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Basal Cell Carcinoma: A Brief Review of Histopathological Types

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ABSTRACT

Basal cell carcinoma (BCC) is the most prevalent form of cancer in the globe. The occurrence of BCC is the result of a complex interaction between genetic and environmental factors. BCC's clinical and histopathological characteristics can vary depending on the tumor's histological subtype, ranging from low-risk tumours such as pigmented, superficial, and nodular tumours to high-risk types such as the basosquamous subtype with sarcomatoid differentiation, micronodular, infiltrating, sclerosing, and morphoeic tumours. This paper aims to provide an overview of the histopathological types of basal cell carcinoma.

Keywords: Basal cell carcinoma; Tumour; Sarcomatoid

INTRODUCTION

BCCs, which are a type of non-melanoma skin cancer along with squamous cell carcinoma (SCC), are the most prevalent malignant tumors in the globe. They may coexist within the same lesion or develop from a benign tumor-like lesion such as verruca vulgaris or a burn scar. Basal cells from the interfollicular epidermis or the hair follicle gave rise to this tumor[1-4]. It is one of the most prevalent forms of skin cancer in some populations, such as those of Asian, African, or Hispanic heritage[5]. Body parts that are exposed to the sun, such as the face, neck, head, trunk, and lower limbs, are where BCC typically develops[6]. Rarely are the mucous membranes, palms, or soles affected[1]. Most patients are middle-aged or elderly[7]. Although these slowly expanding tumors rarely spread, incomplete or delayed medical care may cause serious morbidity. This exists as a result of local invasion, which causes harm to deeper tissues, such as bone and cartilage, and additionally to the skin, especially close to the eyes, ears, and nares[8].

Despite the fact that BCC has a poor prognosis and extremely low rates of metastatic spread, it has a significant incidence of morbidity. This is characterized by local recurrence and destruction, especially when the peri-neural invasion is present. Secondary neuropathy results from BCC spreading contiguously due to peri-neural invasion. Rare cases (11 total) in the literature have described BCC with intravascular invasion, which had a greater rate of metastasis than BCC cases without this aggressive characteristic[9-11]. BCC is now listed under keratinocyte malignancy in the World Health Organization's 2018 classification of skin malignancies, and BCC with sarcomatoid differentiation is now recognized as a distinct histological variation[12]. This paper aims to provide an overview about the histopathological types of Basal Cell Carcinoma.

RISK FACTORS

Certain genetic disorders may increase the risk of developing BCC. Gorlin Goltz syndrome, known also as basal cell nevus syndrome, is an autosomal-dominant condition associated with germline patched 1 mutation. It is characterized by multiple BCCs with early onset, medulloblastoma, cardiac and ovarian fibromas, keratocystic odontogenic tumors, and other skeletal anomalies[13].

Along with genetics, UV radiation is the main environmental risk factor for BCC. Acute intermittent exposure during childhood or adolescence increases the lifetime BCC risk. This danger relies on cumulative exposure and skin tanability[14]. Indoor tanning and a high number of psoralen and ultraviolet A therapy (PUVA) (>100–200) and UVB (>300) treatments increase this risk[15,16]. Several epidemiological studies have linked photosensitizing medications to BCC incidence without a dose-response correlation[17]. Ionizing radiation increases the risk of BCC, especially at the exposure site[18]. Chronic lower-limb ulcers is another risk factor[19]. Chronic exposure to arsenic is also linked to the development of BCC. Arsenic is used only to treat select haematological cancers. It is still found in mining, agriculture, and some countries' drinking water[20].

HISTOPATHOLOGY

Microscopically, BCC is made up of cells with large, elongated nuclei that have palisading along the edges of tumor nodules that vary in prominence. Cytoplasm can vary between being inconspicuous, pale, or lightly eosinophilic. In most cases, mitoses and single-cell apoptoses are noticeable. Retraction artifacts are cleft formations that are noticeable between tumor nests and stroma. In a recent publication, a study highlighted the hypothesis that extracellular matrix degradation, which occurs during tumor growth, may be responsible for the formation of retraction artifacts[21]. However, previously, mucin shrinkage during fixation and staining of the specimen was thought to be the cause of these retraction artifacts[22]. The presence of a mucinous stroma differentiates BCC from other basaloid tumors arising from the skin. The tumor stroma occasionally displays amyloid deposition[22,23].

The growth patterns of basal cell carcinoma can be generally categorized into nonaggressive and aggressive forms. BCC was divided into 26 different histologic types by Wade and Ackerman in 1978[24]. BCC patterns of growth exist on a histologic continuum, and 40% to 75% of the specimens have combinations of different growth patterns within a tumor[25,26]. Furthermore, compared to complete excisions, shave and punch biopsies have an intrinsic error rate of about 20% when classifying BCC subtypes. Despite these limitations, tumor behavior can

be largely predicted by growth patterns[8]. Aggressive-growth BCC types include micronodular, infiltrative, and morpheaform, while Indolent BCC variants are superficial and nodular ones. They had more stromal proliferation, mitotic activity, and greater cell necrosis in common, but less stromal retraction, and circumscription. While metastasis is relatively rare for BCC of any growth pattern, these variants show increased rates of recurrence and metastasis[27,28].

Nodular BCC

Nodular BCC appears as a confined mass. The typical histology result is composed of large tumor nodules that extend deeply into the dermis. Large lesions frequently have ulcerations, giving rise to the historical term "rodent ulcer" for the tumor. A common observation is an epidermal or follicular attachment. Large basaloid lobules are visible in the tumor with peripheral nuclear palisading. The lobule's center region may be solid (Figure 1) or cystic (Figure 2), as a result of an excessive amount of mucin production. The tumor islands are surrounded by fibromyxoid stroma, and clefts are forming between the stroma and the tumor. Mild pleomorphism, varying mitotic activity, apoptosis, and infrequent necrosis are some other characteristics[1,23,29,30].

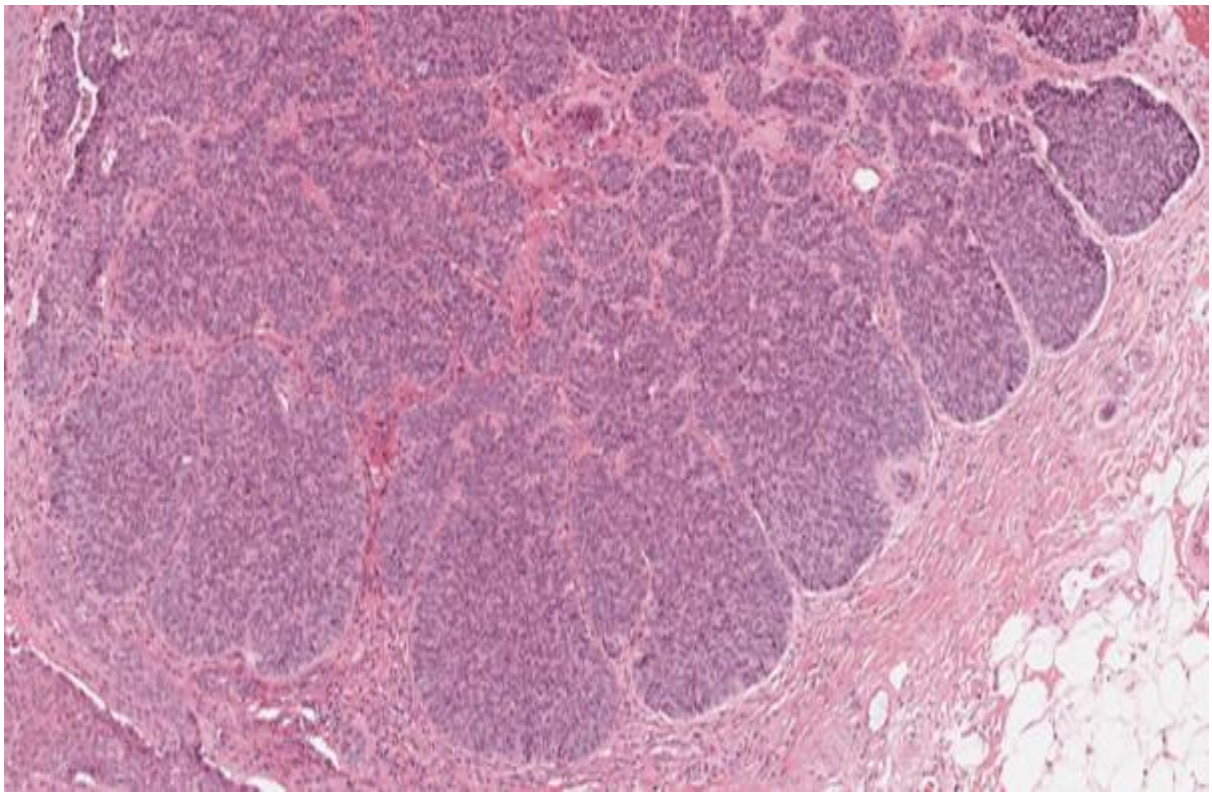

Figure 1: (Nodular BCC H&E stain x40) Large nodules with peripheral palisading and some clefting surrounded by fibrous stroma.

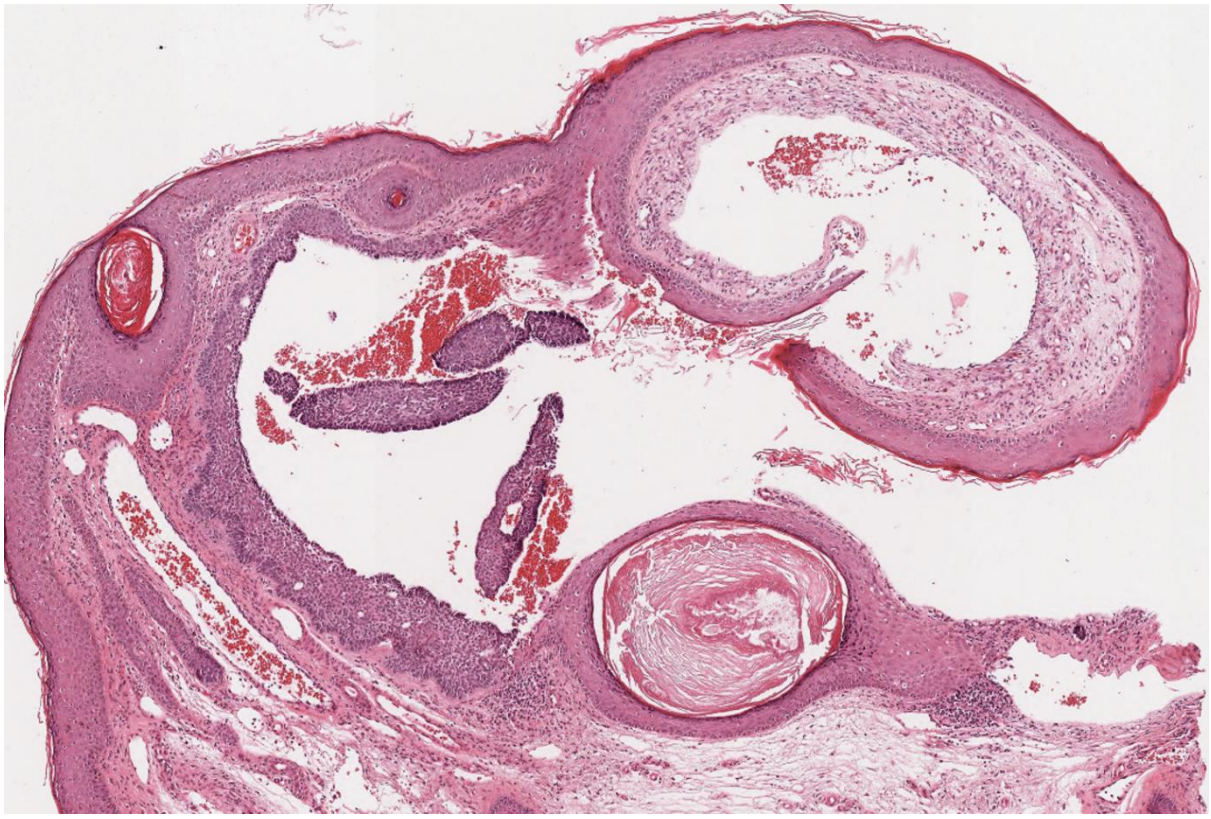

Figure 2: (Nodulocystic BCC H&E stain x40) Biopsy shows nodules of basaloid cells in the dermis. The nodules show peripheral palisading, artificial cleft, central cyst formation, and atypical cells. The neoplasm surrounding with fibrovascular stroma.

Micronodular BCC

The tumor is made up of distinct, small nodules, each measuring less than 0.15 mm in diameter. Normal dermal collagen divides the micronodules, creating the appearance of distinct nodules surrounded by a rim of the stroma. This BCC type is characterized by small basaloid nests that penetrate the dermis diffusely and deeply and extend into the subcutis. The characteristics which distinguish micronodular BCCs (Figure 3) from other BCC types are a less pronounced peripheral palisading and the lack of retraction artifact[1,23,29,31].

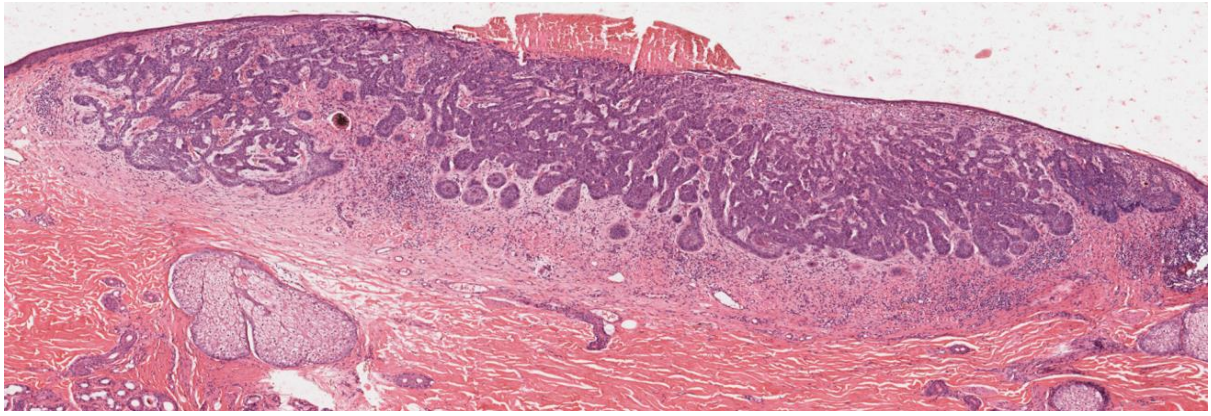

Figure 3: (Micronodular BCC H&E stain x40) Basaloid neoplasm with small nodules of basaloid cells in the dermis. The nodules show peripheral palisading, artificial cleft, and atypical cells.

Superficial BCC

Histologically, solitary basaloid lobules that extend from the epidermis represent superficial BCC (Figure 4). The tumor is only one millimeter thick and doesn't go beyond the papillary dermis. Sometimes, a tumor with nodular, micronodular, or infiltrating forms may also be mixed with superficial BCC[1,23,29,32].

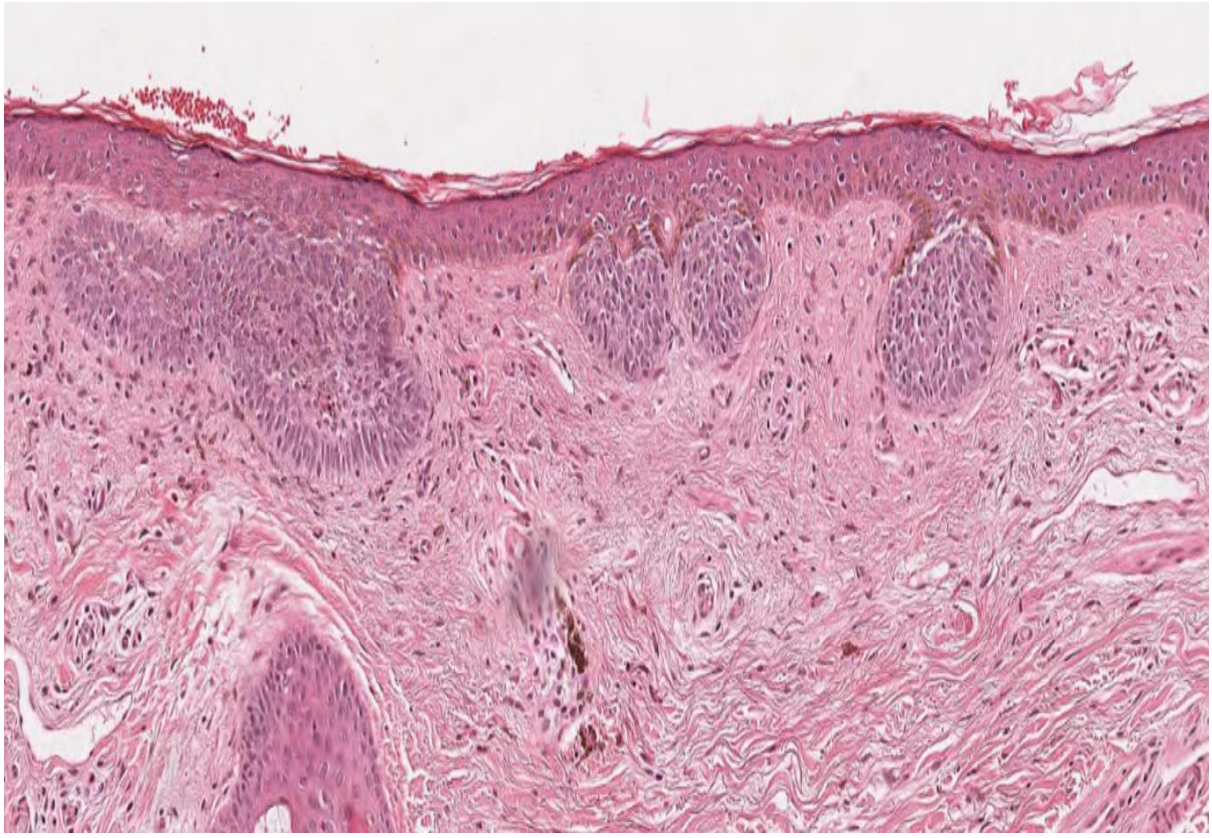

Figure 4: (Superficial BCC H&E stain x40) Isolated basaloid lobules projecting from the lower margin of the epidermis with retraction features. The lobules show peripheral palisading.

Pigmented BCC

Pigmented BCC is characterized by an increase in benign dendritic melanocytes within the tumor islands and by phagocytosed melanin between the tumor cells and peritumoral macrophages. Since the aforementioned modifications can be seen in either nodular or superficial BCC, pigmented BCC (Figure 5) is regarded as a subtype of those two[1,23,29,33].

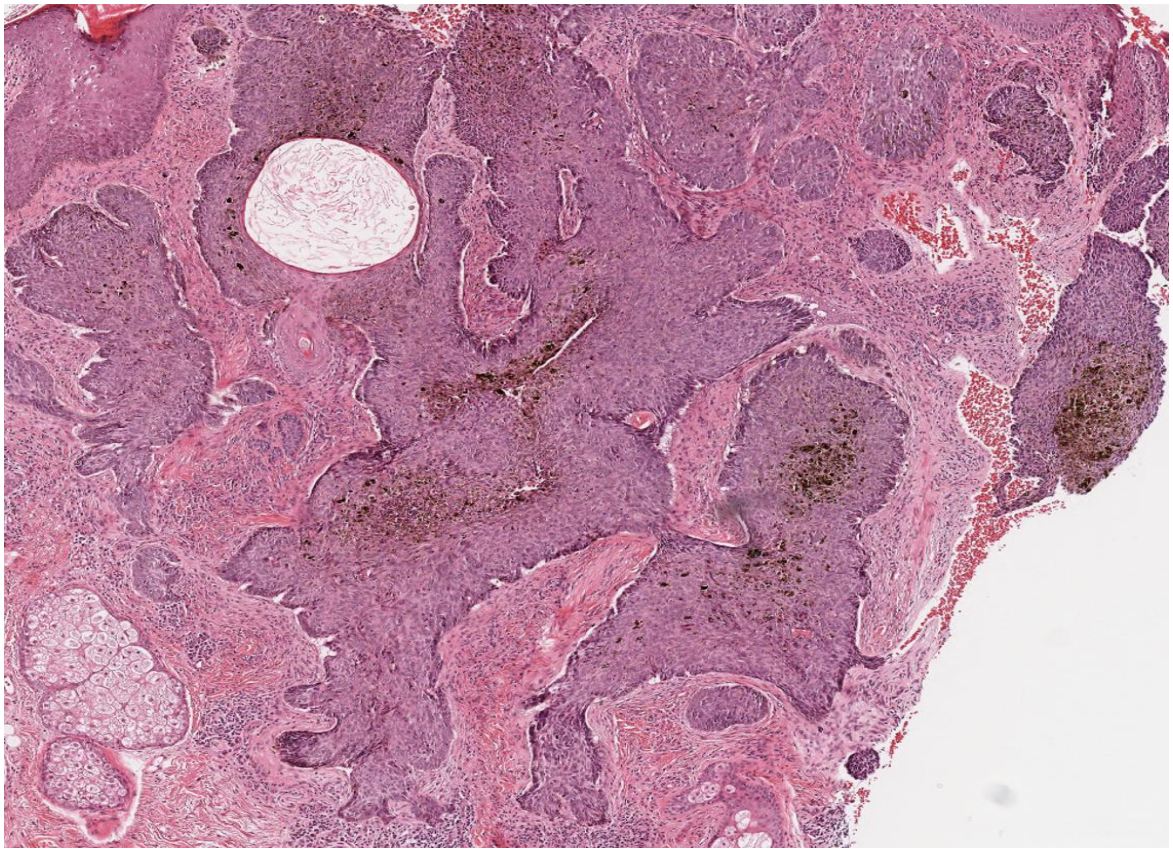

Figure 5: (Pigmented nodular BCC H&E stain x40) Biopsy shows basaloid neoplasm with large nodules of basaloid cells in dermis. The nodules shows peripheral palasiding and clefting along with mitosis and apoptic cells. Melanin pigment deposit in the neoplasm.

Infiltrating BCC

An aggressive form of BCC called infiltrating BCC, exhibits tumor nests that are more than 5-8 cells thick. The histological image is characterized by narrow tumor cords and nests with irregular infiltrative development patterns. Third, infiltrating BCC (Figure 6) cases are associated with nodular BCC. Perineural invasion, which is also found in morphoeic BCC, is a common finding. A higher recurrence rate has also been observed in this type of BCC[1,23,31].

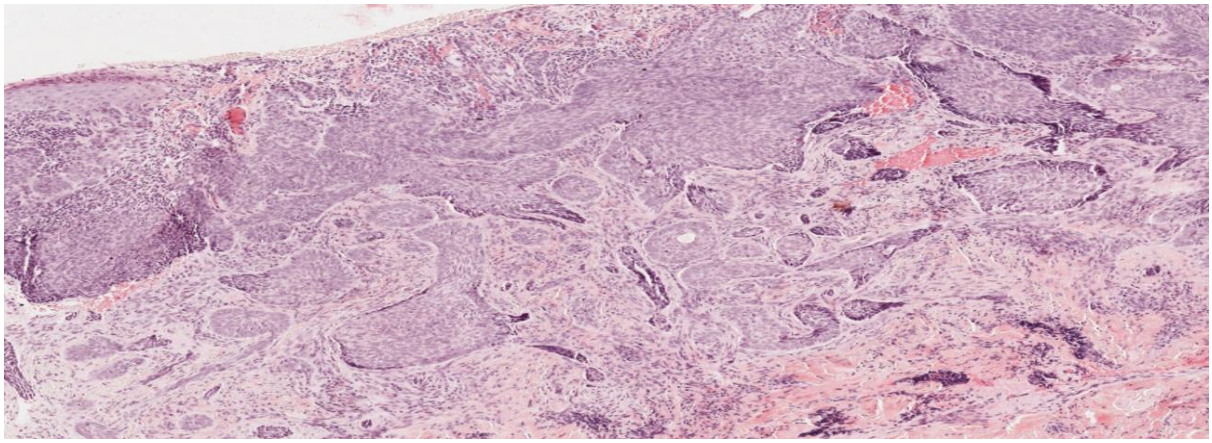

Figure 6: (Infiltrative BCC H&E stain x40) Basaloid masses with irregular strands and elongated cords of tumor cells with conspicuous loose stroma. The masses show peripheral palisading and atypical cells.

Sclerosing/morphoeic BCC

Morphoeic BCC (Figure 7) is characterized by disruption of the normal dermal architecture by extremely thin, narrow cords of basaloid cells that are 1-5 cells thick and destroyed by an overabundance of sclerotic collagenous stroma. Together with the surrounding stroma, the tumor created an irregular, profoundly infiltrative boundary. Retraction artifacts were infrequently observed. Sclerosing BCC is distinguished from the infiltrating form by the presence of extremely collagenous stroma. Perineural invasion is a common symptom of sclerosing BCC and has a high recurrence rate. High-risk BCC requires surgical excision with exact margin control[1,23,29,32].

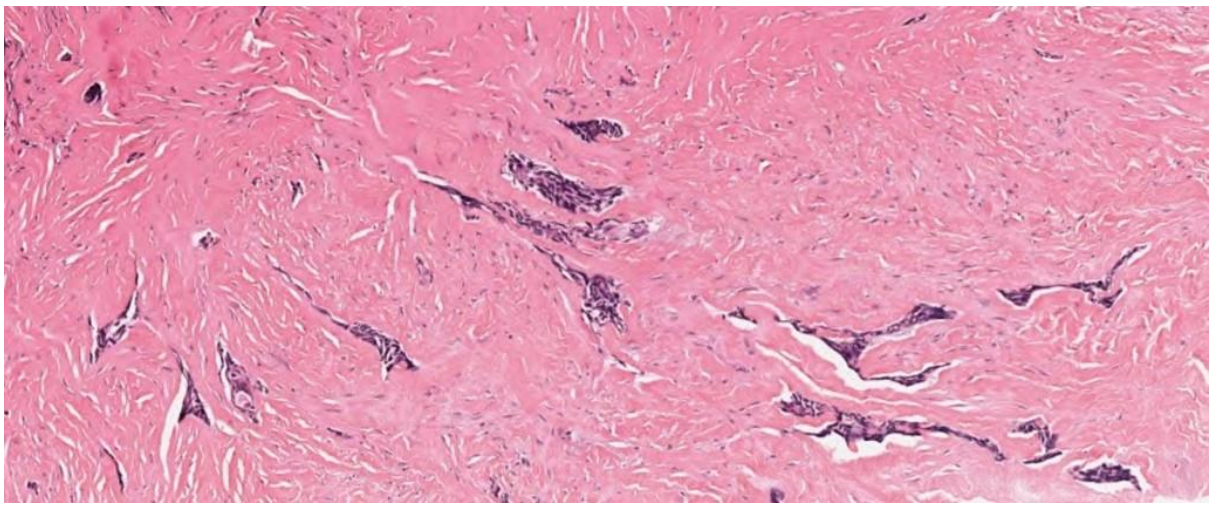

Figure 7: (Morpheaform BCC H&E stain x40) spread of thin strands and nests of basaloid cells with limited peripheral palisading. Stroma is dense and sclerotic.

Adenoid BCC

Adenoid BCC (Figure 8), a rare type of BCC, shows groups of proliferating epithelial cells in the form of islands infiltrating connective tissue. The lesional tissue was arranged in a lobular pattern, showing communication with the epidermis and secondary appendages of the skin. The basaloid epithelial cells showed peripheral palisading, with pleomorphism and mitotic activity. The basaloid cells showed an arrangement in a cribriform pattern, along with the presence of mucin in the ductal spaces. Melanin deposition was also seen in these islands[34,35].

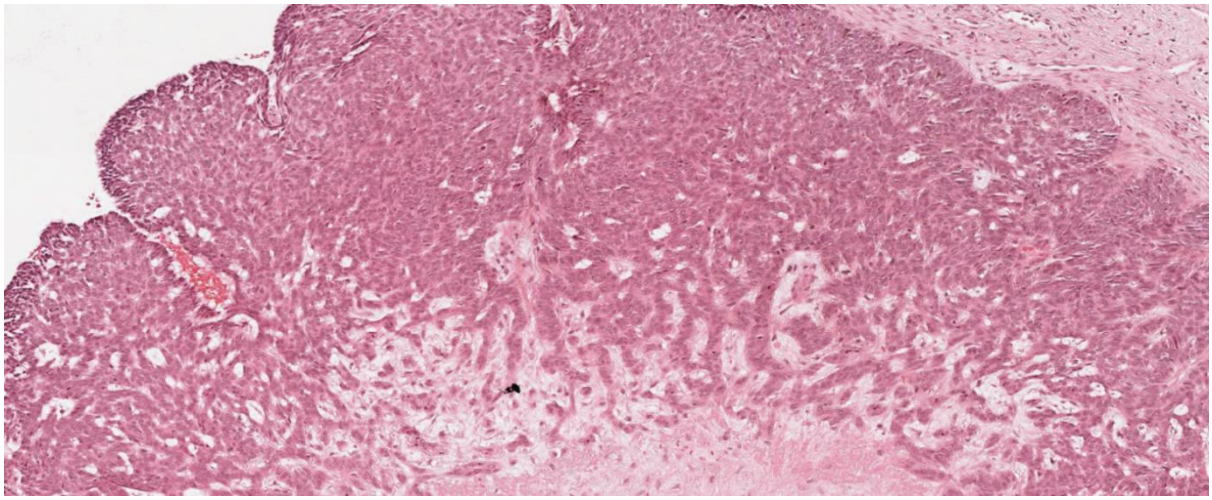

Figure 8: (Adenoid BCC H&E stain x40) Islands of basaloid cells with limited peripheral palisading arranged in cribriform pattern.

Basosquamous carcinoma

Basosquamous or metatypical carcinomas demonstrate the histological characteristics of both squamous cell carcinoma and basal cell carcinoma, as well as the presence of a transition zone between the two[2,3,5]. Atypical squamous cells coexist with islands of basaloid cells. Atypical squamous cells were focally observed or dispersed throughout and had a large eosinophilic cytoplasm. The transition zone is composed of cells with characteristics that lie halfway between SCC and BCC. The densely packed stroma has a fibrotic appearance. Less frequently occurring characteristics included local recurrence (4.5%), lymph node metastases (5%), and perineural invasion (10%)[1,23,29,36].

BCC with sarcomatoid differentiation

Sarcomatoid BCC, metaplastic carcinoma, and carcinosarcomatous BCC are other names for BCC with sarcomatoid differentiation. The tumor has a sarcomatous stroma, which can display a range of histological patterns, and a basaloid epithelial component. The malignant mesenchymal stroma can manifest as osteosarcoma, chondrosarcoma, leiomyosarcoma, rhabdomyosarcoma, and pleomorphic undifferentiated sarcoma. Due to the lack of knowledge on this uncommon variation, the prognosis remains unknown[12,23].

Fibroepithelial BCC

Other names for fibroepithelial BCC include Pinkus tumor and fibroepithelioma of Pinkus (Figure 9). It is composed of basaloid cells that stretch downward from the epidermis in thin, interanastomosing strands. The fibroblastic stroma is thick and encircles the tumor strands. Rarely do basaloid islands appear[1,23,37].

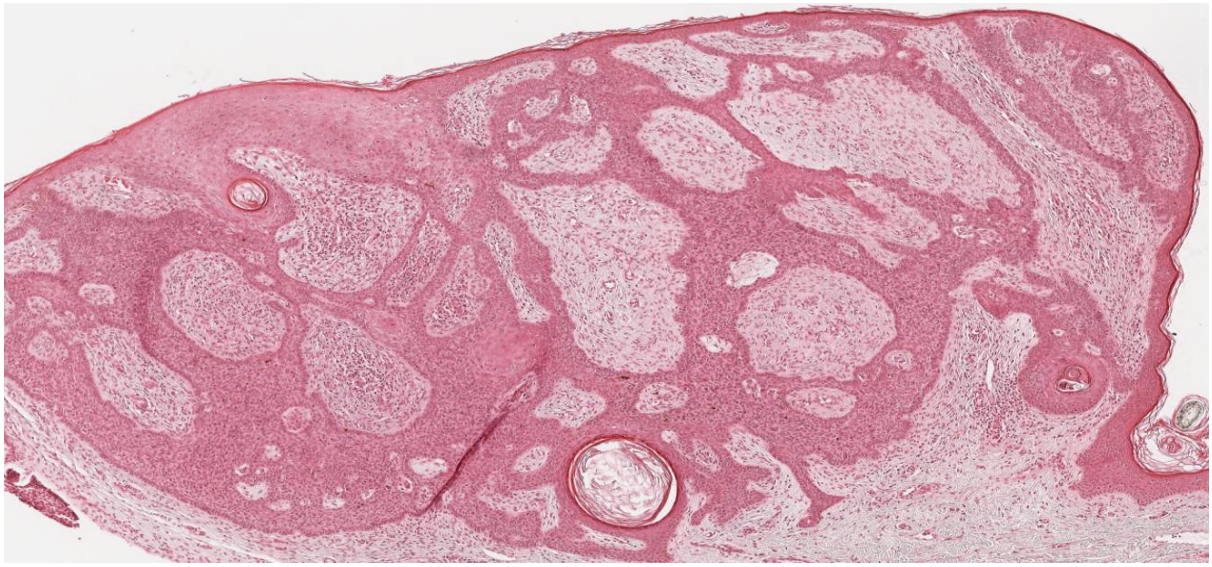

Figure 9: (Fibroepithelial BCC H&E stain x40) Strands of basaloid cells extend from epiderms to deep dermis, they are anastomosing and surrounded by fibromyoxoid stroma. Strands show peripheral palisading, large nuclear-cytoplasmic ratio, atypia, and keratin cyst formation.

Mixed histological BCC types

Basal cell carcinoma with mixed histology demonstrates more than one pathological pattern of the tumor. There is evidence that up to 70% of BCCs with mixed histomorphology exhibit aggressive growth[38,39]. As a result of the marginal involvement and aggressive growth patterns, they typically represent an unfavourable form of cancer with a greater propensity for local recurrence[40]. Among all mixed BCC types, the nodular type is the most common form to be included in the mixed bcc types[38].

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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