Evaluation of Sentinel Node Biopsy in Oral Carcinomas

Aleksandar Milenović[1], Mišo Virag[1], Predrag Knežević[1], Vanja Vučićević Boras[2,3], Karmen Trutin Ostović[4], Dragana Gabrić Pandurić[3,5] and Mato Sušić[3,5]

[1] University of Zagreb, University Hospital Dubrava, Clinic for Oral and Maxillofacial Surgery, Zagreb, Croatia
[2] University of Zagreb, School of Dental Medicine, Department of Oral Medicine, Zagreb, Croatia
[3] University of Zagreb, University Hospital Center Zagreb, Zagreb, Croatia
[4] University of Zagreb, University Hospital Dubrava, MIAC Centre of Clinical Cytology and Cytometry, Zagreb, Croatia
[5] University of Zagreb, School of Dental Medicine, Department of Oral Surgery, Zagreb, Croatia

A B S T R A C T

It is still a matter of debate whether sentinel node biopsy might replace neck dissection in patients with clinically negative neck lymph nodes who suffer from oral squamous cell carcinoma. In 30 patients (26 male, 4 female, average age 59.4 years) with oral squamous cell carcinoma we performed ultrasound guided punction of the lymph nodes which were lymphoscintigraphically seen together with histopatological analysis of the dissected node. Sentinel lymph node was seen in 93% cases. By use of lymphoscintigraphy sentinel node was verified in 23 patients. Ultrasound guided punction showed presence of regional disease in 10% of cases, whereas sentinel biopsy revealed 23 of the converted necks. Histopathological findings were positive in 33% of our patients. The results of this study revealed that sentinel biopsy did not reveal 27% of the patients with positive neck histopathology. In conclusion, sentinel node biopsy should be performed in selective cases as in some localizations it is easier to perform neck dissection in comparison to the sentinel node biopsy.

Key words: *oral squamous cell carcinoma, sentinel node biopsy, histopathology, lymphoscintigraphy*

Introduction

The prevalence of oral squamous cell carcinoma is increasing[1]. Clinically negative necks in early stage of oral squamous cell carcinoma (OSCC) tend to harbor occult disease within cervical lymph nodes in 20–30% of cases[2]. Sentinel node biopsy (SNB) has been proposed for staging of the cN0 neck in early oral/oropharyngeal squamous cell carcinomas (SCC). Because SNB is a minimally invasive procedure, it is thought to be associated with less morbidity than elective neck dissection. The management of the clinically and radiologically negative neck (cN0) in patients with early oral and oropharyngeal squamous cell carcinoma (OSCC) is still a matter of debate, though most centers favor an active policy and perform elective neck dissection (END) for staging of the neck and removal of occult disease. In the past decade SNB has been successfully implemented in early stage head and neck carcinomas[3]. However, Pattani et al.[2] concluded that it is unclear if sentinel node biopsy results in any comparable improvement in survival in comparison to wait and see policy. Therefore we compared ultrasound guided punction of lymph nodes lymphoscintigraphically seen together with histopathological analysis of the dissected nodes.

Materials and Methods

This study was approved by the Ethical Committee according to Helsinki II. There were 30 patients with oral carcinoma with an average age of 59.4 yrs. There were 26 (86%) male patients and 4 (14%) female patients. In 14 (47%) patients modified radical neck dissection was performed and in 16 (53%) patients classic radical neck dissection was performed. Most frequently tumors were located on the tongue (36.7%), followed by floor of the mouth (23.3%), and in the remaining 20% of the patients the tumor was located on the tonsil. Retromolar area and oropharynx were affected in two patients (6.7%) and base

Received for publication November 23, 2013

of the tongue in one patient as well as buccal carcinoma seen in one patient (3.3%). T1 staging had one patient (1%), T2 staging had 22 patients (73.3%) and T3 staging had 7 patients (23.3%).

Comparison between lymph node size was tested by use of t-test for dependent samples whereas number of tested lymph nodes after dissection was tested with t-test for independent samples. In both cases variables were normally distributed which was confirmed by Shapiro-Wilks test. The localization and tumor size with regard to the spread into regional lymph nodes were tested with χ^2-test. Statistical analysis was performed on Statistica 6.0 (Statsoft, Tulsa, USA). As histopathological analysis of the lymph nodes revealed highest number of positive lymph nodes and it was used as a standard. Afterwards, sensitivity and specificity for employed methods was calculated and compared with McNemar test for dependent pairs of proportion.

Results

Out of 30 analysed patients in 28 patients sentinel lymph node was identified (93%). In 23 patients in whom nodes were lymphoscintigraphically seen, these nodes were also shown by intraoperative gamma probe. In seven patients lymphoscintigraphy didnt show sentinel node and five were identified with gamma probe. In 24 patients in whom nodes were recorded as hot, radioactivity was seen in one region whereas in four patients radioactivity was recorded in two regions. In 17 patients region III was identified, followed by region II (6 cases). In two patients regions III and IV were identified and in the remaining two regions were seen IV and V and I and V respectively. In patients whom lymph node was not seen lymphoscintigraphically the suspected lymph node was punctured. The size of the lymph nodes seen by ultrasound varied between 9–22 mm. The average size of the measured lymph node seen by ultrasound was 13 mm. Cytological analysis was performed on several measurments. Firstly out 30 patients, only in one patient was the punctate of the lymph node positive. In five patients imprint cytology was positive. In those five patients smears stained according to Giemsa and Papanicolau were positive as well as immunohistochemistry on cytokeratin. Cytological punction as well as imprint cytology were negative in all other patients.

Final results of the sentinel lymph nodes localisation were obtained by combination of lymphoscintigraphy and intraoperative display by use of mobile gamma probe. By lymphoscintigraphy we showed 23 localisations of potential lymph nodes. Out of remaining seven patients who were not detected, in five we managed to detect sentinel nodes, therefore in 28 patients sentinel lymph nodes were identified. In 30 patients, 44 lymph nodes were extracted and were considered as sentinel lymph nodes. The average size of the sentinel nodes was 12.3 mm (range 5–30 mm). Twenty four sentinel nodes were found in the region III, 17 in the region II and three in the region I. By use of gamma probe no sentinel nodes were seen in the region IV and V.

In our patients the number of sentinel positive lymph nodes varied between one to five. The most frequent finding was one sentinel node in 24 patients (80%). In two patients two lymph nodes were extracted as sentinel lymph nodes (6.7%) and in one patient we extracted three lymph nodes (3.3%) and in one we extracted four lymph nodes (3.3%). In two patients we extracted 5 lmyph nodes (6.7%) which were considered as sentinel lymph nodes. Average number of extracted lymph nodes per patient was 1.5 which were considered as sentinel lymph nodes. Positive lymph nodes were seen in 8 patients (27%). Average number of extracted lymph nodes per patient was 1.5 and they were considered as sentinel nodes. Positive sentinel nodes were seen in 8 patients (27%). In four patients positive sentinel node was the only positive lymph node. In two patients (6%) was sentinel lymph node negative whereas in the dissected neck the same node was found to be positive. Therefore the false negative finding was observed. In one patient sentinel node biopsy as well as results of the dissected neck were negative, whereas during the operation positive lymph node was found parapharyngeally. In total we saw three false negative findings. Two referred to negative sentinel nodes whereas in one patient (no matter of the negative sentinel and dissected neck) one positive node parapharyngeally during operation was found.

In histopathological samples of the lymph nodes, 14 to 45 lymph nodes per patient were isolated. An average number of the lymph nodes was 29.72. In ten patients positive lymph nodes in dissected tissue were found and consequently 6 patients had PN1 (instead of N0) and four patients had PN2 (instead of N0).

There was significant difference between imprint cytology and cytological aspiration according to Mc Nemar analysis ($p=0.0455$). There was no difference between sentinel biopsy and imprint cytology according to Mc Nemar analysis ($p=0.0833$). Additionally there was no difference between histopathology and sentinel biopsy finding ($p=0.1573$). There was a significant difference between histopathology and imprint cytology as a method while diagnosing negative neck ($p=0.0253$).

There were no significant differences between different tumor localizations and metastases. Probability of metastases was not dependent upon T staging. The probability of metastizing into regional nodes was independent upon size of the sentinel lymph node as well as number of the examined nodes.

There was no significant difference between sentinel lymph node measured with ultrasound and sentinel lymph node on the histopathology finding.

Discussion

Gurney et al.[4] performed total of 122 neck dissections in 109 patients. Additional positive nodes were found in 34.4% of cases (42/122: 18 same, 21 adjacent, and 3 non-adjacent neck level). Additional nodes, especially if outside the sentinel node basin, had an impact on outcome. The results are preliminary but suggest that both the

number and the position of positive sentinel nodes may identify different prognostic groups that may allow further tailoring of management plans. Murer et al.[5] investigated 33 patients after SNB and 29 after elective neck dissection. SNB is associated with significantly less postoperative morbidity and better shoulder function than elective neck dissection. The same authors[5] concluded that patients with nodal negative early SCC of the oral cavity should be offered SNB. However, the results of this study show that sentinel node biopsy has drawbacks, therefore we wouldn't recommend it as the results of this study revealed that sentinel biopsy did not reveal 27% of the patients with positive neck histopathology. Contrary to our results, Liu et al.[6], Dequanter et al.[7], Edkins et al.[8] reported that SNB has 100% sensitivity and specificity in oral tongue carcinoma. It might be that sentinel is an excellent method for detection of oral carcinoma and that different results are obtained when oropharyngeal carcinomas are included.

Yamauchi et al.[9] reviewed 22 patients with clinically T1/T2, N0. Three of 11 patients (27%) in the watchful waiting group developed regional recurrence and underwent neck dissection. Only 1 of 11 patients (9.1%) in the sentinel node navigation surgery (SNNS) group developed regional recurrence. Although the groups did not significantly differ, the SNNS group tended to have less regional recurrence. SNNS should be the third strategy for managing early oral tongue carcinoma.

Broglie et al.[10] performed analysis of 79 patients (67% male, median age 60 years, age range 34–87 years). Lymphatic mapping consisted of preoperative lymphoscintigraphy, single photon emission computed tomography (SPECT/CT), and intraoperative use of a handheld gamma probe. Twenty-nine of 79 patients (37%) had positive sentinel nodes (SN). Six of 29 (21%) patients showed isolated tumor cells, 14/29 (48%) micrometastases, and 9/29 (31%) macrometastases. Only the difference in DSS achieved statistical significance. The neck control rate after 5 years was 96% in SN-negative and 74% in SN-positive patients. This difference was statistically significant. SNB is a safe and accurate staging modality to select patients with clinically stage I/II OSCC with occult lymph node disease for elective neck dissection (END). Patients with negative SN and no END achieve an excellent neck control rate which compares favorably with reports on primary END. The neck control rate in SN-negative patients is superior to that in SN-positive patients, which is reflected in superior DSS.

Our results show that in 93% of our patients positive sentinel lymph node was identified which was in concordance with the results of Pitman et al.[11] and also Krag et al.[12]. However, Krag et al.[12] reported that detection is highly dependable upon surgeon as on the same sample the percentage of sentinel node identification varied between 79–98%.

Nieuwenhuis[13] reported that ultrasound guided cytology reduces the need for sentinel biopsy for 50%. This finding is opposite to our results as we found that only one patient with positive histopathological finding had positive aspiration cytology finding by use of ultrasound.

Aspiration cytology was significantly more sensitive when compared to imprint cytology when diagnosing clinically negative neck. According to our results aspiration cytology guided by ultrasound is not method of choice in clinically negative neck. Sentinel node biopsy especially in jugular chain might carry serious consequences upon vital structures.

The number of extracted sentinel nodes in our study was in concordance with other studies[14] and varied between one to five nodes.

Skip metastases were seen in two patients within this study (6.7%). Our results are in concordance with the results of Byers et al.[15] who reported that 15.7% of the patients had skip metastases. These findings might explain recurrences after neck dissection which didn't include all five lymph node regions.

One has to bear in mind that most studies so far have showed results based on the extraction of sentinel nodes during neck dissection, but not based solely on the sentinel node identification. Last but not least, we are still unable to confirm whether sentinel might decrease morbidity and increase patients survival. More studies are needed regarding sentinel node efficacy based on the percentages of the regional recurrences during five year period.

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V. Vučićević Boras

University of Zagreb, School of Dental Medicine, Department of Oral Medicine, Gundulićeva 5, 10000 Zagreb, Croatia
e-mail: borasvanja@yahoo.com

EVALUACIJA SENTINEL BIOPSIJE LIMFNIH ČVOROVA U ORALNOM KARCINOMU

S A Ž E T A K

Još uvijek nije poznato da li sentinel biopsija limfnih čvorova može zamijeniti disekciju vrata u bolesnika koji boluju od karcinoma usne šupljine i imaju klinički negativne limfne čvorove na vratu. U 30 bolesnika oboljelih od oralnog planocelularnog karcinoma (26 muškaraca i 4 žene, prosječne dobi od 59,4 godine) je napravljena punkcija limfnih čvorova uz pomoć ultrazvuka koji su viđeni i limfoscintigrafski te uz patohistološku analizu diseciranih čvorova. Sentinel limfni čvorovi su viđeni u 93% slučaja. Upotrebom limfoscintigrafije su sentinel pozitivni čvorovi verificirani u 23 pacijenta. Punkcija uz pomoć ultrazvuka je pokazala prisutnost regionalne bolesti u 10% slučajeva, dok su uz pomoć sentinel biopsije otkrivena 23 konvertirana vrata. Patohistološki nalaz je bio pozitivan u 33% bolesnika. Rezultati ovog istraživanja pokazuju kako se sentinel biopsijom nije otkrilo 27% bolesnika sa pozitivnim patohistološkim nalazom limfnih čvorova vrata. Zaključno, sentinel biopsija limfnih čvorova se treba napraviti u izdvojenim slučajevima jer je na nekim mjestima lakše napraviti disekciju vrata u odnosu na sentinel biopsiju limfnih čvorova.