Basal cell carcinoma of the head and neck

Basal cell carcinoma

First discovered by Jacob et al. in 1827 and other names are: rodent ulcer, basailoma, basal cell epithelioma (BCC) is the most common skin cancer worldwide.

accounts for about **80% to 85% of non-melanoma skin cancer (NMSC).**

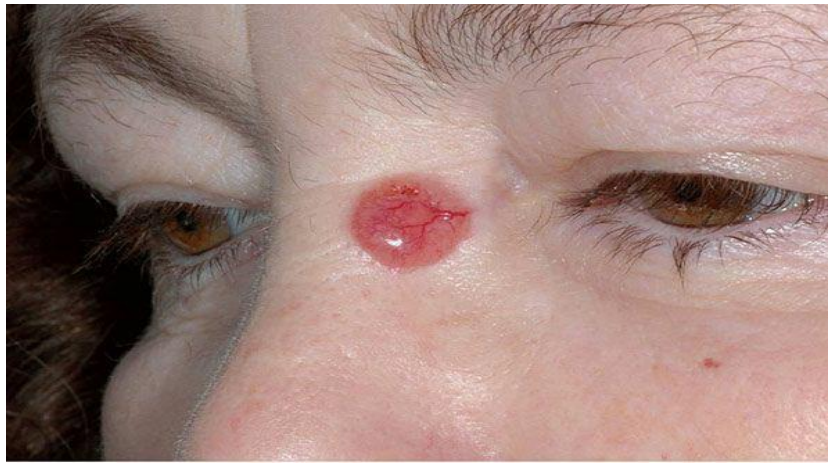
it is clear that there is a 10% per year rise in the incidence of BCC worldwide.

it is estimated that 40–50% of patients with a primary BCC will develop at least one or more BCC within 5 years.

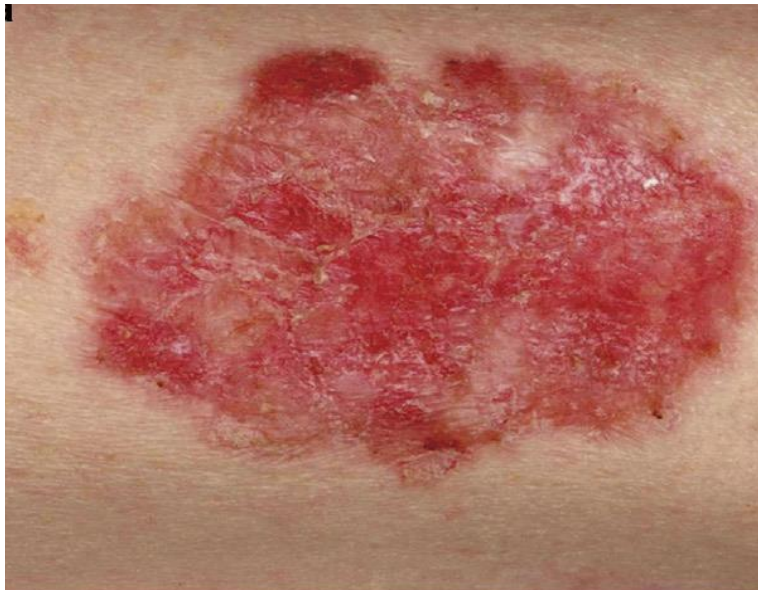
Clinical presentation

The clinical appearance is variable but the most common presentation is that of a slow-growing, red-skin colored nodule with telangiectasia which frequently ulcerates.

Some tumors present as an erythematous macule/patch or an indistinct, indurated, scar-like plaque



Nodular basal cell carcinoma



Superficial BCC.: Well-defined slightly raised erythematous plaque with adherent scale

- Eighty percent of BCCs occur in the head and neck region
- The prevalence of BCC was found to **be twice more in men** than in women, with increasing prevalence with older age
- BCC **rarely found in people under the age of 40** years, although, currently, the incidence in youth continues to rise due to increasing advances in the early diagnosis of BCC
- BCC is **extremely rare in children under 15 years of age**. BCC seen in the pediatric age group is associated with inherited syndromes

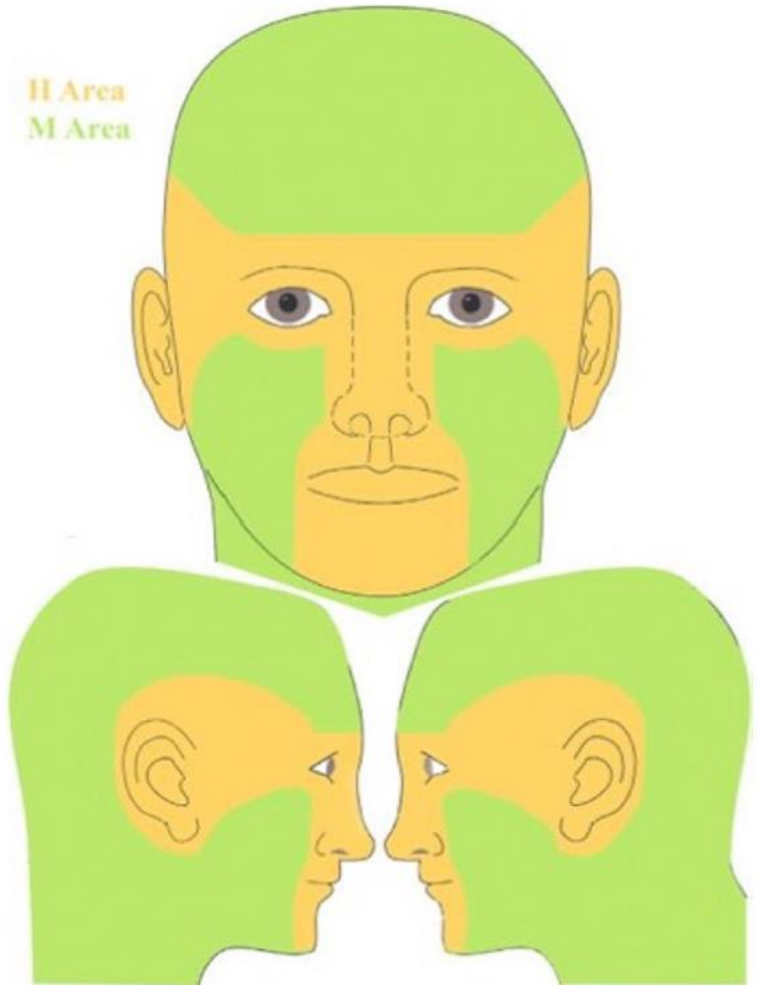
Clinical factors:

Anatomic location is a well-known risk factor for BCC recurrence. National Comprehensive Cancer Network Clinical Practice (NCCN Guidelines)and appropriate use criteria for Mohs micrographic surgery(MMS) designate 3 body areas for risk stratification based on primary tumor location. Area H (the ‘‘mask area’’ of the face) constitutes the highest location-based risk. Lesion size and poorly defined borders are independent risk factors for recurrence. Size cutoffs vary based on location. All recurrent tumors, regardless of previous treatment modality, are considered high-risk.

Area H, ‘‘Mask areas’’ of face (central face, eyelids, eyebrows, periorbital, nose, lips [cutaneous and vermilion], chin, mandible, preauricular and postauricular skin/sulci, temple, and ear), genitalia, hands, and feet.

Area L, trunk, and extremities
(excluding pretibia, hands, feet, nail units, and ankles);

Area M,
cheeks, forehead, scalp, neck, and pretibia.



Risk factors for basal cell carcinomas

- Solar UV radiation
- Human papillomavirus
- Iatrogenic immunosuppression
- Acquired immunodeficiency syndrome and non-Hodgkinlymphoma
- PUVA therapy
- Photosensitizing drugs
- UVB phototherapy
- Ionizing radiation
- Occupational factors
- Arsenic exposure
- Previous history of basal cell carcinoma

Environmental factors:

- The mechanism of UV radiation-induced mutagenesis has been extensively studied. Both UVB and UVA radiation are mutagenic; however, UVB radiation causes direct DNA and RNA damage by inducing covalent bond formation between adjacent pyrimidines.
- UV-induced DNA damage normally results in DNA repair or apoptosis; only very rarely does it lead to tumorigenesis. Patients with Xeroderma pigmentosum (XP), where DNA repair mechanisms are impaired, can have an up to the 2000-fold increased risk of skin Cancer.
- . BCC from anatomical regions with chronic UV exposure are associated with higher mutation rates than those with intermittent exposure.

Occurrence of Metastases.

- Metastatic BCC **(1%)** is more likely attributed to tumors with aggressive histopathologic patterns.
- The typical case history of a metastatic BCC is that of a large, ulcerated, locally invasive, and destructive primary lesion that has recurred despite repeated surgical procedures or radiotherapy.
- Metastatic BCC, hematogenic, & lymphogenic spread show an even distribution.
- 50% of the patients with metastatic BCC have metastases to **lymph nodes** as their first site of spread,
- lungs, and bones also are frequently the first sites of involvement.
- Metastases to the liver, other viscera, and the skin or subcutaneous tissues have occurred.

Molecular Genetic Features:

- More than 80% of BCC overexpress p53 protein, and this figure is even higher in the more aggressive types. Mutation in TP53 is found in approximately 30%–40% of cases.
- Dysregulation of the Hedgehog pathway is a key pathogenetic event in basal cell carcinoma.

In the absence of Hedgehog ligands, protein patched homolog 1 (encoded by PTCH1) normally inhibits the transmembrane protein Smoothened (encoded by SMOH), leading to a cascade that represses expression of the Hedgehog downstream target genes, SMO (20%)

In basal cell carcinomas, inactivating somatic mutation and allelic loss of PTCH1, the gene implicated in the basal cell nevus syndrome, are common (67% and 53% of cases, respectively).

- Another gene related to Gorlin syndrome was called suppressor of fused (Sufu), which is a negative regulator in the hedgehog signaling pathway, SUFU (8%).
- Heterozygous loss-of-function variants in SUFU cause NBCCS. clinical features are milder in individuals with SUFU-related NBCCS with fewer BCCs, and no jaw cysts were reported.

Syndromes that included basal cell carcinoma:

- Nevoid basal cell carcinoma syndrome (NBCCS) also known as the Gorlin–Goltz Syndrome is a multisystem genetic disorder with an autosomal dominant inheritance pattern,. It is characterized by multiple BCC, palmar pits, calcification of dura, keratocysts of the jaws, skeletal anomalies, and occasional abnormalities of the central nervous system, mesentery, and endocrine organs.

- Other genetic syndromes may predispose people to develop NMSC, including xeroderma pigmentosum, epidermolysis bullosa.
- Ferguson Smith Syndrome (Multiple self-healing squamous epithelioma of Ferguson-Smith (MSSE) is a rare autosomal dominantly inherited disease, almost exclusively reported in patients of Scottish origin, with recurrent, histologically malignant tumours that undergo spontaneous regression

- Bazex syndrome (X-linked dominant condition with features of follicular atrophoderma, multiple BCCs, local anhidrosis, and congenital hypotrichosis)

- Rombo syndrome (an autosomal dominant condition distinguished by BCC, atrophoderma vermiculatum, trichoepitheliomas, hypotrichosis, milia, and peripheral vasodilation with cyanosis
- MuirTorre Syndrome (is an autosomal-dominant skin condition of genetic origin, characterised by tumours of the sebaceous gland or keratoacanthoma that are associated with visceral malignant diseases.

HISTOLOGICAL FEATURES OF BCC

Basal cell carcinoma (BCC) shows the following histologic features:

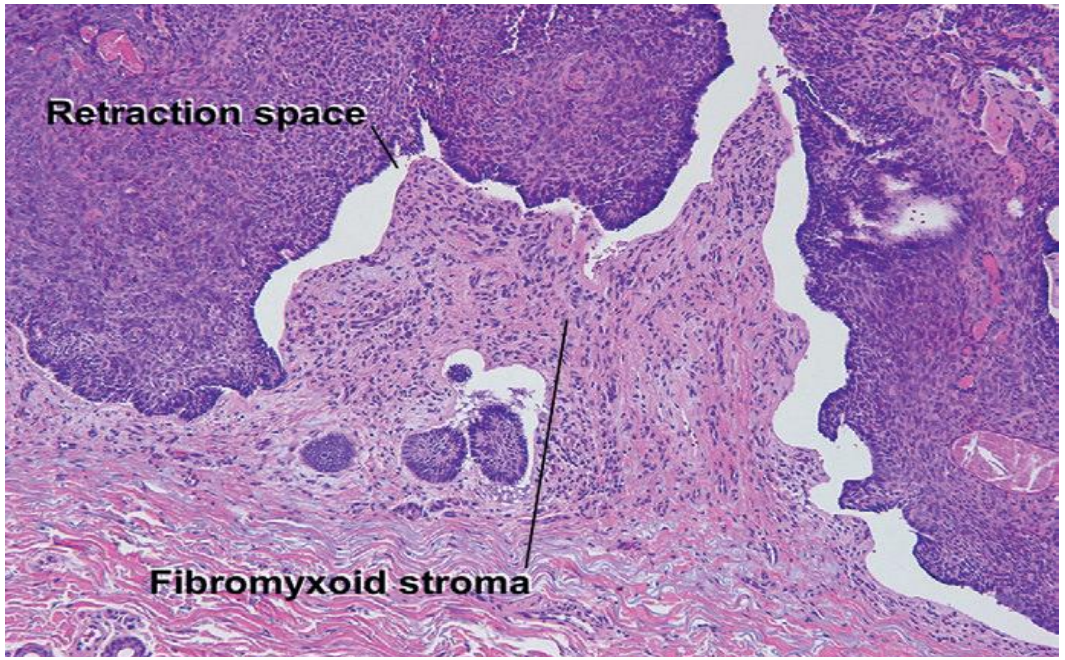
- Neoplastic aggregates that vary in size and shape composed of **basaloid cells**
- Aggregates often arise from the **undersurface of the epidermis** or connect to adjacent hair follicles
- Peripheral palisading of nuclei within the tumor aggregates
- Retraction artifact between the aggregates and surrounding stroma
- Mucinous stroma surrounding the basaloid tumor aggregates
- Tumor cells have large, oval, or elongated nuclei and little cytoplasm
- Necrosis in the center of tumor aggregates and/or individual pyknotic/necrotic tumor cells
- **Lack of striking cytologic atypia and mitoses**
- Solar elastosis often in the surrounding dermis
- Tumor may have surrounding inflammatory infiltrate
- Calcifications may be present in long-standing lesions
- **Within one BCC more than one histologic subtypes may be seen(mixed type).**

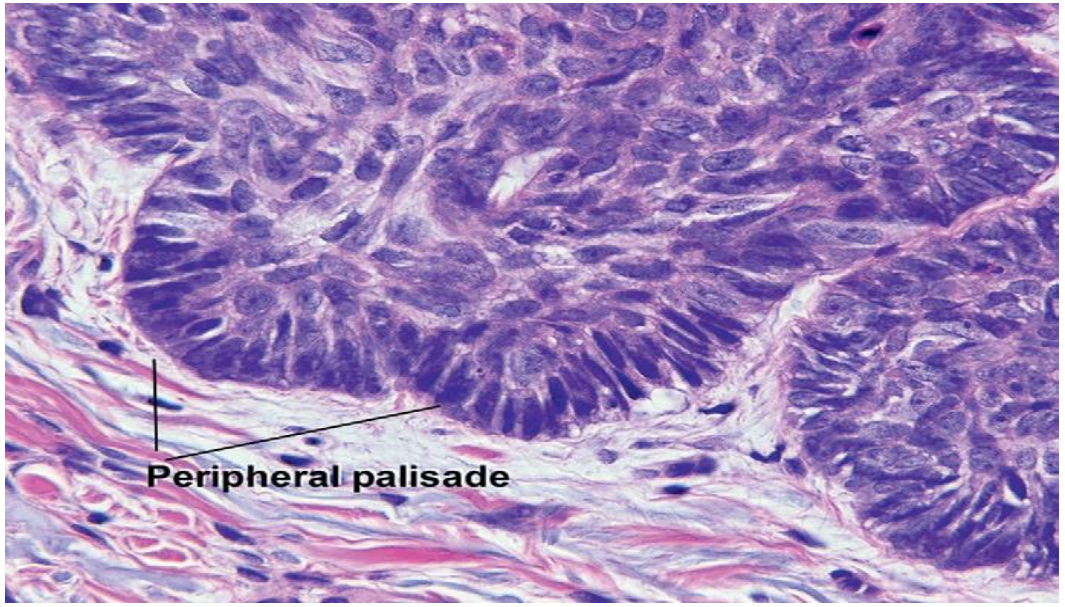
histological sub-typing based mainly on the growth pattern into ‘low-risk’ and ‘high-risk’ variants

Nodular More than half of all basal cell carcinomas are of the nodular type (also known as nodulocystic.

Key features

- Nodular blue islands
- Peripheral palisading
- Retraction artifact
- Distinctive fibromyxoid stroma
- **Low risk-type**



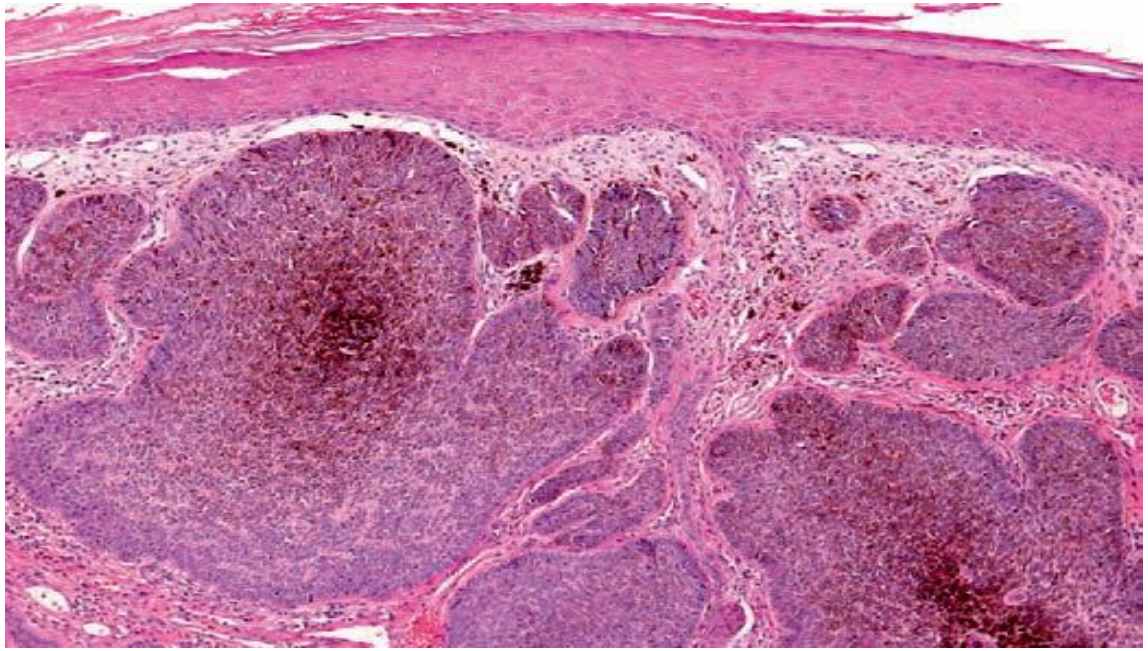


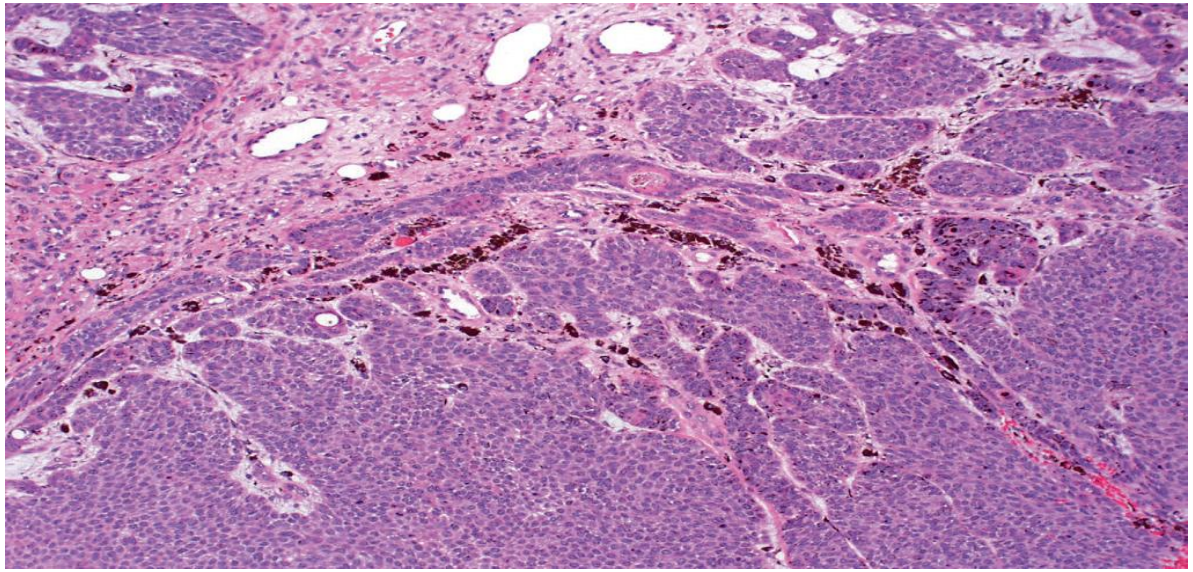
Pigmented BCC

is one of the most difficult-to diagnose lesions.

is a clinical and histological variant of BCC that exhibits increased pigmentation by benign melanocytes that colonize the tumor.

- Melanophages are frequently dispersed within the dermis.
- The frequency of pigmented BCC varies, being 6% of all the BCCs





Micronodular BCC

Key features

• Small blue islands

• Peripheral palisading

• Retraction artifact focally

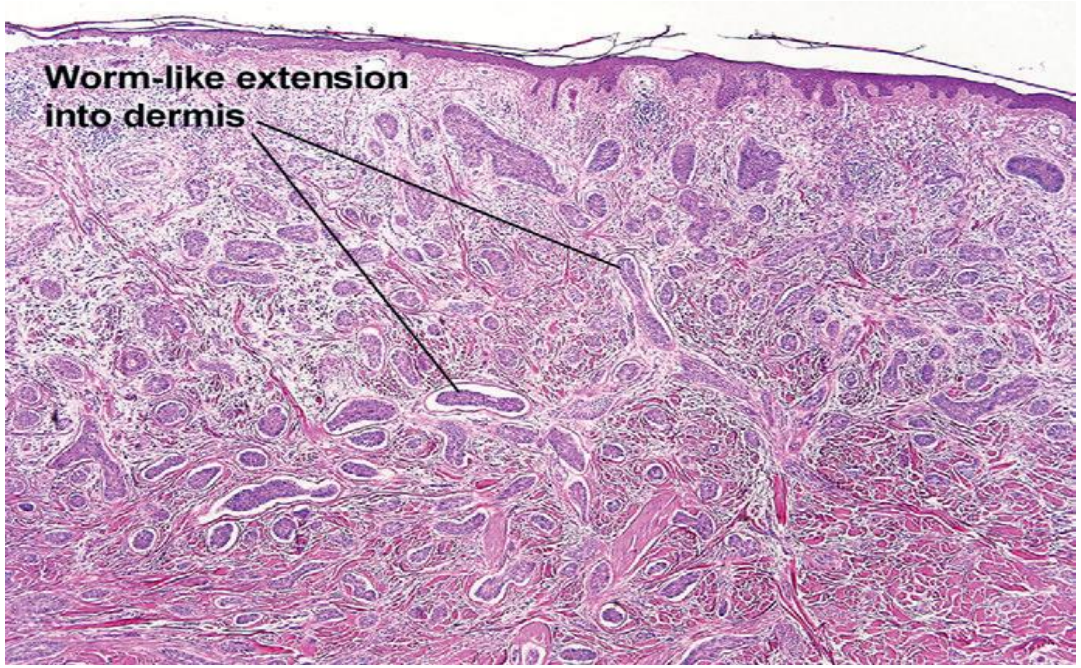
• Distinctive fibromyxoid stroma surrounds individual islands, but normal dermis is present between islands.

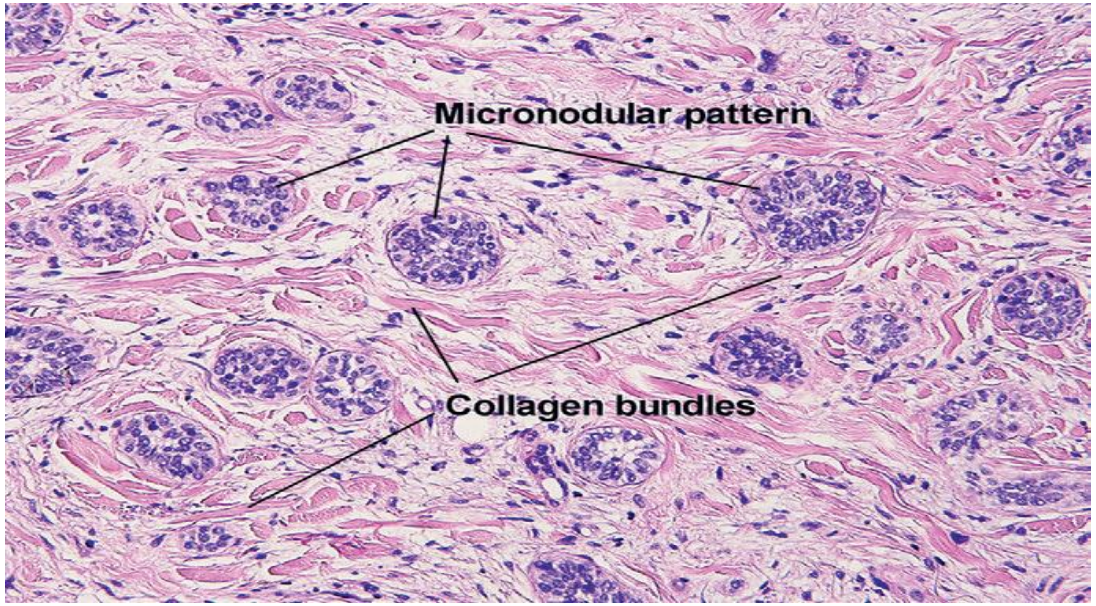
- **High-risk type**

Micronodular BCC is characterized by **aggressive worm-like growth into the dermis.** In cross-section, the appearance is micronodular. Because of the thick dermal collagen bundles between tumor islands, the tumors are poorly defined clinically, and curettage has a high failure rate.

It should be noted that many ordinary BCCs demonstrate small finger-like projections that appear as small round balls in cross-section.

Only tumor stroma separates the islands, with no thick collagen bundles in between. These tumors do not qualify as micronodular BCC.





Superficial multifocal BCC

Key features

• Multifocal blue buds

• Distinctive fibromyxoid stroma displaces solar elastosis downward

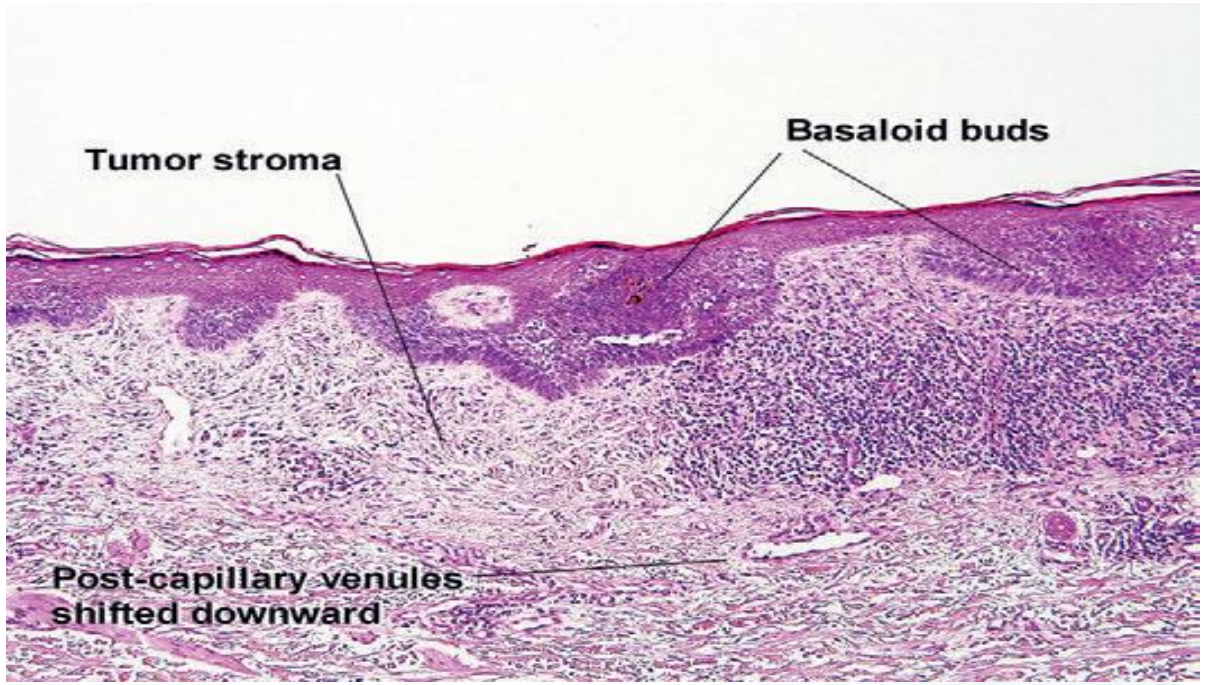
• Retraction artifact common

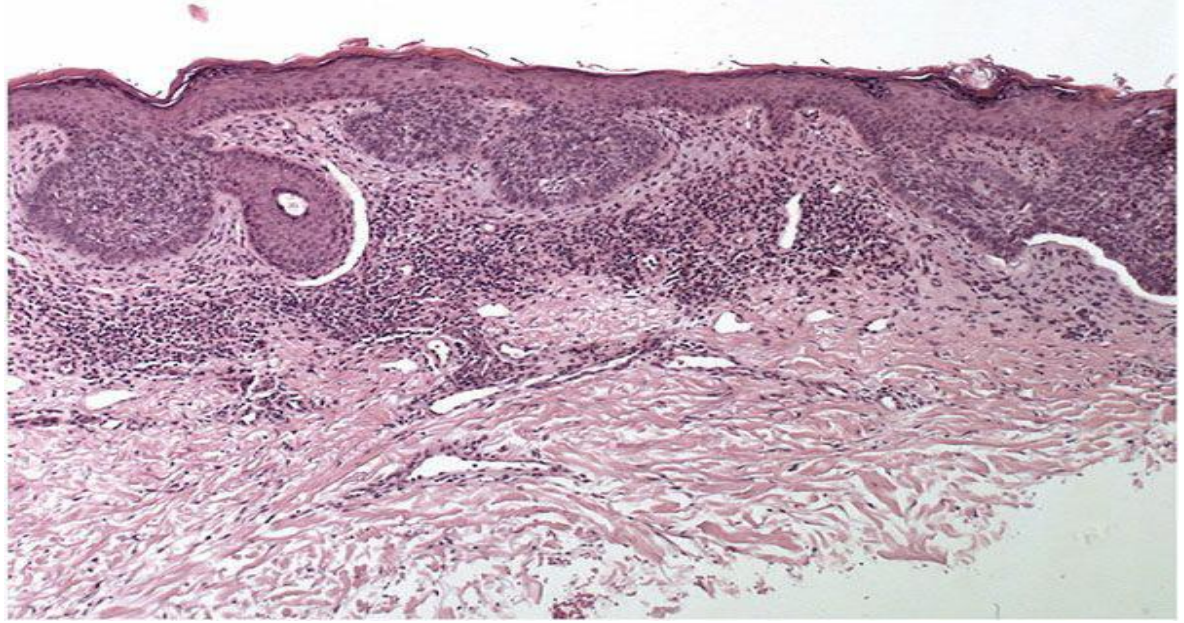
• Low-risk type

Histologically it comprises multiple, superficial, bud-like down growths of basaloid tumour cells arising from the under surface of the epidermis.

The dermis between the superficial tumour lobules show increased vascularity and fibrosis.

It **is sometimes difficult to pinpoint the peripheral extent of a superficial BCC histologically due to an apparently multifocal growth pattern and this explains the high local recurrence rate associated with this subtype.**

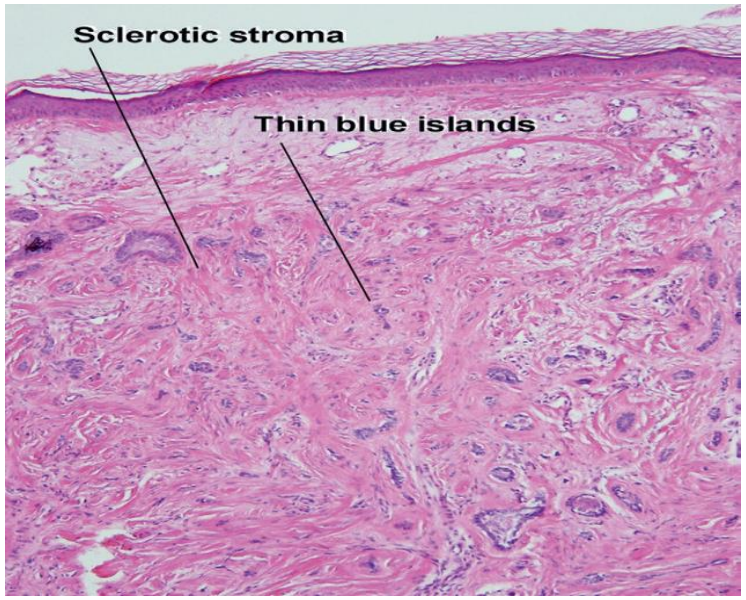


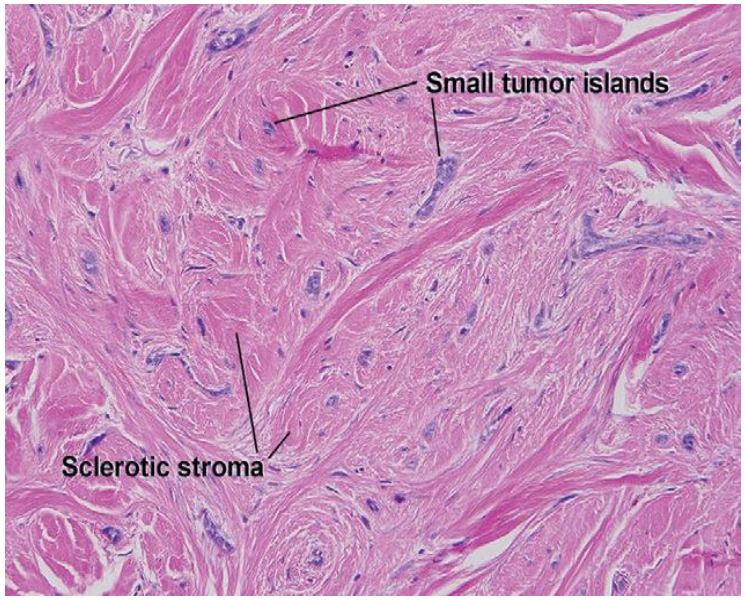


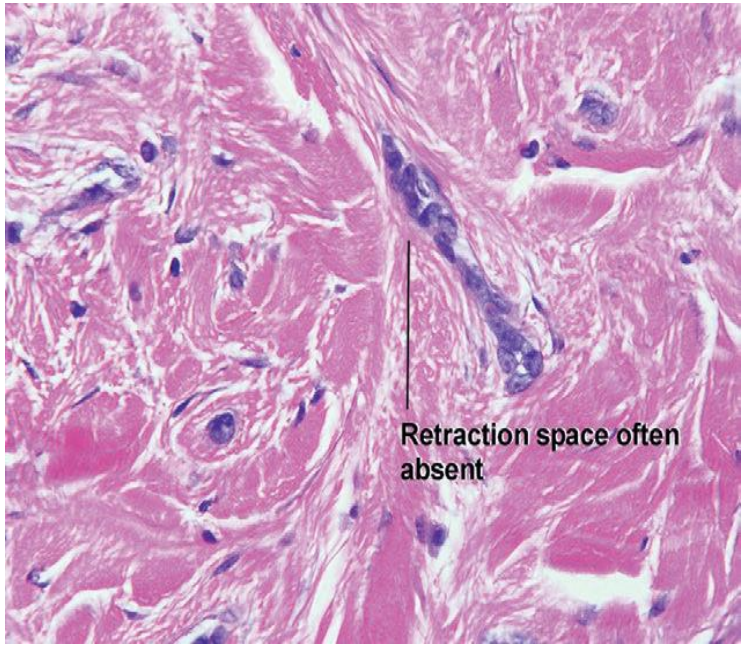
Morpheaform/ Sclerosing BCC

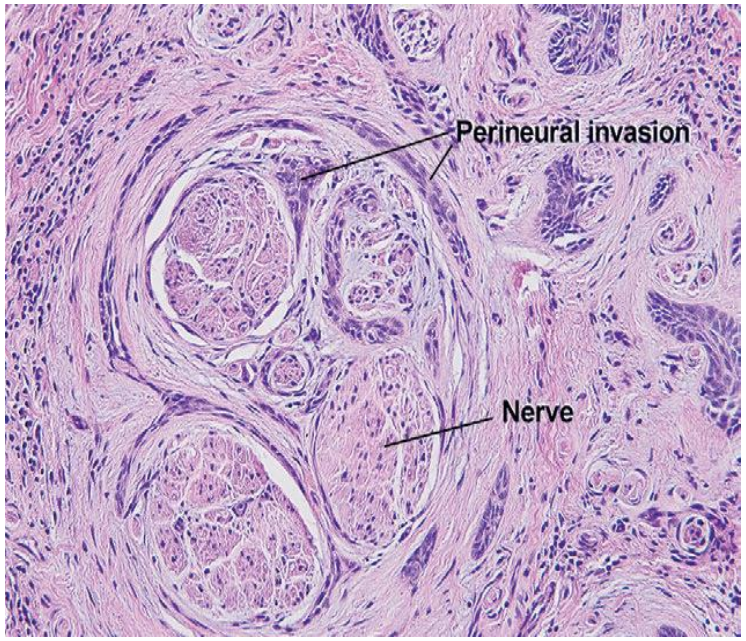
Key features

- Thin infiltrating strands of basaloid cells, usually only two cells thick
- Sclerotic stroma
- Rod-like islands with small horn cysts may be present focally
- High-risk type
- Perineural, lymphovascular invasion and local recurrences are common.





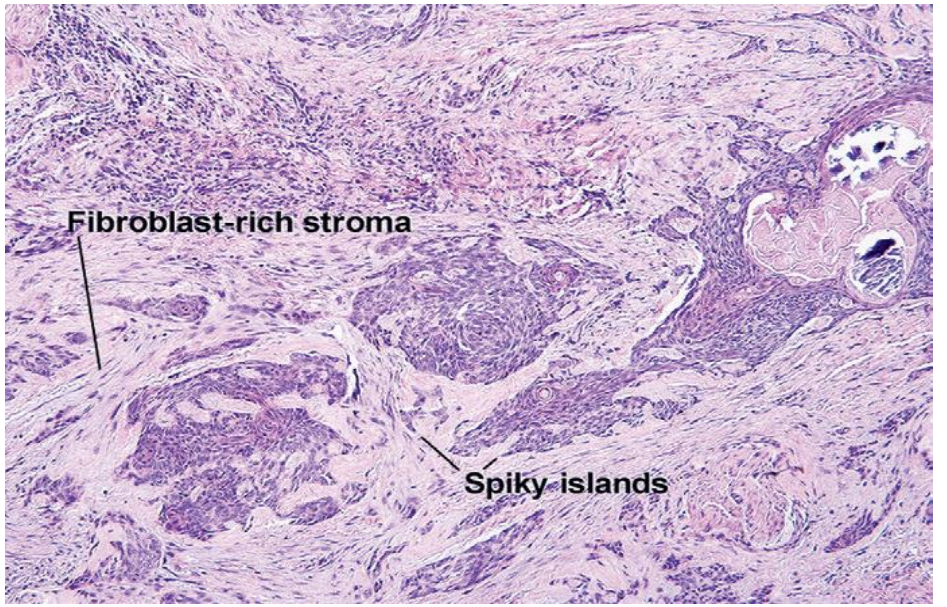


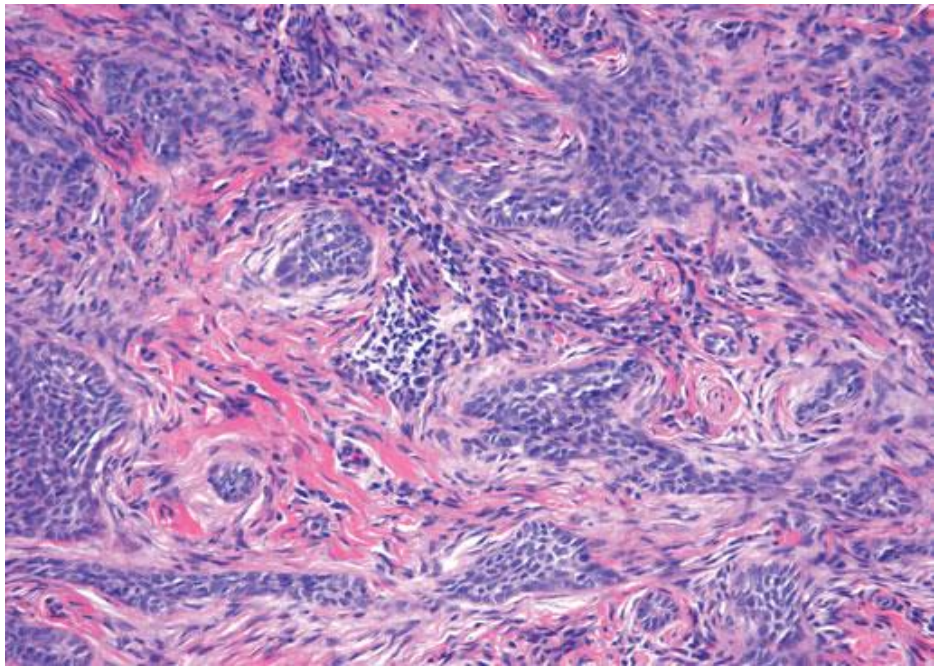


Infiltrative BCC

Key features

- Spiky growth pattern
- Fibroblast-rich stroma with little mucin
- Areas of squamous differentiation common
- Perineural extension common
- The basaloid epithelium exhibits some peripheral palisading of nuclei. The tumor stroma is slightly sclerotic.
- **High-risk type**





Fibroepithelioma of Pinkus

Key features

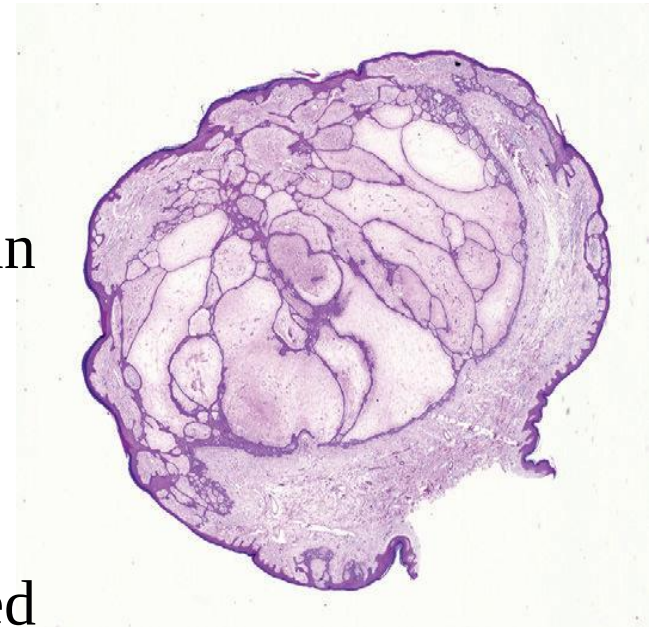
- Pink strands, blue buds
- Eccrine ducts often visible within strands
- Ample fibromyxoid stroma
- Low–risk type

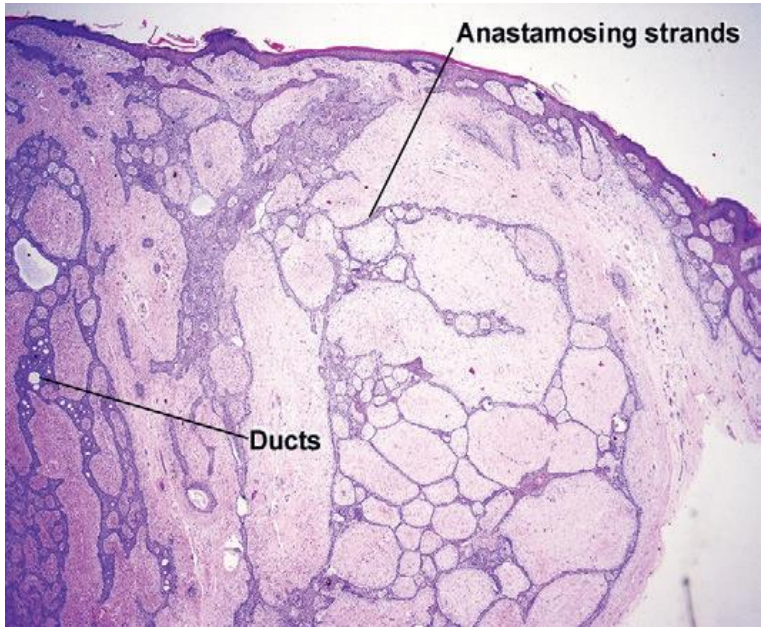
Fibroepithelioma of Pinkus is composed of anastomosing pink

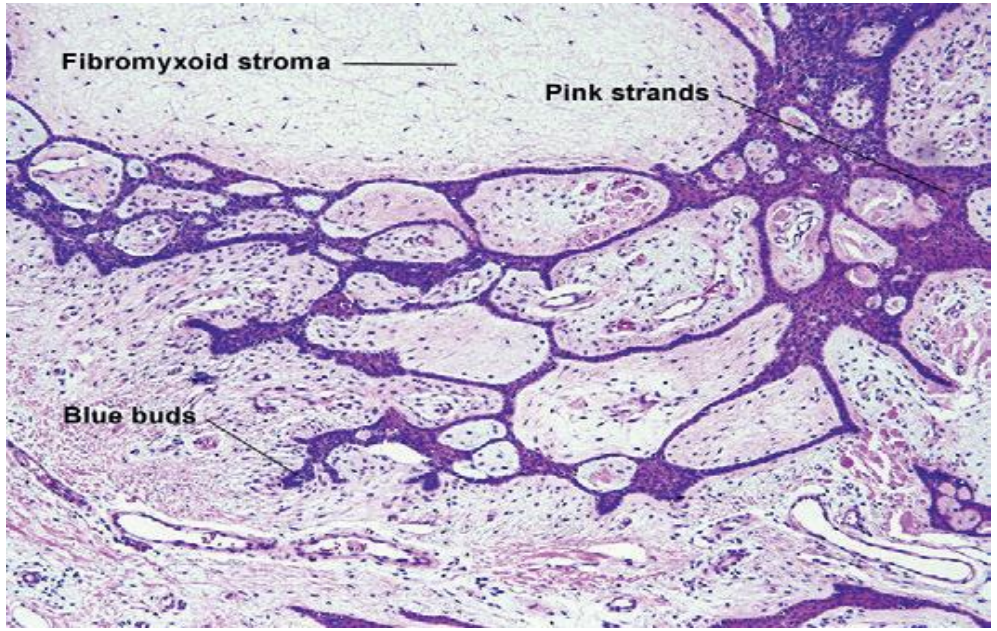
epithelial strands embedded in a fibromyxoid stroma. Ducts are

often visible within the strands. Blue basaloid buds are present

at the tips and periphery of strands.



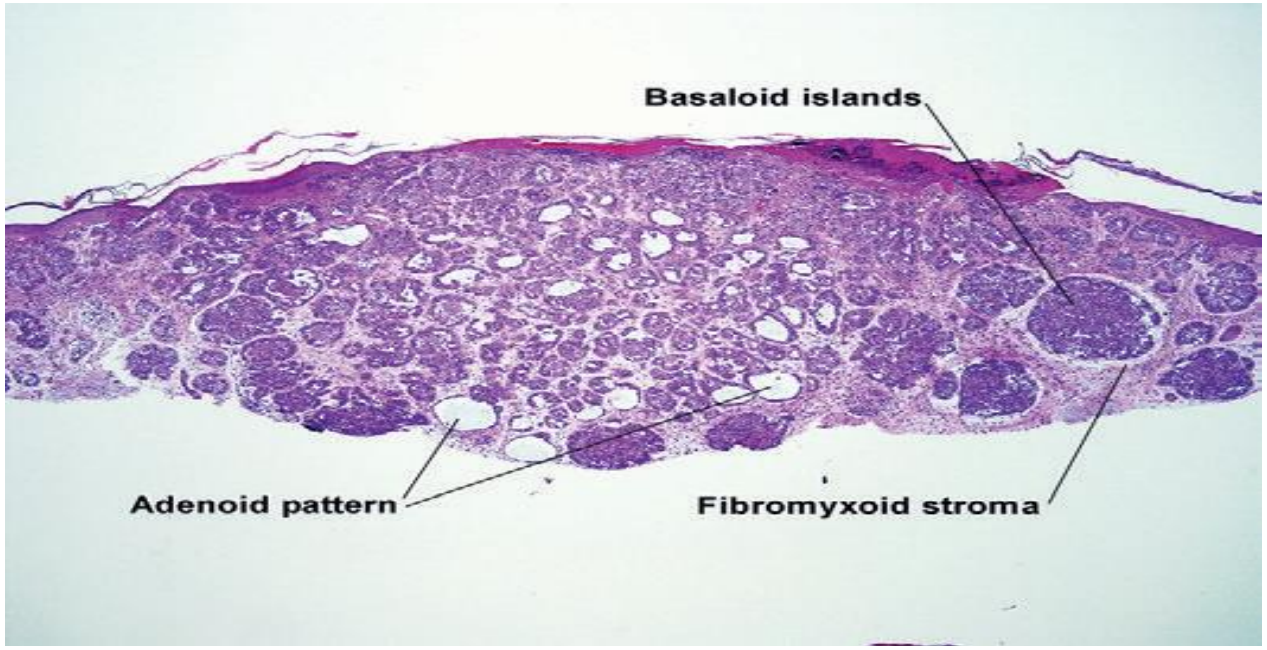


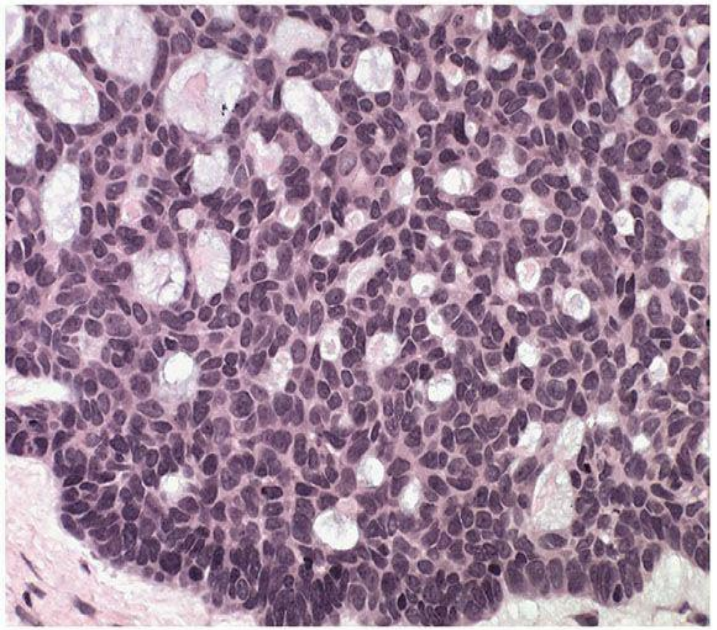


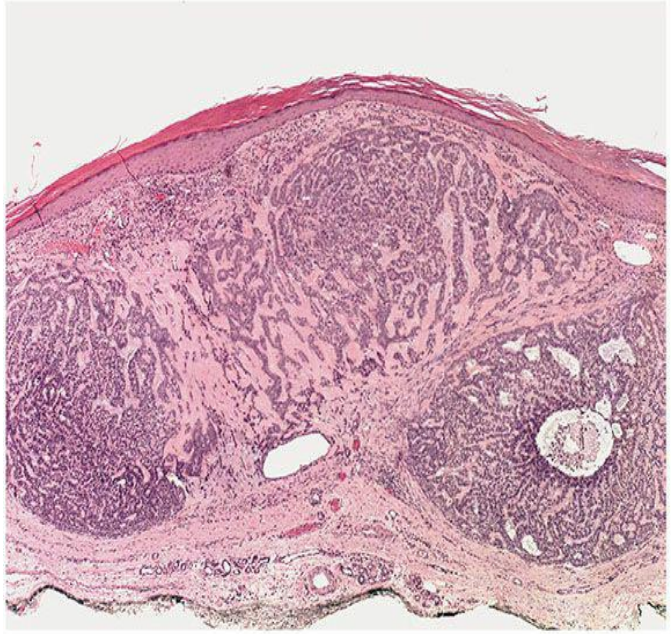
Adenoid BCC

Key features

- Blue islands with adenoid pattern (clear spaces in the middle of islands)
- Peripheral palisading
- Fibromyxoid stroma
- Retraction artifact
- Low-Risk type
- The strands of epithelial cells present a lacelike pattern. The stroma has a mucoid appearance.







Infundibulocystic BCC

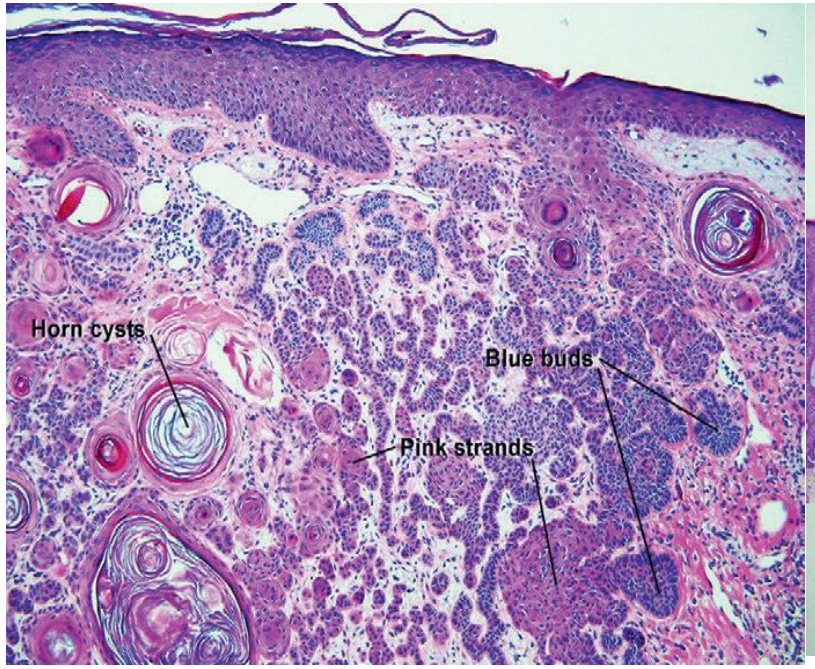
Key features

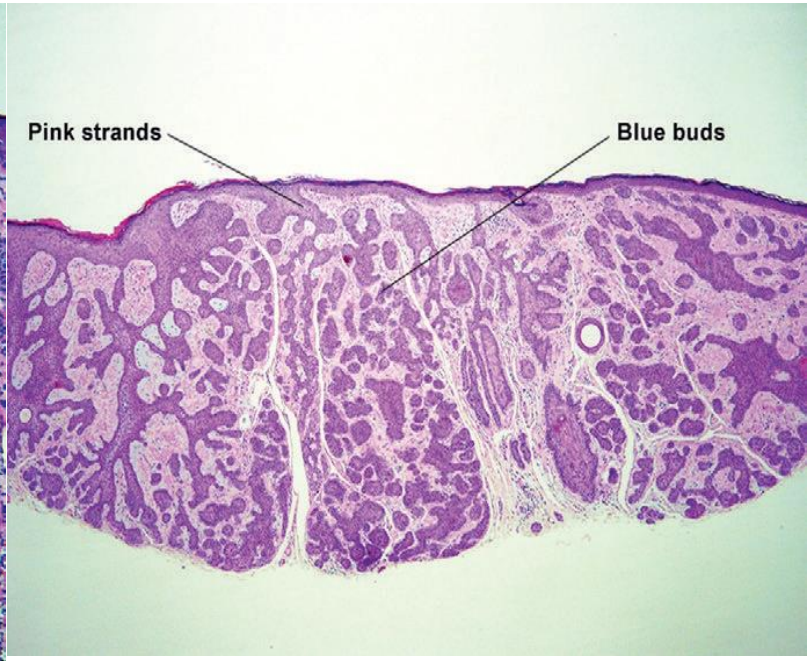
- Pink strands, blue buds
- Horn cysts
- Fibromyxoid stroma
- **Low- risk type**

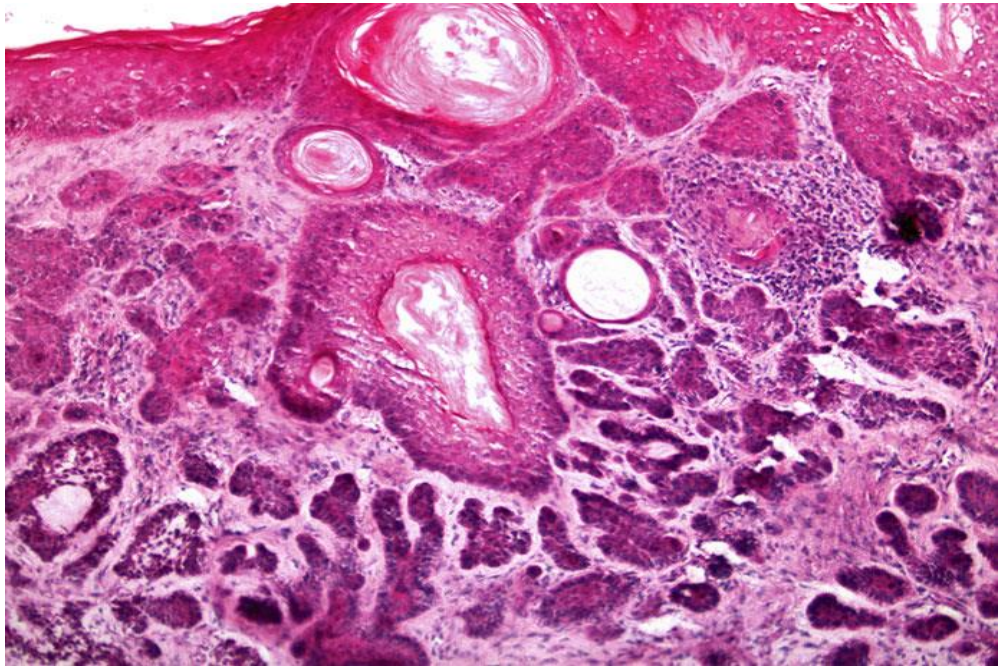
Infundibulocystic BCC differentiates towards the follicular infundibulum.

It is characterized by pink strands of squamous epithelium, blue basaloid buds at the tips of the strands, and horn cysts.

cystically dilated follicular infundibula surrounded by branching basaloid aggregates. These aggregates also diminish as the tumor penetrates deeper in the dermis.







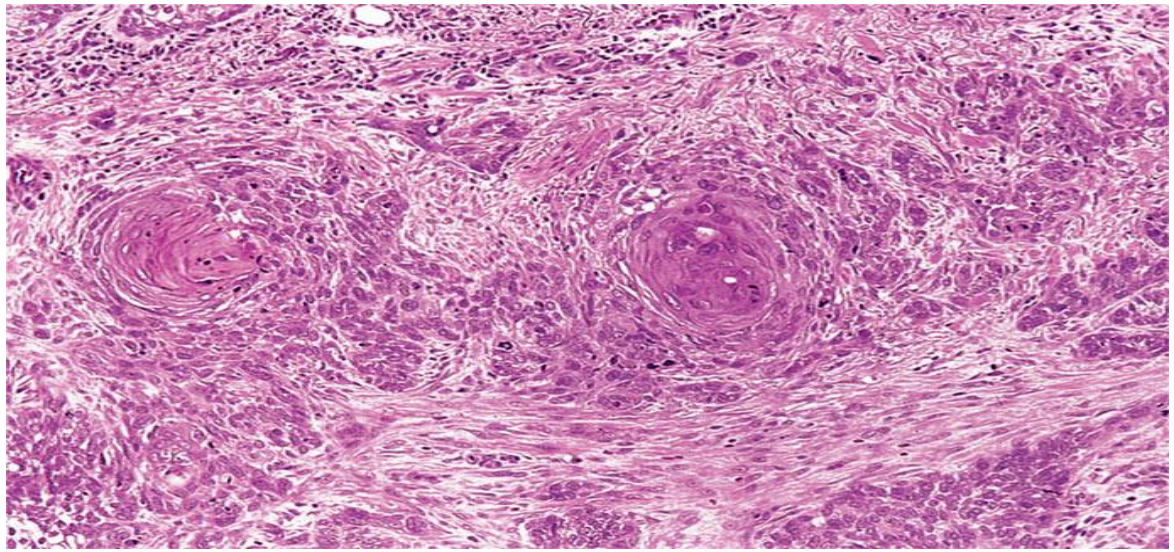
Basosquamous or metatypical basal cell carcinoma

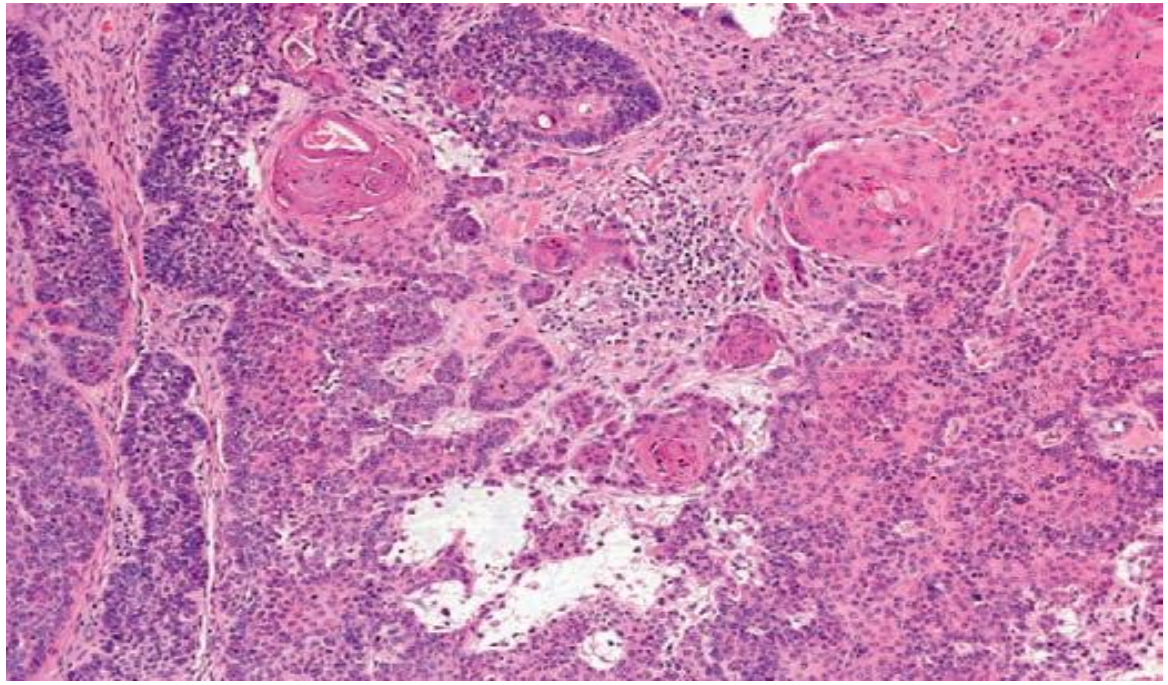
Tumours that on pathological study appear to have features of both BCC and SCC. The biological significance is that this pathological pattern is

associated with a **significantly higher incidence of metastatic spread.**

The pattern in these lesions is of small aggregates of cells lacking classic palisading and embedded in dense and profuse fibrous stroma.

The cells are larger with a larger paler nucleus than in the classic BCC and have a more eosinophilic cytoplasm.



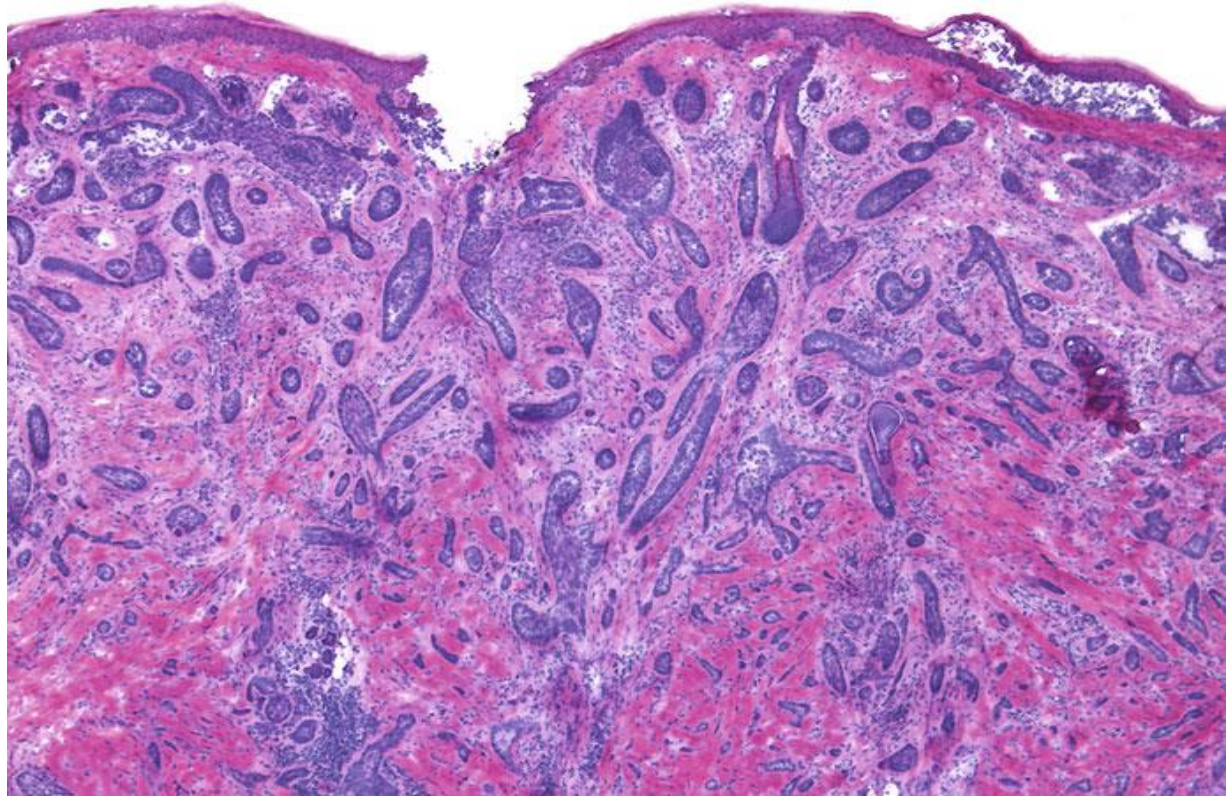


A “mixed” basal cell carcinoma

It is a hybrid tumor.

The term basal cell carcinoma with mixed histology has also been used to refer to tumors demonstrating more than one type of pathologic pattern.

occurs in nearly 40 percent of cases



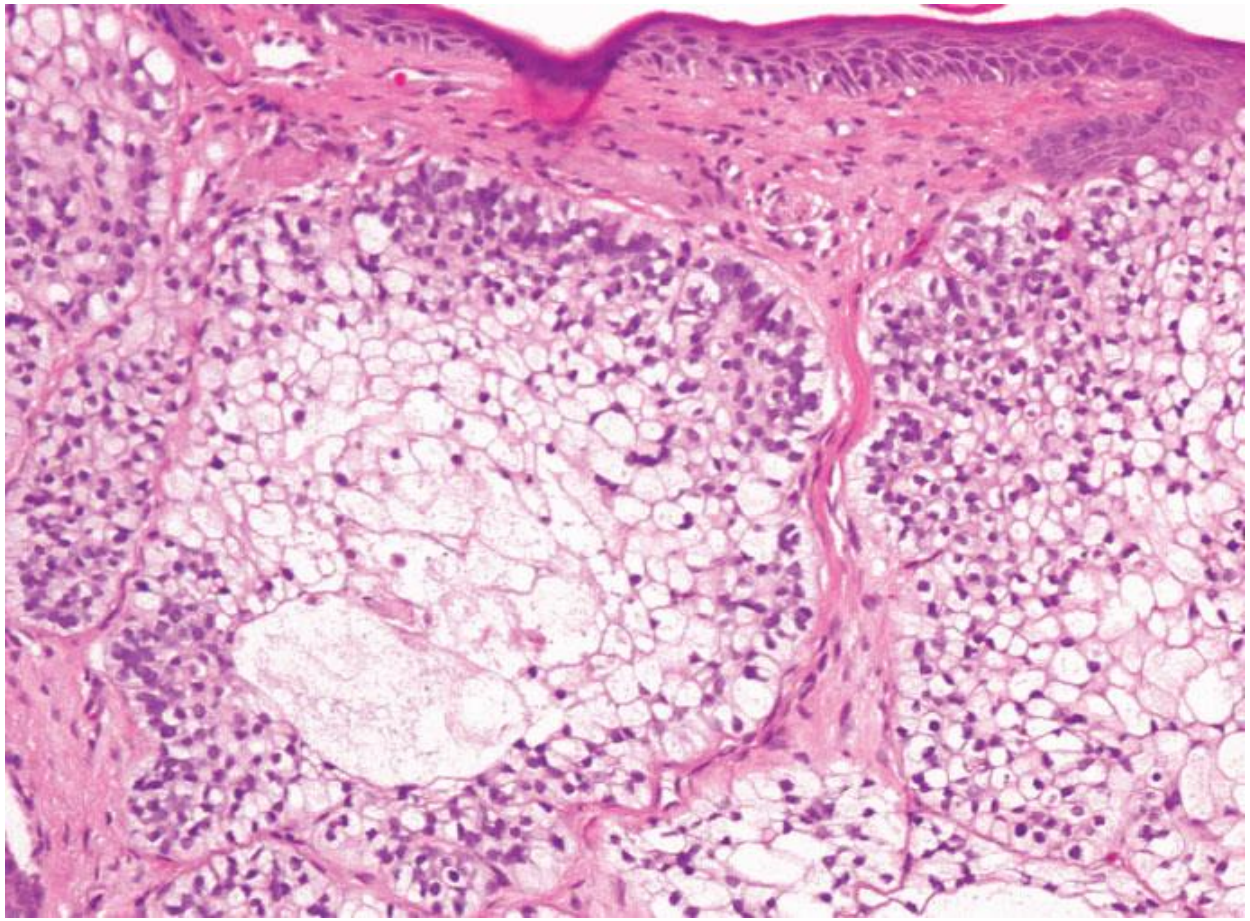
Nodular and infiltrative basal cell carcinoma: infiltrative BCC with larger tumor aggregates near the epidermis that become smaller and angulated deeper in the dermis.
Cords, strands, and individual neoplastic basaloid cells are seen at the bottom of the photograph

Clear cell basal cell carcinomas

- Demonstrate variable numbers of transparent

tumor cells .

- Most tumors have the overall configuration of a nodular basal cell carcinoma, and aggregates of typical basaloid cells are usually present.
- Clear cell changes may be present only at the periphery of a tumor lobule or may involve the whole lobule.
- The affected cells are round to polyhedral with pale, eosinophilic, vacuolated, or finely granular cytoplasms.441 Palisading is usually minimal to absent.
- Nuclei are eccentrically placed and are atypical but not profoundly so.

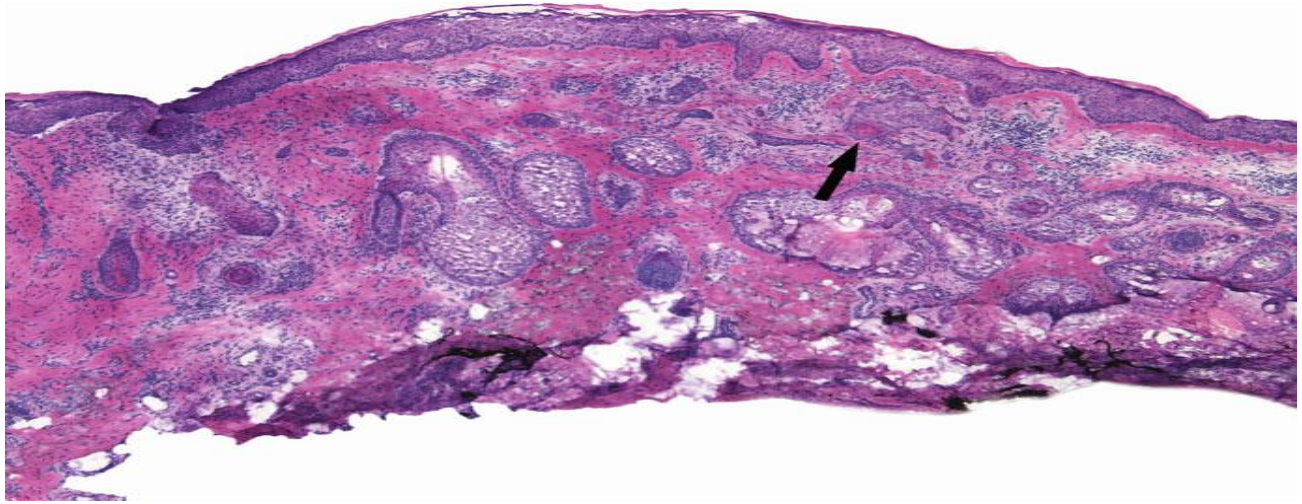


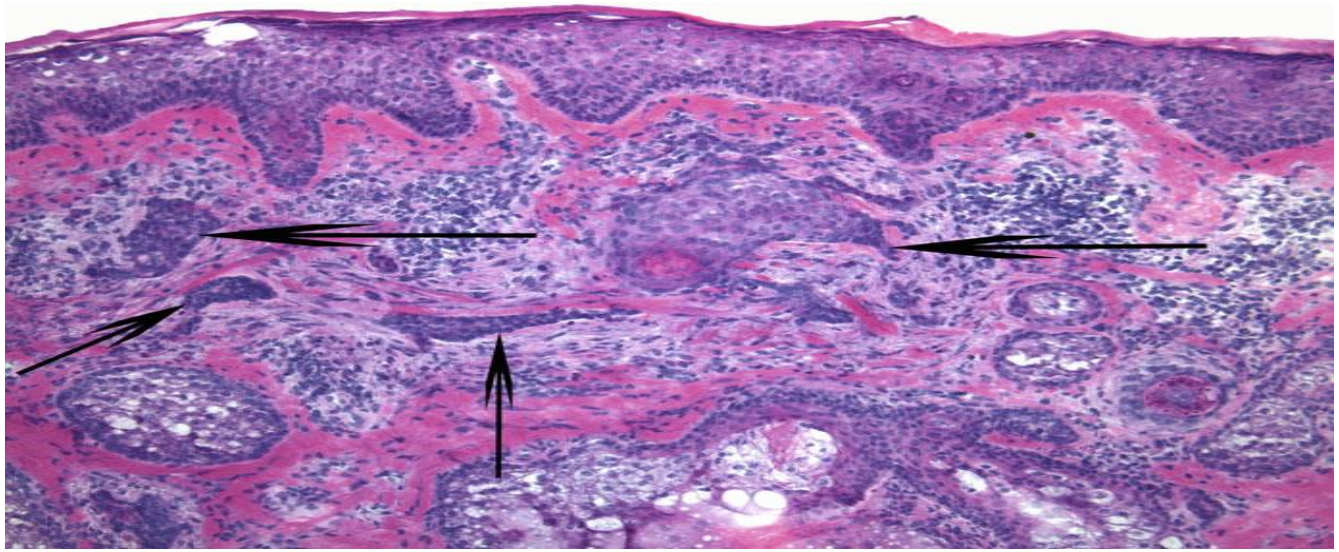
Keratotic basal cell carcinoma

BCCs with follicular differentiation contain small keratinized cysts (that lack a granular layer) within the aggregates of neoplastic cells.

These lesions display differentiation towards hair follicle structures.

addition, prominent clefting between the palisaded tumor islands and the stroma, as well as a myxoid (rather than a fibrocellular) stroma, characterize these BCCs.





(a) there are a few irregular basaloid aggregates in the superficial dermis, some showing angulated shapes. Within the center of a large aggregate is a keratin pearl (arrow).

(b) At this power the neoplastic aggregates (arrows) are more obvious displaying peripheral palisading within the surrounding mucinous stroma

Differential Diagnosis

Nodular, micronodular
Eccrine spiradenoma
Nodular hidradenoma
Trichoepithelioma or trichoblastoma
Superficial
Actinic keratosis
Seborrheic keratosis
Keratotic, infundibulocystic
Trichoepithelioma or trichoblastoma
Basaloid follicular hamartoma
Reticulated seborrheic keratosis
Infiltrative, morpheaform
Microcystic adnexal carcinoma
Desmoplastic trichoepithelioma

Adenoid, fibroepithelioma of Pinkus
Primary cutaneous adenoid cystic carcinoma
Malignant mixed tumor of the skin (malignant chondroid syringoma)
Aggressive digital papillary adenocarcinoma
Clear cell
Sebaceous adenoma
Tricholemmoma
Clear-cell hidradenoma
Clear-cell acanthoma
Balloon cell nevus and balloon cell melanoma
Metatypical
Squamous cell carcinoma

TREATMENT

Surgical and Destructive Procedures

Standard excision

Curettage with electrodesiccation

Curettage alone

Radiation therapy

Cryosurgery

Photodynamic therapy

Laser

Medical Treatment

Combination therapy

Prognosis

The mortality rate from BCC is quite low. The likelihood of relapse after treatment determines its prognosis. The placement of BCC as well as its clinical and histological characteristics are important factors in determining the likelihood of recurrence. Features such as tumor size, histopathology, and whether or not cancer has spread from the original site are all relevant factors. In addition, tumor prognosis is divided into three categories: good, intermediate, and poor according to the previous relevant factors. In the three years after therapy for a primary basal cell carcinoma, the patient faces a 44% probability of acquiring a second basal cell carcinoma and a 6% chance of developing a cutaneous squamous cell carcinoma.