Soft Tissue Deposits in Neck Dissections of Patients With Head and Neck Squamous Cell Carcinoma

Prospective Analysis of Prevalence, Survival, and Its Implications

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Background: Soft tissue deposits of squamous cell carcinoma in the necks of patients with squamous cell carcinoma of the upper aerodigestive tract may represent either total effacement of a lymph node by carcinoma or extralymphatic deposits of carcinoma. There are few reports of their clinical or prognostic significance.

Methods: Data from 215 neck dissections from 155 patients with squamous cell carcinoma of the upper aerodigestive tract were studied prospectively to assess the prevalence of soft tissue deposits within the neck. The case notes of these patients were subsequently reviewed to analyze the effect on both the overall survival and recurrence-free survival.

Results: The prevalence rate for soft tissue deposits occurring alone was 10.3%; the prevalence rate for soft tissue deposits occurring with extracapsular spread was 13.5%. The overall prevalence rate for soft tissue deposits was 23.9%. There was a statistically significant reduction in actuarial and recurrence-free survival in patients with soft tissue deposits compared with patients with pathologically node-negative necks (P=.001), and in patients with soft tissue deposits compared with those with pathologically node-positive necks without extracapsular spread (P=.001). No statistically significant differences were found between patients with soft tissue deposits and patients with pathologically node-positive necks with extracapsular spread, for actuarial survival or recurrence-free survival.

Conclusions: In this series, soft tissue deposits were associated with an aggressive clinical course and poor survival. It is therefore important that histopathologists agree on a uniform terminology when reporting soft tissue deposits and actively look for their presence when examining neck dissection specimens.


The presence of metastatic disease in cervical lymph nodes has been considered to be one of the most important adverse prognostic factors in patients with squamous cell carcinoma of the upper aerodigestive tract.1 We have shown that the presence of extracapsular spread is of paramount importance in determining prognosis, and cervical lymph node metastases without extracapsular spread have only a limited impact on survival.2 We have prospectively investigated the prognostic significance of metastatic squamous cell carcinoma in extranodal tissue in 215 neck dissections performed for the treatment of 155 patients with squamous cell carcinoma of the head and neck, both with node-positive and high-risk node-negative disease. We show that soft tissue disease is an important prognostic factor for patients with head and neck squamous cell carcinoma that has received limited attention in the literature.

Methods

Between August 1, 1995, and November 30, 2001, 215 neck dissections were performed on 155 patients who underwent curative surgery and either ipsilateral or bilateral neck dissection for squamous cell carcinoma of the upper aerodigestive tract. All patients undergoing neck dissections during the study period were included. Patients were excluded only if they were lost to follow-up. Both the site of the primary tumor and the T and N stage influenced criteria for neck dissection. It is our policy to perform a comprehensive (levels I-V) neck dissection in patients who are clinically node positive. Our policy in treating patients with clinically node-negative necks is to dissect levels I to V in patients with an oropharyngeal or oral cavity primary tumor that is larger than a superficial T2 tumor; and to dissect levels I to IV in patients with a hypopharyngeal primary tumor, a laryngeal primary tumor staged T2b
or greater, or recurrent disease. In addition, we perform bilateral selective neck dissections in patients with midline or bilateral disease. Eighteen patients in the series had salvage surgery because of recurrence after radiotherapy.

The neck dissections were separated into node levels intraoperatively by means of landmarks suggested by Robbins et al. The node levels were marked with steel clips and separated immediately after resection. The node levels were fixed in formalin and sent as separately labeled specimens. Each node level was cut into 2-mm-thick slices and embedded in paraffin wax, sectioned at 6-µm thickness, and stained with hematoxylin-eosin. With this technique, microscopic as well as macroscopic extracapsular spread can be detected.

The neck dissections were also examined for the presence or absence of soft tissue deposits of squamous cell carcinoma. A soft tissue deposit was defined as metastatic squamous cell carcinoma in the soft tissues of the neck, with no evidence of a lymph node being present (Figure 1). Microscopic extracapsular spread was defined as tumor extension beyond the lymph node capsule with a desmoplastic stromal response; macroscopic extracapsular spread was visible with the naked eye. Soft tissue deposits of squamous cell carcinoma differ from extracapsular spread in the absence of an identifiable lymph node structure; they may represent a completely effaced lymph node or a metastatic deposit of SCC unrelated to any lymph node within the neck. Extracapsular spread is always related to metastasis of carcinoma to a lymph node.

The presence of extracapsular spread can be a confounding factor when the effect of soft tissue deposits on survival is assessed. Therefore, patients were divided into 3 groups: (1) patients who had pathologically negative nodes (pN0); (2) patients who had pathologically positive nodes (pN+) without extracapsular spread; and (3) patients who had pN+ with extracapsular spread. Kaplan-Meier survival curves were calculated stratified by soft tissue disease against the 3 groups of patients.

The results were analyzed by patient numbers, rather than neck dissection numbers. The analyses were performed with SAS software (SAS Institute Inc, Cary, NC). Both overall survival and recurrence-free survival were calculated from the date of presentation. For overall survival, if patients had not died by the end of the study, they were censored at the date last seen. For recurrence, if they were alive without recurrence at the end of the study, they were censored at the date last seen. If they died without recurrence, they were censored at the date of death.

One hundred fifty-five patients underwent a total of 215 neck dissections during the study period. Eleven patients had previously undergone radical radiotherapy that had failed. The majority of tumors were laryngeal or hypopharyngeal in origin; details of the distribution of patients by primary site and the number of neck dissections per primary site are given in Table 1. Thirty-seven patients (who underwent 48 neck dissections) were found to have evidence of soft tissue disease (Table 1). Locoregional recurrence occurred in 33 patients, 11 of whom had soft tissue deposits. Distant metastasis was seen in 16 patients, of whom 5 had soft tissue deposits. In 5 patients, locoregional failure and distant metastasis occurred; 3 of these had soft tissue deposits.

The mean follow-up of patients who were alive at the end of the study was 45 months (range, 15-86 months). Of the 155 patients, 52 had more than 5 years of follow-up, 20 had 4 years, 31 had 3 years, 34 had 2 years, and 18 patients had a minimum of 15 months of follow-up.

Sixty-five percent of patients (101/155) had pathological evidence of metastasis to cervical lymph nodes (Table 2). Of these, 71% (72/101) had evidence of either extracapsular spread or soft tissue deposits, and in 29% (29/101) there was no extracapsular spread or soft tissue deposits.

Twenty-four percent of patients (37/155) were found to have soft tissue deposits, and of these, 57% (21/37) had soft tissue deposits and extracapsular spread. Forty-three percent (16/37) had soft tissue deposits alone. With regard to stage of disease, 24% (9/37) were T4, 54% (20/37) were T3, 11% (4/37) were T2, and 5% (2/37) were T1. Two cases were Tx with unknown primary tumors.

### RESULTS

#### RECURRENCE AND SURVIVAL

Thirty-five percent of patients (54/155) had pN0 necks; of these, 69% (37/54) were alive and all were disease free at the end of the study period. Sixty-five percent of patients (101/155) had pN+ necks; of these, 43% (43/101) were alive, and 39% (39/101) were alive and disease free.
SOFT TISSUE DEPOSITS AND EXTRACAPSULAR SPREAD

At the end of the study, 50% (8/16) of the 16 patients with soft tissue deposits alone were alive, and 33% (7/21) of those with both extracapsular spread and soft tissue deposits were alive. Twenty-three percent of patients (8/35) with extracapsular spread alone were alive (Table 2).

In total, 41% of patients (15/37) with soft tissue deposits and 32% of patients (23/72) with extracapsular spread and/or soft tissue deposits were alive at the end of the study, compared with 69% of patients (20/29) with no extracapsular spread or soft tissue deposits.

The presence of soft tissue deposits had a statistically significant adverse effect on actuarial and recurrence-free survival when compared with patients with a pN0 neck (P = .001, $\chi^2$ test), and also when compared with patients with a pN+ neck without extracapsular spread (P = .001, $\chi^2$ test) (Figure 2 and Figure 3). There were no statistically significant differences between patients with soft tissue deposits when compared with patients with a pN+ neck with extracapsular spread but without soft tissue deposits for either overall survival (P = .24) or recurrence-free survival (P = .29, $\chi^2$ test; Figure 4).

COMMENT

Squamous cell carcinoma from a primary site spreads by a process of embolization or permeation in the lymphatic vessels draining the site. Other routes of spread include a vascular or neural route. Tumor cells in the lymphatic vessels reach the cervical lymph nodes, after which the fate of these cells depends on the local environment, the host immune response, and the inherent metastatic potential of the cells. Some of the tumor cells are engulfed or localized by the immune system, while the aggressive ones spread beyond the capsule of the node or to the neighboring lymph nodes. The immune response of an individual lymph node is often overwhelmed by the tumor cells, thereby replacing the entire lymph node architecture with squamous cells. Similarly, the tumor cells can extra-
sate out of the lymphatic channels into the soft tissues of the neck. In these 2 scenarios, histopathological examination would show deposits of squamous cell carcinoma in the soft tissues of the neck, with no evidence of lymph node being present. These characteristics reflect the more aggressive nature of tumor compared with those restricted within the lymph node structure.

In a literature search using MEDLINE, we found only 1 report that studied the prognostic significance of soft tissue deposits as defined herein. In that study, Violaris et al reviewed the histologic slides of 497 patients with head and neck squamous cell carcinoma who underwent neck dissection at a period after initial therapy. Their first aim was to confirm the presence of squamous cell carcinoma within the neck, and second, to ascertain whether metastases was to soft tissue, to a lymph node, or to both. Twenty-eight percent of patients had free soft tissue deposits. The survival of patients with soft tissue metastases was significantly reduced when compared with that of patients with ordinary neck node metastases ($P<.001$). Shah et al., in a study of 758 patients with oral cancers, demonstrated statistically significantly ($P<.001$) higher regional failure rate in patients with extracapsular extension of disease in lymph nodes or the presence of soft tissue involvement in the neck. Their study, however, did not define the exact nature of this soft tissue involvement.

Similarly, other studies on pathology of neck dissections of patients with oral cancers describe soft tissue involvement as spread of tumor into pericapsular (extracapsular) tissue, soft tissue spread beyond the lymph node capsule, and extension of tumor through the capsule into perinodal soft tissues; these descriptions are again unclear about the exact nature of soft tissue involvement, that is, whether they represent just extracapsular tumor spread or soft tissue deposits separate from nodal involvement. Carter, in an appraisal of neck dissections, pointed out that most pathologists interpret metastatic tumors that destroy all vestiges of normal nodal architecture as presumptive nodal deposits and suggested that it is sensible to identify them separately.

Our study demonstrates that the presence of soft tissue deposits has a significant adverse impact on survival of patients with squamous cell carcinoma of the upper aerodigestive tract. Survival was significantly lower for patients with soft tissue deposits compared not just with the pN0 group but also with the pN+ group without extracapsular spread. When compared with extracapsular spread alone, there was no clinically or statistically significant difference between the 2 groups, showing that patients with either soft tissue disease or extracapsular spread have a similar prognosis (Figure 4). Moreover, soft tissue deposits might occur early in the disease, even in T1 tumors. These features suggest that its behavior is similar to that of extracapsular spread, both being indicative of an aggressive form of disease and with a similar impact on survival.

In conclusion, soft tissue deposits represent aggressive tumors with a tendency to have early visceral metastases. They act as a surrogate marker for the systemic dissemination of tumor cells. Therefore, it is important that histopathologists agree on a uniform terminology about soft tissue deposits and actively look for and record their presence while examining neck dissection specimens.

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REFERENCES


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