

Original Article

DETERMINATION OF P53 EXPRESSION IN BASAL CELL CARCINOMA TISSUES AND ADJACENT NONTUMORAL EPIDERMIS FROM SUN-EXPOSED AREAS OF THE HEAD AND NECK

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Background: This study determines the expression of P53 protein and the intensity of immunoreactivity in basal cell carcinoma in comparison with the adjacent nontumoral epidermis in sun-exposed areas of the head and neck regions. The mean age of immunoreactivity in tumoral and adjacent nontumoral epidermis is also determined.

Methods: This descriptive-analytical study was performed retrospectively over a 5-year period on 150 basal cell carcinoma cases in the Pathology Department of Alzahra Hospital in Isfahan.

Proper quality paraffin blocks were chosen for immunohistochemical staining for P53 through the immunoperoxidase method. The intensity of immunoreactivity was graded. The age of the patients was also recorded.

Results: Positive P53 immunoreactivity was observed in 123 basal cell carcinoma tissues (82%) and in 117 adjacent nontumoral epidermis (78%) ($P = 0.38$). The frequency of severe immunoreactivity in tumoral tissue and in adjacent nontumoral epidermis was 46% and 32%, respectively ($P = 0.046$). The mean age of P53 expression was 66.2 years for tumoral tissue and 66.1 years for nontumoral epidermis. The mean age of those who did not express P53 was 52.6 and 55.9 years for the tumoral and nontumoral epidermis, respectively ($P < 0.001$).

Conclusion: No significant difference was detected between P53 immunoreactivity in tumoral tissue and adjacent nontumoral epidermis. Intensity of P53 immunoreactivity was greater in tumoral specimens. Comparison of mean ages showed a significant difference between P53-expressing and non-P53-expressing groups.

Archives of Iranian Medicine, Volume 9, Number 1, 2006: 46 – 48.

Keywords: Basal cell carcinoma • immunoperoxidase • P53

Introduction

Basal cell carcinoma (BCC), the most frequent form of skin cancer, occurs predominantly on the sun-exposed skin in direct proportion to the number of pilosebaceous units present therein. Fair-skinned and blue-eyed people, engaged in outdoor occupations, suffer a higher incidence of these tumors.

BCCs may also develop in sunlight-protected

skin,¹ in nevus sebaceous of Jadassohn, in the lower leg in association with chronic venous stasis or other preexisting conditions,^{1, 2} following arsenic ingestion, X-ray exposure, skin injury, chicken pox scars, tattoos, hair transplantation scars, and immune suppression.¹ Histopathologically, in the common solid type of BCC, nodular masses of basaloid cells are formed, which extend into the dermis in relation to a delicate specialized tumor stroma.^{3, 4}

More than 80% of BCCs overexpress the P53 protein.⁵ At a statistical level, the locally more-aggressive tumors show decreased expression of syndecan-1,⁶ bcl-2,⁷ and greater expression of P53.⁸

The tumor-suppressor protein P53 is present in a wide variety of cells. In normal cells, the

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Accepted for publication: 5 March 2005

concentration of the wild type P53 protein is generally below the level at which immunohistochemical methods are detected, presumably because of ubiquitin-mediated proteolysis. However, point mutation, which leads to the accumulation of mutant protein, occurs frequently in the gene coding for P53 protein.^{9, 10}

In this study, the frequency of P53 expression and its intensity in BCC of sun-exposed areas of the skin were compared with that of nontumoral adjacent epidermis. The frequency of P53 expression according to different age periods was studied as well.

Materials and Methods

We studied 150 archival, routinely processed, paraffin-embedded specimens on patients with BCC lesions from sun-exposed areas of the head and neck in Pathology Department of Alzahra Hospital in Isfahan.

We routinely deparaffinized 4 µm-thick sections. Sections, which contained both tumoral and the nontumoral adjacent epidermal tissues, were included in the study. All others were excluded. Immunohistochemical staining with antimouse antibody, streptavidin-HRP, and diaminobenzidin were performed.¹¹⁻¹³

In this study, age was considered as an independent variable and the intensity of P53 expression was considered as a dependent variable. Data were analyzed with SPSS software, using Chi-square and *t*-tests.

Results

Positive P53 immunoreactivity was observed in 123 BCC tissue sections (82%) and in 117 adjacent nontumoral epidermal tissues (68%) of sun-exposed areas of the head and neck regions. There was no significant difference between the presentation of P53 immunoreactivity in tumoral tissues and the adjacent nontumoral epidermis ($P = 0.38$).

Comparison of P53 intensity in tumoral and the

adjacent nontumoral epidermis indicated that the intensity of P53 immunoreactivity was greater in tumoral specimens ($P = 0.046$) (Table 1).

The mean age of P53 expression was 66.2 years for tumoral tissue and 66.1 years for the adjacent nontumoral epidermis. The mean age of those who did not express P53 was 52.6 years and 55.9 years for tumoral and nontumoral epidermis.

The mean age of the P53-expressing group was significantly greater than non-P53-expressing group in both tumoral ($P < 0.001$) and the adjacent nontumoral epidermal tissues ($P < 0.001$).

Discussion

Earlier, research has been done on this subject including studies from Kochi Medical School in Japan, which demonstrated 70.6% immunostaining of BCCs. P53-positive cells were present not only in cancer nests but also in dysplastic and even morphologically normal epidermis-adjointing cancers. Cases with P53-negative cancer nests represented 12.3% of cases and showed P53-positive reactions in dysplastic and morphologically normal epidermis.¹⁴

In studies performed on xeroderma pigmentosum cases afflicted with BCC, P53 expression was 50% and 40%.^{15, 16} Of interest is the increase of P53 expression, which has been detected not only in tumor cells but also in the adjacent nontumoral epidermis. This event is due to early accumulation of P53 immunopositive clones secondary to sun-exposure, in which morphologic disturbance of proliferation has not already occurred.¹⁷ However, the intensity of P53 immunoreactivity in the adjacent nontumoral epidermis is less than that of tumoral tissues ($P = 0.046$).

Considering the mean age of patients, a direct correlation is conferred between P53 expression and age ($P < 0.001$). In a study performed by Liang et al from Kochi Medical School, a statistical correlation between age and P53 expression was confirmed.¹⁴

In a study by the International Agency for

Table 1. Frequency of P53 intensity in tumoral and the adjacent normal epidermis.

Tissue type		No expression	Mild	Moderate	Severe	Total expression
Tumoral	Frequency	27	23	31	69	123
	%	18%	15.3%	20.7%	46%	82%
Adjacent nontumoral epidermis	Frequency	33	31	37	49	117
	%	22%	20.7%	24.7%	32.7%	78%

Research on Cancer, no statistically significant association could be demonstrated between age and P53 mutation frequency in BCC and nontumoral epidermis (mirror-image anatomic site to the cancer site).¹⁸

Our findings suggest three main points. First, overexpression of P53 in nontumoral epidermis and cancer nests of BCC is significantly related to sun-exposure. Second, the expression of P53 in BCC is an age-dependent process and early accumulation of the P53 protein may be a useful predictor for the detection of nonmelanocytic skin cancer.^{15,16} Third, immunohistochemical techniques can not directly detect genomic instability or abnormal cell cycling. Therefore, we recommend molecular techniques for exact and early detection of P53 mutation.

Acknowledgment

We would like to express our deepest gratitude to the staff of the Department of Dermatology, the staff of the Immunohistochemistry Laboratory, and Mr. Hassanzade for their kind help and cooperation.

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