Giant Basal Cell Carcinoma and Cigarette Smoking

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Several recent studies have linked cigarette smoking to an increased risk of squamous cell skin cancer, but previous studies have found no correlation between smoking and basal cell carcinoma. This article is a retrospective chart review of 200 patients who had Mohs' surgery for basal cell carcinoma at the Mayo Clinic in Rochester, Minnesota, between 1986 and 1990. In patients with tumors less than or equal to 1.0 cm, 30% were smokers. In patients with tumors 1.1 to 2.0 cm, 42% were smokers. In patients with tumors 2.1 to 4.9 cm, 56% were smokers; and in patients with tumors greater than or equal to 5.0 cm, 50% were smokers. Cigarette smoking is associated with an increased prevalence of basal cell carcinomas larger than 1.0 cm in diameter.

Basal cell carcinoma (BCC) is the most common malignant tumor known to man and comprises more than 75% of all nonmelanoma skin cancers.[1] A recent study estimated that the incidence of nonmelanoma skin cancer in the United States alone may exceed 1 million cases per year.[2] There are several well-known risk factors for BCC, such as fair skin, significant past sun exposure, tendency to burn rather than tan, increasing age, and genetic predisposition. Giant BCC, defined as those tumors 5.0 cm or greater in diameter, comprise less than 1% of all BCCs.[3] Risk factors for a BCC becoming a giant BCC include aggressive histologic subtype, recurrence after previous treatment, history of radiation exposure, and history of neglect.[4]

It is well known that cigarette smoking has adverse effects on the body, and more specifically, on the skin.[5] Several studies have found a relationship between smoking and squamous cell skin cancer,[6-9] but no relationship has been found to exist between BCC and smoking. For example, Karagas et al[8] found that BCC had no clear relation to cigarette smoking, Griego et al[10] found the incidence of BCC to be unaffected by smoking, and Lear et al[11] found smoking history *not* to be a risk factor for BCC. It should be noted that these studies were examining all BCCs regardless of their size; therefore, the great majority would have been smaller than 1.0 cm in diameter. No one has ever evaluated patients with BCC in relation to the size of the tumor and correlated the results with smoking status.

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Methods

A review of all charts of patients that had Mohs' surgery for BCC at the Mayo Clinic in Rochester, Minnesota, between 1986 and 1990 was performed. Tumor size was recorded based on postsurgical Mohs' defect, and smoking status was ascertained, if available. Data, based on the diameters of the tumors, were obtained from 50 consecutive charts in each of the following categories: less than or equal to 1.0 cm, 1.1 to 2.0 cm, 2.1 to 4.9 cm, and greater than or equal to 5.0 cm. Data on a total of 200 patients were recorded and evaluated. For most patients, data focused only on whether or not they were smokers. Detailed information on number of packs smoked per day and years spent smoking was rarely available.

Results

In patients with tumors less than or equal to 1.0 cm, there were 29 males and 21 females. Mean age was 68.41 years (SD=13.54) and range, 23 to 84 years. In 4 patients, smoking status was unknown, leaving 46 evaluable patients. Of these, 14 were smokers and 32 were nonsmokers, which resulted in a smoking prevalence of 30% (Table 1).

In patients with tumors 1.1 to 2.0 cm, there were 28 males and 22 females. Mean age was 69.10 years (SD=11.47) and range, 27 to 95 years. In 5 patients, smoking status was unknown, leaving 45 evaluable patients. Of these, 19 were smokers

Table 1.

Tumor Size and Cigarette Smoking in Basal Cell Carcinoma

Size	No. of Patients	No. of Smokers	Smokers, %
≤1.0 cm	46	14	30
1.1–2.0 cm	45	19	42
2.1–4.9 cm	39	22	56
≥5.0 cm	40	20	50

and 26 were nonsmokers, which resulted in a smoking prevalence of 42%.

In patients with tumors 2.1 to 4.9 cm, there were 33 males and 17 females. Mean age was 70.10 years (SD=10.72) and range, 44 to 86 years. In 11 patients, smoking status was unknown, leaving 39 evaluable patients. Of these, 22 were smokers and 17 were nonsmokers, which resulted in a smoking prevalence of 56%.

In patients with tumors greater than or equal to 5.0 cm, there were 32 males and 18 females. Mean age was 71.59 years (SD=10.90) and range, 43 to 94 years. In 10 patients, smoking status was unknown, leaving 40 evaluable patients. Of these, 20 were smokers and 20 were nonsmokers, which resulted in a smoking prevalence of 50%.

The smoking prevalence in the state of Minnesota for all adults in 1985 was 28%.[12] Statistical analysis was performed on this data, and cigarette smoking was significantly correlated with increasing size of BCC based on analysis of variance and Fisher's protected least significant difference (PLSD) test ($P<.05$).

Comment

From our data, it appears that cigarette smoking does have an effect on the prevalence of BCC, at least on those tumors larger than 1.0 cm. We found a positive dose-response relationship wherein the larger the BCC, the more likely a patient was to be a smoker. Those patients with small BCCs (≤1.0 cm) were no more likely to be smokers than the general population (in both groups, approximately 30% were smokers), whereas those with larger BCCs had a significantly higher prevalence of smoking than the general population. This result explains why previous studies, which examined all BCCs (the majority of which were <1.0 cm) as one group, failed to find a correlation between smoking and BCC. Our results, therefore, confirm the previous studies that found no relationship between smoking and BCC—but only for tumors less than or equal to 1.0 cm. For the larger, more serious tumors, there appears to be an association between smoking and BCCs (Figure 1).

A possible explanation for this correlation between cigarette smoking and larger BCCs may relate to the adverse effects of smoking on the immune system. Several studies have documented that smoking has a deleterious effect on both cellular and humoral immunity.[13-23] One study found that nicotine caused suppression of the cutaneous inflammatory response,[24] and another study found that chronic nicotine exposure induced T–cell tolerance, which led to immunosuppression.[22]

Depressed cellular immunity plays a role in cutaneous carcinogenesis, as is evidenced by the great increase in squamous cell carcinoma and the modest increase in BCC in patients receiving immunosuppressive or cytotoxic agents.[25] One study found that patients with large BCCs or squamous cell carcinomas (>2 cm) had significantly lower T–cell counts than either those with small tumors or the control group and that these lowered counts persisted even after tumor resection.[26] This study also found that larger tumors have an absent or minimal lymphocytic infiltration, whereas smaller tumors had moderate to marked lymphocytic infiltrates. Another study[27] compared BCCs in immunosuppressed patients with BCCs in immunocompetent patients and found that in the immunocompetent patients, 10% of tumors were infiltrative, and in the immunosuppressed group, 24% of tumors were infiltrative. There was also twice the prevalence of morpheaform BCC in the immunosuppressed group. Therefore, not only does systemic immunosuppression play a role in allowing more and larger BCCs to develop but also it appears to promote the development of more aggressive subtypes.

This study does not prove a causal relationship between smoking and larger BCCs because there are other factors that may predispose smokers to the large tumors. Some factors include lack of concern about

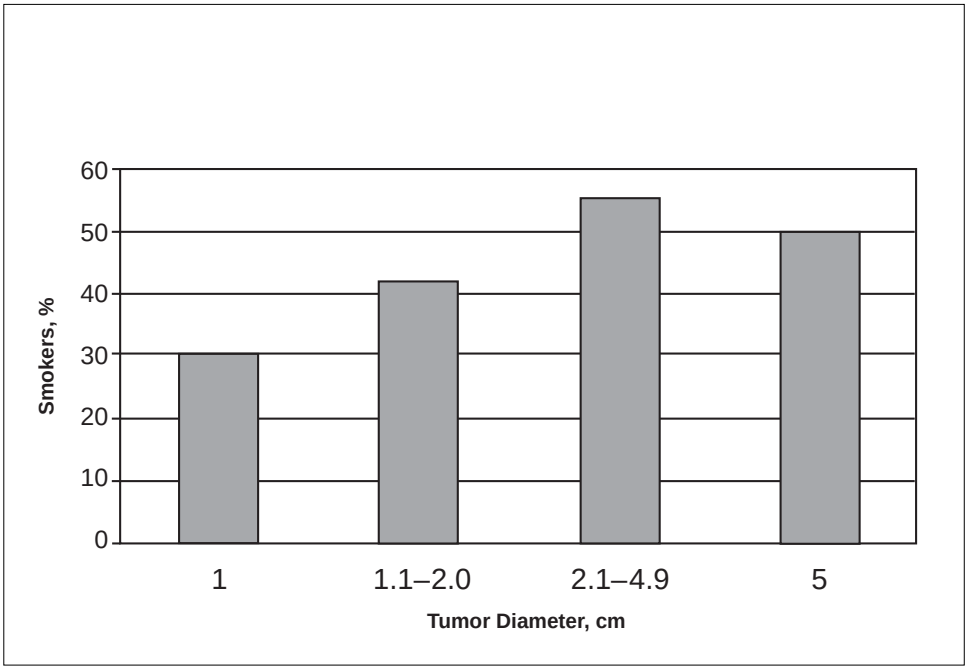

FIGURE 1. Tumor size and prevalence of smoking in basal cell carcinoma.

overall health and patient failure to examine the skin or be concerned over a growing skin lesion. It is also possible that smokers may spend more time in the sun or use less sunscreen, and there may be other behavioral factors that predispose smokers to BCC. This was a preliminary observation and further studies will be needed to confirm our findings.

A weakness of this study is that, because of its retrospective nature, additional information, which would have been helpful, is not available. Detailed information on number of packs smoked per year, duration of existence of the tumors, and history of sun exposure would have been helpful to clarify the association of smoking to the development of large BCCs.

In conclusion, we found that cigarette smoking is associated with an increased prevalence of BCCs larger than 1.0 cm in diameter.

Acknowledgment—Special thanks to Lynn Pershing, PhD, for her assistance with the statistical analysis.

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