BASAL CELL CARCINOMA: HISTOLOGIC DIAGNOSTIC PITFALLS – CASE REPORT

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Abstract: *Basal cell carcinoma (BCC), although a very often dermatological issue, may embrace various morphological forms that the pathologist is required to accurately diagnose. We present the case of a 15 years old girl with a nodular tumor observed, on skin, in a subclavian area, with dimensions within 0,7/0,7/0,4 cm. The microscopic appearance of the tumor resembles a BCC, with basaloid and rare scuamoid features, but no atypia or peripheral clefting, within a normal dermis with marked plasocytic inflammation and reticular areas; differential diagnosis included trichoepithelioma, Merkel cell carcinoma, trichoblastoma and microcystic adnexal carcinoma. The final diagnosis proved to be a trichoepithelioma. Therefore, the importance of differential diagnosis in BCC and BCC-like conditions requires mainly classical histologic criteria, with, depending on case, subsequent molecular confirmation techniques. The article depicts the required attitude in such a situation, allowing an illumination on the matter.*

INTRODUCTION

Basal cell carcinoma (BCC) is a very often dermatological diagnosis, regarded almost as a common primary malignancy within the skin, constituting almost 80% of all cutaneous primary cancers. Around 900.000 new patients are diagnosed with a form of BCC during one year's time, in the United States, with occurrence in all races having a slight predominance for fair or blond skinned people. Almost 85% of BCCs are encountered on the skin of the face, neck or head and scalp, while other may appear on the extremities and rarely on hands. Sometimes, BCCs might be develop in the periocular regions, like in the lower eyelid, medial or lateral canthus.(1) The tumor grows in an indolent fashion, and if left untreated, it may involve profound structures like the hypoderm, skeletal muscles and bones. Clinically, the BSCs is divided in the following types: nodular, ulcerative, superficial, multicentric, erythematous, sclerosing and morphea-like. The median patients age is 40 years old, having a fair skin that are prone to sunburns. Treatment consists of topical application of imiquimod, surgical excision and irradiation.(2,3) Metastatic disease is very rare and might be detectable in neglected BCCs with prolonged evolution and profound spreading.(4)

CASE REPORT

We present the case of a 15-year old girl with a nodular tumor observed in the left subclavian area with surrounding erythema that has been resected by our surgical team. The excised fragment consisted of a round – ovoid, white to tan, elastic structure with dimensions within 1 cm (0,7/0,7/0,4 cm) and inconspicuous ulcerations (figure no. 1). The fragment was fixed in a 4% formalin solution for 24 hours, in order to preserve any immunogenicity. Afterwards, histologic processing included the use of successive ethanol concentrations, i.e 70, 80 and three successive baths of 96, 99 degrees, izopropylic alcohol and acetone submersion in order to freeze any decaying on the tissue. Subsequent paraffin embedding and sectioning in 2-3 µm followed with standard haematoxylin and eosin staining and microscopic examination.

Figure no. 1. Macroscopic appearance of excised nodule (formalin 4%)

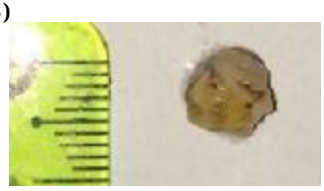

Figure no. 2. Dispersed basaloid cells around a follicular area in the presented case (HE, 400x)

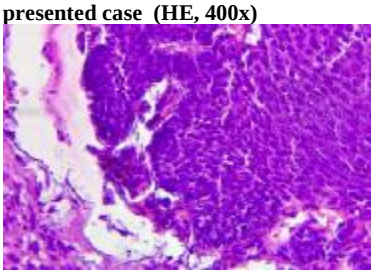

Figure no. 3. Basaloid areas with intermingled haematic infiltrates and surrounding dermis oedema; no visible atypia (H&E, 400x)

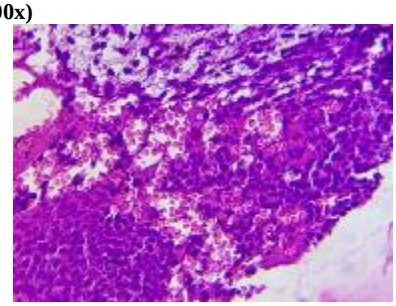

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Figure no. 4. Scuamoid pearls inside basaloid cell areas, with hyaline depositions and brisk inflammatory infiltrates (HE, 100x)

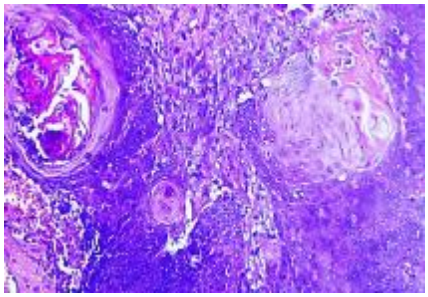
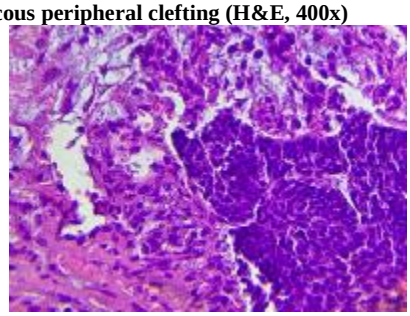


Figure no. 5. Basaloid areas with a whorle appearance pattern, brisk plasmocytic infiltrates and edem with incoscpicous peripheral clefting (H&E, 400x)



The microscopic examination revealed a dermis with frequent hair follicles that surrounds an almost necrotic area with bluish, polygonal, basaloid cells (figure no. 2) with visible nuclei and scant mitosis, intermingled with epidermal and scuamoid areas (figure no. 4), oedema and brisk plasmocytic inflammation (figures no. 3 and 5). There were present pearl-like structures scattered in the basaloid cell population. It is important to note that no peripheral clefts are observable between basaloid areas and healthy dermis (figure no. 4). Regarding histologic criteria, the established diagnosis was that of a trichoepithelioma with areas resembling basal cell carcinoma. The archived tissue and sections were referred for immunohistochemical analysis.

DISCUSSIONS

Ultraviolet radiation exposure is general accepted as the main risk factor for the initiation of BCC. It seems that day-light timing, pattern of distribution and duration of exposure to UV emissions would influence in a significant way the BCC onset. Therefore, recreational exposure of individuals during childhood and adolescence of a individual would have eventually a tremendous influence towards the evolution of BCCs. The presence of any ionizing radiation, oral psoralen, arsenic and ultraviolet A rays could be incriminated in the etiopathogeny of BCCs. Transplant recipients and immunosupression predisposes individuals for BCCs. For example, it has been documented that renal transplant patients have a ten-fold incidence for BCCs than those patients who have not received any renal transplants.(5) Genetic studies have identified that mutations in p53 and PTCH tumor suppressor genes for BCC, in sun-exposed Korean patients, are linked with sporadic cases of BCC. Heterozygocity loss of 9q22 for PTCH loci was found in 53% of cases. Therefore, it is suggested that UV-induced DNA lesions might interfere with the production of different BCC morphologic racial subtypes.(6) Some authors designate BCCs as a trichoblastic carcinoma (TCC), due to its predominant follicular differentiation and a possible follicular origin. It is known that TCC is a rare entity, thought to arise from within a benign trichoblastoma, presenting as a painless mass for a several years period before malignant transformation. However, there are similarities and differences between the morphologies of TCC and BCC: the TCCs may develop clinicopathologic criteria akin to BCC, histological diagnosis is difficult as it must be excluded from the benign counterpart.(7) Although difficult to identify or speculate a hair follicle origin for BCCs on standard haematoxylin-eosin stains, in superficial forms of BCCs this may become conspicuous, however, towards embryonic human hair. It was observable that vellus hair has intense Ep-CAM or epithelial cell adhesion molecule staining. In the terminal stage of hair follicle, only the secondary germ hair becomes the starting point of a new hair cycle with active cellular proliferation with no morphological signs towards any differentiation.

In this stage, the molecular immunohistochemical expression of Ep-CAM is visible, while, in the end of the cell differentiation this becomes inconspicuous. In some studies, most of the BCC variants – morpheiform, nodular, infiltrative, cystic, adenoid or granular consistently express Ep-CAM immunogenicity together with Ber-EP4. Further research prove that Ep-CAM may be involved in the generation of the oblique angle of the hair follicle during development, which is important for proper layering of the shaft and thermoregulation in fur-bearing organisms, thus offering solid evidence for BCC etiology as the most primitive hair follicle tumor.(8) Thus, microscopic appearance for BCC requires the presence of basaloid cells with scant cytoplasm and elongated hyperchromatic nuclei, peripheral palisading with peritumoral clefting and mucinous alteration of intermingled stroma, the latter two being the most important differential features against basaloid or BCC-like tumors. Amiloyd presence, distrophic calcifications and regressive brisk inflammatory infiltrate may be detectable on standard haematoxylin and eosin stains. Tumors with signed ring morphology , Pinkus tumor or fibroepithelioma, granular or infundibulocystic BCC variants might be encountered, although irrelevant to the prognostic factors.(9)

Most disputed differentials are Merkel cell carcinoma, microcystic adnexal carcinoma, squamous cell carcinoma with basaloid feature and trichoblastoma and trichoepithelioma. Merkel cell carcinoma (MCC) is confirmed histopathologically and is classified as trabecular, small cell or intermediate, proving to be a tumor with small, round, bluish cells with large nuclei that stain in a dot-like pattern with CK-20. MCC may be deceptive and misinterpreted in early stages as a BCC, amelanotic melanoma, keratoacanthoma or cutaneous metastatic disease, especially when overlying epidermis is not ulcerated until present in a late stage. Despite BCCs similiraties the MCC has a rapid growth rate with early metastastic disease.The best clue for MCC diagnosis is furnished by the AEIOU acronym, i.e. asymptomatic – lack of tenderness, expanding rapidly, immunosuppression, patient over 50 years of age and site exposed to ultraviolet rays.(10) Microcystic adnexal carcinoma (MAC) is an unusuall, malignant adnexal neoplasm, designated also as a malignant syringoma or syringoid carcinoma – i.e, a low grade sweat gland carcinoma. Grossly, it presents as a smooth, flesh colored to yellow, bulging firm plaque or cystic tumor, with a diameter between 2 to 3 cm, that evolves in a 3 to 5 years period, with initial site on head or neck, including lips. Histologically, MAC is a deep infiltrating tumor with assimetry, with desmoplastic stroma and keratin horn cysts intermingled with basaloid cells nests and tadpole shaped ducts filled with a eosinophilic amorphous substance. Perineural invasion is characteristic, while cords and strands may become very thin

and may have anindian file pattern. The immunohistochemistry panel in MAC may prove the most reliable CK19 positive expression in malignant transformation, along with broad spectrum antikeratin AE1-AE3 antibodies and carcinoembryonic antigen (CEA) positivity. Syringomatous carcinoma as a variant of MAC may be distinguished due to a higher amount of basaloid cells and nests, within a more sclerotic dermis.(11) Trichoblastoma (TCB) is a rare, benign, tumor with origins in rudimentary hair follicles, frequent in pediatric pathology, that arises secondary to another benign lesion, known as nevus sebaceous, due to a rapid development on the scalp or another hairy region during adolescence. Clinically it presents as a skin-colored, large, nodular lesion. The histopathological appearance of TCB may encounter various forms described as small, large nodular, retiform, cribriform, racemiform or columnar. The main feature is characterized by the presence of basaloid follicular germinative cells.(12) Trichoepitheliomas (TES) present as a solitary, fleshy nodule, nonulcerated with raised margins, usually on the upper eyelid margin, in patients with age ranging from 3 to 75 years old. Sometimes, TES present surrounded by milia-like lesions. The pathologic examination reveals that TES occur in 3 varietes: solitary, multiple or desmoplastic. Solitary lesions are non-inherited, while multiple TES may be associated with cylindromas and syringomas known as the Spiegel-Brooke syndrome, determined by a recessive suppressor oncogene located on the chromosome 16q12-13. The desmoplastic form of TES require the presence of concentric laminated keratinous horn cysts with a conspicous desmoplastic stroma and clusters of epithelial cells.(13)

CONCLUSION

In an ever increasing skin primary neoplasm incidence, the attention focused towards the early detection of BCC may offer an additional genetic syndrome diagnose and avoidance of later unfavorable evolution of BCC, regarding deep penetration muscles and bones or esthetic difficulties for face or visible skin localization, especially in young patients.

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