Volume : 5 | Issue : 9 | September 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48



# Clinicopathological Study of Morphological Variants of BASAL CELL CARCINOMA

Medical Science

KEYWORDS :

| | |
|---|---|
| **Dr.Mandakini.B.Tengli** | Associate Professor. Dept . of Pathology KBNIMS Kalaburagi. |
| **Dr. Guruprasad Yelawanti** | Prof.and Head of the Dept. of Dermatology.KBNIMS Kalaburagi. |
| **Dr. Syeda Heena Kauser** | P G Student, Dept.of Pathology. KBNIMS Kalaburagi. |
| **Dr S Mahantappa** | Prof. and HOD Dept. of Pathology. KBNIMS Kalaburagi. |
| **Dr Pratima Sambrani** | Prof.Dept.of Pathology KBNIMS Kalaburagi. |

**INTRODUCTION:**

Basal cell carcinoma is the most common malignant neoplasm of skin in white people. Its incidence is increasing worldwide.[1] The exact incidence in India is not known.[2]

BCC arises from basal cells of the epidermis or follicular structures and is seen mostly in sun-exposed areas. Sunlight is the most frequent association with development of BCC. [3]

Five clinical types of BCC occur. They are 1) Superficial BCC, 2) Nodular BC 3) micronodular BCC, 4) Infiltrating BCC and 5) Fibroepithelioma.[4]

The common diagnostic feature of BCC, at least focally, is the presence of islands of basaloid cells, with peripheral palisading and a retraction (artifactual) cleft between the lobules of tumor and stroma.[5]

Histologically BCC can be divided into two broad groups: 1) Undifferentiated and 2) Differentiated. Differentiated lesions show a slight degree of differentiation towards cutaneous appendanges of hair, sebaceous glands, apocrine glands or eccrine glands.

This is a clinicopathological study of 15 cases of BCC to identify the morphological variants of BCC.

**AIM OF THE STUDY**

To study the morphology of variants of BCC

**MATERIALS AND METHODS**

Skin biopsies of suspected cases of BCC (and later confirmed by histopathology), and a few unsuspected cases(later diagnosed as BCC), received in the Department of Pathology, KBNIMS, , during the period of two years ( from June 2014 to June 2016), which were subjected to routine processing and staining by H&E, were reviewed and the morphology of variants of BCC were studied.

**RESULTS:**

A total number of 15 cases of BCC were studied, of which 14 were biopsies and one entire tumour.

**Table:1**

**In our present study, the age and sex distribution was as follows:**

| Age(yrs) | Males | Females | Total |
|---|---|---|---|
| 21 to 60 | 4 | 2 | 6 |
| 61 to 100 | 3 | 6 | 9 |
| | 7 | 8 | 15 |

**Table: 2**

**Sites of the lesions are as follows**

| Site | No. of cases |
|---|---|
| Face | 12 |
| Scalp | 1 |
| Thigh | 1 |
| Arm | 1 |
| Total | 15 |

Out of 15 cases eight lesions were nodular, six were ulcerated and the one on the back of the thigh was large, (6x5 cms) - Giant basal cell carcinoma.

**The morphology of all these lesions were studied in detail.**

All these cases showed common histological features of BCC consisting of lobules, nests and columns of basaloid cells, having scant cytoplasm and small round to oval nuclei with condensed chromatin. There was characteristic outer palisading of cells, with artifactual retraction spaces between the tumor cell nests and the surrounding loose, fibromucinous stroma infiltrated by lymphocytes and histiocytes.

**Table: 3**

**The histopathological classification of these lesions is as follows:**

| Sl.no. | Histopathological Subtype | No.of cases |
|---|---|---|
| 1 | Undifferentiated -Superficial | 2 |
| 2 | Undifferentiated-Nodular | 4 |
| 3 | Undifferentiated-Nodular –Pigmented | 2 |
| 4 | Undifferentiated-Micronodular | 1 |
| 5 | Undifferentiated-Nodular-Infiltrative Growth | 1 |
| 6 | Undifferentiated-Metatypical (Basosquamous) | 2 |
| 7 | Differentiated –(Nodular with keratotic differentiation | 2 |
| 8 | Differentiated –(Nodular with adenoid differentiation) | 1 |
| | Total | 15 |

There were two cases of superficial BCC, which were ulcerated. There were lobules of basaloid cells which were projecting from the epidermis, confined to the papillary dermis and not involving the reticular dermis. Stroma showed dense lymphocytic infiltrate.

Volume : 5 | Issue : 9 | September 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

There were 11 cases of undifferentiated nodular BCC, which showed large lobules of basaloid cells, in both papillary and reticular dermis. Of these, two cases showed melanin pigment in the tumor nests and also in the macrophages of the stroma(Fig.1), one case showed micronodules, one case showed infiltration into the bone, and two cases showed areas of squamous differentiation (basosquamous or metatypical variant)(Fig.9)..

Two cases showed keratin horn cysts (keratotic differentiation)(Fig.2).

**DISCUSSION**

Basal cell carcinoma derives its name from the cytologic similarity of the tumor cells to the normal basal cells of the epidermis and the belief that it arises from them. All BCCs attempt to differentiate toward adnexal structures (especially pilosebaceous units), but most of them remain at a stage so primitive that, this recognition is not immediately apparent .[6]

Basal cell carcinomas are very frequent tumors, particularly in light skinned individuals living in countries at low altitudes.[7] Basal cell carcinomas constitute approximately 80% of all non- melanoma skin cancers. Australia has the highest rate of basal -cell carcinoma in the world.[8] The exact incidence in India is not known.[2] Purnima Malhotra et al. observed that, a higher percentage of pigmented lesions and delayed diagnosis in dark-coloured skin is noted in BCC of Indian population.[9]

Risk factors for the development of BCC include Type -1 skin (which always burns ,never tans);red or blonde hair; blue or green eyes; freckling in childhood; family history of skin cancer; immunosuppressive treatment and ingestion of Arsenic.[1]

Exposure to ultraviolet radiation is the major cause of BCC. Intense, intermittent exposure to the sun is associated with a higher risk of BCC than is a similar degree of continuous exposure . A latency period of 20 to 50 years is typical between the time of UV damage and the clinical onset of BCC. It is observed that, in most cases ,BCC develops on chronically sun-exposed skin of elderly people, especially in the area of head and neck.UVB radiation damages DNA and its repair system and alters the immune system leading to genetic alterations and formation of neoplasm. UV – induced mutations in the $P^{53}$ tumor suppressor gene have been found in about 50% of the cases.[10]

BCCs are found to occur in older people. In our study of 15 cases, age of the patients ranged from 52 to 84 years. In a study of 34 cases by Purnima Malhotra et al[9], the age of the patients ranged from 28 to 102 years, and in a study of 25 cases by Prema Saldanha et al[2], the age of the patients ranged from 50 to 95 years.

Upto 80% of all lesions are found on the head (Fig. 6) and neck, and in half of them they occur on the skin of the cheek (Fig.8) and nose (Fig.7),15% develop on the shoulders ,back or chest ,and the rest may be seen on the lower extremities, the clitoris and the vulva, perianal region etc.[11] In our study, lesions of 13 cases (87%)were on the head and neck and one on the posterior aspect of the arm and one on the back of the thigh. In a study of 25 cases by Prema Saldanha[2] ,22(88%) had lesions on the head and neck region and remaining one each on the back chest and abdominal wall. .

BCCs present clinically as pearly papules, often containing subepidermal telangiectatic blood vessels. some of them contain melanin and appear similar to melanocytic nevi or melanomas. Advanced lesions may ulcerate and extensive local invasion of bone or facial sinuses may occur .[12] The term-Rodent ulcer was coined by Jacob Arthurin in1827.[3]

In most cases clinical diagnosis is not difficult for an experienced clinician. But in some unclear cases, Actinic keratosis, Seborrheic dermatitis,Pyogenic granuloma,Merkel tumor,Psoriasis,Bowen disease, Non-pigmented melanocytic naevus,Malignant melanoma,and Squamous cell carcinoma have to be considered.

Several genetic conditions are associated with the risk of developing BCC such as albinism, xeroderma pigmentosa, Bazex syndrome and the naevoid basal cell carcinoma syndrome (Gorlin syndrome,which is an autosomal dominant disorder characterized by multiple BCCs).[13]

BCCs have characteristic histopathologic findings that facilitate accurate diagnosis. The insular pattern is the most characteristic, accounting for most of nodular clinical presentations. Variably sized, separate or fused, cystic or solid islands of basaloid cells, usually bordered by a palisaded outer row of cells, separated from the stroma by retraction artefact, are seen.[4]

The Royal College of Pathologists has published a minimum dataset for the histopathological reporting of BCC and this has been written to be compatible with the British Association of Dermatologists' management guidelines. Growth patterns to be reported include nodular, superficial, infiltrative/morphoeic and micronodular types, together with differentiation when of severely atypical or malignant squamous type (basosquamous carcinoma). Deep and peripheral excision margins will be reported to be either involved or clear. The latter will include a comment of a clearance of less than 1 mm for close margins and a measured distance in whole millimetres for other excisions.[14]

Histopathological classification of BCC.[13]

**Undifferentiated BCC :**

Superficial BCC – Characterised by proliferation of atypical basaloid cells that form an axis parallel to the epidermal surface and demonstrate slit- like retraction of the palisaded basal cells from the subjacent stroma. A band like lymphoid infiltrate may be present.

Nodular BCC – Represents the most common form of BCC. It is characterised by discrete, large or small nests of basaloid cells in either the papillary or reticular dermis accompanied by slit- like retraction cleft from the stroma. Any of the differentiated elements may be seen. The surrounding stroma may show myxoid change.

Micronodular BCC – Manifest tumour nests which are smaller and widely dispersed in an often asymmetric distribution extending deeper into the dermis and/ or subcutis.(Fig.4). Retraction spaces are not common and the surrounding stroma shows either a myxoid or collagenized morphology suggesting that these lesions may be an intermediate step between nodular and aggressive subtypes.

Aggressive growth BCC – Includes the prototypic morpheaform BCC, infiltrative growth BCC and metatypical BCC.

Morpheaform BCC/ Sclerosing BCC – Is characterised by columns of basaloid cells, 1-2 cells thick, enmeshed in a

densely collagenized stroma containing proplastic fibroblasts.

Infiltrative growth BCC – Comprises of irregularly sized and shaped nests of tumour cells. They may show invasion of subcutis and adjacent muscular and other structures. (Fig.5).

Metatypical BCC (Basosquamous BCC) – Is a form of aggressive growth BCC with areas that show intercellular bridge formation and / or cytoplasmic keratinzation.

**Differentiated BCC:**

Keratotic BCC (Pilar BCC) – Appears to differentiate along pilo sebaceous units. There are large basaloid tumour nests which are rounded and show central keratinisation and degeneration.(Fig.2). True hair production is absent.

Infundibulocystic BCC – The proliferating basaloid cells, typically in continuity with the overlying epidermis, proliferate as oblong and rounded nests surrounding keratin field structures lined by stratified epithelium that shows a granular cell layer. The cells that line these keratin filled cyts manifest progressive squamoid differentiation with an outer basaloid rim.

Follicular BCC – Show matricial differentiation, whereby shadow cells adjacent to islands of proliferating basaloid cells are present and so mimic a pilomatrichoma.

Pleomorphic BCC – Particularly of nodular architecture show strikingly enlarged giant hyperchromatic nuclei with amorphous nucleoplasms.

BCC with sweat duct differentiation – With typical eccrine and sometimes apocrine differentiation.(adenoid).(Fig.3).

BCC with sebaceous differentiation – Is differentiated from sebaceous adenoma by having a germinative cell component which occupies greater than 50% of the transverse diameter of tumour lobules that typically manifest a rounded morphology with areas of slit- like retraction accompanied by mitosis and apoptotic debris.

Fibroepithelioma of Pinkus – Typically arises above the natal cleft or on the lower trunk as a pink or flesh coloured nodule. In this tumour, elongated basaloid epithelial strands manifesting slit- like retraction from stroma, are enmeshed in a myxoid matrix or a background of proliferating spindle cells with abundant collagen.

Unusual cases may have zones with giant tumor cells, clear cells, granular cells, signet-ring cells.[15] Basaloid simulants -Ameloblastoma, Cloacogenic carcinoma,and Mucinous carcinoma have been described by Lori Lowe and Ronald P Rapini

Differential diagnosis: 1)Squamous cell carcinoma –areas of retraction clefts, aid in the differentiation of BCC from squamous cell carcinoma. 2)Desmoplastic trichoepithelioma can be differentiated from fibrosing BCC by the presence of considerable number of horn cysts.[4]

BCC are slow growing tumors which rarely metastasize. Most of them are diagnosed at an early stage and are cured by local excision. However, a few tumors (<0.5%) are locally aggressive and potentially disfiguring or exceedingly rarely may metastasize to distant sites.[3]

**CONCLUSION**

In this study of 15 cases of BCC, we have identified various morphological variants of BCC and have classified them into undifferentiated and differentiated. There was one case showing micronodular pattern and another case showing bone infiltration, which are high risk factors of invasion. The other patterns were nodular- pigmented, keratotic, adenoid , and basosquamous variants.

There is a need for introduction of National screening program including mandatory annual skin examination by trained health professionals. Early detection and treatment of lesions are crucial to decrease functional and cosmetic morbidity and costs. Clinical assessment and histopathological diagnosis remain the 'gold standard' for evaluating BCC and cancers in general. Although the mortality from basal cell carcinoma is low, its morbidity level can be very high and its potential adverse cosmetic effects can be distressing to patients.

**BCC pictures; (NINE )**

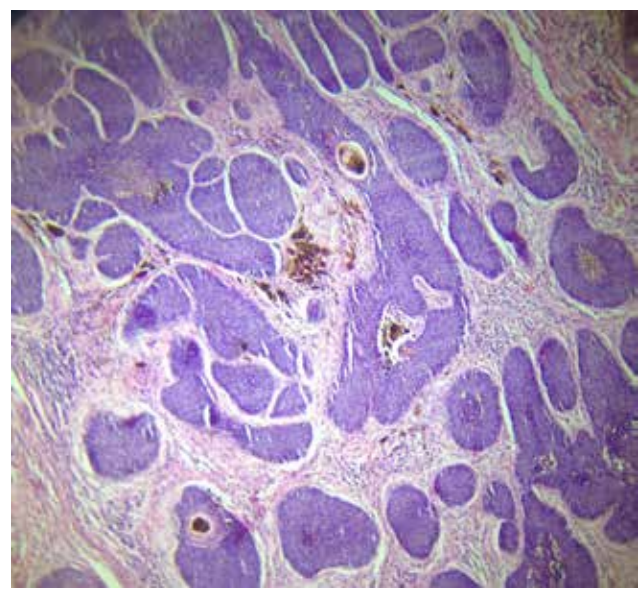

Fig. 1 Nodular ,Pigmented BCC (10 x 10x)

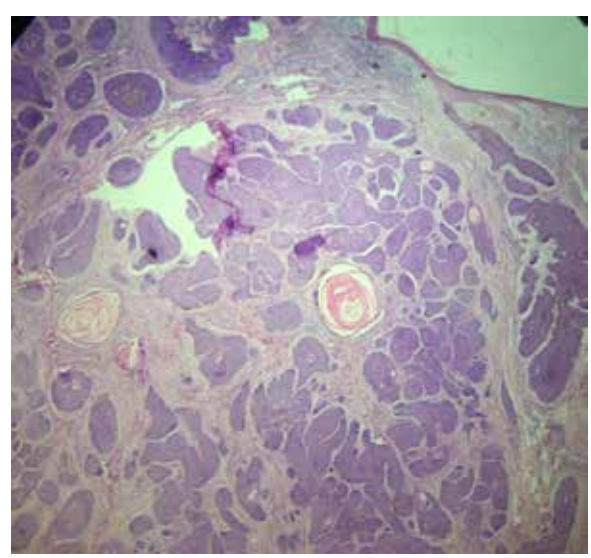

**Fig. 2. Nodular, Keratotic BCC (10 x 10x)**

Volume : 5 | Issue : 9 | September 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

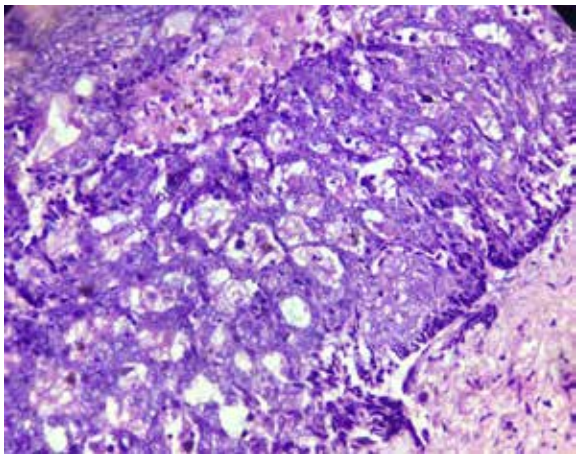

**Fig. 3 Adenoid BCC (40 x 10x)**

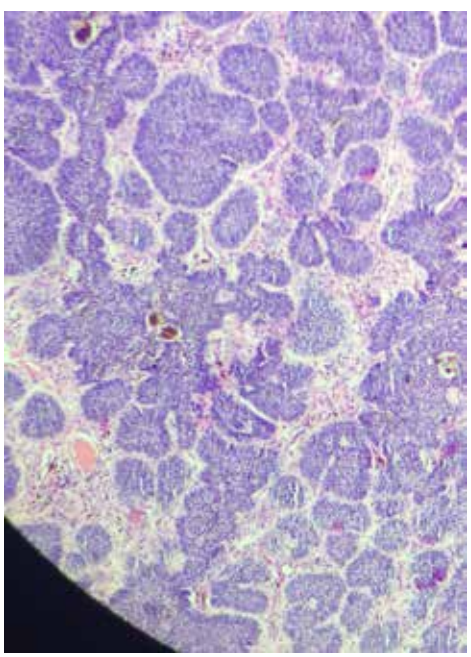

**Fig. 4 Micronodular BCC (10 x 10x)**

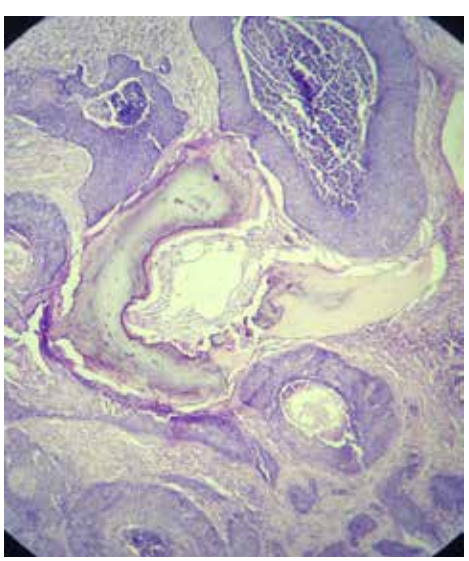

**Fig. 5 Nodular BCC invading the bone(10 x 10x)**

**Fig. 6 BCC of the scalp**

**Fig. 7 BCC on the nose**

**Fig. 8 BCC at the angle of the mouth.**

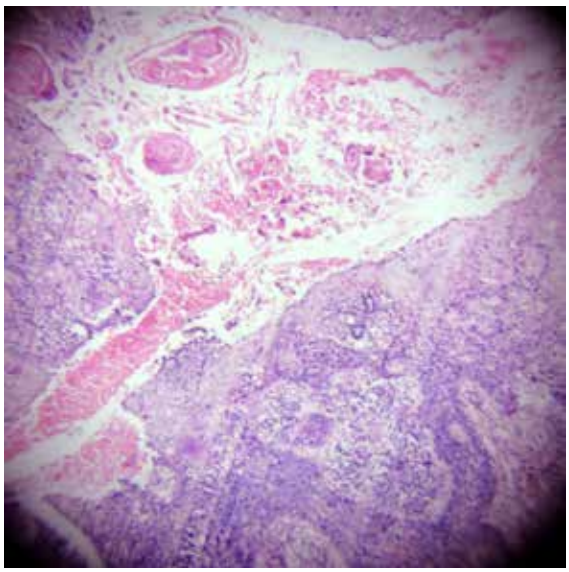

**Fig.9 Basosquamous BCC (10x10x)**

## REFERENCES

1. C S M Wong,R C Strange,J T Lear.Basal cell carcinoma.BMJ 2003;327:794-798
2. Prema Saldanha,PR Shanthala,Krishnaraj Upadhaya.Cutaneous basal cell carcinoma:A morphological spectrum.Archives of medical and Health Sciences 2015;3:24-28
3. Sumir Kumar,Bharat Bhushan Mahajan,Sandeep Kaur,Ashish Yadav,Navtej Singh and Amarbir Singh.A Study of Basal Cell Carcinoma in South Asians for Risk Factor and Clinicopathological Characterization: A Hospital Based Study.Journal of Skin Cancer 2014;2014:Article ID 173582:9 pages
4. David E.Elder,Rosalie Elenitsas,Bernett L.Johnson,Jr,GeorgeF.Murphy,Xiaowei Xu.Lever's Histopathology of The Skin.10th ed.Wolters Kluwer:Lippincott Williams & Wilkins;2011
5. R.A.Carr,S.M.Taibjee,D.S.A.Sanders.Basaloid skin tumours:Basal cell carcinoma. Current Diagnostic Pathology2007;13:252-272
6. Juan Rosai.Rosai and Ackerman's Surgical Pathology.10th ed.Vol 1.Elsevier Mosby;2012
7. LeBoit P.E., Burg G., Weedon D, Sarasain A. (Eds.): World Health Organization Classification of Tumours. Pathology and Genetics of Skin Tumours. IARC Press: Lyon 2006
8. Adam i. Rubin,M.D., Elbert H.Chen,M.D., and Desiree Ratner,M.D. Basal Cell Carcinoma .N Engl J Med2005;353:2262-2269
9. Purnima Malhotra, Avninder Singh, V Ramesh.Basal Cell carcinoma in the North Indian population:Clinicopathologic review and immunohistochemical analysis. Indian Journal of Dermatology,Venerology and Leprology2011;77:328-330
10. Mirna Situm,Marija Buljan,Vedrana Bulat et al.The role of UV radiation in the development of Basal Cell Carcinoma.Coll.Antropol2008;32:167-170
11. Lyubomir A Dourmishev Darena Rusinova, Ivan Botev .Clinical variants,stages, and management of basal cell carcinoma;Indian Dermatology Online Journal2013;4:12-17
12. Alexander J.F.Lazar. George F. Murphy in Kumar,Abbas,Aster.Robbins & Cotran Pathologic Basis of disease.9th ed Vol 2.Elsevier;2015
13. A Neil Crowson.Basal Cell carcinoma:biology, morphology and clinical implications;Modern Pathology2006;19:127-147
14. G Saldanha,A. Fletcher,D.N. Slater.Basal cell carcinoma:a dermatopathological and molecular biological update;British Journal of Dermatology-Wiley Online Library2003;195- 202
15. Christopher DM Fletcher.Diagnostic Histopathology of tumours.4th ed.vol 2.Elsevier;2013