on the left side of the neck. A diagnostic biopsy of the mass reveals melanoma which leads to a series of scans, 18F-FDG-PET/CT (Fluorodeoxyglucose-Positron Emission Tomography/Computed Tomography) and 123I-MIBG-SPECT (Metaiodobenzylguanidine-Single Photon Emission Tomography), intended to differentiate the extent of disease [1,2]. It is anticipated that the biopsy results, patient physiology and interpretation of the scan results guide in determining the appropriate medical treatment plan and the prognosis of the patient.

Discussion

Melanoma

Melanoma is cutaneous cancer where malignant cells arise from skin pigment-producing cells (melanocytes) and are commonly observed as the irregular shaping and/or discolouring of new or rapidly growing moles [3].

The skin is considered as the largest organ in the body and its epidermis (outer layer) is entirely externally exposed, it absorbs more natural (Ultra-Violet) UV radiation from the sun than any other part of the body. Exposure to UV light has been linked to many, if not all, forms of skin cancers and it is estimated that UV exposure plays a role in (it is not directly responsible for) the majority of skin cancers, including melanoma. Similarly, the use of sunbeds and tanning increases the exposure the UV radiation in a process designed to increase the pigmentation levels in melanocytes to achieve a darker complexion. Due to this deliberate additional UV exposure, studies show a correlation between the incidence of melanoma and sunbed/tanning use [4-6].

There are also hereditary genetic mutations of the genes such as CDKN2A which can be passed down from parent to child [5]. Offspring who inherit genetic mutations in select genes are shown to be at higher risk of developing cancers such as melanoma. While the hereditary passing of mutations leading to melanoma is not as likely a cause as environmental factors, an estimated 10% of melanoma cases show a close relative also with the disease [7-9].

With the environmental and hereditary causes of melanoma in mind, it is important to consider the risk factors which contribute towards the likelihood of developing the disease. Studies have shown that demographic variations such as differences in natural complexion dictate the probability of developing melanoma from factors relating to UV exposure. For example, darker-skinned individuals are seen to resist melanomas resulting from UV exposure more than fairer skinned individuals [4].

Biopsy

In addition to the melanoma confirmation, tests performed on the biopsy sample could also provide insight into the staging of the disease and the genetic alterations in the melanoma. This information can be used to indicate prognosis and guide a treatment plan, as certain therapies respond better to different cancer staging and targeted therapies are only deployed against cancers with expressions to which the therapy is designed. An example of a genetic mutation which biopsy test could confirm is the presence of a mutated BRAF gene, which is observed in approximately 50% of melanomas. The

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***Corresponding author:** Mesharck Gariba, Department of Life Science, University of Hull (Alumni), Central Bedfordshire College, England, UK, E-mail: megshito@yahoo.com

presence of this mutation will guide decisions as to how to combat the disease most efficiently [10].

FDG-PET/CT

The patient also underwent an 18F-FDG-PET/CT scan which initially revealed six diagnostically relevant regions of FDG uptake. 18F-FDG-PET/CT is widely considered to be among the most powerful imaging modalities when detecting, staging and monitoring cancers such as advanced melanoma. This is due to the superior sensitivity and specificity saw on PET/CT compared to other imaging modalities, for example, standalone PET or CT which lack the combined functional and anatomical data. MRI (Magnetic Resonance Imaging) scans could be considered a viable alternative; however, Pfannenberg & Schwenzer shows that only a few early studies compare the diagnostic practicality of MRI against PET/CT [11]. In the future, PET/MRI could prove to be a stronger diagnostic tool due to the simultaneous data acquisition, however, given that the infrastructure for PET/CT is readily supported compared to PET/MRI, the use of PET/CT appears to remain the most reliable diagnostic tool for confirming the staging of melanoma and identifying the location of metastases. The use of CT coupled with PET provides the important anatomical data with which the PET data can be overlaid. This allows the region of PET tracer uptake to be mapped precisely to a point in the anatomy. As CT provides a 360-degree map of the anatomy, this modality is considered superior to most other anatomical modalities such as planar x-ray which would not provide the 3-dimensional breakdowns. As a result, the use of CT coupled with PET realises the option of computerised 3-dimensional reconstructions [12-14].

It should be noted that despite the aforementioned superior sensitivity of PET/CT compared with other modalities, PET sensitivity for lesions less than 1cm diameter is considered poor. This means that the use of a PET scan may not have been ideal in cases of early-stage melanoma, indicating that the biopsy strongly suggests melanoma of an advanced stage. Furthermore, the use of combined PET/CT requires that the images should undergo attenuation correction to produce an image which reliably shows regions of interest against its respective anatomical location. The patient moving and breathing during the scan can also influence the anatomical features shown on the resulting images [11].

The multiple lesions observed from the 18F-FDG-PET/CT uptake further suggest that the melanoma is of an advanced stage; stage IV, having spread away from the primary tumour in the left of the neck. The breakdown of the PET/CT confirms that the mass located on the neck is indeed a primary melanoma (as opposed to a metastasis) as this is the only lesion which appears on the skin. As well as the six lesions outlined from the PET/CT scan, significant FDG uptake is observed in the bladder as well as moderate uptake in the brain and heart. This is because the FDG tracer used in this PET scan targets areas of increased glucose uptake. While this makes FDG an ideal target for cancers of unregulated growth, it also accumulates in areas such as the brain and heart which naturally have higher levels of glycolysis than other areas of the body. The intense uptake in the bladder is explained as the FDG tracer is excreted through the renal pathway. For these reasons, these areas of uptake should be excluded when considering regions of potential cancer [15,16].

The remaining six regions of FDG uptake, from the head down, are the pituitary gland (Figure 1), the left posterior neck (Figure 2), the right T9 vertebra (Figure 3), the left retroperitoneal region (Figure 4), the left sacrum (Figure 5) and the right superior pubic ramus (Figure 6).

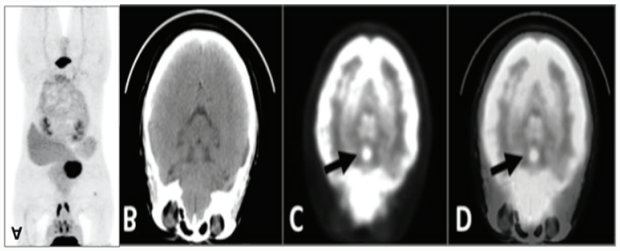

Figure 1: (A) Shows an area of diffused abnormal hypermetabolism, (B) increase metabolic activity of FDG, (C) Corresponding CT scan showing the elevated level of FDG metabolism (D) shows fusion of images. The images are indication of possible metastasis or pituitary adenoma.

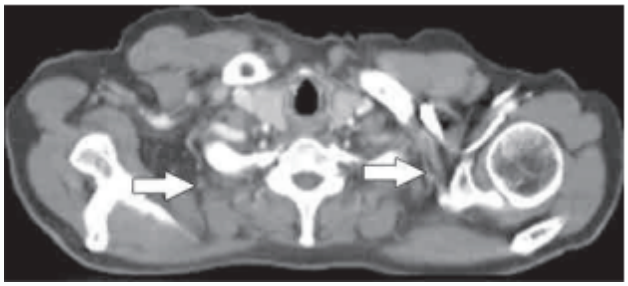

Figure 2: Image shows an intense FDG uptake in the neck and a site of the biopsy indicates melanoma.

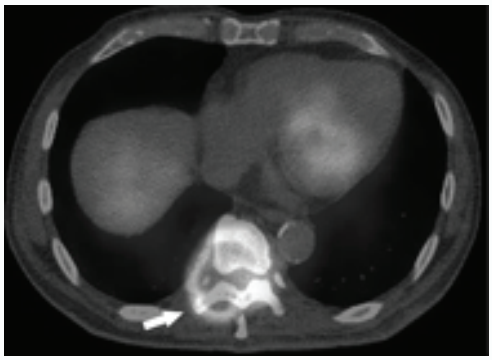

Figure 3: Reveals abnormal uptake in the lesion of T9-vertebral body an indicating metastasis.

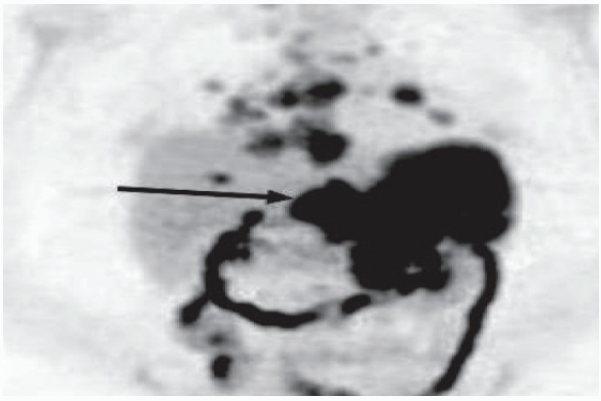

Figure 4: Image shows a widespread involvement of the retroperitoneal mass reveal an intense FDG uptake.

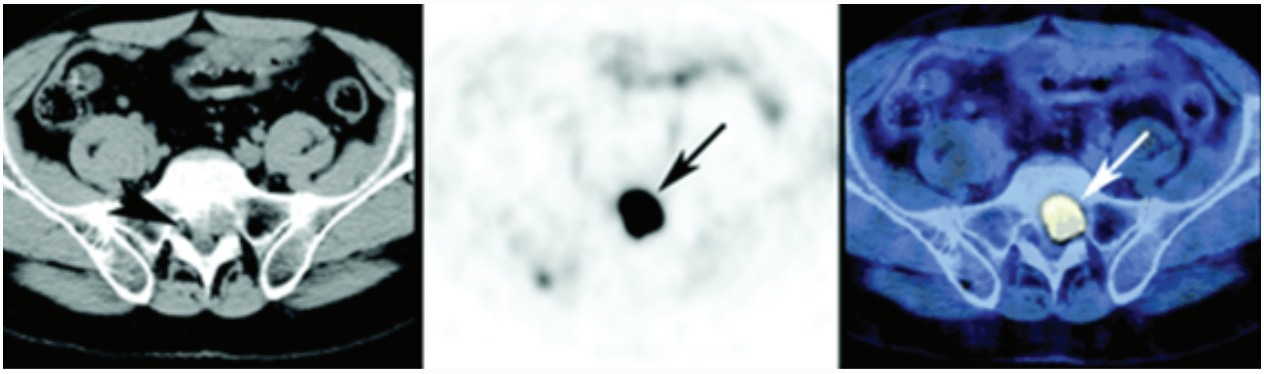

Figure 5: The PET/CT scan reveal metastatic deposit in the sacrum.

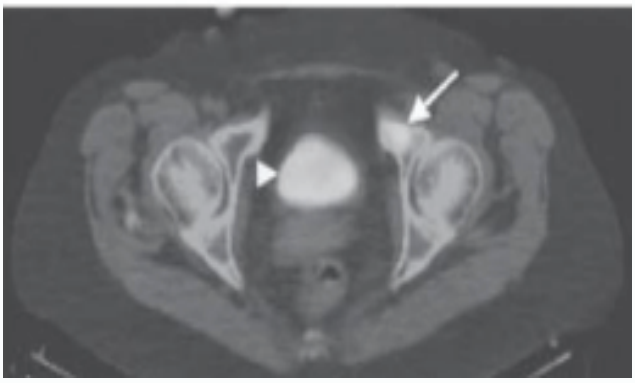

Figure 6: Image shows intense uptake in the superior pubic ramus and also an incidental FDG uptake in the bladder.

The Table 1 below is a summary of the regions of the FDG uptake in the patient with regards to the relative size, the extend of growth and their characteristics.

The CT scan performed as part of the PET/CT was a contrast-enhanced CT, meaning that a contrast agent is applied to the patient, likely through injection, before the scan resulting in a better quality image, allowing for stronger differentiation between organs and surrounding tissue densities. This makes imaging the head and brain much clearer than CT without the contrast enhancement. As melanoma is known to metastasize to the brain, the use of contrast-enhanced CT is a better choice of modality in this instance as opposed to a regular CT without contrast enhancement [17-19]. The contrast-enhanced CT also reveals additional characteristics on the left retroperitoneal mass showing hypodensity around the centre of the mass; a distinction which contrast enhancement intensifies through clearer boundaries of tissue density. The proximity of the left retroperitoneum mass to the adrenal glands, the size of the mass compared to the other lesions and the central hypodensity observed support a possible paraganglioma diagnosis, where the hypodense, heterogeneous appearance could be a result of necrosis, calcification and/or haemorrhaging in the centre of the tumour. Should the retroperitoneal lesion prove to be a paraganglioma, it is most likely that this would be the primary tumour due to its size and location. A paraganglioma diagnosis raises an additional possible source of metastasis observed in the remaining four regions of FDG uptake [20,21].

MIBG-SPECT

To differentiate which of the metastases are secondary to the melanoma and which are secondary to the paraganglioma, an additional scan using 123I-MIBG as a tracer instead of FDG can be used (Table 2). Unlike a biopsy, this non-invasive functional imaging technique can be compared against the FDG-PET/CT uptake levels and shows which areas contain uptake consistent with paraganglioma cancers, to which 123I-MIBG is more sensitive [22]. The better sensitivity and specificity towards paragangliomas makes MIBG a preferential tracer over other SPECT tracers such as Tc99m, however, the use of this tracer requires thyroid blockade treatment before imaging as the thyroid has a high Iodine uptake [23]. The biopsy of each lesion would be avoided at this stage as it is an invasive test and the paraganglioma diagnosis can be supported through non-invasive imaging.

123I-MIBG-SPECT can be used in particular to target cancers of paraganglioma and pheochromocytoma because the 123I-MIBG tracer is an analog of norepinephrine, which is mediated by the norepinephrine transporter system. This means that the 123I-MIBG analogue is highly sensitive to neuroendocrine cancers, such as paraganglioma and less so towards other cancers [22,24-26]. This feature supports the confidence in the 123IMIBG and FDG comparison, which will provide evidence towards differentiating melanoma and paraganglioma metastases.

The 123I-MIBG-SPECT scan reveals uptake in five regions: the retroperitoneal mass, the right T9 vertebra, the left sacrum, the right superior pelvic ramus and the liver. This uptake is consistent with the FDG uptake except for the additional liver uptake and the lack of uptake in the pituitary gland and neck lesion.

The regions with 123I-MIBG uptake indicate the paraganglioma and its metastasis whereas those regions which were seen to have FDG uptake with no 123I-MIBG uptake indicate the melanoma with its metastasis. As those regions of only FDG uptake are limited to the masses located on the neck and the pituitary gland, this possibly alters this initial interpretation of the extent of melanoma throughout the patient, showing only a single possible metastasis in the pituitary. Furthermore, it is plausible that the pituitary gland lesion is, in fact, pituitary adenoma onset through the paraganglioma as literature is supportive of the notion that pituitary neoplasms such as adenomas can arise in coincidence with paraganglioma and pheochromocytoma [27,28]. However, it would be unusual to see the FDG uptake in the pituitary should the lesion be adenoma [29]. This, along with the

fact that biopsy results appear to have prompted a full-body PET/CT further suggests that melanoma has metastasised and the MIBG scan supports that the pituitary uptake is likely the only metastasis of the melanoma. Note that it could be argued that there is a minimal trace of FDG uptake seen in the liver and kidney; however, it is probable that this interpretation would not be clinically relevant and would also be explained through normal metabolism.

As the FDG tracer shows the extent of glycolysis in a region, it is expected that the FDG uptake is observed in all the cancerous legions, however, it noted that the MIBG tracer expressed an uptake in the liver where the FDG tracer did not. Upon observation of the CT and planar x-rays images provided for the liver in this uptake, no anatomical abnormality is distinguished. Based on the lack of FDG uptake, the lack of anatomical supported data and an understanding of the normal physiological pathways of MIBG excretion, it is believed that liver uptake is of little concern and unrelated to any cancer [30]. The basis of this exclusion is similar to that of the FDG uptake exclusion seen in the heart, brain and bladder.

Treatment Recommendations and Future Imaging

A common treatment consideration for both benign and malignant paraganglioma is surgery with the intent of removing the tumours. However, given the patient age of 78 and the sensitive area of the mass located on the vertebra, it is advised that a thorough physiological assessment of the patient is undertaken before determining the rationale of surgery. Radiotherapy is shown to be another viable option, particularly for patients with bone metastases and maybe a better course of action to the surgery. Chemotherapy is shown to have little long term benefits to paragangliomas which have metastasised. It is recommended that radiotherapy is performed on the secondary paragangliomas and surgery is considered for the primary tumour, given its size, and followed up with radiotherapy to any residual mass. This treatment recommendation assumes that the uptake in the liver is nonmalignant [31].

Given the patient age, brain surgery to treat the melanoma to the pituitary gland and even the lesion to the neck may be deemed too high risk. Likewise, radiotherapy may cause some small collateral damage to healthy tissue which is much higher risk around the brain. It is recommended that, given the stage of the melanoma, combined chemotherapy treatment is optimal. Exact chemotherapy agents used would depend on the results of the biopsy, for example, BRAF inhibitors [32].

To monitor the response to treatment, follow up scans of both PET/CT and MIBG-SPECT would be performed to assess the changes in lesion size. In chemotherapy treatment, this would typically occur after 2 or 3 cycles of treatment. Should surgery be performed, immediate scans would also be undertaken to confirm that the entire intended lesion was removed and how much remains [33].

Should the patient present with any additional symptoms suggestive of liver dysfunction (yellowing eyes etc.), it may be deemed necessary to perform an additional scan of the liver such as an MRI to gather any evidence of abnormality. Otherwise, the monitoring of response to treatment would provide more clues as to the true nature of the liver uptake, which is believed to be normal metabolic activity [15,16].

References

1. Cantalamessa A, Caobelli F, Paghera B, Caobelli A, Vavassori F. Role of 18F-FDG PET/CT, 123I-MIBG SPECT, and CT in restaging patients affected by malignant pheochromocytoma. Nucl Med Mol Imaging. 2011;45(2):125-31.
2. Bleeker G, Tytgat GAM, Adam JA, Caron HN, Kremer LCM, Hooft L, et al. 123I-MIBG scintigraphy and 18F-FDG-PET imaging for diagnosing neuroblastoma. Cochrane Database Syst Rev. 2015;2015(9):CD009263.
3. NIH - National Cancer Institute (No Date) Melanoma of the Skin.
4. D'Orazio J, Jarrett S, Amaro-Ortiz A, Scott T. UV Radiation and the Skin. Int J Mol Sci. 2013;14(6):12222-48.
5. American Cancer Society. What causes melanoma skin cancer? 2016.
6. Erdei E, Torres SM. A new understanding in the epidemiology of melanoma. Expert Rev Anticancer Ther. 2010;10(11):1811-23.
7. Hayward NK. New developments in melanoma genetics. Curr Oncol Rep. 2000;2(4):300-6.
8. Hayward NK. Genetics of melanoma predisposition. Oncogene. 2003;22(20):3053-62.
9. Ranaweera A. Genetics of melanoma. 2011.
10. American Cancer Society. What causes melanoma skin cancer? 2016.
11. Pfannenberg C, Schwenzer N. [Whole-body staging of malignant melanoma: advantages, limitations and current importance of PET-CT, whole-body MRI and PET-MRI]. Radiologe. 2015;55(2):120-6.
12. Almuhaideb A, Papathanasiou N, Bomanji J. 18F-FDG PET/CT Imaging in Oncology. Ann Saudi Med. 2011;31(1):3-13.
13. Griffeth LK. Use of PET/CT scanning in cancer patients: technical and practical considerations. Proc (Bayl Univ Med Cent). 2005;18(4):321-30.
14. Subesinghe M, Maria Marples M, Scarsbrook AF, Smith JT. Clinical impact of 18F-FDG PETCT in recurrent stage III/IV melanoma: a tertiary centre Specialist Skin Cancer Multidisciplinary Team (SSMDT) experience. Insights Imaging. 2013;4(5):701-9.
15. Sarji SA. Physiological uptake in FDG PET simulating disease. Biomed Imaging Interv J. 2006;2(4):e59.
16. Shreve PD. Anzai Y, Wahl RL. Pitfalls in Oncologic Diagnosis with FDG PET Imaging: Physiologic and Benign Variants. Radiographics. 1999;19(1):61-77.
17. AIM at Melanoma Foundation. Brain Metastases. 2014.
18. Cancer Research UK. CT scan. 2015.
19. Rawson JV, Pelletier AL. When to Order Contrast-Enhanced CT. 2013. Am Fam Physician. 2013;88(5):312-6.
20. Baez JC, Jagannathan JP, Krajewski K, O'Regan K, Zukotynski K, Kulke M, et al. Pheochromocytoma and paraganglioma: imaging characteristics. Cancer Imaging. 2012;12(1):153-62.
21. The American Association of Endocrine Surgeons. Paraganglioma (adrenaline-producing tumour outside the adrenal gland).
22. Milardovic R, Corssmit EP, Stokkel M. Value of 123I-MIBG Scintigraphy in Paraganglioma. Neuroendocrinology. 2010;91(1):94-100.
23. Mahdoubi K. Protecting the thyroid: I-123 MIBG blockade passes the test. 2014.
24. Wiseman GA, Pacak K, O'Dorisio MS, Neumann DR, Waxman AD, Mankoff DA, et al. Usefulness of 123I-MIBG Scintigraphy in the Evaluation of Patients with Known or Suspected Primary or Metastatic Pheochromocytoma or Paraganglioma: Results from a Prospective Multicenter Trial. J Nucl Med. 2009;50(9):1448-54.
25. Kantorovich V, Pacak K. Pheochromocytoma and paraganglioma. Prog Brain Res. 2010;182:343-73.
26. Ilias I, Divgi C, Pacak K. Current role of MIBG in the diagnosis of pheochromocytoma and medullary thyroid cancer. Semin Nucl Med. 2011;41(5):364-8.

27. Perez FG, Gil AL, Robledo M, Iglesias P, Artero CV Pituitary adenoma associated with pheochromocytoma/paraganglioma: A new form of multiple endocrine neoplasias. Endocrinol Nutr. 2016;63(9):506-8.

28. Denes J, Swords F, Xekouki P, Kumar AV, Maher ER, Wassif CA, et al. Familial Pituitary Adenoma and Paraganglioma Syndrome -A Novel Type of Multiple Endocrine Neoplasia. 2012.

29. Ryu SI, Tafti BA, Skirboll SL. Pituitary adenomas can appear as hypermetabolic lesions in (18) F-FDG PET imaging. J Neuroimaging. 2010;20(4):393-6.

30. Nakajo M, Shapiro B, Copp J, Kalff V, Gross MD, Sisson JC, et al. The normal and abnormal distribution of the adrenomedullary imaging agent m-[I-131] iodobenzylguanidine (I131 MIBG) in man: evaluation by scintigraphy. J Nucl Med. 1983;24(8):672-82.

31. Fliedner SMJ, Lehnert H, Pacak K. Metastatic Paraganglioma. Semin Oncol. 2010; 37(6):627-37.

32. Tan WW. Malignant Melanoma Treatment Protocols. 2016.

33. Chemocare. How Can We Tell if Chemotherapy is Working? 2016.