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Biopsy of the sentinel lymph node in oral squamous cell carcinoma: analysis of error in 100 consecutive cases

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Abstract

UK national guidelines in 2016 recommended that sentinel lymph node biopsy should be offered to patients with early oral cancer (T1-T2 N0) in which the primary site can be reconstructed directly. This study describes the pitfalls that can be avoided in the technique of biopsy to improve outcomes. We retrospectively analysed the data from 100 consecutive patients and recorded any adverse events. Lymphatic drainage of tracer failed in two patients as a result of procedural errors. Two patients with invaded nodes developed recurrence after total neck dissection, one after micrometastases had been diagnosed, and the other as a result of extranodal spread that had led to understaging and therefore undertreatment. Two results would not have been mistakenly classified as clear if all the harvested nodes had been analysed histologically according to the protocol. The disease-specific (96%) and disease-free (92%) survival were better than expected for a group of whom a third had stage 3 disease. If all harvested nodes had been analysed by the correct protocol then two of the three nodes wrongly designated clear would have been detected, two deaths potentially avoided, and the false-negative rate would have fallen from 8.3% to 2.7%. We conclude that minor deviations from protocol can result in a detrimental outcome for the patient.

Keywords: Sentinel Lymph Node Biopsy; oral oncology; oral cancer; oral squamous cell carcinoma

Introduction

Recent evidence has confirmed that elective neck dissection gives better survival than a "watch and wait" policy in patients with early oral squamous cell carcinoma (SCC) and a clinically N0 neck.[1] Meta-analyses have shown that sentinel lymph node biopsy can identify early metastases reliably,[2–4] and neck dissection can therefore be restricted to the 20% or 30% who have invaded nodes.[5–7] United Kingdom guidelines recommended that biopsy should be offered to patients (T1-T2 N0) with oral SCC as it is in Denmark and Holland.[8]

Sentinel lymph node biopsy has a sensitivity and specificity between 79% and 87% depending on the location of the malignancy, but a false negative rate of up to 14%.[5] It is necessary to report positive results to gain confidence in the technique, but more informative data may be gained by

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analysing failures. We have therefore analysed the adverse events in 100 consecutive biopsies. Our intention was to identify pitfalls that can be avoided to improve outcomes.

Material and methods

We retrospectively analysed the results of 100 consecutive patients with T1-T2 N0 tumours who had sentinel lymph node biopsies between 2005–2013. The technique followed a standard protocol,[9] which involved radionuclide lymphoscintigraphy over one day (20–40 MBq) or two days (40–80 MBq) depending on the availability of resources. Static and dynamic imaging was used in all patients with the addition of single-photon emission computed tomography (SPECT/CT) in the final 26 cases (after 2011).

A blue dye optical tracer was used during operation. Lymph nodes retrieved were either hot or blue, or hot and blue, and firm nodes were also sampled. There were initially evaluated on haematoxylin and eosin (H & E) smears and, if these were clear, on serial sections with H & E, and pan-keratin AE1/AE3 staining at 150 μm intervals.[5] If more than three nodes were harvested, the one with the highest gamma count was taken as the sentinel node, and processed according to the full protocol. The remainder were processed by single section staining through the hilum with H & E. If the lymph nodes were clear it was assumed that no metastases were present and a "watch and wait" policy was adopted. If they were invaded, a level 1–4 completion neck dissection was done. These were examined by a single H & E section of hilum, or from multiple cassette slices (2 mm thick) if the node was thicker than 5 mm (Fig. 1).

Contemporaneous data were stored in a bespoke database (InfoFlex v.5, CIMS Ltd) that consisted of personal and clinical characteristics, findings from lymphoscintigraphy, condition of sentinel lymph node, complications of the procedure, and details of the tumour. The type, site, date, and subsequent treatment of any recurrences were noted.

Failure was defined as recurrence at any site, death from disease, a false negative biopsy, or failure to find a sentinel lymph node. A false negative biopsy was diagnosed if there was subsequent development of an isolated metastatic SCC of the neck.

Statistical analysis

R (R-Project, R Core Team) was used for the statistical analysis. The independent *t* test was used to examine any statistical relations between the patients' clinical and personal characteristics and their outcomes. The significance of the differences between the groups that developed complications and those that did not were compared with chi-squared, Fisher's exact, or Welch's two-sample *t* test as appropriate. Probabilities of less than 0.05 were accepted as significant.

Table 1
Outcome of disease and result of the sentinel lymph node biopsy.

Type of recurrence	Sentinel lymph node biopsy result	
	Negative (n = 65)	Positive (n = 33)
Local	0	0
Local and neck	0	0
Neck only	3	4
Local and distant	0	0
Local, neck, and distant	0	1
Total recurrence	3	5

NB: Lymphatic drainage of tracer failed in two patients as a result of procedural errors.

Results

Details of 100 consecutive patients with oral SCC (T1 n = 74: T2 n = 26), N0 M0, were retrieved. In two cases lymphoscintigraphy had failed to show a sentinel lymph node but one was present in 98 patients, of which 86 were ipsilateral to the tumour (10 bilateral, and two contralateral). About 2.5 nodes were retrieved/patient (range 1–6), with 19 patients having more than three excised. In these patients only the hottest was subjected to the full histological protocol.

A total of 36 patients had occult metastases in the neck (22/74 of the pT1 and 14/26 of the pT2), 33 were identified by biopsy examination and the remainder discovered as isolated recurrences during follow up (Table 1). The false negative rate was therefore 8%. There were 12 deaths, giving a crude survival of 88%. Eight of the patients who died had new primary tumours and these were censored in the outcome analysis. Four patients died from recurrence of the original carcinoma (disease-specific survival 96%), and three of these may have been preventable (Cases 3,7, and 8 in Table 2).

Of the 33 patients with invaded sentinel nodes, 32 were treated by complete neck dissection and one by radiation alone, which was an error of medical assessment. After biopsy this patient was too frail for neck dissection and had radiotherapy that failed to cure the disease (Case 8, Table 2). If it had been predicted that the patient would not manage the two separate procedures, neck dissection would have been the primary treatment. Statistical analysis was completed on the pathological tumour factors with significant factors shown in Table 3.

Isolated recurrence in the neck

Seven patients (excluding Case 8) developed isolated neck recurrences (Fig. 1), four after biopsy and neck dissection, and three after false negative biopsy results.

The patients with invaded nodes (n = 32) were subsequently treated by neck dissection and in 25 no further lymph node metastases were detected. Four of the 32 subsequently developed isolated recurrences in the neck. In two patients (Cases 9 and 10, Table 2), these developed in the other side of the neck and were treated. In the other two (Cases 6 and 7, Table 2), recurrences were ipsilateral and both died of

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