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Clinical and Histopathological Features of Aggressive Basal Cell Carcinoma

Ülker Gül,*[1] MD, Seçil Soylu,[1] MD, Emine Benzer,[2] MD, Işın Pak,[2] MD

Address: [1]Ministry of Health, Numune Education and Investigation Hospital, Dermatology Department, Ankara, Turkey; [2]Ministry of Health, Oncology Education and Investigation Hospital, Pathology Department, Ankara, Turkey

E-mail: ulkergul@yahoo.com

** Corresponding Author:* Ministry of Health, Numune Education and Investigation Hospital, Dermatology Department, Ankara, Turkey

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Abstract

Background: Basal cell carcinoma (BCC) is the most frequent type of skin cancer in humans. A minority of BCCs have an aggressive biological behavior, causing extensive deep tissue invasion, metastasis and recurrence. The object of this study was to evaluate clinical and histopathological features of aggressive BCC.

Material and Methods: The study group was consisted of 19 recurrent and/or invasive BCC and control group was consisted of 19 nonaggressive BCC patients.

Results: At the aggressive group 3 had only recurrent tumor, 6 were recurrent and invasive and 10 had only invasive tumor. Localization of the lesions was at periorbital site most frequently. Histopathologically, at the aggressive group, the loss of regularity in palizading was revealed at 16 cases, morpheiphorm or sclerozing stroma at 14 cases, infiltrative tumor type at 15 cases, squamous differentiation at 15 patients and increase in tumor cells nuclear pleomorphism at 14 cases.

Conclusion: There is no any standardized certain diagnostic criterias of aggressive BCC. Therefore, by the evaluation of the histopathological criterias of scalp and neck sited BCCs according to the features that were above mentioned, can supply the estimation of the biological behaviors of BCCs.

Introduction

Basal cell carcinoma (BCC) is the most frequent type of skin cancer in humans [**1**]. Most BCCs are slow-growing, relatively nonaggressive tumors [**1, 2, 3**]. However, a minority of BCCs have an aggressive biological behavior, causing extensive deep tissue invasion, metastasis and recurrence [**1, 2, 3, 4, 5**]. The object of this study was to evaluate clinical and histopathological features of aggressive BCC (AG-BCC).

Materials and Methods

Our study group was consisted of 19 recurrent and/or invasive BCC (**Figure 1**) and control group was consisted of 19 nonaggressive BCC patients. All of the patients' age, gender, localization of the lesions were recorded. For recurrent and/or invasive BCC cases, the number of recurrences, the time interval between the first and recurrent lesions occurence, the tissues that they invaded were also noted. At both group, histopathologically squamous differentiation, the number of mitoses, the loss of regularity in palizading, cystic changes, morpheiphorm or sclerozing stroma, increase in tumor cells, nuclear pleomorphism, the cell group

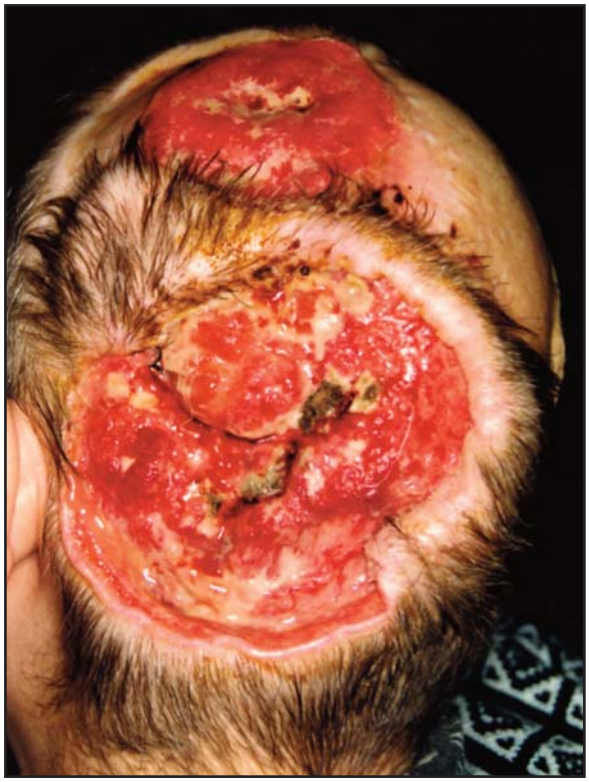

Figure 1. Aggressive BCC lesions

Table 1. The Biological Behaviour of AG-BCC According to Gender

	Recurrence	Recurrence + Invasion	Invasion
Female (n=7)	2	2	3
Male (n=12)	1	4	7
Total (n=19)	3	6	10

type, growth pattern and existence of ulceration were examined.

Results

Aggressive group was consisting of 7 female and 12 male; total of 19 patients (**Figure 1**). The age interval was between 41 and 73 (mean: 58.74). Three had only recurrent tumor, 6 were recurrent and invasive and 10 had only invasive tumor (**Table1**). Localization of the lesions was at periorbital site most frequently. Interval between recurrence time was changing between 6 months to 8 years (**Table 2**). The age interval of the nonaggres-

Table 2. The Age, Gender, Anatomical Location, Recurrence and Invasion Features of AG-BCCs

No	Age	Sex	Location	The interval time of recurrence	The number of recurrence	Invasion to Front Tissues						
						Perineural	Cartilage	Bone	Muscle	Orbita	Dura	Salivary gland
1	73	F	Nose	4 years	1							
2	63	M	Nose	2 years	1							
3	46	F	Nasolabial fold	6 months	1							
4	63	M	Ear	1 year	1		+					
5	61	M	Cheek	1 year	1	+						
6	58	M	Periorbita	7 months	1			+	+	+		
7	59	M	Periorbita	7 months	1	+		+	+			
8	72	F	Nose	8 years	1	+		+	+			
9	54	F	Periorbita	4 years, 5 years	2	+			+			
10	55	F	Periorbita			+			+	+		
11	54	M	Neck			+			+			
12	50	M	Cheek			+			+			+
13	61	M	Scalp					+			+	
14	41	M	Periorbita						+	+		
15	58	M	Ear				+					
16	69	M	Periorbita			+			+	+		
17	60	F	Temple				+					
18	59	F	Scalp			+			+			
19	60	M	Forehead						+			

Table 3. The Age, Gender, Anatomical Locations of Nonaggressive BCC

No	Age	Sex	Location
1	62		
2	63	M	Nose
3	57	M	Temple
4	75	F	Nose
5	61	F	Periorbita
6	54	F	Chin
7	87	M	Nose
8	66	M	Scalp
9	51	M	Forehead
10	64	F	Forehead
11	50	M	Hand
12	71	F	Cheek
13	55	M	Nose
14	69	M	Nose
15	65	F	Nose
16	60	M	Ear
17	71	F	Cheek
18	59	M	Nose
19	72	F	Nose

sive group was between 50 and 87 (mean: 63.78). There was 11 male and 8 female patients. The most frequent localization of the lesions was the nose (**Table 3**). Histopathologically, at the AG-BCC group, the loss of regularity in palizading was revealed at 16 cases, morpheiphorm or sclerozing stroma at 14 cases, infiltrative tumor type at 15 cases, squamous differentiation at 15 patients and increase in tumor cells nuclear pleomorphism at 14 cases (**Table 4**). At the control group, the loss of regularity in palizading was revealed in 6 cases, morpheiphorm or sclerozing stroma in 3 cases, infiltrative tumor type in 6 patients, squamous differentiation in 13 patients, increase of tumor cell nuclear pleomorphism in 6 cases (**Table 5**).

Discussion

Aggressive BCC can be clinically defined in 3 forms as; recurrent, deeply invasive and metastatic [**1, 2, 3, 4, 5**]. Our study group was consisted total of 19 patients; 3 had recurrent BCC, 10 had deep tissue invasion, 6 had both recurrent BCC and invasion. There was no metastasizing case.

In the literature, AG-BCC was found to be more frequent at males in two study, however another study observed that AG-BCC was more frequent at females [**2, 6, 7**]. In our both study groups of patients with aggressive and nonaggressive lesions, the men outnumbered women.

The age of patients who develop AG-BCC is reported at 7th decade of life [**1, 2**]. However *Leffell* et al reported that AG-BCC was more frequently noted in patients under 35 years of age than in those older [**5**]. Our AG-BCC patients were between 41-73 years of age (mean 58).

In the literature, the localization of the lesions of AG-BCC was as follows: according to the study of *Dixon* et al. the most frequent sites were the nose (10 cases), ear and preauricular region (9 cases), forehead and temple (6 cases); according to the study of *Jacobs* et al. the nose, eyes or cheeks (11/20 cases), ear (3/20), neck and chin (4/20), lip and forehead (2/20); according to *Dellon*, nose 11, cheek 4, ear 4, forehead 5, eyelid 2, lip 1, neck 2 and chest 1 [**1, 2, 4**]. *Leffell* et al. noted that the majority of AG-BCC in men were found on the forehead and temples, whereas in women, the majority of AG-BCC occurred on the nose [**5**]. In the review of *Koplin* et al. 97 percent of all recurrent lesions are located in the head and neck region; among these, the combined nasal, malar and periorbital areas comprise over 75 percent of all recurrent BCC [**8**]. The AG-BCC lesions of our patients were all located in the head and neck region; respectively; periorbital region (33 %), nose (16 %), cheek (11 %), ear (11 %), scalp (11 %), nasolabial fold (6 %), temple (6 %), neck (6 %). In the nonaggressive BCC group, the most frequent site was the nose (42 %).

The mean interval time between excision and recurrence ranges between 15.6 months and 30 months according to *Koplin* et al. and 24.6+11.8 months according to *Silva* et al. [**8, 9**]. In our study the mean interval time was between 6 months and 8 years (mean 32 months). The recurrence rate was 2 in only one case, and one in 8 cases.

'Squamous differentiation, mitotic rate, irregularities in peripheral palisade, cystic change, morphea-like or sclerosing stroma, presence of nuclear pleomorphism, the shape of cell groups, growth pattern and ulceration'

Table 4. The Histopathological Features of AG-BCC

No		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	Total
Squamous differentiation		+	+	+			+		+	+	+	+	+	+	+	+	+	+	+		15
Mitotic Rate	≤ 5		+	+						+	+	+	+	+					+		8
	6-10						+	+	+							+	+	+			6
	> 10	+			+	+									+					+	5
Irregularities in peripheral palisade			+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		16
Cystic change		+	+			+		+	+	+	+			+		+	+	+			11
Morphea-like or sclerosing stroma			+		+	+	+	+	+		+	+	+		+	+	+	+	+	+	14
Nuclear pleomorphism			+		+	+	+	+	+			+	+	+	+	+		+	+	+	14
The shape of cell groups	Round	+																			1
	Spiky							+					+				+				3
	Mixed		+	+	+	+	+		+	+	+	+		+	+	+		+	+	+	15
Growth pattern	Nodular																				0
	Nodulo-ulcerative	+								+											2
	Morphea-like																				0
	Infiltrative				+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	15
	Superficial multicentric		+	+																	2
Ulceration		+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	18

are investigated for histologic criterias of AG-BCC in the literature. Basal cell carcinomas that had one or more of these criterias was defined as aggressive form [**1, 2, 3, 4, 7, 10, 11, 12**].

For the presence of squamous change, *Dixon* et al. found 30 %, *Jacobs* et al. found 23 %, *Dellon* et al. found 67 % squamous change at the aggressive group [**1, 2, 4**]. This rate was found 79 % in our AG-BCC group and 68 % in our nonaggressive BCC group. However the prognostic value of squamous differentiation is still controversial [**13**].

In the study of *Jacobs* et al. although there was no statistically significant difference between the mitotic counts in aggressive and non-aggressive lesions, 2 cases in the aggressive series had over 50 mitoses per 10 high-power fields (HPF) [**2**]. *Dixon* et al. found no difference between the recurrent and nonrecurrent group [**1**]. However, *Hauben* et al. and *Rosa* et al. suggested that high mitotic activity was associated with aggressivity [**7, 10, 12**]. In our AG-BCC group; the mitotic rates were 26 % for over 10 mitoses per 5 HPF and for nonaggressive BCC group, the rate was higher as 47 %. Our result was not consistent with the findings of the last authors.

Irregularities in the peripheral palisade of AG-BCC was found between 67-86 % in the literature series [**1, 2, 4**]. In our study, consistent with literature, the irregularities in the peripheral palisade was found to be 84 % at the AG-BCC and 32 % at the nonaggressive BCC patients.

Some authors observed less degree of cystic change in non- aggressive group. Most investigators have found no association between cystic change and aggressive behavior [**1**]. In our study, cystic change rate was found to be 58 % in AG-BCC group and 53 % in the nonaggressive group, so our results are consisted with the sight that there is no association between cystic change and aggressive behavior.

Most studies in the past have observed a relationship between morphea-like /sclerosing stroma and tumor aggressiveness, but some of them have not [**1, 4**]. We found 74 % morphea-like /sclerosing stroma in our AG-BCC group and the rate was 16 % in the nonaggressive BCC group. Our finding was consistent with the general exception in the literature.

A marked degree of nuclear pleomorphism also appeared to be associated with aggressivity [**1, 2, 10**]. In our study group, the rate of nuclear pleomorphism was found to be 74 % for AG-BCC and 32% for nonaggressive BCC. We observed a significant difference in the

Table 5. The Histopathological Features of Nonaggressive BCC

No		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	Total
Squamous differentiation		+	+	+	+	+		+	+	+				+	+	+			+	+	13
Mitotic Rate	**≤ 5**		+							+	+	+			+						5
	6-10					+		+						+			+			+	5
	> 10	+		+	+		+		+				+			+		+	+		9
Irregularities in peripheral palisade				+			+	+	+							+				+	6
Cystic change		+		+			+	+			+		+	+	+		+	+			10
Morphea-like or sclerosing stroma				+			+	+													3
Nuclear pleomorphism				+	+		+	+								+			+		6
The shape of cell groups	**Round**	+	+		+					+	+	+	+	+	+		+	+	+		12
	Spiky																				0
	Mixed			+		+	+	+	+							+				+	7
Growth pattern	**Nodular**									+				+	+		+		+		5
	Nodulo-ulcerative		+		+				+				+								4
	Morphea-like																				0
	Infiltrative			+		+	+	+								+				+	6
	Superficial multicentric	+									+	+						+			4
Ulceration			+	+	+	+	+	+	+				+			+	+		+		11

degree of nuclear pleomorphism between the ratio of the two groups.

According to *Jacobs* et al. the cell groups tended to be small with spiky or irregular outline in 90 % of aggressive lesions [**2**]. *Dixon* et al. found the spiky shape 27 %, mixed pattern 33 %, round shape 40 % of the recurrent group and, noted that the predominant pattern in the recurrent group was spikey and in the nonrecurrent was round [**1**]. *Rosa* et al. also emphasized that the cell groups tended to be spiky or irregular outline were consistent with aggressive lesions [**10**]. The cell groups of our AG-BCC lesions were found to be 79 % mixed pattern, 16 % spikey and 5 % round pattern. There was no spiky pattern and the most frequent pattern was round in our nonaggressive BCC group.

At the aggressive lesions, 82 % were ulcerative, ulcero-infiltrative, or infiltrative type in the study of *Jacobs* et al. [**2**]. *Dixon* et al. found the total rate of infiltrative, morphea and superficial multicentric growth pattern as 50 % of the recurrent group and accepted these histologic criterias as being associated with aggressivity [**1, 3**]. *Sloane* also determined that infiltrative and multifocal types were more associated with recurrence than nodular type of growth pattern [**11**]. The rate of growth pattern in our AG-BCC group was 78 % for infiltrative type, 11 % for nodulo-ulcerative type, 11 % for superficial multicentric type. There was no nodular or morphea-like growth pattern. When compared with the results of our control group; nodular pattern was significantly more frequent in our nonaggressive BCC group and infiltrative type was significantly more frequent in the AG-BCC group.

The previous studies showed that aggressive lesions had frequently involved subcutaneous tissues, cartilage, or bone [**2, 5**]. We observed that the aggressive lesions were invaded 58 % muscle, 47 % perineural, 21% bone, 21 % orbita, 16 % cartilage, 5 % dura mater and 5 % salivary glands, respectively.

Ulceration of the tumor rates was found to be 87 % according to *Dellon*, whereas *Shanoff* et al. found no difference between the rate of recurrence for ulcerative and non-ulcerative group [**4,14**]. In our study group, 95% of AG-BCC and 58 % of the nonaggressive BCC group were ulcerated.

As a result, the early diagnosis with the aid of a well-designed clinicopathological correlation and a radical therapy of AG-BCC are recommended. However because of the nonaggressive course of BCCs, the AG-BCC cases can be overlooked. In addition, there is no standardized certain diagnostic criterias of

AG-BCC. Therefore, by the evaluation of the histopathological criterias of scalp and neck sited BCCs according to the features that were above mentioned, can supply the estimation of the biological behaviors of BCCs.

References

1. Dixon AY, Lee SH, McGregor DH. Factors predictive of recurrence of basal cell carcinoma. Am J Dermatopathol 1989; 11: 222-232. PMID: 2729527
2. Jacobs GH, Rippey JJ, Altini M. Prediction of aggressive behavior in basal cell carcinoma. Cancer 1982; 49: 533-537. PMID: 7059912
3. Dixon AY, Lee SH, McGregor DH. Histologic features predictive of basal cell carcinoma recurrence: results of a multivariate analysis. J Cutan Pathol 1993: 137-142. PMID: 8320358
4. Dellon AL. Histologic study of recurrent basal cell carcinoma. Plast Reconstr Surg 1985; 75: 853-859. PMID: 4001205
5. Leffell DJ, Headington JT, Wong DS, Swanson NA. Aggressive-growth basal cell carsinoma in young adults. Arch Dermatol 1991; 127: 1663-1667. PMID: 1952969
6. Silverman MK, Kopf AW, Bart RS, Grin CM, Levenstein MS. Recurrence rates of treated basal cell carcinomas. J Dermatol Surg Oncol 1992; 18: 471-476. PMID: 1592998
7. Hauben DJ, Zirkin H, Mahler D, Sacks M. The biologic behavior of basal cell carcinoma: analysis of recurrence in excised basal cell carcinoma: part II. Plast Reconstr Surg 1982; 69: 110-116. PMID: 7053498
8. Koplin L, Zarem HA. Recurrent basal cell carcinoma. Plast Reconstr Surg 1980; 65: 656-664. PMID: 7367506
9. DeSilva SP, Dellon AL. Recurrence rate of positive margin basal cell carcinoma: results of a five-year prospective study. J Surg Oncol 1985; 28: 72-74. PMID: 3968892
10. DeRosa G, Vetrani A, Zeppa P et al. Comparative morphometric analysis of aggressive and ordinary basal cell carcinoma of the skin. Cancer 1990; 65: 544-549. PMID: 2297645
11. Sloane JP. The value of typing basal cell carcinomas in predicting recurrence after surgical excision. Br J Dermatol 1977; 96: 127-132. PMID: 843446
12. Hauben DJ, Zirkin H, Mahler D, Sacks M. The biologic behavior of basal cell carcinoma: part I. Plast Reconstr Surg 1982; 69: 103-109. PMID: 7053497
13. Leffell DJ, Fitzgerald DA. Basal cell carcinoma. In: Freedberg I, Eisen E, Wolff K et al. Fitzpatrick's Dermatology in General Medicine. 5th ed. New York: McGraw-Hill; 1999. 857-864.
14. Shanoff L, Spira M, Hardy S. Basal cell carcinoma: A statistical approach to rational management. Plast Reconstr Surg 1967; 39: 619. PMID: 6026420