Lymphatic drainage map of the head and neck skin squamous cell carcinoma detected by sentinel lymph node biopsy

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Abstract. – OBJECTIVE: Squamous cell carcinoma of the skin often affects the scalp and neck region and has a potential for complex lymphatic metastases. The aim of this study was to examine the pattern of lymphatic drainage that would enable better insight and prediction of lymphatic metastasis of head and neck squamous cell carcinoma (HNSCC) in relation to the anatomical localization of the primary process.

PATIENTS AND METHODS: A prospective analysis included 64 patients who underwent sentinel lymph node (SLN) biopsy. The biopsy was performed in patients with high-risk cutaneous head and neck squamous cell carcinoma between 2006 and 2010.

RESULTS: SLNs in tumors of the forehead, temporal region, lateral cheek, and auricle were found in the cervical region at level II and parotid lymph nodes (p<0.001). In tumors of the nose, periorbital region, and postauricular tumors, SLNs were found in parotid lymph nodes (p<0.001), in tumors of the medial cheek in level I cervical lymph nodes and parotid lymph nodes (p=0.003). In tumors of the neck, SLNs were detected in the cervical region at level IV, whereas in tumors of the posterior scalp they were found in the occipital region (p<0.001).

CONCLUSIONS: The results of SLN biopsy in high-risk cutaneous HNSCCs show the regularity of metastasis based on which a lymphatic drainage map can be constructed and thus potential metastatic sites depending on the primary tumor localization predicted.

Key Words: Sentinel lymph node biopsy, Head and neck, Squamous cell carcinoma, Skin.

Introduction

Non-melanoma skin cancer is one of the most common malignancies in white patients¹⁻². Squamous cell carcinoma accounts for an average of 20% of all cases of non-melanoma cancers³ and is most commonly localized in the head and neck region⁴. According to available data from the literature, the cutaneous form of squamous cell carcinoma metastasizes in about 0.3% to 16% of cases⁵. However, it is considered that this percentage is significantly greater in high-risk patients (11-47.3%)⁶⁻⁸. This type of carcinoma characteristically spreads to local lymph nodes first, and then, metastasizes to distant tissues and organs⁶⁻¹¹. It has been proven that squamous cell carcinoma of the skin, primarily localized in the head and neck region, metastasizes locally to lymph nodes of the parotid region, as well as to lymph nodes of the neck¹². Population analyzes estimate that the mortality rate of this type of carcinoma is around 0.7%¹³. Many cases of local metastases in lymph nodes are potentially curable. However, a small number of patients, unfortunately, suffer a fatal outcome despite treatment. The five-year survival rate among patients with operable, metastatic, cutaneous squamous cell carcinoma of the head and neck region amounts to 70-75%¹⁴. Given the fact that the presence of metastases in regional lymph nodes is a key prognostic indicator for survival in patients with squamous cell carcinoma, special attention should be paid to the prevention of nodal disease during treatment¹⁵.

Sentinel lymph node biopsy (SLNB) plays a significant role in the treatment of high-risk cutaneous squamous cell carcinomas without clinical or radiological evidence of the metastatic disease¹⁶⁻¹⁸. Early identification of micrometastases could enable a selective and timely inclusion of high-risk patients in more aggressive treatment protocols, as well as scheduling more frequent follow-ups by physicians, thereby potentially improving the survival rate¹⁶,¹⁷. To date, an accurate
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A map of metastasis of cutaneous forms of squamous cell carcinoma of the head and neck region has not been formed. SLNB is a minimally invasive method that examines the presence of metastases in the nodal basin.

On the other hand, in patients with a parotid gland-affected tumor process and a clinically negative cervical region, optimal treatment remains controversial. Furthermore, determining the presence of metastases in clinically negative lymph nodes of the neck remains a challenge. Elective nodal treatment is appropriate in a significant number of subclinical metastases in lymph nodes of the neck. In addition, in patients undergoing neck dissection, it is necessary to perform the dissection up to the level of lymph nodes considered most likely to be affected by the tumor process.

Our hypothesis is that metastases may vary regarding the anatomical localization of the primary tumor process, as well as that an appropriate map of lymphatic drainage of the head and neck skin may enable the prediction of potential metastases. Therefore, the aim of this study was to correlate the primary localization of cutaneous squamous cell carcinoma of the head and neck region with the localization of the sentinel lymph node (SLN).

**Patients and Methods**

This prospective study included 64 high-risk patients with cutaneous squamous cell carcinoma of the head and neck and clinically negative lymph nodes subjected to SLNB between 2006 and 2010 at the Clinic for Plastic, Reconstructive and Aesthetic Surgery of the Clinical Center in Niš, Serbia. Patients were selected based on the presence of high metastatic risk defined by the criteria published in the literature.

The study included patients whose biopsy indicated the presence of squamous cell carcinoma of the skin in the head and neck region. Furthermore, following clinical and ultrasonographic examinations, no enlarged lymph nodes or signs of potential metastatic disease were detected in any of the included patients. Patients in whom the presence of metastases was detected during the above examinations were excluded from the study.

Control follow-ups and ultrasonographic examinations of lymph nodes were performed every 3 months after the surgical intervention. In case we were not able to come to a follow-up at the scheduled time, information was collected from medical records and via telephone interviews. The study was approved by the Ethics Committee of the Faculty of Medicine of the University in Niš, and the written consent was obtained from all participants in the study.

The primary malignant process on the skin is divided into 12 different anatomical areas: anterior scalp, posterior scalp, retroauricular region, periorbital region, temporal region, frontal region, medial cheek, lateral cheek, nose, auricle, chin, and neck (Figure 1). Primary squamous cell carcinoma of the lips was excluded from the study given that the lips anatomically belong to the oral cavity.

Lymphoscintigraphy was performed after injecting 30-50 MBq of Technetium-99m radiolabeled nanocolloid at the tumor site. Following all valid guidelines, after 3-18 hours, surgical excision of the primary tumor with wide margins and SLN was performed, followed by SLNB using a manual gamma camera for SLN detection.

The excision of the primary lesion was made immediately before SLNB to prevent the “shine through” phenomenon. Radiolocalization was combined with the intradermal injection of vital blue dye at the primary site of the tumor at the onset of the surgical procedure. Tissue cross-sections 3 mm-thick of biopsied SLNs were em...
bedded into paraffin blocks. Thereafter, ten 5 μm-thick sections were obtained from each preparation and examined microscopically using hematoxylin-eosin and immunohistochemical staining for cytokeratins AE1 and AE3. Finally, lymphatic drainage patterns were analyzed. The anatomical localization of the tumor was correlated with lymphatic drainage to levels I, II, III, IV, V, occipital and parotid lymph nodes. The external jugular lymph nodes, located in the immediate vicinity of v. jugularis externa, as well as lymph nodes in the region of the anterior border of the sternocleidomastoid muscle, were specially considered through level II. Superficial parotid lymph nodes were considered within the same region.

The StatCalc program and Fisher’s exact test were used for the statistical analysis of the obtained data, while results were interpreted as statistically significant for probability values not greater than 0.05 (p<0.05).

Results

The study included 64 patients, 40 males and 24 females. The mean age of the patients was 71.5±7.9 (ranging from 58 to 84 years). The overall follow-up averaged at 9.2 years (ranging from 7-11 years). SLNB was performed under general anesthesia in 46 patients, whereas in 18 patients this procedure was accomplished under local anesthesia and analgesia. The patients were discharged from the clinic on the second day after the surgery.

In patients in whom the presence of micrometastases in SLN was not proven after the biopsy,
there was no subsequent development of metastases at the level of other lymph nodes.

Lymphoscintigraphy identified 122 SLNs in 64 treated patients (on average 1.91 lymph nodes per patient, ranging from 1 to 4). In 10 patients, SLNs were localized at two levels. The anatomical distribution of primary sites and the distribution of lymphatic drainage in accordance with the localization of the primary tumor are shown in Table I. A large number of tumors were localized on the auricle (21.6%). Level II was the most common localization of SLNs, in as many as 44.6% of patients. Regarding 33 SLNs localized at level II, drainage into external jugular nodes was detected in 24 (72.7%) (Figure 2). Drainage into parotid lymph nodes amounted to 31.1%, and all SLNs were from the superficial parotid group. Level I and occipital lymph nodes had a lower rate of drainage (8.1%).

Drainage into level III was detected in 1.4% of cases. There were no localized SLNs at level V. In general, in 71.6% of cases, drainage was into superficial lymph nodes, followed by 24% into external jugular nodes, 23% into superficial parotid, and 6% into occipital lymph nodes.

The data were analyzed to examine whether the localization of the primary tumor affects the probability of drainage nodes at certain levels of the neck and parotid region. There was a statistically significant correlation between tumor localization and drainage in certain groups of lymph nodes. In patients who had a primary tumor on the frontal region, temporal region, lateral cheek, and the auricle, SLNs were found at level II and parotid lymph nodes ($p<0.001$). On the other hand, in tumors of the nose, periorbital region and posterior auricular region, SLNs were found in parotid lymph nodes ($p<0.001$), while in tumors of the medial cheek, SLNs were detected at level I and parotid lymph nodes ($p<0.003$). Finally, in tumors localized on the neck, SLNs were found at level IV ($p<0.001$), while in tumors of the posterior scalp SLNs were detected in occipital region ($p<0.001$).

Among the 64 patients with clinically negative lymph nodes who underwent SLNB at our clinic, 14 patients (21.9%) had histologically positive SLNs. The distribution of metastases regarding the localization of the primary tumor is illustrated in Figure 4.

Our study reported three small complications, such as the appearance of seroma (two cases in
which a lymph node of the parotid region was biopsied and one case in which a biopsy of level II lymph nodes was performed), which did not require further surgical treatment. No other complications were reported.

The incidence of metastases in high-risk squamous cell carcinoma patients undergoing SLNB ranges between 12.5% and 44.4%.

The results of our study have shown that 21.9% of patients had histologically positive SLNs. Therefore, the construction of lymphatic drainage patterns of the head and neck in relation to the primary anatomical localization of malignancy could potentially be of great importance in the treatment of patients. Several studies conducted at Royal Prince Alfred Hospital have also tackled this issue and pointed out that SLNB should be considered for high-risk tumors and should be evaluated individually for each patient with squamous cell carcinoma, while for patients with cutaneous malignant melanomas of the head and neck, tumors metastasized to clinically predicted nodal groups in 92% of patients.

Sentinel lymph node biopsy has become the standard in the assessment of clinically negative lymph nodes in patients with malignant melanoma. On the other hand, the use of SLNB in cutaneous forms of squamous cell carcinoma is still in the initial study phase, with only a few studies conducted on a small number of patients.

Several studies have described levels of neck region involvement in patients with squamous cell carcinoma of the head and neck, and the results are based on the material obtained after neck dissections. To date, there are no studies that have analyzed lymphatic drainage according to the data obtained by SLNB in high-risk patients with squamous cell carcinoma of the head and neck. The authors of the conducted studies on the cutaneous form of squamous cell carcinoma recommend neither regional lymph node dissection nor SLNB, suggesting that this disease is quite common, and that the frequency of lymph node involvement is relatively small.

Once squamous cell carcinoma metastases appear, the overall survival rate is only 34.4% which highlights the crucial importance of early diagnosis and treatment of this disease.

A high incidence of lymphatic drainage into level II in this study is consistent with the findings of previous studies.

The data on the involvement of superficial lymph nodes is scarce, especially in the area of v. jugularis externa. Lymph nodes in this region, being mostly solitary, are not located at a certain, specific level, but represent a frequent place for metastatic spread of the primary skin cancer. Vauterin et al. drew special attention to these nodes and recommend their removal by any lymphadenectomy for skin carcinoma, including squamous cell carcinoma and melanoma. Chu and Osguthrope also highlighted the involvement of external jugular and occipital lymph nodes. In our study, lymphatic drainage was mainly into the superficial lymph nodes - in external jugular nodes, superficial parotid, and occipital lymph nodes. In addition, lymphatic drainage of cutaneous squamous cell carcinomas has been shown to be predictable regarding the anatomical localization. Therefore, this study provided further understanding of the lymphatic drainage map of the head and neck in patients with squamous cell carcinoma of the abovementioned regions.

In clinical practice, SLNB can be a challenge for the surgeon. When performing in the cervical region, this diagnostic procedure is particularly
complex for an inexperienced surgeon due to the presence of large blood vessels and nerves. In addition, in some cases, atypical localization of the sentinel lymph node is also possible. Finally, due to the limited space between tumor area and SLN in the head and neck region, radiolocalization can be difficult due to diffuse radiation or signal superposition.

Early treatment of patients with the confirmed nodal disease could lead to a reduction in the number of fatal outcomes in association with squamous cell carcinoma.

Conclusions

The lymphatic drainage map is useful for predicting potential metastatic sites based on the primary location of the tumor. With the knowledge of the lymphatic drainage map, it is recommended to perform a thorough clinical examination of lymph nodes of the head and neck region where lymph is drained from the area of the primary tumor, given that it enables early diagnosis and appropriate treatment of patients with present metastases.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References


