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Case Report

PET Scan Misses Cutaneous Melanoma Metastasis with Significant Tumour Size and Tumour Thickness

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Abstract

BACKGROUND: Although PET-scan is an advanced, innovative and widely used method for monitoring patients with different types of cancer diseases, it is important to note that its application in patients with cutaneous melanoma is limited and should be reconsidered.

CASE REPORT: To affirm this new statement, we are presenting a case from our clinical practice of a patient with melanoma of the interdigital space (with resected in sano primary melanoma and performed complete lymphadenectomy) that showed locoregional and systemic progression in two months post operation. The PET scan performed within the second hospitalization (and before the second operation) did not detect the presence of any cutaneous metastases, which were clinically and histologically verified after the second operative procedure.

CONCLUSIONS: This data suggests that shortly more reliable and sensitive imaging methods for monitoring patients with cutaneous melanoma should be found. Having in mind that our patient has been operated twice in the area of the primary lesion (as the surgical wound underwent secondary healing), theoretically, the abundant cicatrization could have led to reduced glucose uptake in the surrounded cancerous tissue. Monitoring of a larger number of patients with locoregional metastases and surgical interventions in different locations would shed light on the observations shared by us.

Introduction

Positron emission tomography (PET) is a non-invasive nuclear imaging technique with uncomparable ability to assess functional and biochemical processes in tissues [1]. Due to its high sensitivity and specificity, it has a wide application in oncology for cancer diagnosis, staging, restaging, detection of the extent of local and regional disease spread, as well as in the monitoring of response to cancer treatment [2]. An important feature of PET is its ability to detect the earliest stages of many diseases due to its possibility to assess the biochemical and functional processes in tissues. This great advantage of PET explains the importance of the method to the clinical oncology practice [3]. It is important to emphasise that this characteristic significantly differs it from other high sensitivity methods like MRI (magnetic resonance imaging) and CT (computer tomography), which detect only anatomical or functional changes that have already occurred [4].

Specifically, about melanoma malignum, FDG-PET takes an important place in its detection and imaging [5].

Case report

A 58-year-old male patient presented to the

department of dermatologic surgery because of the dark lesion on his right foot. Clinical examination revealed a dark brown to black pigmented macula, located in the interdigital space between the first and the second finger of the right foot, with uneven distribution of colour and irregular borders. The lesion was removed by surgical excision under local anaesthesia, with 0.5 cm field of safety margins in all directions. Also, a lymph node dissection under general anaesthesia was performed with retroperitoneal entrance toward the iliac and femoral vessels. Intraoperatively were established dark coloured packages of enlarged lymph nodes with a firm texture and a diameter of 2.5 cm. Enlarged lymph nodes were observed in the obturator whole, with the same characteristic. A lymph node was found in the pelvis immediately adjacent to the v. iliaca external, infiltrated the vein wall. Radical lymph dissection was performed in a femoral, obturator and paraphiliac area.

Histological examination of the cutaneous lesion revealed moderately atypical cells with vesiculous nuclei, suspicious for melanoma, with tumour thickness 2 mm (Breslow).

Histological examination of the dissected lymph nodes verified total and non-total metastasis from melanoma, some with capsular infiltration, some of them without.

The patient was diagnosed in stage IIIC and referred for a PET-scan in 2 months. Two months later the patient presented to the department with two pigmented lesions with uneven borders in the same location (Fig. 1a).

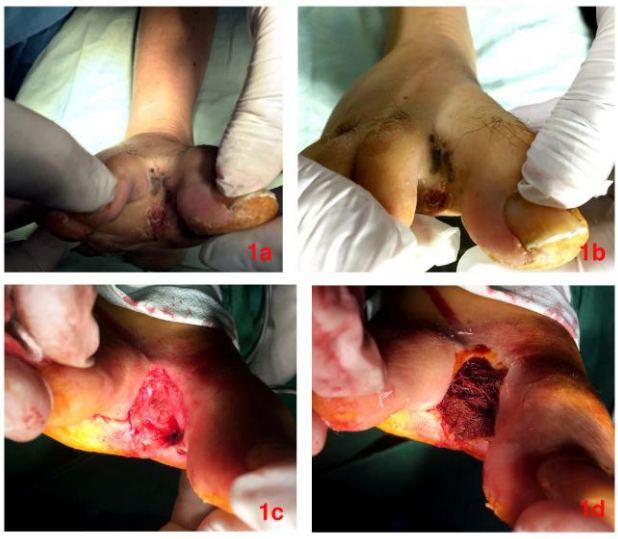

Figure 1: A, B) Clinical manifestation of interdigital malignant melanoma cutaneous metastases; C) Postoperative results after the second excision of a primary tumour, followed again with secondary healing; D) Surgical excision of the interdigital cutaneous metastases under local anaesthesia. Disinfection intraoperatively with povidone-iodine solution 10%

Preoperatively, PET-scan examination was performed, and it detected one right prevertebral lymph node (L3), measured 10mm with SUVmax 3.2; three enlarged paraaortic lymph nodes at the level of the bifurcation, measured up to 13 x 6 mm with SUVmax up to 4.9; and distal right parailiac lymph nodes, measured up to 17 x 10 mm with SUVmax 10.0. Infiltrative, probably inflammatory parenchymal changes of the right lung in the interlobe and paracardial with SUVmax up to 2.6 were also observed. However, no cutaneous metastases were detected on the PET-scan.

The cutaneous lesions were removed by surgical excisions, and the histological examination verified nodular melanoma malignum 1cm in diameter, with no ulceration; mitoses 1-2; Clark II-III; Breslow – 2.

By the clinical results, a restaging is performed in stage IV. The patient was referred for therapy with Pembrolizumab (KEYTRUDA) after hospitalisation in the oncology department.

Discussion

Nowadays, malignant melanoma is showing a tendency to increase in incidence – since 1970 it has approximately doubled with an estimated 68,720 new diagnosed in 2009 [6]. Early stages of melanoma are effectively treated with surgical excision [7]. However, by the time of diagnosis 15% of patients are presented with metastases or locally advanced tumor process [8].

FDG-PET has a wide application in oncology because of its significant role in cancer diagnosis, staging, restaging and therapeutic response monitoring in the most common cancers [9]. FDG (fluorodeoxyglucose) is an analog of glucose used as a radiotracer in order to detect tumor cells which are distinguished to have elevated glucose uptake [10]. It is a well-known fact that tumor cells have high metabolic needs of glucose, lipids and amino acids. PET imaging is based exactly on this distinctive feature of tumors, which explains the high sensitivity and specificity of the method when it refers to cancer diagnosis, staging and therapeutic response monitoring [11]. Glucose, as well as oxygen, growth factors and nutrients are critical factors that ensure the progress of cancer cells into solid tumors by activating their specific metabolic pathaways [12]. Microenvironment, especially hypoxia takes important place in the evolution of tumors [13]. In hypoxic conditions of 100-150 μm distance between the tumor cells and the nearest blood vessel, their ability to endure profound hypoxia is condition for their progress [14]. An adapting mechanism of cancerous

cells is the ability to rely on anaerobic glucose metabolism, which ensures the major needs of energy for tumour growing [15].

Nowadays, PET takes a significant place in oncology where it is widely used for cancer diagnostic, staging and therapy response monitoring [16]. Soon, in 1998, the limitations of PET were overcome with the development of the first combined PET/CT, firstly installed in University of Pittsburgh Medical Center [17]. This imaging technique provides an assessment of both biochemical and anatomic characteristics of tissues and is a significant advance in the evaluation of primary tumours, metastases, staging, therapy response monitoring and post-treatment recidives [18].

FDG-PET has a large application in evaluation of the extent of local and regional disease spread [19, 20]. Results of a meta-analysis evaluating the ability of PET in staging and restaging of cutaneous melanoma confirmed its usefulness in the detection of distant metastases. However, not so desirable results were observed in the evaluation accuracy of regional metastases as it does not detect microscopic disease [21]. Another report of Crippa et al. affirms reliable sensitivity and specificity in detection of lymph node metastases in patients with malignant melanoma. The presented results are showing that FDG-PET detected 100% of metastases ≥10 mm, 83% of metastases 6-10 mm, and 23% of metastases ≤ 5 mm. It is important to emphasise that the FDG-PET had high sensitivity (> or = 93%) only for metastases with more than 50% lymph node involvement or with capsular infiltration. However, this imaging method is not sensitive enough to detect subclinical microscopic disease [22]. The fact that PET sensitivity for melanoma lymph node metastases is dependent on tumour volume is also reported in data presented by Wagner et al. [23]

However, despite the successful results of PET in cancer diagnosis and evaluation, it has some important limitations that should not be neglected: (1) no quantitative system in assessing changes in FDG-metabolism in the therapeutic response. In the USA the development of such system is based on PET Response Criteria in Solid Tumors (PERCIST) [24]; (2) False-positive results. False positive results are possible because of increased FDG uptake in some normal body areas, such as lymphoid tissue and brown adipose tissue [25]. Another reason for false positive results may be the increased accumulation of FDG in some benign processes as inflammation or infection [26]; (3) low sensitivity. Low sensitivity may be observed in hypocellular cancers such as desmoplastic or mucinous tumours, as well as in micrometastases in breast cancer and melanoma [27]. Also, PET presents low sensitivity in well-differentiated low-grade tumours, which have lower glucose uptake, such as carcinoid tumours, renal cell carcinoma, bronchoalveolar-cell carcinoma and most prostate cancers [28].

We present a case of a patient with a malignant melanoma where two satellite cutaneous metastases measured 2 x 0.7 cm were not detected via PET-scan examination. With the presented case we want to report the unreliable results of PET-imaging when it refers to cutaneous melanoma metastases.

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