Indian Journal of Mednodent and Allied Sciences
Vol. 4, No. 2, June 2016, pp- 101-106

IndianJournals.com
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DOI : 10.5958/2347-6206.2016.00016.9

Case Report

Morpheaform Basal Cell Carcinoma: A Case Report with Review of Literature

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ABSTRACT

Basal cell carcinoma (BCC) is the most frequently occurring skin cancer. Most cases are not life threatening, as very small proportions of BCCs metastasise. However, a high tendency to recurrence makes characterising BCCs and tumour margin areas obligatory. It will assist in better understanding their pathogenesis and in more effective treatment through prevention of recurrence and second primary disease.Various morphological subtypes have been described, nodular BCC being the most common type. Morpheaform or sclerosing BCC is a rare but high risk variant of BCC. One such case of Morpheaform, BCC in a 30-year old female patient is reported here to emphasise the nature and early diagnosis of this malignancy.

KEYWORDS: Basal cell carcinoma, Infiltrative, Morpheaform BCC, Skincancer, Malignancy, Ulcer, Nevoid basal cell carcinoma syndrome

INTRODUCTION

Basal cell carcinoma (BCC) is the most common malignancy in humans. It is the most prevalent skin cancer, accounting to 90% of all skin cancers [1]. It was first described by Jacob in 1827 [2] and then by Krompecher in 1900 as 'carcinoma epithelialea denoides' [3]. BCC develops most commonly on sun-exposed areas of the skin, face and scalp in middle aged or elderly individuals [4]. Lesions occurring on sun-protected and sun-exposed skin have a different biology and morphology in these locations [2]. BCC arises from pluripotential stem cells in basal layer of the epidermis or from hair follicle (outer root sheath area), hair follicle stem cells which present just below sebaceous gland ducts [1,4].

CASE REPORT

A 30-year old female patient reported with the chief complaint of an ulcer on the face since last 2 years. Patient was apparently alright 2 years back when she noticed an ulcer on the left side of the nose.The ulcer was initially small in size and grew to the size of 3×3 cm over a period of 2 years.No history of skin lesions elsewhere was noted. Patient is a farmer by profession and performs outdoor work in the sun since childhood.

On inspection, a large ulcer was seen on the left lateral wall of the nose with irregular borders ranging in size from 3 × 3 cm. The ulcer showed scarring, crusting and white keratotic base. Colour ranges from brown to black and no fresh granulation tissue was seen at the base. The area of ulcer was depressed than the adjacent structures. Left nostril appeared distorted and there was asymmetry between right and left nostril. There was no nasal stuffing and discharge from the nose (Figure 1).

On palpation the ulcer was non-tender. The base of the ulcer was indurated. Temperature of skin was not elevated. Based on the clinical examination provisional

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diagnosis of BCC was given. Wide local excision was performed and histological examination was done.

On histopathological examination, the H & E stained section showed epithelium and sparse connective tissue.The epithelium was stratified squamous or the keratinised in nature. Epithelial cells showed basilar hyperplasia, nuclear hyperchromatism, prominent intercellular bridges, increased Nuclear: Cytolasmic ratio. Mitotic figures were seen in some cells. The basal cells showed melanin pigmentation (Figure 2). Some cells were also present with vesiculated nuclei. Basement membrane was intact. Adnexal structures like hair follicle and sebaceous glands were seen extending from connective tissue in to the epidermis. The underlying connective tissue showed islands of malignant epithelial cells. The islands showed basal cells in the periphery with palisaded arrangement of nuclei (Figures 2a,b and 3). Deeper areas of connective tissue also showed small round islands and thin chords of basaloid cells (Figures 3 and 4). The islands showed clear spaces surrounding them suggestive of retraction artefact (Figures 5). Connective tissue also showed collagen fibres, fibroblasts and inflammatory cell infiltrate chiefly of lymphocytes.Based on clinical and histopathological examination, final diagnosis of 'Morpheaform Basal cell carcinoma' was given.

DISCUSSION

BCC is a slow-growing, locally invasive skin malignancy, infiltrating the underlying tissues three-dimensionally by the irregular growth of subclinical finger-like outgrowths which remain contiguous with the main tumour mass. The main reason for morbidity is local tissue destruction and invasion. It has extremely rare metastasis [5]. Sun exposure is the major risk factor in development of BCC, specially, in persons with a fair skin complexion type-I (including red or blonde hair, light coloured eyes, freckling) and people with a history of intermittent sun exposure and severe sunburn during childhood are at highest risk. The effect of UV radiation is inversely proportional to the amount of pigmentation [6].

Other risk factors for BCC include the exposure to arsenic, coal tar derivatives and irradiation. BCC may, like squamous cell carcinoma, arise in the previous scars, ulcers, burn sites and areas of foci of chronic inflammation [2]. Immune compromised states are also regarded as one of the factors in provoking an increased risk of BCC and this can be due to impaired immune surveillance of oncogenic viruses [7]. The genodermatoses associated with the risk of BCC include the xeroderma pigmentosum, Rasmussen syndrome, Rombo syndrome, Bazex–Christol–Dupre syndrome, albinism and Darier's disease. These syndromes variably either decrease epidermal pigmentation, and thus, increase the risk of UV light-induced oncogenic transformation or promote genotypic instability in the epidermis [2]. Though sporadic BCCs are not life threatening, their occurrence with syndromes such as Nevoid Basal Cell Carcinoma Syndrome (NBCCS) can be life threatening because of associated systemic involvement. Dental involvement that is presence of odontogenic keratocysts can be one of the key diagnostic features of the syndrome, and hence, dentist can be the 1st person to encounter such cases. Hence, here we have also emphasised on the NBCC, as its presence must be ruled out.

Nevoid Basal Cell Carcinoma Syndrome

NBCCS is also referred to as Gorlin–Goltz Syndrome, Basal cell nevomatosis and NBCCS [8]. The NBCCS was probably first reported by Jarish in 1894, who published a case of multiple jaw cysts associated with skeletal abnormalities and basal cell nevi. But, it has been a well-recognised entity after Gorlin and Goltz published their paper in 1960 after analysing 150 cases from the literature [9]. It is a hereditary condition transmitted as an autosomal dominant trait and exhibits high penetrance and variable expressivity. It is characterised by several developmental defects and a predisposition to cancer with extremely varied clinical manifestations [8]. Gorlin and Goltz described the condition as a syndrome comprising the principal triad of multiple basal cell nevi, jaw keratocystic odontogenic tumours and skeletal anomalies. Wide range of other

neurological, ophthalmic, endocrine and genital manifestations are variables associated with this triad [8].

The diagnosis is however made clinically, using the major criteria suggested by Kimonis *et al*. NBCCS can be considered, if the clinician finds any 2 major and 1 minor criteria or 1 major and 3 minor criteria in the suspected patients (Table 1). Additionally, laboratory testing for PTCH gene in the diagnosis of this syndrome is important [10]. The principal causative mutations in NBCCS occurs in the human homologue of the drosophila 'patched' gene (PTCH), on long arm of chromosome 9q (22.3–q31), which is part of the Hedgehog (HH) – signalling pathway which is important in determining embryonic patterning and cell fate in the developing embryo [11]. This gene mainly functions as a tumour-suppressor gene along with other important roles such as in odontogenesis. The mutations in this gene result in loss of control of several genes known to play a role in both organogenesis and carcinogenesis [8].

BCC occurs most frequently in 4th decade of life, with male to female ratio of 3:2. BCC is commonly seen in the middle third of the face, but can also occur in other sun-exposed areas. It does not arise in the oral mucosa, and thus, never seen inside the oral cavityunless it arrives there by invasion or infiltration from skin [4].

Clinical manifestations are very diverse, including papulonodular lesions with a pearly transparent rim, destructive ulcerative lesions called ulcusrodens, pale foci with various degrees of induration, erythematous foci with obvious telangiectasia or cystic nodules [12]. Depending on different clinical and histological features, BCC is subdivided into many categories. Up til now, many histopathological types of BCC have been described by various authors.The highest number was 26, described by *Wade and Ackerman* in 1978. Histological growth pattern and histological differentiation are the two basic criteria in the creation of classification of histological types by most authors. The histological growth pattern is thought to be of the greatest biological significance. Classification based on the histological growth pattern is useful in creating of the concept of low-risk and high-risk types of BCC. A greater probability of subclinical spread, aggressive local behaviour of the tumour with a more frequent occurrence of local recurrences and incomplete excision are characteristic of high-risk types. High-risk types include infiltrative and superficial types; whereas, low-risk types include nodular type BCC [12].

Most commonly encountered subtypes of BCC are as follows.

Nodular BCC is the most common variety of BCC, representing 30–75% of all BCC [12]. It begins as a

Table 1: Criteria In diagnosing Nbccs

Major Criteria	Minor Criteria
More than 2 basal cell carcinomas (BCCs) or one BCC in patients younger than 20 years of age	Macrocephaly
Odontogenic keratocysts of the jaw (proven by histologic analysis)	Congenital malformations (e.g. cleft lip or palate, frontal bossing, coarse faces and moderate or severe hypertelorism)
Three or more palmar or plantar pits	Other skeletal abnormalities (e.g. sprengel deformity, marked pectus deformity and marked syndactyly of the digits)
Bilamellar calcification of the falxcerebri	Radiological abnormalities (e.g. bridging of the sellaturcica, vertebral anomalies, modelling defects of thehands and feet, or flame-shaped lucencies of the hands and the feet)
Bifid, fused or markedly splayed ribs	Ovarian fibroma or medulloblastoma
A first degree relative with NBCCS	

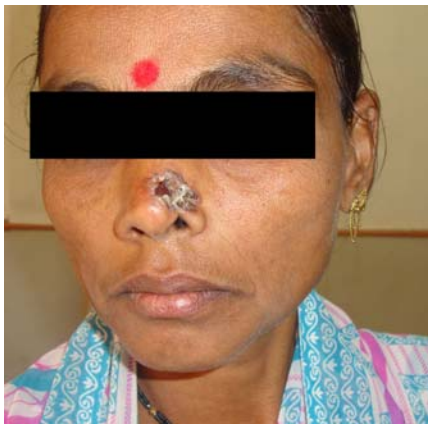
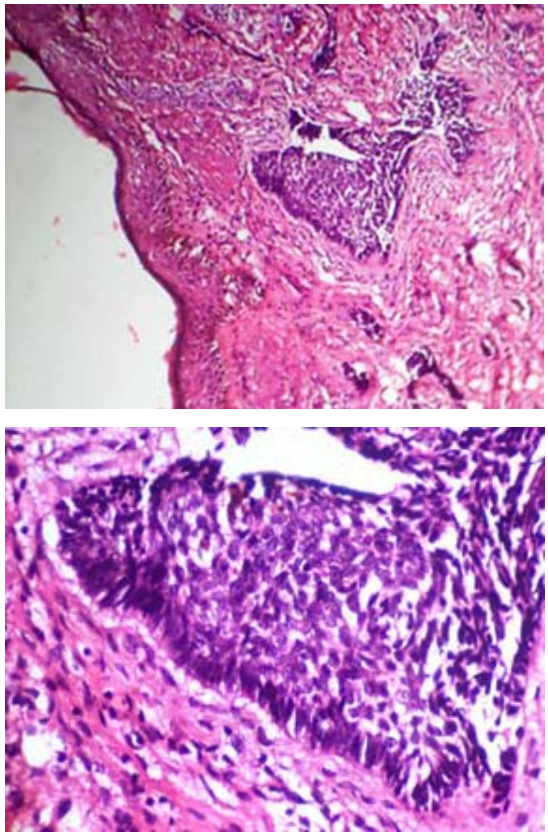


Figure 1: A large ulcer on the left lateral wall of the nose with irregular borders with scarring, crusting and white keratotic base



(a)

(b)

Figure 2: (a) Basal cells with melanin pigmentation and basaloid islands in the connective tissue (10× view). (b) Islands showing basal cells in the periphery with palisaded arrangement of nuclei (40× view)

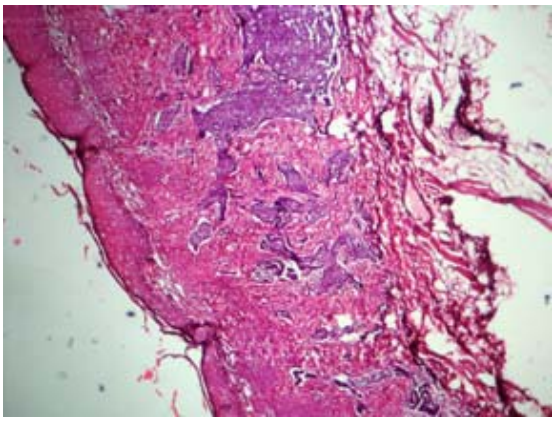


Figure 3: Deeper areas of connective tissue showing small round islands and thin chords of basaloid cells (4× view)

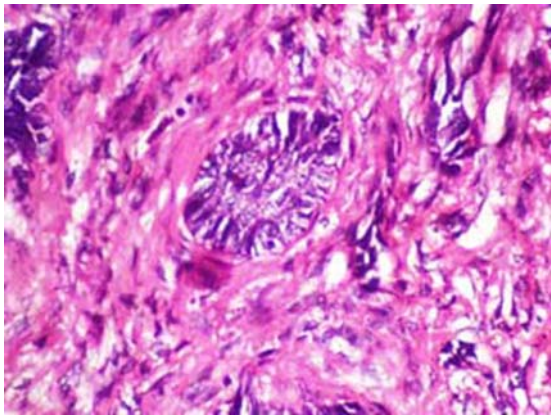


Figure 4: Small round islands of basaloid cells with peripheral palisading (10× view)

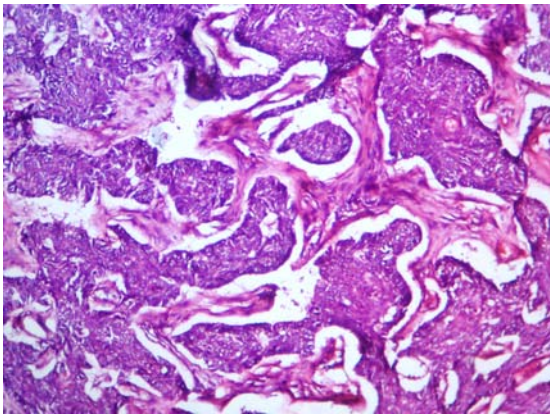


Figure 5: Basaloid islands in the connective tissue showing clear spaces surrounding them suggestive of retraction artefact (10× view)

small, elevated papule with central depression which ulcerates, heals and breaks down again. Telangiectatic vessels are usually seen coursing over the borders. Eventually, the crusting ulcer which appears superficial, develops a smooth, rolled border representing tumour cells spreading laterally beneath the skin [4]. Pigmented BCC, Superficial BCC, Micronodular BCC, Cystic BCC and Infiltrating BCC are other common variants of BCC. Infiltrating BCC comprising 10% of all BCC, has been divided into two categories as Sclerosing (5%) and Non-Sclerosing BCC. Histopathologically, BCC is an epithelial malignant tumour with a low-malignant potential, consisting of cells resembling the basal epidermis layer. The diagnostic histological features, common for all types of the tumour, are basaloid cells with a thin pale cytoplasm surrounding round or oval nuclei with a roughly granulated chromatin pattern. The peripheral borderline cell layers show characteristic palisaded arrangement and the surrounding stroma is often separated by artificially created slits, known as 'retraction artefacts', whereas the internal arrangement of the cells is more chaotic. Most tumours originate in the epidermis and invade the dermis in the form of solid or cystic nodules or streaky projections creating various growth patterns. Mitoses may be rare or multiple; often, especially in greater tumour nodules, there is presence of central necrosis [12].

Morpheaform BCCs represent roughly 1–5% of all BCCs, clinically presenting as white or yellow depressed fibrotic scars that rarely ulcerate or bleed [2]. This sclerosing (morpheic, fibrosing, cicatricial or desmoplastic) variant of infiltrative BCC has characteristically increased number of fibroblasts and the presence of fibrotic desmoplastic stroma, giving the tumour a characteristic clinical picture of a morphea or keloid scar [12]. It is an aggressive variant with sclerotic plaques or papules. The border is usually not well defined often extending beyond clinical margins. Histopathologically, it exhibits growth patterns resulting in strands of cells rather than round nests of cells [4]. Individual cell necrosis and mitotic activity are brisk considering the relative volume of tumour. The neoplasms themselves are poorly demarcated, showing widespread invasion tillreticular dermis and penetration into the subcutaneous tissue. Slit-like retraction from the stroma is less common than the nodular and superficial variants but is still often demonstrable as in our case. These neoplasms are thought to coexist along with other aggressive growth morphologic variants. Although typically, one to two cells in thickness, cords up to five cells in thickness may also be seen; the architecture sometimes comprises sharp angulation of such cords. Pronounced stromal fibroplasia and fibrosis surrounds the tumour tongues [2].

The different forms of BCC carry with them a different set of differential diagnostic possibilities. Considering aggressive growth BCCs, the morpheaform BCC must be distinguished from other desmoplastic adnexal tumours including desmoplastic trichoepithelioma and microcystic adnexal carcinoma. Desmoplastic trichoepitheliomas manifest an epidermal 'dell', which is a downward indentation of the epidermal surface, accompanied by proliferating basaloid cells, keratin cysts and only rarely mitosis in the tumour cells. Dermal mucin production and apoptosis are absent although calcification may be seen. In the microcystic adnexal carcinoma, a widely invasive tumour is seen which typically goes to the edges of a punch biopsy specimen and comprises columns of vertically-oriented atypical cells manifesting individual cell necrosis and mitotic activity surmounted by keratin-containing cystic structures lined by differentiated squamous epithelium [2].

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