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Pathological Variants and Diagnosis of Basal Cell Carcinoma

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Background

Basal cell carcinoma (BCC) is the most common form of non-melanoma skin cancer occurring in the skin. It is a locally destructive tumour with varied clinical and histological appearances. It is the most common cancer in white-skinned individuals with increasing incidence rates worldwide. BCC arises from the inter-follicular or follicular epithelium. It is the most common malignant tumour type in humans and is a local aggressive course. It has low disease associated death rate and metastases to lung and bone exceptionally rare. When multiple, associated with a number of genetic conditions, including basal cell nevus (Gorlin), Bazex-Dupré-Christol, Rombo syndromes and xeroderma pigmentosum. Patients with BCC place a large burden on healthcare systems, because of the high incidence and the increased risk of synchronous and metachronous BCCs and other ultraviolet radiation (UVR) related skin cancers (i.e. field cancerization). As a result, the disability-adjusted life years and healthcare costs have risen significantly in recent decades. The key feature of basal cell carcinoma at low power magnification is of a basaloid epithelial tumour arising from the epidermis. The basaloid epithelium typically forms a palisade with a cleft forming from the adjacent tumour stroma. Centrally the nuclei become crowded with scattered mitotic figures and necrotic bodies evident. A useful distinguishing feature from other basaloid cutaneous tumors is the presence of a mucinous stroma. Some tumors may also show foci of regression, seen as areas of eosinophilic stroma with lack of basaloid nests**.**

BCC is a complex disease, in which the interplay between UVR, phenotype (UVR-sensitive) and genotype (somatic mutations and germline mutations/polymorphisms) fulfils a key role in an etiopathogenesis. Prevention programs with continual refinements and improvements could be of major importance in tackling the growing skin cancer problem. Nests of basaloid cells with peripheral palisading associated with a fibro myxoid stroma are the essential feature of BCC. It stains positively with cytokeratin, though favoring cytokeratin's from the follicular epithelium. BerEP4 is diffusely present in most tumors, while EMA is infrequently positive. The incidence rates in the United Kingdom appear to be increasing at a greater rate when compared with the rest of Europe. Indoor tanning with UV radiation-emitting lamps is common among adolescents and young adults. Rising incidence rates of basal cell carcinoma (BCC) have been reported for the United States and particularly among those diagnosed at younger ages. Recent epidemiologic studies have raised concerns that indoor tanning may be contributing to early occurrence of BCC, and younger people especially are vulnerable to cancer risk associated with this exposure.

Variants of Basal Cell Carcinoma

Superficial BCC: This variant show multifocal nest of atypical basaloid epithelium arising as buds from the basal layer of the epidermis. These nests remain confined to the papillary dermis.

Nodular BCC: The tumour forms a solid tumour nodule or nodules which may extend into subcutaneous tissues. Cartilaginous invasion is unusual.

Pigmented BCC: Focal deposits of melanin are evident throughout the tumour. An increased number of melanocytes may also be seen within the tumour, and scattered melanophages may be present in the surrounding stroma.

Micronodular BCC: While commonly forming a nodular architecture, the tumour is comprised of multiple small nests. This tumour may also exhibit extensive infiltration into surrounding tissue and is included within the poorer prognosis subtypes of tumour given the increased risk of local recurrence.

Basosquamous carcinoma: While this tumour may also be considered in the differential diagnosis as within the umbrella of squamous cell carcinoma, the clinical and histological features more closely resemble basal cell carcinoma. The cellular morphology shows areas of large, pale squamous cells, but lack keratinization. This therefore shows close resemblance to the metatypical type. These tumors will stain positively with BerEP4 while usually negative for EMA.

Different Diagnosis of BCC

Trichoepithelioma: The epithelium of trichoepithelioma demonstrates intimate integration with the surrounding matrix which is often cellular and fibro myxoid and show stroma. In contrast, basal cell carcinoma typically exhibits at least some retraction (clefting) between the epithelial cells and the surrounding epithelium and may show mucin deposition. Papillary mesenchymal bodies can serve as an important clue to trichoepithelioma. Immunohistochemistry is typically unhelpful but numerous stains are sited in the literature including Bcl-2, Ber-Ep4 and CD34. BCL2 staining is diffusely positive in basal cell carcinoma, while highlighting the basal layer of trichoepitheliomas. CD10, while positive in basal cell carcinomas and trichoepithelioma, tends to show peritumoral stromal reaction also.

Sebaceoma: This tumour will usually show a more lobulated architecture, and lack palisading, clefting and mucinous stromas. Immunostaining may be helpful with sebaceoma rarely positive for BerEP4, while typically positive with EMA.

Microcystic adnexal carcinoma: This can be difficult to distinguish from infiltrating basal cell carcinoma and desmoplastic

trichoepithelioma. Deep invasion, extensive perineural invasion and convincing ductal (glandular differentiation) may favor microcystic adnexal carcinoma. Immunohistochemical studies with CK20 can be extremely useful.