Hibernoma as an incidental finding in the ^{18}F-FDG PET/CT of a patient with melanoma

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Despite being benign tumors, hibernomas show intense fluorine-18-fluorodeoxyglucose uptake, as they are derived from brown fat, which is frequently seen as hypermetabolic fatty areas on PET/CT. We present the case of a patient with cutaneous melanoma, diagnosed with a cervical hibernoma mimicking a metastatic lymph node at fluorine-18-fluorodeoxyglucose PET/CT. Being aware of the metabolic behavior and radiologic appearance of this entity may prevent reporting false-positive lesions, especially in an oncologic setting. ***Melanoma Res*** **00:000–000**

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Introduction

PET/CT with fluorine-18-fluorodeoxyglucose (^{18}F-FDG) represents an established imaging tool for diagnosis, staging, and restaging of multiple neoplasms, based on the principle that malignant cells have higher metabolic needs and, therefore, show an increased glucose consumption in the form of ^{18}F-FDG, allowing PET imaging. However, glucose is the energetic substrate of many physiological processes and benign conditions, which can represent a source of pitfalls and false-positive findings in ^{18}F-FDG PET/CT. Hibernomas are uncommon benign fatty tumors with high avidity for ^{18}F-FDG because of their mitochondrial content. Keeping this entity in mind, regarding its both metabolic behavior and radiologic appearance, could prevent a wrong interpretation of this pitfall.

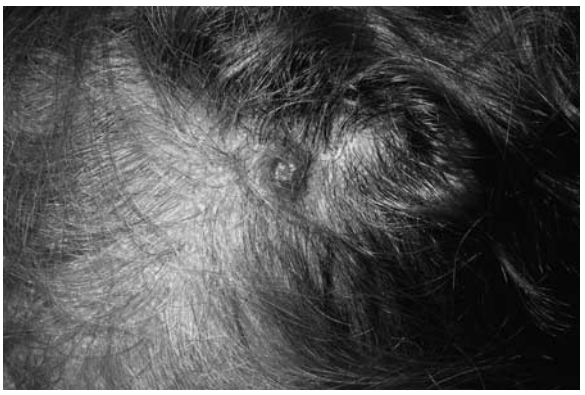
Case report

A 63-year-old woman with a history of hypertension and dyslipidemia was referred to the Department of Dermatology with a nodular, pigmented lesion of 9 mm of diameter that had been growing for 4 months in her left temporal area (Fig. 1). A biopsy confirmed a nodular melanoma with a Breslow index of 4.78 mm and focal ulceration, so a wider excision with 2-cm margins was performed, as well as a sentinel lymph node biopsy, obtaining five lymph nodes, none of them with metastatic cells. Therefore, the lesion was staged as a IIC melanoma with high-risk features, and a PET/CT with ^{18}F-FDG was requested to rule out other sites of disease.

A whole-body PET/CT with a dedicated head and neck acquisition was performed, detecting a highly hypermetabolic right cervical area [maximum standardized uptake value (SUV_{max}) 16.4; cervical level III] (Fig. 2a and b), without pathologic findings in the rest of the body. This image did not correlate with any anatomic structure at the low-dose computed tomography (CT) of the PET/CT, as only a mild increase in the density of the fat was detected (Fig. 2c). A contrast-enhanced CT was recommended, which suggested that the hypermetabolic area detected on the PET/CT corresponded to a necrotic lymph node (Fig. 2d).

Considering that necrotic tissues should not have such a high uptake of ^{18}F-FDG, and to rule out the possibility of a metastatic lymph node, even if contralateral to the primary lesion, an ultrasound-guided fine-needle aspiration biopsy of the area was requested. The neck ultrasound detected a heterogeneous lesion, not accessible to a needle aspiration. As two months had passed since the

Fig. 1



Clinical aspect of the nodular melanoma in the skin of the left temporal area.

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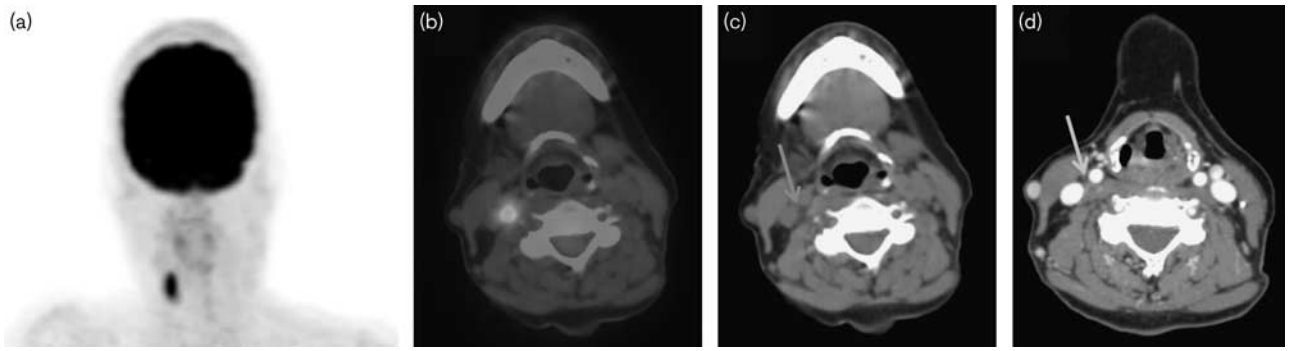
Fig. 2



Radiologic appearance of the hibernoma. (a) Maximum intensity projection of the baseline PET/CT showing a highly hypermetabolic focal area in the right neck ($SUV_{max} = 16.4$), located at cervical level III at the fusion images (b). However, at the low-dose computed tomography (CT) sequence (c), no apparent lesion was identified in this area (arrow), observing only a mild increase in the density of the fat. Therefore, a contrast-enhanced CT was performed (d), distinguishing a small nodular image with peripheral contrast enhancement (arrow), oriented as a necrotic lymph node. SUV_{max}, maximum standardized uptake value.

first PET/CT, another PET/CT was performed to update the situation of both the lesion and the rest of the body. On the new PET/CT, the hypermetabolic right cervical area showed a mild increase on activity ($SUV_{max} = 18.2$), without changes in shape or extension, even if it persisted with no anatomic correlation on the low-dose CT; there were no other findings in the rest of the body. Finally, a surgical excision of the lesion was performed, obtaining fragments of fatty tissue, histologically compatible with a hibernoma.

Discussion

PET/CT with ^{18}F-FDG is increasingly used in staging and follow-up of patients with melanoma, as the technique is becoming more available, and new therapies for melanoma improve survival and the possibility of alternative treatments if first line fails. However, as it is widely known, ^{18}F-FDG uptake in non-neoplastic tissues such as inflammatory or infective processes, or physiologically hypermetabolic areas as the bowel or the brown fat, can represent a source of false-positive results.

Two types of fatty tissue have been identified in mammals: white fat, which cells are specialized in storing energy and act as an insulator, and brown fat, from which adipocytes can generate heat as a response to hypothermia or ingestion of food, basically thanks to their high content in mitochondria [1]. Small mammals are rich in brown fat, but larger mammals often lose it as they grow old, remaining sometimes in the neck and supraclavicular areas, armpits, around big vessels in the mediastinum, paravertebral and intercostal spaces, and perirenal [2]. Because of its mitochondrial content, brown fat has a high uptake of ^{18}F-FDG, being detected on PET/CT, and sometimes representing a confounding factor in image interpretation [3].

In a study with 6867 patients, brown fat showed high ^{18}F-FDG uptake in 298 (4.33%) of them, being more prevalent in female and in those with lower weight and lower body mass index, with a range of SUV_{max} in brown fat between 1.6 and 23.3 [3]. It is also known that brown fat metabolism increases with cold [2], a common situation in PET/CT units and the reason why patients are often covered with a blanket during the radiopharmaceutical-uptake period and the scanning time.

Hibernomas are infrequent, slow-growing tumors, originating from brown fat [4]; their name is taken from fatty tissue of hibernating animals, to which they resemble. They represent less than 2% of benign fatty tumors [5], and macroscopically they are usually well-delimited, lobulated and partially encapsulated, showing a yellowish-brown color, sometimes with a mucoid surface. Contrary to classic lipomas, which are formed by univacuolated adipocytes with peripheral nuclei, hibernoma cells are multivacuolated with central nuclei; they are rich in mitochondria, and are associated with capillary proliferation and fibrovascular septa. Because of its high vascularization, core needle biopsy is not recommended [4]. They were classically considered to be located in places with persistence of fetal fatty tissue [2], though in a study with 170 cases, the most common location was the thigh, representing 30% of the total [4].

Few cases of hibernomas detected on PET/CT are described in scientific literature [6,7], all showing high hypermetabolism, with SUV_{max} over 10, as is the case of our patient; despite their benign nature, they show an elevated glucose metabolism because of their high mitochondrial content and rich vascularization. Differential diagnosis includes lipomas and liposarcomas. Radiologically, hibernomas are frequently heterogeneous on CT or MRI, as they can have septa, similar to normal fat. Sometimes a dominant vessel can be identified after intravenous contrast administration, with the presence of a large vessel within a fatty lesion being highly suggestive of

hibernoma [8]. Although hibernomas show a high ^{18}F-FDG uptake, lipomas are normometabolic, and liposarcomas tend to show lower SUV_{max} values [9], though there does not exist a cutoff value to reliably distinguish hibernomas and liposarcomas. Recent research describes that oral administration of propranolol one hour before the radiopharmaceutical injection significantly decreases ^{18}F-FDG uptake in hibernomas, and helps distinguish them from liposarcomas [10], though more research is needed before incorporating this procedure in routine practice.

In the reported case, bearing in mind the primary tumor and the location of the hypermetabolic area, the first diagnostic that was considered was a metastatic lymph node. However, as it showed no correspondence to any anatomic structure on the low-dose CT, and the fact that it was contralateral to the primary lesion (which had showed no metastatic ipsilateral lymph nodes at the sentinel lymph node biopsy) made this diagnostic less probable; that is why, additional imaging procedures were recommended. When the patient was referred for the second PET/CT, the known area showed a mild increase in metabolism with respect to the previous PET/CT, but at this time, there were other areas of slightly hypermetabolic brown fat in supraclavicular and intervertebral spaces, so despite contrast-enhanced CT reported a necrotic lymph node, the possibility of a circumscribed active area of brown fat was brought into consideration, and subsequently surgically confirmed.

Therefore, when reporting PET/CT, one has to consider not only the history of the patient and of his disease but also the potential presence of pitfalls that may change the interpretation of the results.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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