Review Article

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Basal Cell Carcinoma Mixed Histological Subtype: Case Report and Review of Literature

Sunil V Jagtap[1], Shubham S Jagtap[2], Ramnik Singh[3], Devika Borade[4], Harshkumar Machhi[5]

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Abstract

Background: Basal cell carcinomais a slow growing malignant cutaneous non melanocytic tumor that is locally aggressive but it rarely metastasizes. Case of 61 year male presented to the outpatient department with a round, nonhealing ulcer with hyperpigmentation, measuring 2.5x2.1x0.8cm over the right side of face, 1.8 cm below the right eye region for the last 1.5 years. Patient had history of swelling at same site 1.5 year back, as small nodular lesion which was excised. The general physical and systemic examinations were normal. The lesion was surgically excised with wide margins. The specimen on gross measured 2.3x2.1x0.6cm, firm, grey brown to black colored hyperpigmented with rolled out margins and central ulceration measuring 1.6x1.4x0.6cm. Cut section was grey white, nodular with blackish pigmentations. On microscopic examination showed a circumscribed nodular lesion composed of neoplastic cells arranged in large basaloid lobules with peripheral nuclear palisadations. The neoplastic basaloid cells with scant cytoplasm and hyperchromatic nuclei were seen. The stroma was fibromyxoid with focal inflammation. The surface ulceration was noted. The nodules are variable size of more than 0.3cm diameter. Tumor showed epidermal attachment. In areas the reticulate, pseudoglandular pattern of basaloid neoplastic cells were noted with a mucinous stroma. Focal areas of colonization of tumor's complexes with melanocytes and stromal melanophages pigmentation was noted. The tumor showed 0.5cm depth of invasion. The mitotic activity was low, minimal atypia and apoptosis were noted. The lymphovascular, perineural invasion was absent. All peripheral and deep surgical margins were free from tumor. On histopthological findings reported as Basal cell carcinoma-nodular, adenoid cystic and pigmented: mixed histological subtype over face. The patient was kept on regular follow up. There was no evidence of recurrence or any metastasis.

Conclusion: We present this rare case of Basal cell carcinoma-nodular, adenoid cystic and pigmented: mixed histological subtype for its clinical and morphological findings. The pathological diagnosis and classification of BCC are essential for the evaluation of the tumour type, its biological behaviour, risk assessment of the recurrence and treatment.

Keywords: Basal cell carcinoma; Adenoid; Pigmented BBC; Mixed histological subtype.

Author Affiliation: [1]Professor, Department of Pathology, [2]Resident, Department of Medicine, [3,4,5]Resident, Department of Pathology, Krishna Vishwa Vidyapeeth (Deemed to be University), Krishna Institute of Medical Sciences, Karad 415539, Maharashtra, India.

Corresponding Author: Sunil Vitthalrao Jagtap, Professor, Department of Pathology, Krishna Vishwa Vidyapeeth (Deemed to be University), Krishna Institute of Medical Sciences, Karad 415539, Maharashtra, India.

E-mail: drsvjagtap@gmail.com

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INTRODUCTION

Basal cell carcinoma (BCC) is most common skin tumor, accounting for about 80% of all non-melanoma skin cancers.[1] BCC as per clinical behaviour with histopathologic subtypes and according to the risk of tumor recurrence are classified as low-risk and high-risk subtypes. The most common histological types of BCC is nodular (40-50%), other are infiltrative, (15 to 25%), ulcerative morphea like, sclerosing, mixed, basosquamous, pigmented etc.[2] The BCCs are classified with a low risk of recurrence are nodular, superficial, pigmented and infundibulocystic and fibroepithelial subtypes. And with a high risk of are recurrence are micronodular, infiltrating, sclerosing or morphoeic and basosquamous BCCs, and BCCs with sarcomatoid differentiation. The overall prognosis for patients with BCC is excellent. Basal cell carcinoma-nodular, adenoid cystic and pigmented: mixed histological subtype are rarely noted. Various BCC contain more than one histological types and there is no uniformity from what percentage of individual types the BCC should be determined as a mixed histological subtype.

CASE REPORT

A 61 year male presented to the outpatient department with a round, nonhealing ulcer with hyperpigmentation, measuring 2.5x2.1x0.8cm over the right side of face, 1.8cm below the right eye region for the last 1.5 years. On examination lesion was an ulceration firm, tender, black colored hyperpigmented with rolled out margins and central area of ulceration with exudation (Fig. 1). Patient had history of swelling at same site 1.5 year back, as small nodular lesion which was excised. The history of excessive sun light exposure related to occupation was there. The general physical and systemic examinations were normal. The lesion was surgically excised with wide margins. The specimen was send for histopathological examination. On gross lesion measured 2.3x2.1x0.6cm, firm, grey brown to black colored hyperpigmented with rolled out margins and central ulceration measuring 1.6x1.4x0.6cm. Cut section was grey white, nodular with blackish pigmentations. On microscopic examination showed a circumscribed nodular lesion composed of neoplastic cells arranged in large basaloid lobules with peripheral nuclear palisadations (Fig. 2,3,4). The stroma was fibromyxoid stroma with inflammation. The surface ulceration was noted. The nodules are variable size of more than 0.3cm diameter. Tumor showed epidermal attachment. In areas the reticulate, pseudoglandular pattern of basaloid neoplastic cells were noted with a mucinous stroma (Fig. 5,6,7). Focal areas of colonization of tumor's complexes with melanocytes and stromal melanophages pigmentation was noted (Fig 5).

The tumor showed 0.5cm depth of invasion. The mitotic activity was low, minimal atypia and apoptosis were noted. The lymphovascular, perineural invasion was absent. All peripheral and deep surgical margins were free from tumor. On histopthological findings reported as Basal cell carcinoma-nodular, adenoid cystic and pigmented: mixed histological subtype over face. The patient was kept on regular follow up. There was no evidence of recurrence or any metastasis.

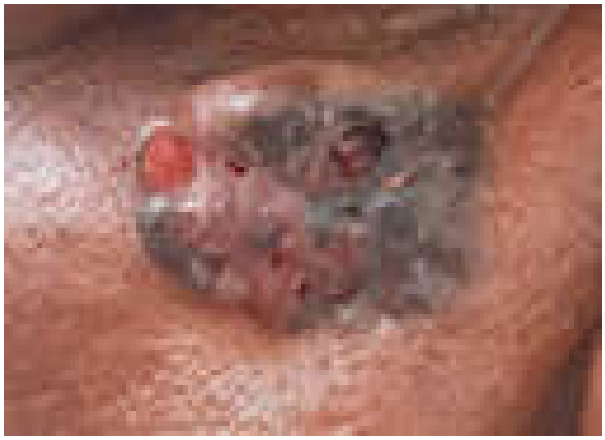

Fig. 1: Nodular lesion with ulcer and hyperpigmentation over the right side of face.

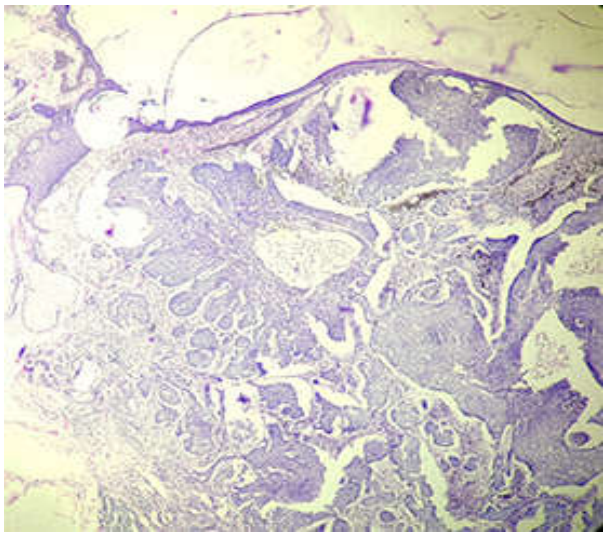

Fig. 2: nodular lesion composed of neoplastic cells arranged in large basaloid lobules with peripheral nuclear palisadations. (H &E stain,40x)

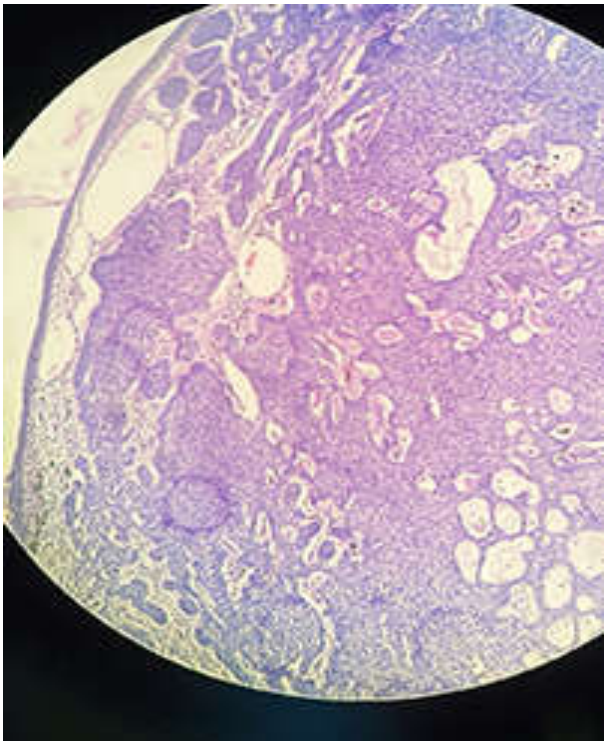

Fig. 3: nodular lesion with adenoid cystic BCC.(H &E stain,40x)

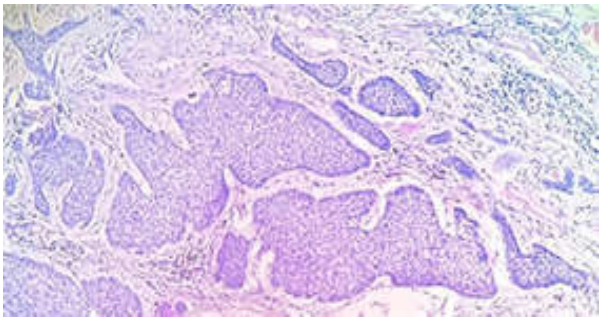

Fig. 4: nodules of neoplastic cells arranged in large basaloid lobules with peripheral nuclear palisadations. (H &E stain,100x)

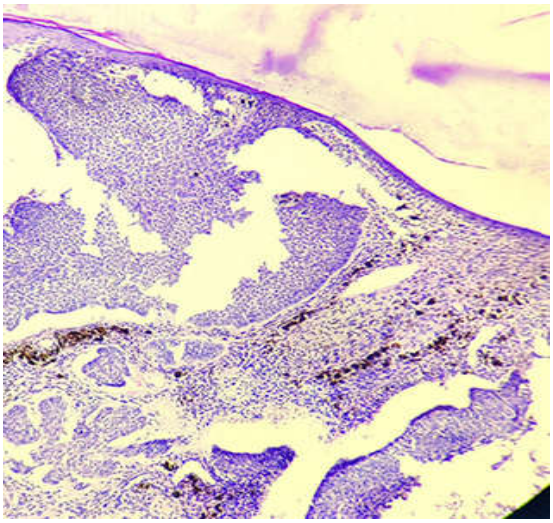

Fig. 5: nodular with melanin pigmentations. (H &E stain, 40x)

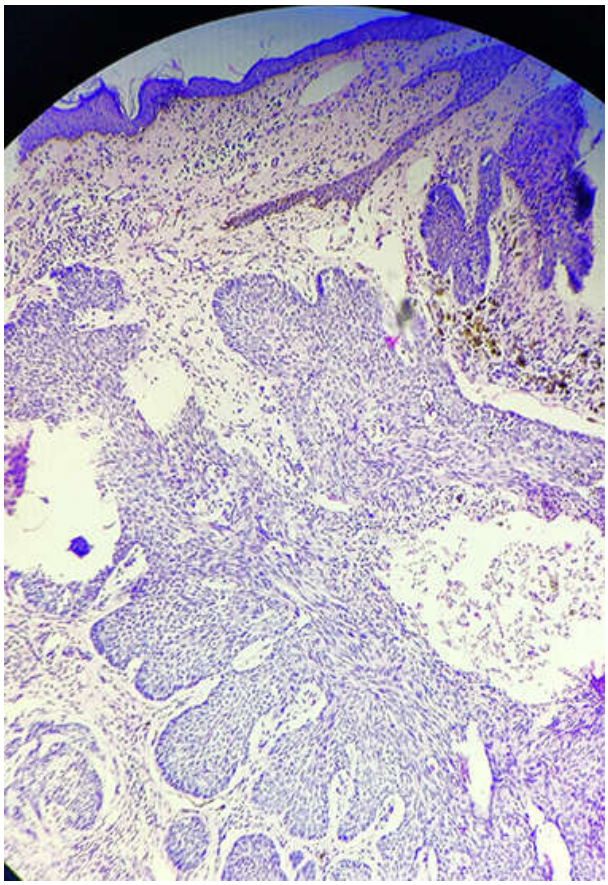

Fig. 6: nodular with melanin pigmentations. (H &E stain, 100x)

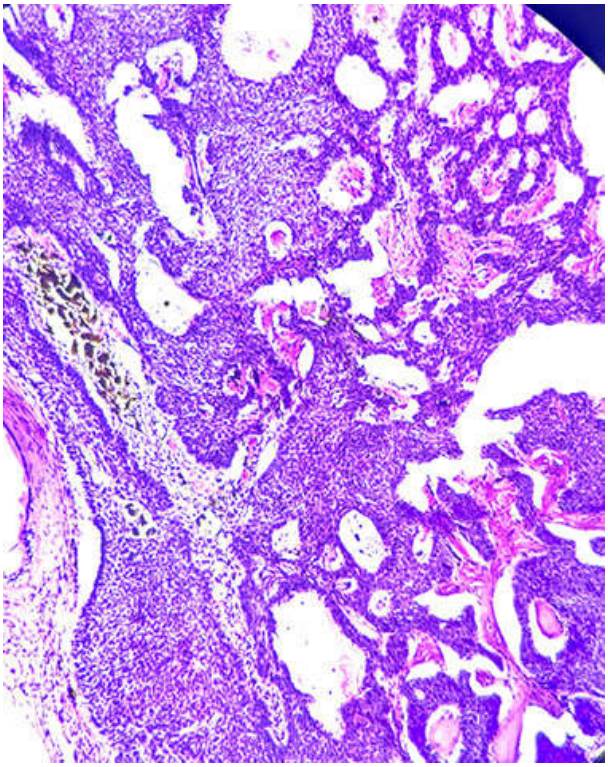

Fig. 7: nodular, adenoid cystic and Pigmented BCC. (H &E stain, 40x)

DISCUSSION

The origin of BCC is from the basal cells located in the interfollicular epidermis or the follicular bulges. The pathogenesis is excess exposure to sunlight may cause DNA damage, mutagenesis, and decreases immune surveillance. A gene commonly found to be mutated in BCC is the PTCH gene. A PTCH gene mutation at chromosome 9q22.3, that inhibits the Hedgehog signaling pathway, BCC is common in light-skinned individuals with a family history of BCC and increases in incidence closer to the equator or at higher altitudes. Incidence is relatively low in Asians, Blacks, and Hispanics.

Epidemiology and clinical

Basal-cell cancer accounts for at least 32% of all cancers globally.[3] In the U.S. population more than 2 million people were treated in 2006 for non-melanoma skin cancer, mostly were BCCs.[4]

Basal cell carcinoma (BCC) is the most common malignant tumor of the skin which was first described by Jacob in 1827.[5]

BCC is characterized as a locally invasive, slow-growing carcinoma, with infrequent rate of metastasis (0.0028-0.5%).[6]

As per Clark CM et al, BCC is classified into 4 main groups on its: anatomical location, histopathology, lesion size, or recurrence.[7]

The various risk factors for development of BCC was given, sun exposure (to ultraviolet light, particularly in childhood) is the most important risk factor. Other risk factors include genetic conditions, chronic exposure to arsenic, photosensitizing drugs, industrial chemical substances such as vinyl chloride, polycyclicaromatic hydrocarbonates, ionizing radiation, and immunosuppression.[8]

The anatomical location of BCCs is approximately 70% on the face. It was most commonly on the, nose and eyelid, other sites are the trunk and extremities.[9,10] Rare location areas such as anogenital region, nail unit, palm and sole are also seen. The most of cases occur on areas of skin that are regularly exposed to sunlight or ultraviolet radiation. Clinically patients of BCC presents with an slowly enlarging, nonhealing, ulcerative, painful lesion that may sometimes bleeds. The ulcer edges raised or rolled out. The most of BCCs are solitary tumors, those occurring in the Gorlin-Goltz syndrome are often multiple.

The lesions may with pink-red, scaly, macule or patch with pruritus. The macules of black-blue or brown areas may resembles naevus.[11]

Evaluation and Histomorphology

The diagnosis is done on clinical features, dermatoscopy, biopsy of lesion with histological features, where IHC helps in confirmation and differential diagnosis. In the 2006 World Health Organization classification, BCCs were classified in the skin adnexal tumor group. There are >26 various subtypes of BCC appear in the literature, the common and distinctive clinicopathologic types are nodular, Micronodular, Adenoid, Superficial, Pigmented, Ulcerative, Morpheaform, Infiltrative and Fibroepithelial BCCs. Others are Keratotic, Basosquamous (metatypical), Clearcell, Signet cell BCCs.[12]

In our case BCC was of mixed histological type consists of nodular, adenoid and pigmented subtypes. A study by Bartoš V, et al observed that in mixed type BCC subgrouphistomorphology was found comprising a mixture of two to four different subtypes in various proportions. The most frequent combinations included nodular-infiltrative, superficial-nodular, nodular-trichoepithelial and nodular-micronodular subtype. The prevalence of mixed BCCs was 35.1%.[13]

Nodular BCCs present as nodular or papule with a telangiectatic vessel. Later on shows ulceration called as rodent ulcer. The nodules may be pigmented in various extents the cystic change may occurs. The tumor forms a solid nodule which may extend into subcutaneous tissues. The other form may with superficial, well circumscribed erythematous macular lesions with a fine filamentous pearl rim.

BCC on morphological features are the islands and nests with peripheral palisading basaloid cells with scant cytoplasm and hyperchromatic nuclei, often with stromal retraction and fibromyxoid stroma.[14] The clefting, mucoid or myxoid stroma with spindle cells, with or without amyloid deposits are other findings. Sometimes the tumor stroma has a collagenous, keloidal-type.

The definition of the micronodular subtype improved in the fourth edition of the WHO Classification of Skin Tumors, where alongside the required size of micronodules (less than 0.15 mm in diameter), it also states that they should make up to more than 50% of the tumor.[15]

In our case nodular subtype was associated with Adenoid BCC. On microscopy shows reticulate pattern of tumor growth. This subtype may shows differentiation of tubular, gland-like structures or pseudoglandular pattern of basaloid tumor cells. The stroma shows mucinous material. Tumor can mimic true gland formation, resulting in diagnostic confusion with a sweat gland adenocarcinoma. Bastiens MT et al. study showed an the adenoid variant is a very uncommon subtype and accounts for approximately 1.3% among all the histopathological types of BCC, and this variant in its pure form is less often seen.[16]

In our case nodular BCC was mixed with pigmented subtype. Pigmented BCC is a subtype of nodular or superficial BCC. It is characterised by melanin pigment derived from an increased number of dendritic melanocytes within the malignant tumor nests, being found within the malignant basaloid cells or the macrophages which surround the malignant proliferation. The presence of melanophages in the dermis have no influence on the biological behaviour of the tumor.[17] Pigmented BCC can mimics seborrheic keratosis or malignant melanoma.

The superficial BCC shows multicentric, small islands or lobules of malignant basaloid cells with peripheral palisading, localized in the superficial dermis, with a connection to the epidermis. They may shows inflammatory infiltrate. It can be part of a mixed-pattern tumor, with micronodular, nodular, or infiltrating BCCs.

It is important to classify BCCs according to histological type associated with risk of local recurrence. The lower risk subtypes are nodular, superficial, pigmented, infundibulocystic, fibroepithelial. While higher risk BCCs are basosquamous, sclerosing or morpheaform, keloidal, infiltrating, BCC with sarcomatoid differentiation and micronodular subtypes.

Immunohistochemistry is very useful in distinguishing BCC from other basaloid tumors such as trichoepithelioma and basaloid SCC. Compton LA, et al observed that on immunohistochemistry BCC tumor cells are positive for pancytokeratin (100%), BerEP4 (80–100%), p63 (100%), CAM5.2 (20–95%), androgen receptor (33–66%), p53 (74.5–83%).[18]

Investigation of mutations in the patched-1 (PTCH-1) gene has provided important insights into the pathogenesis of BCC, and points to a key role in the Hedgehog (Hh) signalling pathway in its pathogenesis.[19]

Treatment

The staging of BCC is made according to Tumor, Node, Metastasis (TNM) classification and is essential for performing the adequate treatment.

Early diagnosis and complete excision of the primary lesion is important to prevent invasion, metastasis and recurrence.

The surgery is the treatment of choice of primary BCC. The various surgical options include Mohs micrographic surgery, curettage and electrodessication, and cryosurgery. The chemotherapy is used for metastatic BCC. The other options are radiation.[7] In superficial BCC cases treatment option is topical agents like5% imiqoimod, 5-fluorourasil, etc.

Prognosis

As prognostic factors in BCC, the Bcl-2 expression was directly correlated with nonaggressive BCC with favorable outcome. While the expression of p53 was correlated with the aggressive histological subtypes.[20]

The aggressiveness in BBCs is related to expression of the proliferation marker Ki67/MIB1 directly.

BCC is known as an indolent cancer with a high rate of local recurrence. It has very low incidence of nodal or distant metastases. Approximately 40% of patients with BCC have a recurrent skin lesion within 5 years. Surgical excision is generally curative with 5-year cure rates of more than 99% for primary tumors not involving the head.[21]

Our patient responded well to surgical excision. On regular follow up there was no evidence of recurrence or any metastasis.

CONCLUSION

We present this rare case of Basal cell carcinoma-nodular, adenoid cystic and pigmented: mixed histological subtype over face for its clinical and morphological findings. In lesions suspicious for BCC a biopsy should be performed. The pathological diagnosis and classification of BCC are essential for the evaluation of the tumour type, its biological behaviour, risk assessment of the recurrence and treatment.

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