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Хибридна SPECT/CT за детекция на интранзитни сентинелни лимфни възли и насочване на терапията при ранен малигнен меланом

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Hybrid SPECT/CT for detection of in-transit sentinel lymph nodes and treatment tailoring in early stage malignant melanoma

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Abstract. The status of sentinel lymph nodes (SLN) in the regional to the tumor lymphatic basin is a well known prognostic and therapy-tailoring factor in early stage malignant melanoma (MM). Nuclear medicine mapping of lymph flow is a major prerequisite for successful intra-operative SLN detection and hybrid SPECT/CT allows a precise topographic and morphologic characterization both of the SLN and the whole scanned region. This case report from our clinical routine demonstrates the possibility on modern nuclear medicine to detect a sentinel node not only in the regional basin but also in-transit lymph nodes, neighboring the primary tumor lesion. A close interdisciplinary collaboration is needed - nuclear medicine physicians, oncodermatologists, surgeons, pathologists and medical oncologists should work closely together for the standardization of procedures and the consequent adjuvant treatment tailoring.

Key words: SENTINEL LYMPH NODES, MALIGNANT MELANOMA, SPECT/CT

Резюме. Статусът на сентинелните лимфни възли (СЛВ) в регионалния на първичната лезия лимфен басейн е добре известен прогностичен и определящ терапевтичния подход фактор при ранния малигнен меланом. Нуклеарно-медицинското картиране на лимфния дренаж е основна предпоставка за успешна интраоперативната детекция на СЛВ, а прицелната хибридна SPECT/CT позволява точна топографска и морфологична характеристика на СЛВ и дава структурно-анатомична характеристика на целия скениран регион в зоната на интерес. Представеният клиничен случай от нашата практика демонстрира възможностите на съвременната нуклеарно-медицинска технология да детектира СЛВ, не само в регионалния за първичния тумор лимфен басейн, но и интранзитни лезии в близост до първичния тумор. Необходимо е тясно интердисциплинарно сътрудничество между специалистите от клиниките по нуклеарна медицина, онкодерматология, хирургия, патология и медицинска онкология, за стандартизиране на диагностичните протоколи и своевременно насочване на адювантното лекарствено лечение.

Ключови думи: СЕНТИНЕЛНИ ЛИМФНИ ВЪЗЛИ, МАЛИГНЕН МЕЛАНОМ, SPECT/CT

Introduction

The sentinel lymph node (SLN) is the first lymph node in the regional for the tumor lymphatic basin, receiving direct lymph flow from the primary. In some cases however, lymphoscintigraphic mapping discovers a SLN in a region, lying between the primary and the expected regional drainage zone. These "in-transit" lymph nodes, located at more than 2 cm from the primary along the lymph path to the regional basin, are treated as "sentinel" as well and their status has the same prognostic potential and therapeutic consequences.

We present a case of malignant melanoma patient, in which sentinel lymphoscintigraphy with targeted SPECT/CT detected an in-transit SLN in the proximity of the primary lesion of the torso.

Clinical case

We report a case of 49-years old patient with a primary skin lesion of the back, in the left dorso-

lumbar region. The histologic subtype of the primary was superficial spreading malignant melanoma (SMM), after diagnostic excisional biopsy T-stage pT4b, clinical stage IIC, without clinical and ultrasound suspicion for metastatic lymph nodes in both inguinal regions, without other skin lesions.

Preparing for the wide local excision with SLN biopsy, we performed sentinel lymphoscintigraphy in a two-day protocol in the Clinic of Nuclear medicine. The radiopharmaceutical ^{99m}Tc -Nanotop was applied with standard procedure – at 4 injection sites, 0,1 ml each, around the cicatrix. The acquisition protocol included planar scans in the area of the primary with both inguinal and both axillary regions. Planar imaging showed fast lymphatic drainage leading to left axilla with a notable hot spot – a SLN (Fig. 1A). No lymphatic flow to both inguinal areas was noted. For structural and topographic clarity we extended the acquisition with hybrid SPECT/CT in the area of the primary and both axillae. The summed 3D-SPECT image showed a focus of high tracer uptake close to the injection site but apart from all 4 spots of application (Fig. 1B). The hybrid image with low-dose

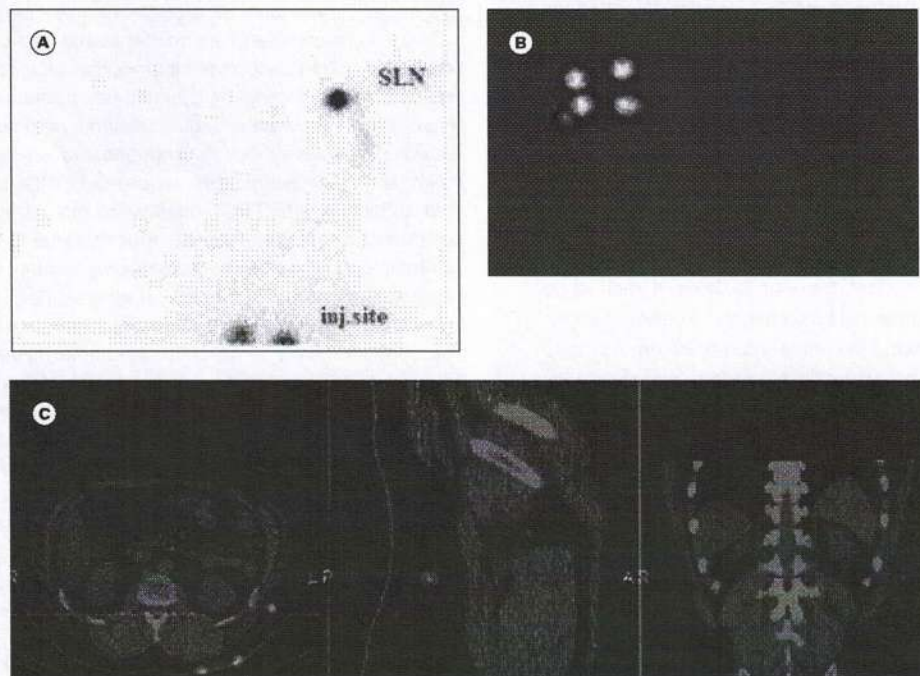


Fig. 1. SVD, 49y. Superficial spreading melanoma (SSM) of the skin in left dorso-lumbar region, after excisional biopsy, pT4b, stage IIC. SPECT/CT-sentinel lymphoscintigraphy. (A) Planar scan of the SLN in left axilla. (B) SPECT-MIP of injection site with an additional hot spot in the neighbouring area (red arrow). (C) Hybrid SPECT/CT image with a corresponding oval subcutaneous lesion of ~4 mm – an in-transit SLN – histologically proven metastatic (0,4 cm micrometastasis) - pT4bpNsn1a(0) cM0, stage - IIC.



Fig. 1. (D) SLN in left axilla – histologically negative for metastases; a second-tier LN in dorsal parascapular region, not removed surgically (arrow). (E) low-dose CT image of an enlarged LN – 15-16 mm, with no tracer uptake



Fig. 2. Intraoperative gamma probe detection of the in-transit SLN

CT showed a rounded subcutaneous lesion of d~4-5 mm in the left lumbar region with intense radiotracer uptake (Fig. 1C). The presence of a structural lesion excluded the possibility for a false-positive transitory lymph "depot". Hybrid images showed also focal tracer uptake in left axilla (d~15mm) and left parascapular region (d~6-7 mm) with CT-correlating lymph nodes of 15 mm and 6-7 mm respectively (Fig. 1 D-E). Both hot spots were defined as sentinel and second-tier lymph nodes, respectively. The focus in the left lumbar region was described as in-transit, appointed for intra operative correlation. During surgery, apart from the "typical" SLN in the left axilla, the above described in transit lymph node was detected with the help the gamma probe, with gamma-photon activity of 646 counts/sec (Fig. 2).

According to protocol, the removed lymph node was measured for rest-activity outside the patient's body – 607 counts/sec – confirmed as sentinel and corresponding to the one described in the SPECT/CT report. There was no remaining activity in the operation theatre in the left lumbar region after the removal of the node (Fig. 3). Single pigmentations could be seen in the in-transit node, suspicious for micrometastases (Fig. 4).



Fig. 3. Measuring activity of the in-transit SLN using gamma probe outside the patient's body

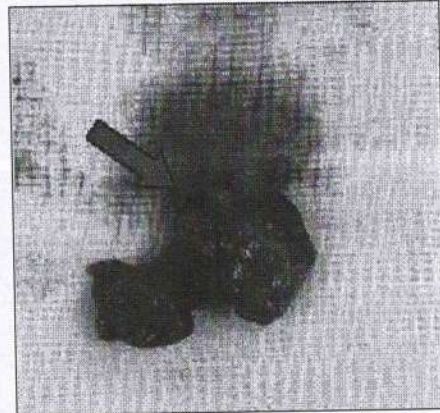
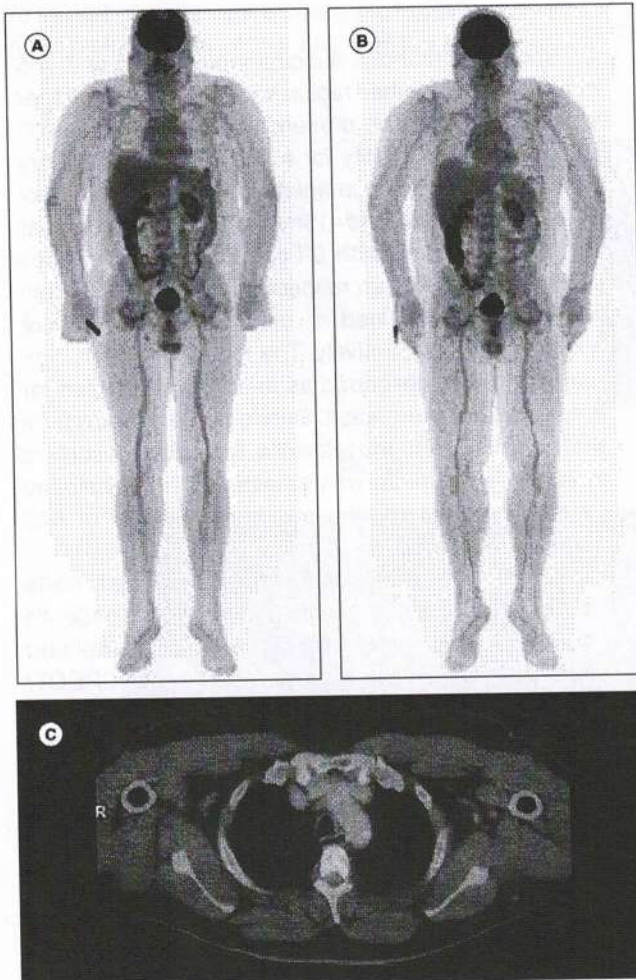


Fig. 4. Macroscopic pigmentations in the in-transit LN <2 mm, suspicious (red arrow)



The left axillary SLN was negative for metastases, while the in transit sentinel contained a micrometastasis of d~1-2 mm. SPECT/CT-lymphoscintigraphy managed to upstage the patient into stage IIIc, with consequent personalized treatment - start of adjuvant target therapy after proven BRAF-positivity.

To exclude further undiagnosed metastatic foci in the higher stage, two consecutive ^{18}F -FDG-PET/CT scans were performed in the follow-up of this patient so far, with single moderately metabolic lymph nodes in the left axilla and left iliac region, not changing significantly over a period of 6 months (Fig. 5).

Discussion

The decades of clinical studies in early stage MM led to the so called "change of paradigm" – SLNB is not a referral for regional lymphadenectomy any more, but a prerequisite to select patients for adjuvant systemic treatment (immune – and target therapy) in stage III – using anti-PDL-1 or BRAF/MEK-inhibitors [1-4]. The

Fig. 5. ^{18}F -FDG- PET/CT during follow-up after SLNB and under ongoing target therapy. (A) Whole-body PET 05'22. (B) Whole-body PET 12'22. (C) PET/CT of a metabolically nonactive LN in left parascapular region;

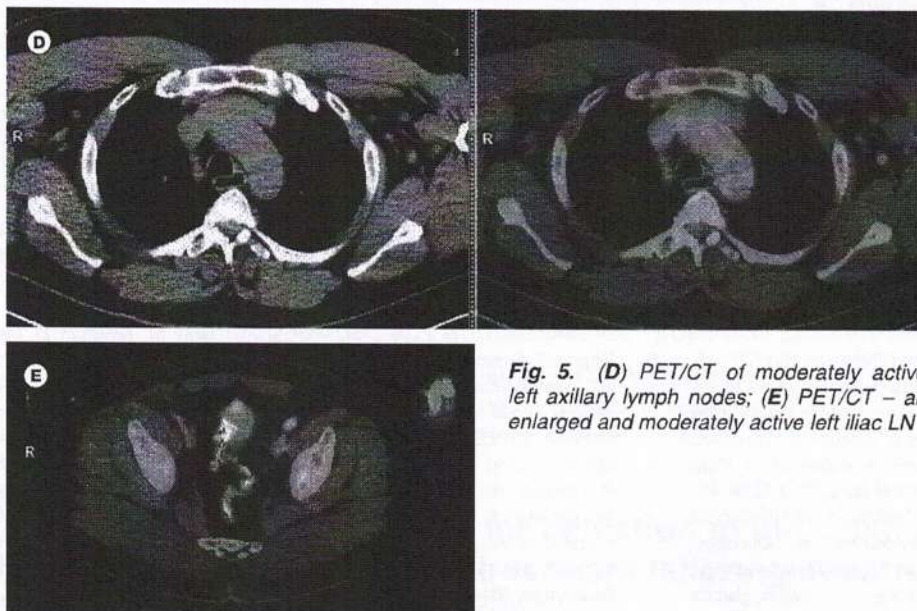


Fig. 5. (D) PET/CT of moderately active left axillary lymph nodes; (E) PET/CT – an enlarged and moderately active left iliac LN

national reimbursement of these medications in our country since 2020 allowed their use also for Bulgarian patients. The adoption of contemporary therapeutic algorithms implicates also an establishment and standardization of diagnostic protocols as well. Sentinel lymphoscintigraphy combined with modern hybrid technologies in NM is the main guide for the surgeon in SLNB [5]. Three-dimensional SPECT/CT images have a better contrast and spatial resolution than planar, allowing easier discrimination of SLNs in close proximity to the injection site, with higher detection rate of SLNs as a whole, especially in anatomically complex areas as head and neck, for example [6, 7]. SPECT/CT imaging has higher accuracy for the number of SLNs – e.g., two closely located separate lymph nodes could look as one only on a planar image. The used in the SPECT/CT-protocol low-dose CT without intravenous contrast medium is diagnostic enough for anatomic localization, gamma-photon attenuation and scatter correction. The big prospective multicenter study of IAEA demonstrated in 2015 the possibilities of SPECT/CT to modify surgical approach in 37% of melanoma patients with significantly improved accuracy in head and neck and torso [8]. A metaanalysis of Quartuccio et al showed higher detection rate of SLN and registration of more than one SLN with SPECT/CT compared to planar scintigraphy [9]. The conclusions of Moncrieff M et al. [10] are quite similar, noting a trend to find more lymph drainage regions with SPECT/CT. In a

study by Ortín-Pérez et al over 900 melanoma patients, in transit SLN were found in 80 patients, with 19,4% of them containing micrometastases and no metastases in the regional LN in 4 patients [11]. Another study of 1223 SLNB [12] found in transit SLN in 5,2% of patients, with 21,9% of them having micrometastases. The same study found statistically significant earlier relapse and death of melanoma in the case of in transit lymphatic drainage. All patients with newly detected in transit lymph node metastases are classified as N1c and the patient is upstaged into stage III with following adjuvant therapy even without pathologic regional lymph nodes.

Conclusion

Sentinel lymphoscintigraphy with hybrid targeted SPECT/CT is an obligatory component for the correct detection and localization of in transit lymph nodes while planning SLNB in malignant melanoma. Though the incidence on in transit SLNs is relatively low in MM, the presence of micro-metastases has the same prognostic and therapy-tailoring significance, as in regional “regular” sentinels. The detection of in transit SLN is an indication for surgical removal and stressing the need for careful diagnostic follow-up, including ^{18}F -FDG-PET/CT.

The authors declare no conflict of interest!

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