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Importance of sentinel lymphatic node biopsy in detection of early micrometastases in patients with cutaneous squamous cell carcinoma

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Summary *Background:* Cutaneous squamous cell carcinoma (CSCC) is the second most common malignant skin cancer with a tendency to spread through the lymphogenic pathway. Metastases are found in 2–6% of cases. The aim of this study was to determine CSCC micrometastases when non-invasive examination methods do not detect them.
Method: A total of 88 patients were included in the study with clinically diagnosed, histologically confirmed CSCC and no distant or regional lymph node metastases detected during instrumental tests. The patients were grouped into low- and high-risk CSCC groups. They underwent one-stage surgery – radical tumour excision and sentinel lymph node/nodes biopsy (SLNB). Significance level of 0.05 was chosen for testing statistical hypotheses.

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Results: One hundred and fifty-three sentinel lymph nodes (SLNs) were detected and excised in 88 patients. Micrometastases were found in five SLNs of three patients with high-risk CSCC. The rate of micrometastases was 3.4%; however, in the high-risk group it was 6.5%. The mean diameter of CSCC with micrometastases in SLN was 5.6 ± 3.5 cm, and that without micrometastases was 1.5 ± 1.1 cm ($p = 0.003$). The depth of CSCC according to Breslow in the patients with detected micrometastases in SLN was 3.5 ± 1.2 mm, and that without detected micrometastases was 2.2 ± 1.4 mm ($p = 0.047$). Patients with micrometastases in sentinel lymphatic nodes underwent radical lymphadenectomy. There was neither recurrence of CSCC metastases in regional lymph nodes nor distant metastases during the research period detected.
Conclusions: In patients with CSCC the rate of micrometastases directly correlates with the depth and diameter of the tumour. In patients with high-risk CSCC the rate of micrometastases is 6.5%.

Background

Skin cancer is one of the most topical problems in the world.[1,2] There are three major types of skin cancer: basal cell carcinoma, squamous cell carcinoma and melanoma. The morbidity of all types skin cancer has been increasing for the past two decades at a fast pace worldwide. In the United States more than 1.3 million new cases of all skin cancer forms have been recorded, which is a substantial number for a country with 324 million residents.[1–6] The most common non-melanoma type skin tumour is basal cell carcinoma, which is less aggressive than other skin cancer types. The second most frequent type of skin cancer accounting for 20% of non-melanoma type skin tumours is cutaneous squamous cell carcinoma (CSCC) which is an aggressive tumour prone to metastases, especially lymphogenous.[7–11]

The risk of CSCC increases from a few to a dozen of times for individuals who have freckles, fair or red hair, fair eyes and who are prone to sunburn or are not able to get sunburnt. A number of epidemiological studies have proved the association between occurrence of CSCC and exposure to strong sunburn.[5,11–17] According to the world data, the metastases are found in 2 – 6% of CSCC patients.[18] In case of a tumour with ≥2 cm diameter, the rate of recurrence increases to 15% and the rate of metastases to 30%.[18] For CSCC on the lip or the ear, the rate of recurrence and metastases is 10 – 25%. For poorly differentiated CSCC, the rate of metastases reaches 28.6%.

Survival prognosis of CSCC patients depends on tumour morphology and spread. The 5-year survival upon determination of CSCC and no metastases in regional lymph nodes is up to 96%. Further, the 5-year survival upon determination of CSCC with metastases in regional lymph nodes and combined treatment of surgery and radiotherapy applied is 72%. When metastases are present in regional lymph nodes and no treatment is applied, the 5-year survival is only 25 – 35%.[7–10]

Currently, metastatic CSCC is determined when increased regional lymph nodes are detected clinically and/or distant metastases are determined by way of non-invasive methods. This proves that clinically detected metastases are a sign of CSCC that is already advanced or has spread. For more precise evaluation of CSCC, there is an idea to perform sentinel lymph node biopsy (SLNB), which is supported globally and is usually applied in patients with melanoma and breast cancer in order to determine possible tumour metastases and apply appropriate treatment as early as possible.

The aim of our study was to determine CSCC micrometastases when non-invasive (clinical or ultrasound) examination methods may still not detect them. As the majority of CSCC metastases (80 – 85%) spread by lymphogenous ways, investigation of sentinel lymph nodes (SLNs) would allow us to achieve improvement in the diagnosis of CSCC spread and timely application of adequate treatment, which could reduce tumour spread, improve the prognosis of the disease and prolong survival.

Methods

A prospective clinical study was carried out from July 2012 to January 2016 at the Clinic of Plastic and Reconstructive Surgery of the Hospital of the Lithuanian University of Health Sciences. The purpose of this study was to test the research hypothesis whether SLNB has an impact on the early diagnosis of micrometastases in patients with squamous cell carcinoma of the skin. Study was approved by the Ethics Committee of Kaunas Regional Biomedical Research.

A total of 88 patients with clinically diagnosed (by dermatologists) and histologically confirmed CSCC met the inclusion criteria of the study (Table 1). Chest x-ray, abdomen ultrasound and regional lymph nodes ultrasound were performed to the patients before including them to the study. The patients with detected distant metastases or metastases in regional lymph nodes were not selected. The patients were grouped into low- and high-risk CSCC groups according to the guidelines of the National Comprehensive Cancer Network.[19] The groups of low-risk and high-risk CSCC were selected according to the risk factors summarised in Table 2. If at least one high-risk criterion of CSCC was present along with low-risk CSCC criterion, the patient was included into the group of high-risk CSCC.

All the patients underwent one-stage surgery – radical tumour excision and SLNB. On the hospitalisation day, the patients underwent radionuclide lymphoscintigraphy with radiopharmaceutical preparation (RF, 99mTc-albumin nanocolloid, *Nanocoll*, *Amersham Health*, 0.1 – 0.2 mL). Then, a planar gamma camera (*Siemens e.cam*) was used to perform a dynamic lymphoscintigram in order to determine lymph leakage from the tumour and the greatest RF