The Role of Frozen Section Histological Analysis in the Treatment of Head and Neck Skin Basal and Squamous Cell Carcinomas

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Abstract

Background: Skin basal and squamous cell carcinomas together account for over half of all newly diagnosed cancer cases. Frozen section control of surgical margins is often required in the head and neck region. A paraffin permanent section does not always confirm the results of a frozen section.

Objectives: To test the diagnostic accuracy of frozen section histopathological analysis in determining the free margins of excised tumors.

Methods: This was a retrospective study of 169 cutaneous basal and squamous cell carcinomas excised with surgical margins diagnosed by frozen section and confirmed by permanent paraffin sections. The data included patients' age, gender, clinical and histopathological diagnosis, as well as characteristics of the lesions.

Results: There were 149 (88%) basal cell carcinomas and 20 (12%) squamous cell carcinomas. False negative margins were found in 19 cases (11.2%) and false positive margins in 11 (6.6%). We did not find any correlation between false positive or false negative margins and patients' age, gender, tumor size, tumor location, or the presence of sun-damaged skin. A significantly lower rate of false negative results was found in the residual tumor group.

Conclusions: Our findings support the use of frozen section margin control in selected patients suffering from non-melanoma skin cancer of the head and neck.

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Non-melanoma skin cancer is the most common type of cancer. Surgical treatment often involves the sacrifice of normal-appearing skin in order to eradicate tumor invasion into the surrounding tissue [1,2]. In the head and neck area such extensive excision may cause large scars and disfigurement. Conservative skin excision may result in incomplete tumor extirpation and recurrence. To ensure complete removal of the cancerous tissue immediate examination of the excised tissue margins using frozen section histological diagnosis technique is frequently performed [3-5]. The objective of the present study was to test the diagnostic accuracy of frozen section diagnosis in determining free margins of the excised tumors in non-melanoma skin cancer.

Patients and Methods

We conducted a retrospective study of the charts of all patients treated in the department of plastic surgery at the Soroka University Medical Center between 1 January and 31 December 2004. Altogether, 169 basal and squamous cell carcinomas were excised with surgical margins diagnosed by frozen section and confirmed by permanent paraffin sections. After initial frozen section diagnosis the specimens were fixed, stained and re-examined. Indications for frozen section analysis were residual tumors, lesions with poorly defined clinical border, and cases before flap reconstruction. Data regarding patients' clinical and histopathological parameters were collected. We compared the accuracy of frozen and permanent sections in diagnosing surgical margin involvement. A false negative result was determined by the presence of negative margins in the frozen section and positive margins in the permanent section. A false positive result was determined by the presence of positive margins in the frozen section and negative margins in the permanent section. Correlations between independent variables, false positive, false negative, and negative frozen section margins were tested using chi-square test for contingency tables or Fisher exact test when appropriate. A P value < 0.05 was considered significant.

Results

We retrieved 169 histopathological reports of patients with basal cell carcinoma or squamous cell carcinoma of head and neck skin for which frozen section had been used in excisional surgery; 149 (88%) were basal and 20 (12%) were squamous cell carcinomas [Table 1]. The basal cell carcinoma group (n=149) was divided into two subgroups – primary tumor excisions (75 specimens) and previously diagnosed incompletely excised lesions (residual tumors, n=74).

It should be noted that in the residual tumor subgroup only 20 of the 74 basal specimens contained tumor cells after re-excision (tumor positive). This is similar to our previous report [6].

Table 1. False negative and false positive results

Tumor type	Subgroup	No. of tumors	False negative	False positive
Basal cell carcinoma	Primary tumor	75	14 (18.7%)*	8 (10.7%)**
	Residual tumor	74	3 (4.1%)*	1 (1.4%)**
Squamous cell carcinoma	Primary tumor	13	2 (15.4%)	2 (15.4%)
	Residual tumor	7	0	0
Total		169	19 (11.2%)	11 (6.6%)

* $P = 0.0028$

** $P = 0.017$

In the squamous group only one of the seven residual tumors contained cancer cells.

Table 1 presents an analysis of data according to false negative and false positive results in the various subgroups. In the primary tumor excision group, false negative results were obtained in 14 cases (18.7%) and false positive in 8 (10.7%). In contrast, the residual tumor subgroup showed significantly lower false negative and false positive rates – 4.1% (P = 0.028) and 1.4% (P = 0.017) respectively. Similar results were found in the squamous group. Overall, false negative results were found in 19 specimens (11.2%) and false positive in 11 (6.6%). The negative predictive value for residual tumors was 94.8% and only 27.3% for primary tumor excisions. We did not find any correlation between false positive or false negative margins and patient's age, gender, tumor size, tumor location, or the presence of sun-damaged skin.

Clean surgical margins were achieved in the first excision session in 136 of the 169 cases. Two excisions were required in 54 patients and 3 patients were operated three times. We did not find any difference between basal and squamous cell carcinomas with regard to the number of re-excisions.

Discussion

Over 10,000 new cases of non-melanoma skin cancers are diagnosed in Israel annually. Basal and squamous cell carcinomas together account for over half of all new cancer cases [7]. Although seldom fatal it affects many patients, causing considerable morbidity and requiring substantial resources. Most skin cancers are easily treatable by surgical excision, with 3–6 mm clinically diagnosed tumor-free skin margins, and are closed by simple linear suturing. In these cases the surgical margins do not need frozen section confirmation. In cases where tumor borders are visually difficult to determine, in cases with previously incompletely excised lesions, or in aesthetically significant areas, intraoperative tumor-free margin confirmation is required. Our policy is to confirm surgical margins before flap reconstruction.

Despite our caution, we still find ourselves in a situation where the permanent histological section does not confirm the frozen section diagnosis of free margins. These cases led us to review our series of frozen sections in an effort to determine the weakness of our approach and to better inform our patients of their prognosis. Our results show an average false negative rate for the entire group – 11.2% (19/169), which is in the range of previous reports [3,8]. We did not find any correlation to tumor size, type, location or presence of pre-malignant lesions as might be expected.

The false negative rate was relatively high in the primary excision group – 18.7% and 15.4% for basal and squamous cell carcinoma respectively. In the residual tumor group the false negative results were significantly lower (4.1–0% only). This significant difference can be explained by selection bias. It is well known that re-excision of residual tumors reveals malignant cells in about 25–30% of specimens only [6]. Some authors attribute this to the theory of the "disappearance" of tumor cells that occurs as part of the wound-healing process after the first excision when not enough tumor cells are left to survive [9].

Generally, the rate of false negative results is closely related to the rate of malignancy in the examined group. In the residual tumor cohort the rate of malignancy was 26.8%, which was significantly lower than in the primary excision group. This finding correlates well with our previous report on a different group of patients where the rate of malignancy found in re-excision specimens was 28% [6]. With regard to the false positive results the only feasible explanation was the presence of atypical epithelial cells close to the surgical margins, or a possible technical error.

Analyzing data on the number of excisions made to obtain clean surgical margins revealed that the overall rate of complete tumor excision at the first surgery was 70.5%. This leaves about 30% of patients who would have had an incomplete excision had frozen section not been used. This is about three times the rate of incomplete excision in our general non-melanoma skin cancer population and about twice the rate in our head and neck skin cancer population of our previous study [6]. This means that this preselected group can benefit from the use of frozen section margin control. One may argue that these cases should be treated by Mohs surgery with no need for traditional frozen section margin control. However, Mohs surgery is not always available, in particular in the southern Israel region.

Our findings serve as a basis according to which we can offer our patients a fairly accurate prediction of their chance for completeness of tumor excision. This will allow them to make an educated choice.

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