Original Paper

Histopathological Features of the Eyelid Basal Cell Carcinomas

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ABSTRACT: Basal cell carcinomas (BCC) make up about 90% of malignant tumors of the eyelids. Although they are generally slow-growing tumors, in the periocular region can cause significant morbidity due to orbital invasion. In the present study we followed the associations between the various types of BCC with the depth of invasion, respectively the Breslow stage (BS) and with the pT category. The study included a number of 92 cases of eyelid BCC from the Plastic Surgery and Ophthalmology Departments of the Craiova County Emergency Clinical Hospital which were processed and diagnosed in the Pathological Laboratory of the same hospital. Histopathological analysis of the 92 BCCs indicated that in 72 cases the tumors were composed of a single growth pattern, and in 20 cases they were composite, associating two or more growth patterns. The cases with a single growth pattern corresponded in 53 cases of nodular BCC, in 9 cases of infiltrative BCC, in 2 cases of superficial BCC and in 8 cases of micronodular BCC. The composite types corresponded in 10 cases to the association of the nodular type with the micronodular one, in 8 cases to the association of the nodular type with the infiltrative one and in 2 cases to the association of the infiltrative type with the micronodular one. Statistical analysis indicated significant associations between BS, pTa and the histopathological type of tumors, the mixed types being frequently present in cases with high SB and advanced pT.

KEYWORDS: *Basal cell carcinoma, Breslow stage, pT category.*

Introduction

Basal cell carcinomas (BCC) represent about 90% of malignant tumors of the eyelids [1-3].

Although are slow-growing tumors, they can lead to significant morbidity through orbital invasion.

BCCs have very varied histological subtypes, and their different clinical behavior is the basis of the WHO classification system [4].

However, there is no universally accepted classification for these tumors, but mainly two systems are used based on the histopathological model of growth and histological differentiation.

Of the two systems, the classification based on the growth model is accepted, which also has the greatest clinical significance.

Types of nodular and superficial BCC are the most common histopathological varieties and tend to be less aggressive [5].

In contrast, the morpheaform, infiltrative, and basosquamous subtypes are rarer and more aggressive because they are associated with a higher rate of positive resection limits, as well as a higher risk of recurrence and metastasis [6].

In the eyelid location, these three subtypes constitute over 80% of the BCC cases with orbital invasion [7,8].

In the present study we followed the associations between the various varieties of BCC with the depth of invasion, respectively Breslow stage (BS) and with the pT category.

Material and Methods

This study was performed retrospectively on a number of 92 cases of basal cell carcinomas of the eyelids, from the Plastic Surgery and Ophthalmology Departments of the Craiova County Emergency Clinical Hospital, the biological material being processed in the Pathology Laboratory of the same hospital.

The specimens of tumor surgical excision were fixed in 10% buffered formalin, then processed by paraffin embedding technique and hematoxylin-eosin stained.

The classification of the lesions was done according to the WHO recommendations [4].

We aimed to evaluate the different varieties of BCC in relation to the Breslow stage (BS) and the pT category according to the recommendations of UICC (Union for International Cancer Control) and AJCC (American Joint Committee on Cancer) in the TNM8 system [9].

The acquisition of images was done using the Panthera L research binocular microscope, with

a built-in 5 Mpixel digital camera (MoticEurope SLU, Barcelona, Spain) and integrated software, which allowed the appreciation of the two parameters, BS and pT respectively.

Statistical analysis used comparison tests (χ2-chi square test) within the SPSS10 software (Statistical Package for the Social Sciences).

The study was approved by the local ethical committee, and written informed consent was obtained from all the patients.

Results

Histopathological analysis of the 92 BCCs indicated that in 72 cases (78.3%) the tumors were composed of a single growth pattern, and in 20 cases (21.7%) they were composite, associating two or more growth patterns.

The 72 cases of BCC with a single growth pattern corresponded in 53 cases (57.6%) to nodular BCC, in 9 cases (9.8%) to infiltrative BCC, in 2 cases (2.2%) to superficial BCC and in 8 cases (8.7%) to micronodular BCC.

The composite types of BCC that associated a combination of two or more of the above types, which in 10 cases (10.8%) corresponded to the association of the nodular type with the micronodular one, in 8 cases (8.7%) to the nodular type associated with the infiltrative one, and in 2 cases (2.2%) to the infiltrative type associated with the micronodular one.

The nodular variant of BCC diagnosed in 53 cases (57.6%), was composed of nests of basaloid cells with large sizes and various shapes, located in the papillary and reticular dermis. In the periphery of the tumor islands the cells were arranged in a palisadic pattern, with retraction artifacts at the border with the surrounding stroma (Figure 1A).

Mitosis and apoptosis have often been identified, especially towards the periphery of neoplastic islands.

Some lobules indicated degeneration of neoplastic cells in the center of tumor nests with the formation of cystic structures (Figure 1B), or in other cases had a cribriform or nodular adenoid pattern (Figure 2A).

Also, in 5 cases of solid BCC, we noticed the appearance of squamous differentiation, often with a focal character (Figure 2B).

The superficial variant of BCC was identified in 2 cases (2.2%), characterized by the presence of small tumor nests, with basaloid morphology, attached to the lower part of the epidermis (Figure 2C).

The lesions were multifocal, due to the presence of interconnected tumor nests.

The micronodular variant of BCC was identified in 8 cases (8.7%), presented tumor nodules with small, uniform size, with minimal palisade pattern and we found the absence of retraction artifacts (Figure 2D).

Tumor nodules were separated by septa made of normal collagen and invaded the deep dermis.

The infiltrative variant of BCC was present in 9 cases of BCC (9.8%) and it was composed of thin cords of cells with basaloid morphology, with reduced cytoplasm and large hyperchromic nuclei (Figure 2E).

Peripheral palisade pattern and retraction spaces were only rarely identified.

The 20 cases of composite BCC corresponded in 10 cases (10.8%) to the association of the nodular type with the micronodular one, the latter being identified especially in the periphery of tumors, often at the level of deep resection limit (Figure 2F).

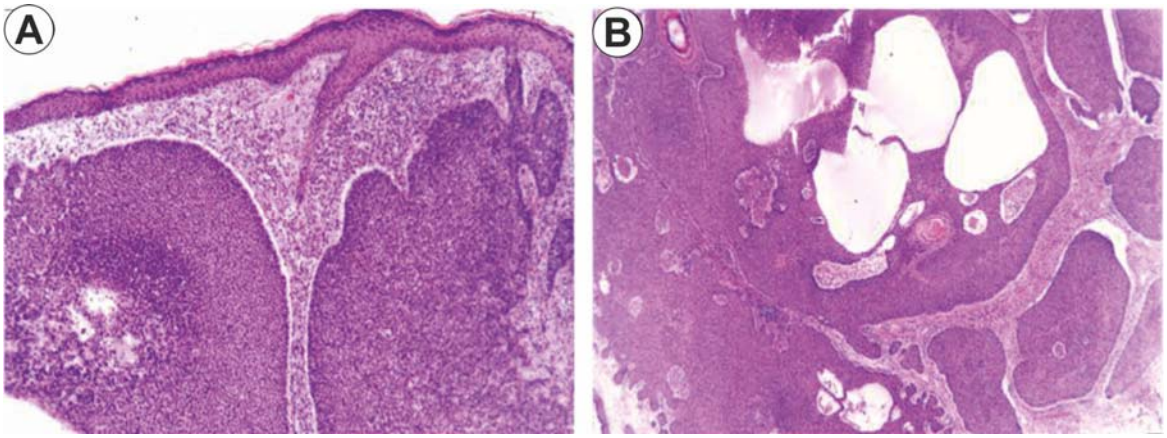

Figure 1. A. Nodular BCC, HE staining, x40; B. Nodular cystic BCC, HE staining, x40.

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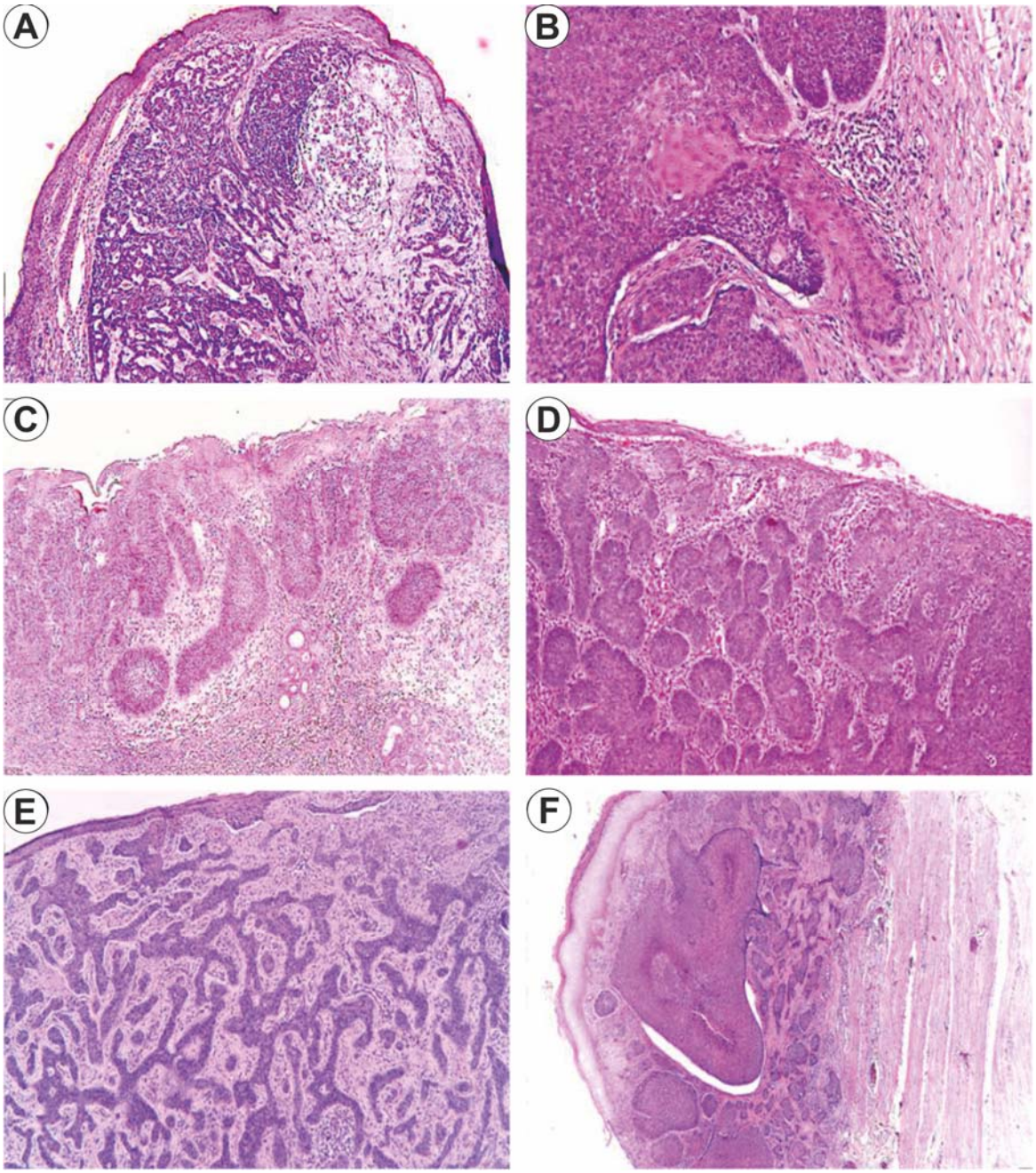

Figure 2. A. Nodular adenoid BCC, HE staining, x40; B. Nodular BCC with squamous differentiation, HE staining, x200; C. Superficial BCC, HE staining, x40; D. Micronodular BCC, HE staining, x100; E. Infiltrative BCC, HE staining, x100; F. Nodular, infiltrative and micronodular BCC, HE staining, x40.

Also, we identified in 8 cases (8.7%) the association of the nodular type with the infiltrative one, the areas with infiltrative pattern being also identified in the deep area of the tumors, at the invasion edge and in 2 cases (2.2%) the association of the infiltrative type with the micronodular one, where along with the cords of basaloid cells there are also small nests of tumor cells.

The assessment of the pT category was performed in relation to BS, which allowed the observation that all the tumors analyzed corresponded to the pT1 or pT2 stage, most of them being included in the pT1b stage (Table 1).

Table 1. BCC distribution according to pT and BS categories.

Category pT/BS		BS I	BS II	BS III	BS IV
T1	T1a	2	2	6	5
	T1b	-	11	15	17
	T1c	-	-	1	2
T2	T2a	-	7	9	7
	T2b	-	-	-	8

The relation of BS to the pT category indicated for the pT1a category 15 cases, corresponding for BS I and BS II in two cases each, BS III six cases and BS IV five cases; for category pT1b 43 cases, corresponding to BS II in 11 cases, BS III 15 cases and BS IV 17 cases; for category pT1c three cases, corresponding in one case to BS III and in two cases to BS IV.

For the pT2 subcategories we observed: for the pT2a category 23 cases, corresponding in seven cases to BS II, nine cases to BS III and seven cases to BS IV; for category pT2b eight cases, corresponding SB IV.

The statistical analysis indicated significant associations between the Breslow score and the histopathological form of BCC, the mixed forms being frequently present in cases with high BS (III, IV) ($p=0.000$, $p<0.001$, $\chi 2$ test) (Figure 3A).

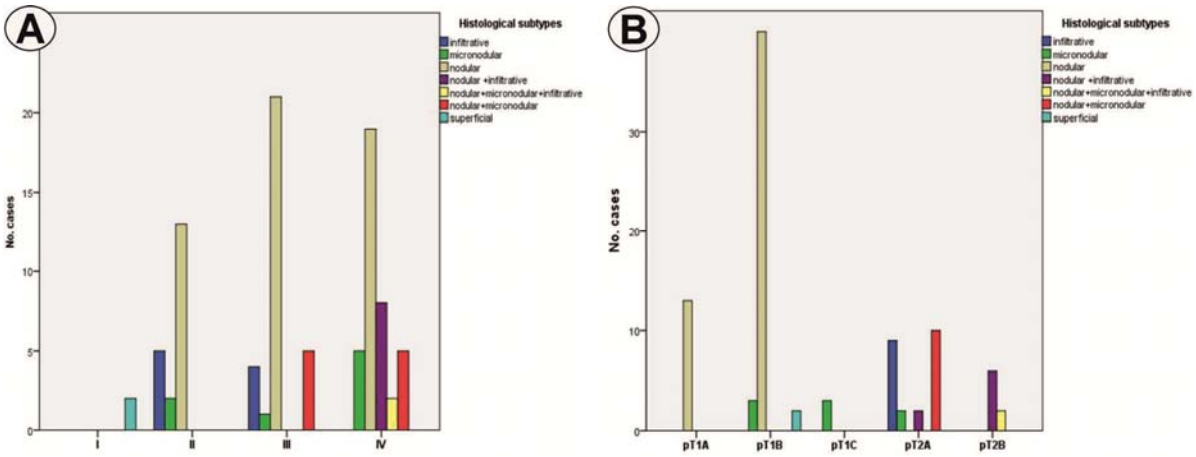

Figure 3. A. BCC distribution according to histopathological type and BS; B. BCC distribution according to histopathological type and pT category.

The tumor extension was significantly associated with the histopathological type, the cases with mixed histopathological pattern being included in the categories pT2a, respectively pT2b ($p=0.000$, $p<0.001$, $\chi 2$, test) (Figure 3B).

Discussions

Because the clinical presentation can be highly variable, biopsy is recommended for all suspected lesions.

In addition, BCC management must be individualized, taking into account clinical factors, tumor characteristics and histological subtype.

The accuracy of the diagnosis on biopsy specimens is around 80% compared to surgical excision specimens [10,11] and represents 40% of cases of discordant diagnosis [10].

As a result, the histopathological examination is important to confirm the diagnosis, define the histological type, assess the presence of microscopic ulcers, determine the involvement of surgical resection limits, and to identify the distance at which the tumor develops from these edges [12].

In our study, the nodular BCC subtype represented 57.6%, followed in order of frequency by the infiltrative type with 9.8%, the micronodular type with 8.7%, the superficial type with 2.2% and the mixed type with 21.7%.

The incidence of different types of BCC in the eyelids varies quite a lot in different studies.

Paavilainen et al. found that the most common histological type was the nodular variant (84.5%), followed by the sclerosing type (5.8%), micronodular (4.9%), keratotic (2.9%) and superficial 1.9%) [13].

Simon et al. reported that most lesions were solid nodular ulcerative (75.9%), followed by morpheaform or infiltrative type (10%) and cystic or nodular (8%), other less common histological types including the basosquamous and plexiform (adenoid) ones [14].

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Wu et al. reported that the two main types of BCC are the solid type that correlates mostly with the nodular clinical type, and the morpheaform/sclerosing type that correlates with the infiltrating clinical type [5].

Pe'er et al. describe in the eyelids a number of common types such as nodular and nodular-ulcerative type, pigmented and infiltrating (morpheaform and sclerosing), as well as less common variants such as superficial BCC [15].

Similarly, other studies report that the most common subtype is the nodular one (66.5%), followed by the superficial, infiltrative and micronodular type, very frequently in the same lesion being found several subtypes, and the most common association was represented by association of nodular and micronodular subtypes [16].

A recent study reports that the most common histological subtype was nodular BCC, accounting for 66.7% of cases, the adenoid type was identified in 10.3% of cases, the morpheaform type in 2.6% of cases, and squamous differentiation of was identified in 20.5% of cases [17].

The eyelid carcinomas continue to have a different staging system than the skin in general, and the system is substantially revised in TNM8 [9].

In TNM8, eyelid tumors are framed using a different system compared to previous editions. The 8th edition of TNM introduced the principle of transition from T1 or T2 to T3, in the presence of deep invasion, defined as tumor thickness/depth greater than 6 mm and/or invasion beyond subcutaneous fat [9,18].

Tumor thickness is measured from the granular layer of the adjacent normal epidermis to the deepest point of the tumor, except for the superficial BCC [18].

Modified SB excludes parakeratosis/crust and the measurement should be made from the base of the ulceration, if present [19].

The AJCC states that staging refers more to squamous cell carcinomas than to BCC, but both UICC and AJCC maintained these conditions in the 8th edition of TNM for BCC cases [9,18].

In TNM8, the depth of tumor invasion is defined as the thickness/depth of tumor invasion greater than 6mm and/or invasion beyond subcutaneous fat. UICC and AJCC maintained these data in TNM 8 for BCC cases [9].

Breslow stages are universally used in assessing the depth of malignant melanoma invasion and is defined in relation to the granular layer to the base of the tumor.

In our study, the mixed forms of tumors that frequently associated aggressive subtypes of BCC were correlated with high SB (III, IV) and with more advanced pT categories, falling into pT2a and pT2b categories, respectively.

In a recent study, the most common category T according to the criteria of the 7th edition was T2a, as opposed to the most common category T according to the criteria of the 8th edition which was T1b [20].

Of the 163 patients, 39% had a lower T category in the 8th edition than compared to the 7th edition criteria, 36% had a higher T category, and 25% had the same pT category [20].

Conclusion

The mixed types of BCC, represented by combinations with/between the aggressive subtypes were correlated with the deeper invasion (higher BS) and the higher pT category (pT2b).

Conflict of interests

None to declare.

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