

Lymphatic mapping and sentinel node biopsy in a patient with upper limb Merkel Cell Carcinoma: a case report and brief review of literature

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[Received 19 IX 2014; Accepted 3 IX 2015]

Abstract

Sentinel node mapping is an integral part of regional lymph node staging in many solid tumors and plays an important role in surgical oncology. This technique has been used with excellent results for non-melanoma skin cancers including Merkel Cell Carcinoma (MCC). In the current study, we reported our first MCC patient who underwent successful sentinel node mapping. We also reviewed the available literature regarding the prognostic significance of sentinel node mapping in cN0 MCC patients.

KEY words: lymphoscintigraphy, radiotracer, Tc-99m-Phytate, Merkel Cell Carcinoma, sentinel node, lymphatic mapping

Nuclear Med Rev 2016; 19, 1: 42–45

Background

Merkel Cell Carcinoma (MCC) is a rare aggressive neuroendocrine skin tumor with high rate of recurrence and distant metastasis [1]. Pathological status of regional lymph nodes is one of the most important prognostic factors in MCC. Patients with clinically involved regional nodes have far worse prognosis compared with cN0 patients [2, 3].

However there is a group of cN0 patients with occult lymph node metastasis which also have poor prognosis and outcome. Sentinel node mapping is an important technique for regional lymph node staging in many solid tumors which has also been used for MCC [4].

We reported a cN0 MCC of the upper limb which was treated with sentinel node mapping and briefly reviewed the available literature regarding the prognostic importance of sentinel node mapping in MCC.

Case report

A 65-year-old male presented with a 0.8 cm painless erythematous mass over the lateral aspect of the left elbow. The mass had been present for more than 1 year and slowly growing. He didn't

have any history of trauma or previous skin lesions. He didn't have any history of malignancy.

The patient underwent excisional biopsy of the lesions. Hematoxylin and Eosin and cytokeratin 20 staining lead to the diagnosis of MCC.

The patient was referred to the nuclear medicine department for sentinel node biopsy the morning of the surgery. The patient received two injections of 0.5 mCi/0.2 mL ^{99m}Tc-phytate subcutaneously around the scar of the tumor biopsy, 30 minutes before surgery. Ten minutes post-injection, lymphoscintigraphy images of the patient was performed (ANT-POST views, 5 minutes/view, using ^{99m}Tc photopeak and a dual head variable angle gamma camera (E.CAM Siemens) equipped with high resolution low energy collimator). Hue of the patient (scatterogram) was imaged simultaneously by the technique of Momenzad et al. [5]. Scatterogram is imaging of the scatter photons of the Tc-99m simultaneous with the original lymphoscintigraphy images. In this technique, no additional time or radiation is needed and a hue of the patient can be imaged. As scatterogram can be done without any additional time, radiation and cost; it can be recommended with all planar lymphoscintigraphy imaging.

Lymphoscintigraphy images of the patient showed a single sentinel node in the axillary region (Figure 1). Intra-operatively the tumor site was excised with a wide margin and an axillary sentinel node was harvested by a gamma probe (EUROPROBE, France). The sentinel node was not pathologically involved by frozen section examination and axillary dissection was not performed. Permanent H&E examination of the sentinel nodes was done after serial sectioning and was also pathologically negative.

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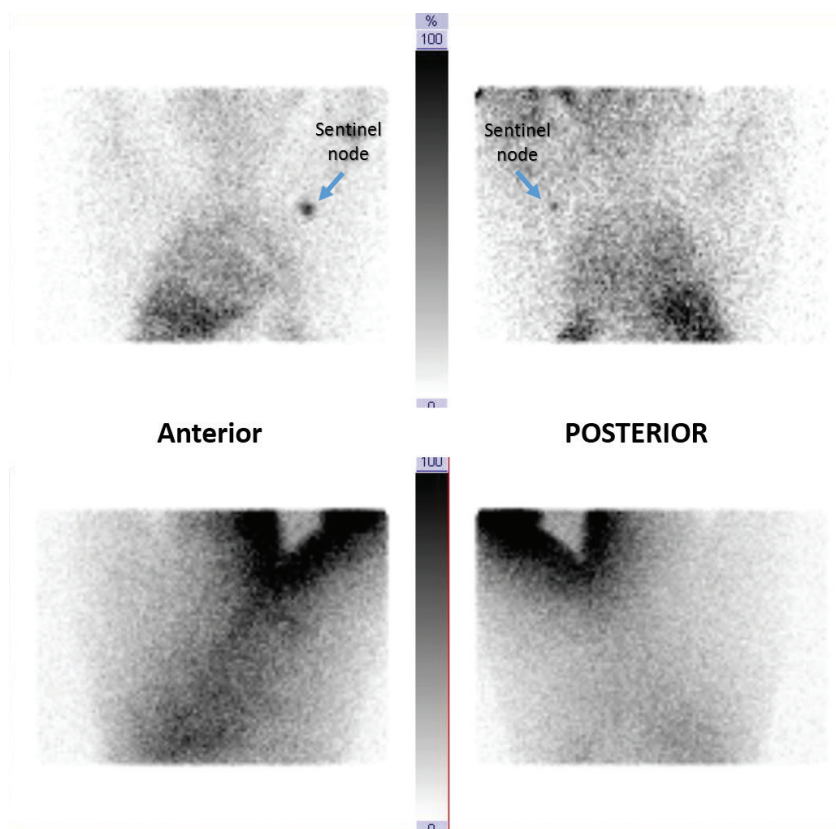


Figure 1. Lymphoscintigraphy images of the patient. The lower row images are scatterograms of the corresponding upper row lymphoscintigrams. A sentinel node could be identified in the left axilla. Injection site is out of the field of imaging

The patient underwent local radiotherapy for the primary site of the tumor. At 7 months follow up the patient didn't have any evidence of local or regional recurrence.

Literature review and discussion

Sentinel node mapping is the standard method of regional lymph node staging in breast cancer and melanoma [6, 7]. Its application in other solid tumors such as gynecological and urological cancers is growing with very promising results [8, 9].

Lymphatic mapping and sentinel node biopsy has also become very common in the high risk squamous cell carcinoma (SCC) of the skin [10, 11] including SCC of the genital area [12, 13].

Sentinel node mapping for MCC has been performed with excellent accuracy since 1998 [14]. By identifying subgroup of patients with regional lymph node involvement in clinically node negative patients, sentinel node mapping can help planning treatment in MCC patients. Our department has an extensive experience in sentinel node mapping in different solid tumors since ten years ago [15]. The current case was the first MCC patient who underwent sentinel node mapping in our department. An axillary sentinel node could be harvested successfully intra-operatively and was not pathologically involved. Axillary node dissection was not performed and the patient didn't receive any specific treatment for axillary area. Thus far the patient is recurrence free.

Nuclear medicine plays a pivotal role in the lymphatic mapping of solid tumors and nuclear physicians are the integral part of sentinel node mapping team. Pre-operative lymphoscintigraphy

is also an integral part of lymphatic mapping in surgical oncology. Lymphoscintigraphy can help the surgeons to plan the surgery due to sentinel node localization before surgery, can identify the unusual locations of sentinel nodes and may decrease detection failure and false negative rate [16, 17].

Thus far three systematic reviews have addressed lymphatic mapping in MCC [4, 18]. Mehrany et al. in the 2002 systematic review gathered all cases of sentinel node mapping in MCC by comprehensive search of the literature. They could gather information of 60 patients, 67% of whom had pathologically negative sentinel nodes. These sentinel node negative patients had no evidence of regional nodal recurrence at follow up visits (no false negative case) [18]. In the 2006 systematic review, Gupta et al. gathered information of 122 MCC patients with lymphatic mapping. They reported that sentinel node mapping upstaged 39 patients (32%) due to pathologically involved sentinel node. This finding has an important clinical implication as these patients may not have received treatment to the involved node bed. Recurrence rate (overall regional and distant) was three times higher in sentinel node positive patients as compared with the sentinel node negative ones [4]. The last systematic review by Sadeghi et al. in 2014 showed the prognostic importance of SLN mapping in cN0 MCC patients as sentinel node mapping can improve disease free and overall survival in cN0 MCC patients as compared with nodal observation [19].

Thus far, six studies reported survival benefit of sentinel node mapping in cN0 MCC patients [20–25]. Table 1 summarizes the characteristics of these studies in addition to their main prognostic findings. Overall, these prognostic studies showed that operative

Table 1. Characteristic of the studies evaluated prognostic significance of sentinel node mapping in MCC

First author	Publication year	Total number of patients	Duration of follow up	Major findings
Tarantola	2013	114	3.3 year (mean)	OS in the patients underwent SLN mapping was higher, HR: 1.04 [0.51–2.15], $p = 0.91$
Kachare	2014	1193	Median of 21 months	DFS was higher in patients underwent SLN mapping, HR: 1.43 [1.01–2.05], $p = 0.04$
Bajetta	2009	63	Median of 65 months	Operative nodal staging with SLN biopsy (HR 3.44 [1.17–10]; $p = 0.023$) predicted better DFS
Sattler	2013	47	Median 20 months	SLN mapping predicted better DFS and OS as compared with nodal observation
Tseng	2014	4038	N/A	DFS was higher in patients underwent SLN mapping, HR: 1.72 [1.37–2.14]; $p = 0.000001$
Asgari	2014	218	2.4 years	Both OS and DFS were better in the SLN mapping group as compared with nodal observation (HR = 2.5 for both)

OS — Overall Survival; SLN — Sentinel Lymph Node; HR — Hazard Ratio; DFS — Disease Free Survival

Table 2. Characteristic of the studies evaluated the prognostic significance of sentinel node pathological involvement in MCC

First author	Publication year	Total number of patients	Duration of follow up	Major findings
Fields	2011	153	41 months (median)	OS and DFS in the patients without involved SLN was higher, HR: 1.86 [0.22–15.6], $p = 0.56$; and 1.69 [0.37–7.68], $p = 0.49$
Kouzmina	2013	28	3.6 years (mean)	OS was higher in patients without SLN involvement, HR: 4.8 [0.79–29.37], $p = 0.08$
Fritsch	2014	721	34 months	DFS was higher in patient without SLN involvement especially in non-head and neck locations: HR: 2.2 [0.84–5.86], $p = 0.1$ for head and neck, and 3.01 [1.77–5.11], $p = 0.0001$ for non-head and neck locations

OS — Overall Survival; DFS — Disease Free Survival; SLN — Sentinel Lymph Node; HR — Hazard Ratio

nodal staging with sentinel node biopsy is associated with improved overall and disease free survival as compared with nodal observation in cN0 MCC patients. In addition, 3 studies evaluated the prognostic significance of pathological involvement of the sentinel nodes in MCC [26–28]. Brief prognostic data of these studies are available in Table 2.

In conclusion, sentinel node mapping is an important method for regional lymph node staging in cN0 MCC patients. Medical literature supports that sentinel node mapping in cN0 MCC patients is associated with improved overall and disease free survival.

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