Case Report

Missing sentinel lymph node in cutaneous melanoma

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ABSTRACT

The American Society of Clinical Oncology guidelines recommend sentinel lymph node biopsy (SLNB) for all patients with melanoma tumors of intermediate thickness (between 1 and 4 mm). In case of patients with thick melanoma tumors (>4 mm), SLNB may be recommended as well, for staging purposes and to facilitate regional disease control. We report a case of an 82-year-old man, undergone excision of a cutaneous melanoma of the right thigh, which shows some limitation of SLNB in thick melanoma. Lymphoscintigraphy, performed as single-photon emission computed tomography/computed tomography (SPECT/CT), failed to identify the real sentinel lymph node, as tracer uptake was seen in A right inguinal node. Due to the presence on CT co-registered images of another suspicious node (with no radiopharmaceutical uptake) in the crural region, and considering the "high-risk" pathologic features of the removed primary lesion, a 18F-fluorodeoxyglucose positron emission tomography/CT (18F-FDG PET/CT) staging scan was planned. PET/CT showed high metabolic activity in the suspected crural lymphadenopathy. Histopathology demonstrated massive invasion of the crural ("sentinel") node and no metastatic cells in the inguinal node. This report highlights both the higher accuracy of lymphoscintigraphy, when performed as SPECT/CT and the potential utility of 18F-FDG PET/CT in regional staging.

Keywords: ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography, cutaneous melanoma, lymphoscintigraphy, sentinel lymph node biopsy, single-photon emission computed tomography/computed tomography

INTRODUCTION

The technique of lymphatic mapping and sentinel lymph node biopsy (SLNB) has emerged in the last two decades as a minimally invasive approach to evaluate regional lymph node basins in patients with intermediate and high-risk primary cutaneous melanoma.[1] In particular, SLNB is now recommended as a staging procedure for patients with T2, T3 or T4 melanomas and clinical uninvolved regional lymph nodes (clinical stage Ib and II) and suggested also for patients with T1 melanomas and pathologic features associated with an increased risk of nodal micrometastases (ulceration, high mitotic rate,…).[2]

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Also positron emission tomography (PET) with 18F-fluorodeoxyglucose (18F-FDG) has been extensively investigated in patients with melanoma and plenty of studies have shown its effective role in detecting distant metastases, further increased after the introduction of co-registered computed tomography (CT) scan (18F-FDG PET/CT).[3]

In this article, we introduce a case of pT4b thigh melanoma, in which both procedures were performed, together with ultrasonography.

CASE REPORT

An 82-year-old white male, with a clinically-confirmed cutaneous melanoma of the right thigh, presented to our unit to undergo lymphoscintigraphy, in order to perform SLNB at the same time of tumor excision. An ultrasonographic evaluation of the lymphatic basin had shown no evidence of adenopathies. Lymphoscintigraphy with ^{99m}Tc-nanocolloids was performed on a hybrid system Philips single-photon emission computed tomography/computed tomography (SPECT/CT) Precedence

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16 slices (Philips Healthcare, Eindhoven, The Netherlands) after intradermal injection of the radiopharmaceutical around the primary lesion (four separate injections, 0.1 ml for each aliquot, total activity 100 MBq). Low dose helical CT scan was performed: 120 kV, 100 mA, D-DOM control dose, 3 mm slice thickness, 1.5 mm detector collimation, pitch 0.8, rotation time 0.75 s. SPECT scan was acquired with the following parameters: 128 × 128 matrix size, 120 view angle, 10 s time/angle, 5 mm pixel size. SPECT/CT images showed uptake of the radiocolloids in a right inguinal lymph node. On CT co-registered images, anyway, another lymph node with no radiopharmaceutical uptake but with suspicious aspect (globular morphology, absence of hilum) was detectable in the crural region, much closer to the primary tumor [Figures 1 and 2 - left panel].

For this reason, and due to the adverse pathologic features of the removed lesion (Clark's level IV, Breslow's depth 4.6 mm, ulceration, 8–9 mitoses/mm^2, poor inflammatory infiltrate, pT4b), the patient was further staged with a ^{18}F-FDG PET/CT scan after surgery. PET/CT showed pathologic uptake of the tracer in the suspected right crural lymph node, which was removed: no other nodal or visceral metastases were seen [Figures 2 - right panel and 3]. Histology demonstrated signs of chronic inflammation and no neoplastic cells in the inguinal lymph node (analysis of slices from the whole node with hematoxylin and eosin (H and E) stain and confirmation with immunohistochemical staining for S-100 protein in each "blank" slide), while a massive metastasis from melanoma was seen in the crural node (H and E).

Neither inguinal lymphadenectomy nor systemic therapy was proposed, due to age and co-morbidity (hypertensive cardiomyopathy) and a follow-up based on abdominal, and inguinal ultrasonography was organized.

Ten months after surgery the patient developed a metastatic disease, further depicted by a follow-up ^{18}F-FDG PET/CT scan [Figure 4].

DISCUSSION

The prognostic factors for cutaneous melanoma have been recently revised in the 7th Edition of the American Joint Committee on Cancer (AJCC) (2009), based on analysis of data for over 50,000 patients of AJCC database. Apart from the features of the primary lesion (thickness, mitotic rate, ulceration), the histologic status of regional nodes has been confirmed as the most powerful independent predictor of survival in clinically node-negative patients.[4]

The technique of SLNB, first proposed in the 1980s, made inroads once it was clear that the treatment of regional node disease while still microscopic afforded a survival benefit compared to waiting for clinically evident disease.[5]

This strategy, minimally invasive, allows the use of more aggressive surgical approaches and systemic therapies only in higher-risk patients, with occult Stage III disease. It has shown high sensitivity (especially when performed with SPECT/CT-aided lymphatic mapping and multiple peri-tumour injections) with very low false-negative rate, mainly related to technical problems associated with identification of the true sentinel node (SN) by nuclear medicine physicians and surgeons and errors in tissue sampling and interpretation by pathologists. Thus, even if new and more sensitive molecular techniques have already shown promising results,[6] SLNB with pathological assessment is now the recommended staging procedure for all Stage I and II patients with primary melanomas >1.0 mm in thickness.

Nonetheless, with the introduction and the development of noninvasive metabolic imaging techniques (such as ^{18}F-FDG PET/CT) also in patients affected by melanoma, the hypothesis that even SLNB could be avoided and replaced by the analysis of tumor metabolism in the lymphatic basin has emerged.

In the last 15 years, almost 20 papers concerning the diagnostic performance of ^{18}F-FDG PET/CT in comparison to SLNB (and ultrasonography) can be found in literature, all pointing out, with few exceptions, a very low sensitivity of ^{18}F-FDG PET/CT in discovering small lymph node metastases if compared with SLNB.[7]

In this scenario, our report looks somewhat interesting, suggesting the possible utility of PET/CT even in the evaluation of regional disease in selected patients.

The key point seems to be the missed identification of sentinel lymph node by lymphoscintigraphy, probably due to the

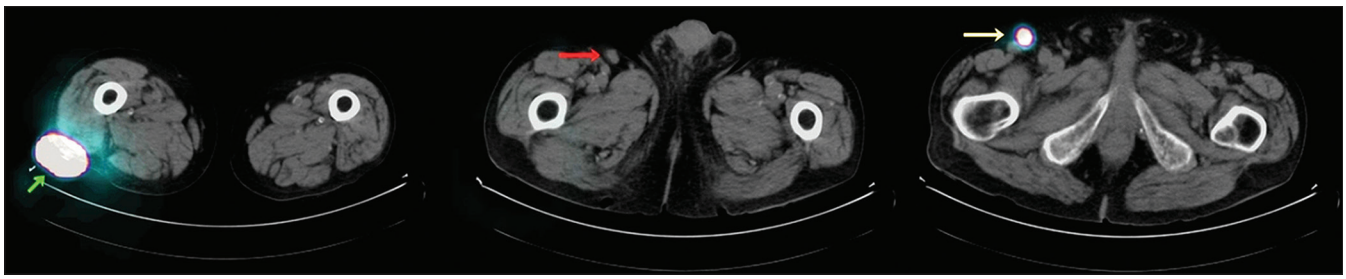

Figure 1: Axial views of single-photon emission computed tomography/computed tomography (CT) lymphoscintigraphy with ^{99m}Tc-nanocolloids. Tracer uptake can be seen in the site of injection/primary tumor (green arrow) and in a right inguinal node (yellow arrow), while there is no uptake in a crural node with suspicious aspect on CT images (red arrow)

obstruction of lymphatic flow to the true SN and the consequent deviation of the flow to another node.[8]

This situation has already been described in some papers about SNs in melanoma and also in breast cancer. In 2009, for example, Lam *et al.* described three cases in which preoperative lymphoscintigraphy failed to show SNs containing metastatic melanoma (all with significant tumor involvement), that were discovered by ultrasound and then confirmed by fine-needle aspiration biopsy and histopathology.[9] The same circumstance was previously described by Estourgie in 2003 in two breast cancer patients: in that report, both lymphoscintigraphy with ^{99m}Tc-nanocolloid and patent blue dye administration failed to identify the true SN, completely invaded by tumor and discovered by intra-operative palpation of the biopsy wound.[10]

What seems new here is that not only lymphoscintigraphy, but even preoperative ultrasonography failed to identify the metastatic crural node. In this setting, in our opinion, a double lesson can be learnt. First, this report confirms that a small risk of missing sentinel lymph node by lymphoscintigraphy exists (especially in thick melanoma) and highlights the added value of a hybrid tomographic study (SPECT/CT), that allows a morphologic evaluation of the interested region too. Second, it shows that ^{18}F-FDG PET/CT, usually performed for "M staging" rather than "N staging" (for the well-known lack of sensitivity in the study of the lymphatic basin), could give important information also about regional disease in selected patients.

The selection of the staging procedures to perform should always be individualized, considering general and local features of the

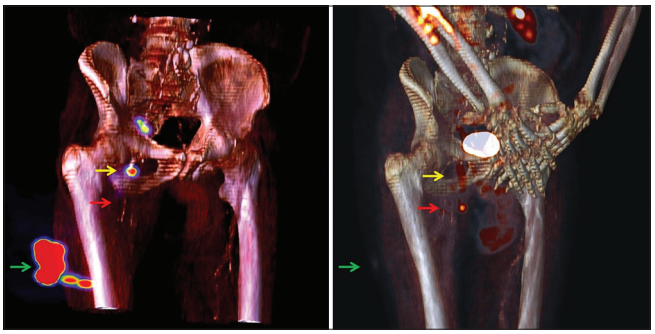

Figure 2: Volume rendering of technetium-labeled radiocolloids single-photon emission computed tomography/computed tomography (left panel) and ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (right panel). The arrows show the sites of primary lesion (green), true "sentinel" crural node (red), false "sentinel" inguinal node (yellow)

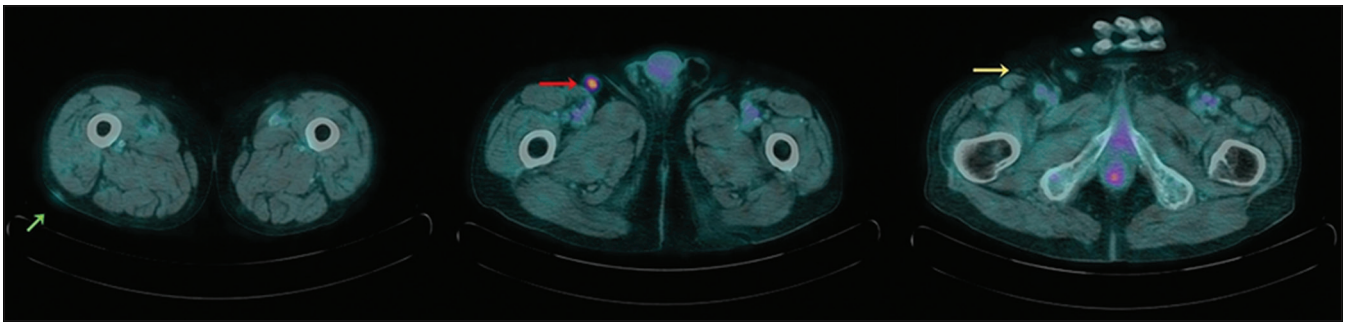

Figure 3: Axial views of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography. No significant uptake can be seen in the site of the removed primary tumor (green arrow) and right inguinal node (yellow arrow), while high metabolic activity is demonstrated in the crural node (red arrow)

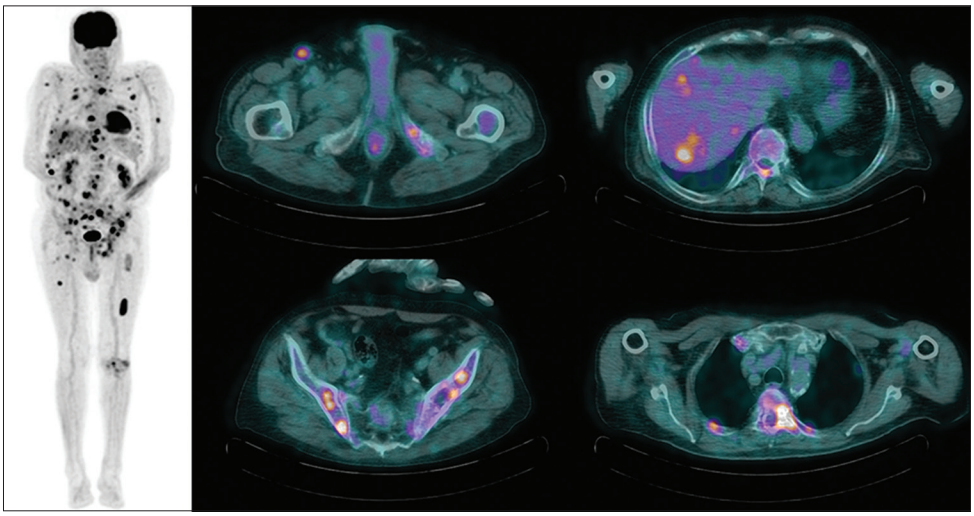

Figure 4: Follow-up ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography scan (1 year after tumor excision): multiple secondary lesions can be seen in right inguinal nodes, in the liver and in many skeletal segments

disease, and evaluating together with the patient the risks and benefits of each technique.

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