DOES BASAL CELL CARCINOMA ARISING IN YOUNGER PATIENTS HAVE A MORE INVASIVE BEHAVIOR THAN THAT ARISING IN OLDER POPULATION?

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Abstract- There is an impression that basal cell carcinomas (BCC) occurring in younger population may be of more invasive behavior in comparison to those arising in older patients. The purpose of this study was to investigate this hypothesis by comparing the histological types of BCC in a large cohort of young and old patients. A total of 287 histological reports and clinical records were evaluated. A consecutive series of 95 patients less than 45 years old were compared with a consecutive series of 192 patients over 45 years of age. Tumors were classified according to the accepted definition of aggressive (morpheic, infiltrative and micronodular) and less aggressive (nodular and superficial) histological growth patterns. Aggressive growth types were found in 32% of patients over 45 and 29% of patients under 45, a difference which was not significant. There was a higher rate of incomplete excision in younger patients and this was highly significant (17% compared to 5%, $P < 0.01$). This study found that BCCs arising in young patients are not histologically different from those found in the older population. Clinically observed aggressive behavior of BCC in young patients may result from inadequate surgical excision due to cosmetics and diagnostic doubt.

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INTRODUCTION

Basal cell carcinoma (BCC) represents the most common cancer worldwide (1-3). The incidence of BCC increases with age and occurs relatively infrequently in people under 50 (4). However, it has been postulated that those BCCs that do arise in younger patients tend to be more aggressive, are particularly mutilating and difficult to eradicate whilst older patients seem less likely to suffer troublesome lesions (1). The question that arises is whether inherently more aggressive tumors arise in young patients or whether other factors determine this observation.

Binstock *et al.* described a particularly aggressive form of BCC in a case study of 20 patients less than 50 years old (5). These BCC were unusually large and located mainly on the scalp. Leffell *et al.* also described aggressive growth of BCC in young adults (1). They observed that there was an apparent increased incidence of infiltrating and morpheic types and a higher rate of recurrence in a series of 51 patients younger than 35. They reported the incidence of aggressive histological types to be 31% in the patients over 35 whilst, in those under 35, the incidence rose to 57%. Although outwardly this might provide evidence for more aggressive disease in young patients, it may also be related to referral patterns associated with a specialist Mohs unit in which there is a bias towards treating more aggressive lesions. Interestingly, in the small group of patients not specially referred for Mohs surgery,

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the aggressive growth lesions accounted for 14% of young patients and 10% of older patients and this difference was not significant.

This study attempts to clarify the issue of age by investigating differences in patients, tumor and treatment factors in a larger population of patients than previously reported to determine which feature is responsible for the clinical observation of aggressive BCC in young patients.

MATERIALS AND METHODS

All histopathology reports with a diagnosis of BCC were reviewed over a period of 5 years (from July 1992 through July 1997). The specimens were derived from a variety of clinical sources including plastic surgery, oncology, dermatology and general surgery practice departments.

Within this group of patients there were 95 patients aged less than 45 years. The older patient subgroup of 192 patients was then identified from the same consecutive 5 years period (from July 1992 through July 1997). Patient factors such as age, sex and anatomical site were recorded. In order to include treatment factors, information concerning the size of excision and whether or not the specimen had been completely excised was noted from the original histology report.

The histological type of these BCCs were reviewed by a consultant pathologist who was blinded to all details of the patient. The tumors were described according to growth pattern (Table 1) and differentiation using a classification previously described (6) and based on the system devised by Sexton *et al.* (7).

Chi squared analysis, Student's *t* test and Wilcoxon rank tests were used to analyze the data.

Table 1. Histological typing

Histological growth	Description
Non-aggressive	
Superficial	Directly attached to the epidermis
Nodular	Large rounded groups of cells with peripheral palisading
Aggressive	
Micronodular	Small island of tumor with wide intervening bridges of stroma
Infiltrating	Spiky tumor edges with poor palisading
Morpheic	Closely packed strands of tumor within fibrous stroma

RESULTS

There was an excess of females in the younger group with BCC but this was reversed in the older group. Of the patients under 45, 55% were female compared to 45% in the over 45 group. A summary of data is found in table 2.

The most common site for BCC in all patients was the middle face including upper lip, nose and cheeks. In young patients the location was less likely to be on head and neck than in other parts. In young patients 28% of BCCs were on sites other than head and neck compared to 19% in older group. The older patients were more likely to have BCC located on the leg (7%) than the younger patients (4%). In both age groups the most common site, other than midface, was the trunk.

Table 2. Comparison of patient, treatment and histological factors between older and younger patients (total 287 cases)*

Variable	Under 45 years (n= 95)	Over 45 years (n= 192)
Sex		
Male	43 (45)	108 (56)
female	52 (55)	84 (44)
Site		
Head and neck	68 (72)	155 (81)
Trunk and limbs	27 (28)	37 (19)
Margin of excision		
Complete	70 (74)	163 (85)
Incomplete	16 (17)	10 (5)
Biopsy only	9 (9)	19 (10)
Histology		
Aggressive growth pattern	28 (29)	61 (32)
Non-aggressive growth pattern	67 (71)	131 (68)

*Data are given as number (percent).

There was no difference in the histological subtyping of BCC between the age groups. A total of 29% of young patients had BCC classed as aggressive compared to 32% of patients over 45 (P= 0.69). The proportions of aggressive to non-aggressive histological types were similar, regardless of site: 31% had aggressive type in head and neck sites compared with 32% in all other areas (P = 0.96).

There was a significant difference in incomplete excision rate for histologically aggressive BCC when compared to the non-aggressive nodular and superficial types. This was the case in all age groups. In total, 18% of the infiltrative and micronodular BCCs were incompletely excised as compared to 5% of the non-aggressive types (P<0.001). The likelihood of incomplete excision was greater in head and neck areas at 11% compared to just 5% in other sites but this didn't reach significance (P=0.12).

There was a trend for younger patients to have an incomplete excision reported. This is in spite of the trend in younger patients to have a higher incidence of trunk BCC which are more likely to be completely excised. Of the patients under 45, 17% were reported to have had an incomplete excision compared to just 5% of older patients. This was highly significant (P<0.001) and was in spite of more scrupulous histologic reporting in a population perceived as high risk.

DISCUSSION

Most BCCs can be cured relatively easily, but a few behave far more aggressively resulting in recurrence and mutilation. It has been suggested that this occurs more frequently in younger patients. Whilst it has proved extremely difficult to reliably predict which BCC will be problematic, their histological appearance has been considered one of the best indicators of potentially aggressive clinical behavior. This could be ascribed either to certain histological types being inherently more invasive or because their occult pattern of growth makes an incomplete excision and thus a recurrence more likely. This study demonstrates that younger patients have tumors that are histologically indistinguishable from those of an older population. Any difference in clinical behavior must then be due to factors related to the patient or their treatment.

The hypothesis that tumor factors cause differences in clinical behavior has been investigated previously in small series (1). It has been reported that younger patients are more likely to have BCC of the more aggressive histological subtypes (1, 5). The present study does not support this: the patient groups studied had nearly identical proportions of aggressive compared to non-aggressive BCCs. It was found that regardless of age, the more aggressive histological types of BCC are significantly more likely to be incompletely excised and this is particularly the case in the younger patients. This may explain their subsequent clinical behavior. Close margin for any BCC with aggressive histology should be avoided.

Other factors may also influence tumor behavior (8). Patient factors may affect the interaction of a tumor with its host. Wei *et al.* have examined DNA repair capacity in young and old patients with BCC (9). They found that young patients with BCC were more likely to have impaired DNA repair capacity and that this increased their risk of BCC, particularly in females, with overexposure to UV light. Other differences in skin metabolism with age have also been reported (10). These differences in genetic expression could possibly explain differences in the behavior of BCCs despite similar appearance of the histology.

Treatment factors may also affect the clinical behavior of a tumor in a young person. These include delay in diagnosis due to the rarity of BCC in the young. Inadequate treatment such as compromised margins may occur in young people as the relative cost to their appearance is greater. We found that younger patients are more likely to have an incomplete excision.

A high rate of recurrence of BCCs in young women has been described (11). It has been suggested that this aggressive behavior might be due to inadequate excision because of cosmetic considerations in a relatively benign cancer. Cox in 1992 reviewed 150 patients under 35 years of age (12). He found a reversal of the usual male preponderance and that the lesions have on average been present for 3 years before diagnosis. These patients had a high rate of incomplete excision at

21% and correspondingly high rate of recurrence. That study suggests that there may be differences in the presentation and management of BCC in younger patients.

In present study the same distribution of histologic types in all age groups was found. This would suggest that any observed increase in clinically aggressive behavior in young patients must be due to other factors. In this study there was a greater tendency for younger patients to have incomplete excision. When compared to an older population this was in spite of a lower incidence of head and neck tumors which would be expected to have a high incomplete excision rate. We believe that the cosmetic considerations leading to incomplete excision in younger patients lead to an elevated risk of future recurrence and mutilation and have given rise to the suggestion that BCC in young patients have a more aggressive phenotype than those arising in older population.

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