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The Convergence of Basal and Squamous: A Deep Dive into Basosquamous Cell Carcinoma – A Case Report

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Abstract

Basosquamous carcinoma is a rare, non-melanotic and aggressive variant of BCC having features of both basal cell component and squamous cell component diagnosed histopathologically. We report a case of Basosquamous carcinoma in a 75-year-old female patient who came with complaints of an ulcer over the left cheek for 1 month. Initially edge wedge biopsy was sent and it was to be BCC. Later on, the patient underwent a wide local excision biopsy. On microscopy sections showed skin and a tumour arising from the basal layer arranged in nests with peripheral palisading with foci of retraction artifacts and also desmoplastic stromal reaction. Also shows squamous differentiation with an increased mitotic rate. This case report highlights its distinctive histologic appearance and emphasises the aggressive nature of the tumour.

Keywords: *Basal Cell Carcinoma(BCC), Basosquamous Carcinoma(BSC), BerEP4, EMA, Mustarde Flap, Squamous Cell Carcinoma.*

Introduction

Basosquamous Cell Carcinoma is a poorly known entity. It's a rare variant of Basal Cell Carcinoma. It has features of both basal cell carcinoma and squamous cell carcinoma [1, 2, 3]. In recent studies incidence of BSC which was previously 1.7% to 2.7% has increased to 4.8% of all cutaneous tumours [3, 4, 20]. It is an aggressive cutaneous tumour with increased chances of metastasis and recurrence. Its Characteristics have more similarity to that of squamous cell carcinoma though it's a variant of basal cell carcinoma [16, 17]. Most Basosquamous carcinomas are located in the cranial and cervical region, mainly the upper half of the face over the nasal & periorbital region and rarely over the ear, trunk and back.

We discussed a case of BSC over the face which was initially suspected to be a BCC and turned out to be Basosquamous Carcinoma. This report describes the clinical presentation of BSC along with its Surgical Management and histology of this rare form of malignancy.

Materials and Methods

We present a case of Basosquamous Cell Carcinoma over the face which was initially diagnosed as a basal cell carcinoma and turned out to be Basosquamous Histology. Here the clinical presentation and Surgical Management were studied.

Case Presentation

A 75-year-old female farmer by occupation came with complaints of a non-healing ulcer on her left cheek for the past month. It was insidious in onset which gradually progressed to attain the present size [Figure 1]. She was not experiencing any pain over the ulcer. There was no active bleeding or discharge from the ulcer. There were no fever episodes, there was no loss of weight or appetite. No history of trauma. No

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history of ulcers or swellings elsewhere on her body, no known comorbidities, and no prior surgical history.

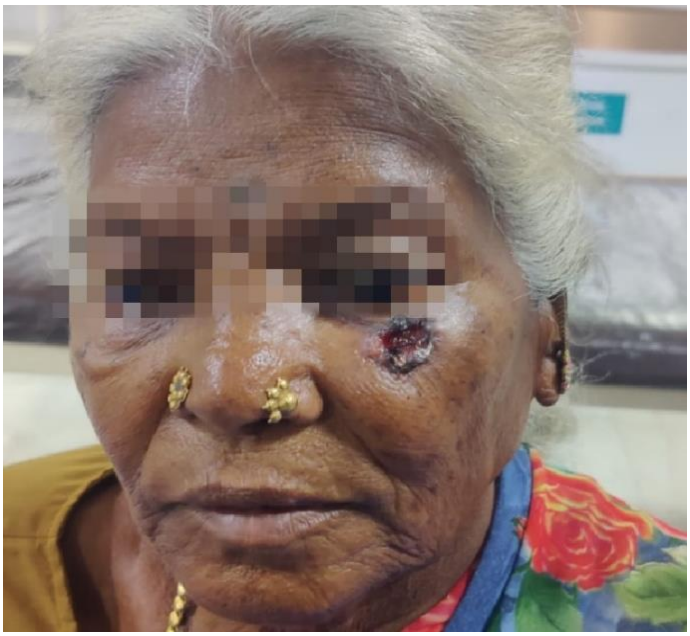

Figure 1. Patient With Basosquamous Cell Carcinoma Over Left Cheek

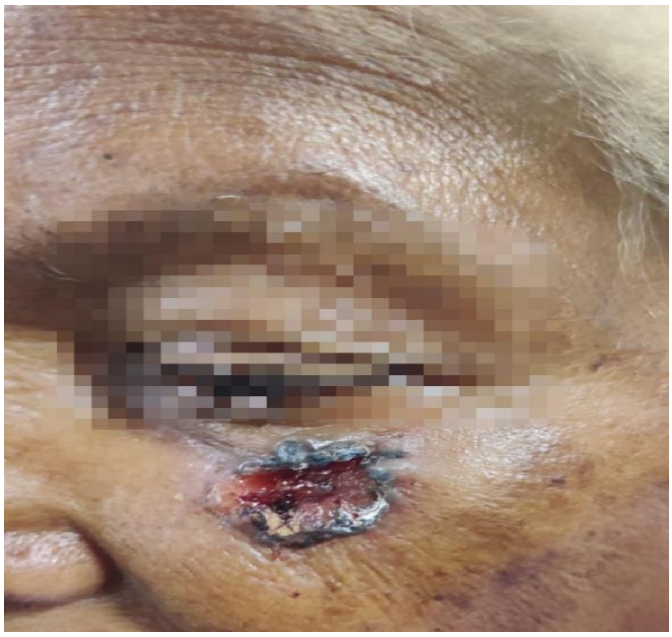

Figure 2 Basosquamous Cell Carcinoma Over Left Cheek

The ulcer was 3x4cm in size over the left cheek extending 2cm from the left side of the nose's ala to 5 cm from the tragus of the left ear. It was irregular in shape with raised pearly beaded edges and irregular margins. Necrotic tissue was seen over the floor of the ulcer. The surrounding skin appeared normal. There was no warmth or tenderness. The ulcer was not bleeding on the touch. Induration is present over the edge of the ulcer [Figure 2]. The ulcer was not fixed to deeper structures. No palpable lymph nodes are present.

All routine investigations were within normal limits. An ultrasound of the neck showed no enlarged lymph nodes.

Edge wedge biopsy: Fragmented Biopsy with tiny fragments of islands of BASALOID CELLS consistent with the clinical diagnosis of BASAL CELL CARCINOMA.

Wide local excision made with a 5mm margin. The specimen was sent for a frozen section. The floor of the excised specimen was not free of tumours [Figure 3]. Further excision was done including periosteum and infraorbital fat. The re-excised tissue was sent for the frozen section. Infraorbital fat and all the margins and deeper tissue were free of tumours [Figure 4]. After confirming clear margins flap cover was planned [Figure 5]. Markings were made for cheek rotation flap (Mustarde cheek Rotation Flap) [Figure 7]. Incision made along the markings and flap raised. Flap mobilized into the defect. Haemostasis was achieved and a drain was placed. Flap sutured [Figure 6]. A sterile compression dressing is done.

Figure 3. Excised Specimen Gross Image

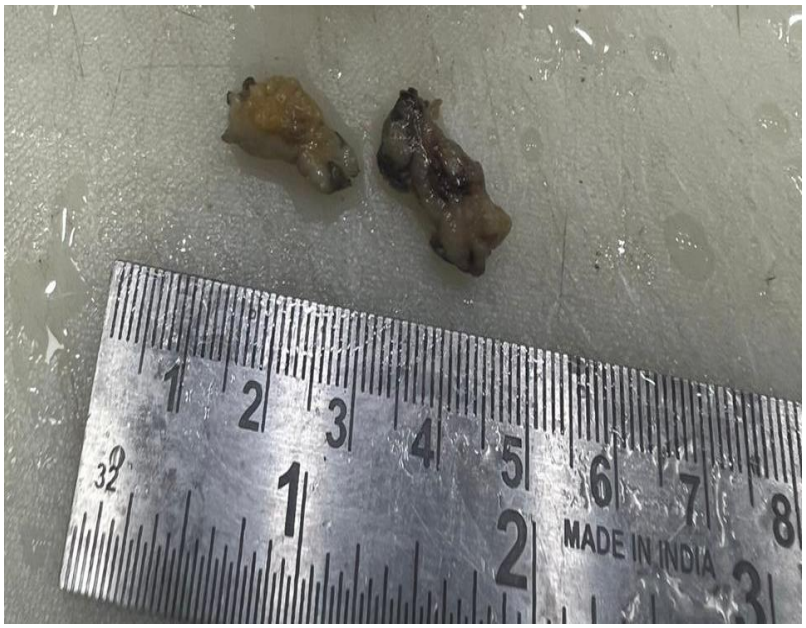

Figure 4. Re-excised Specimens – Remaining Tissue Including Periosteum and Infra Orbital Fat

Figure 5. Intra-Op Picture Post Excision with Flap Marking

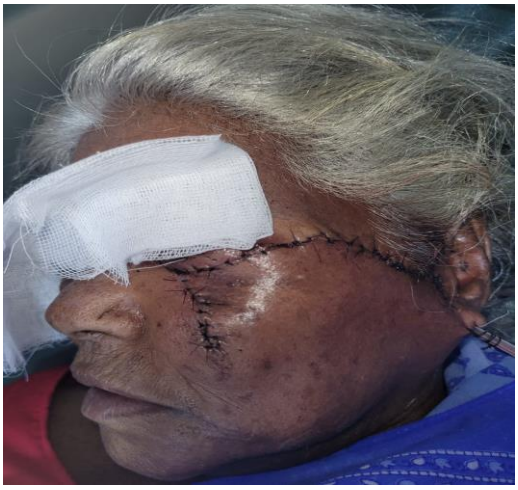

Figure 6 Immediate Post-Operative Picture

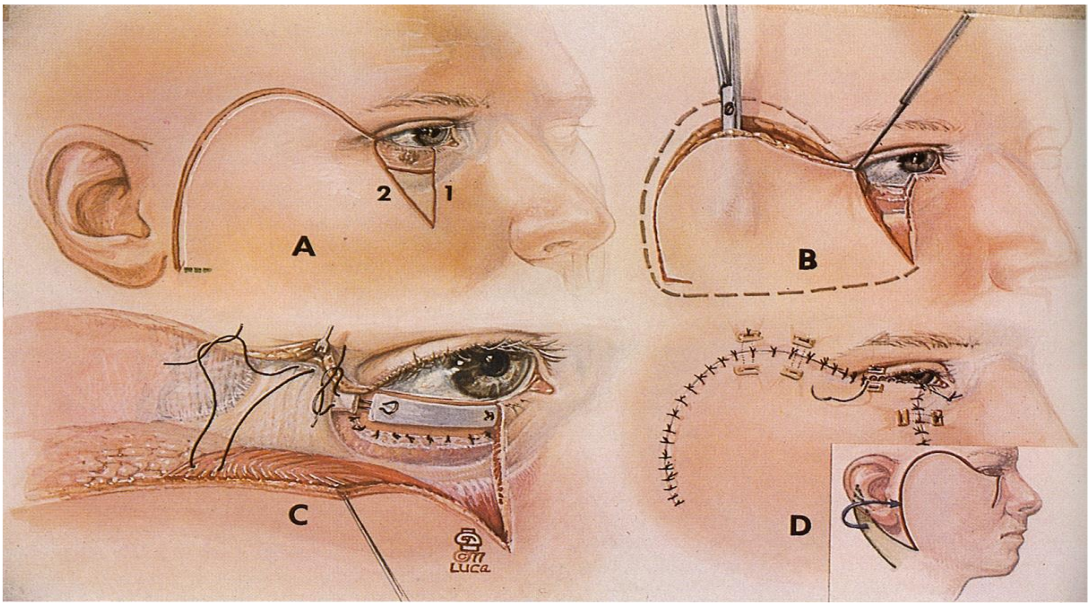

Figure 7 Picture Depicting the Technique of Mustarde Cheek Rotation Flap

(image source: Michael A. Callahan, Alston Callahan, mustardé flap lower lid reconstruction after malignancy, ophthalmology, volume 87, issue 4, 1980, pages 279-286, issn 0161-6420, https://doi.org/10.1016/s0161-6420(80)35237-8.)

Histopathology

The excised specimen was sent for routine tissue processing. In the frozen section, all margins were free of tumour. In H& E sections show skin and a tumour arising from the basal layer arranged in nests with peripheral palisading. There are foci of retraction artefacts. However, there are large nests of tumour cells surrounded by desmoplastic stromal reactions. The cells are large with abundant eosinophilic cytoplasm with vesicular nucleus. There is an increase in mitosis (average mitotic count is 9/10 HPF). Many nests of tumour cells show comedonecrosis [Figure 8]. The tumour is infiltrating the deeper skeletal muscle tissue in the sections examined. There are focal areas of keratinization forming keratin pearls [Figure 9]. The possible diagnosis is Basosquamous carcinoma (an aggressive variant of BCC).

Immunohistochemistry Ber EP4 was focal positive [Figure 10], and EMA was negative [Figure 11].

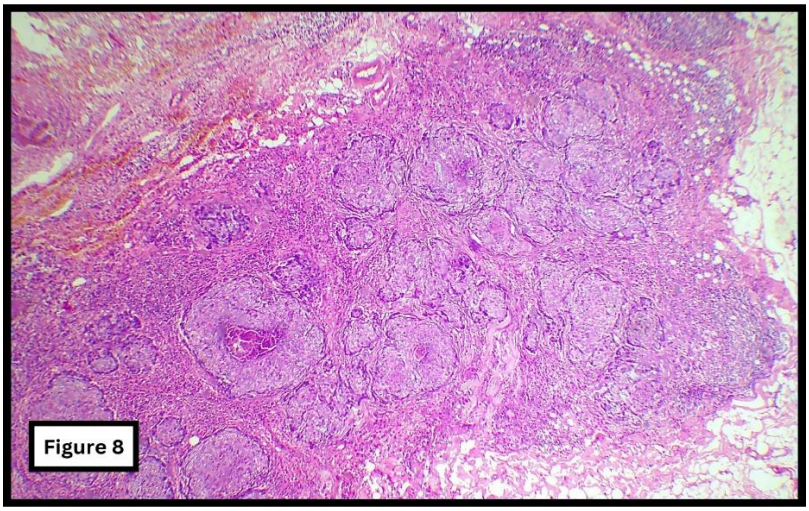

Figure 8. Shows Tumour Nests with Comedonecrosis Surrounded by Desmoplastic Stromal Reaction. The Tumour Nests are Seen Infiltrating Into the Deeper Tissues

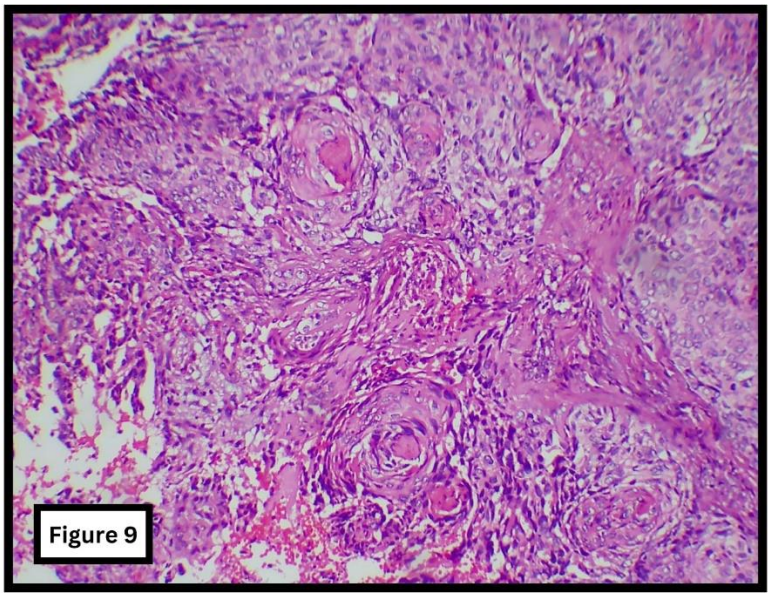

Figure 9. Shows Focal Areas of Squamous Differentiation Forming Keratin Pearls

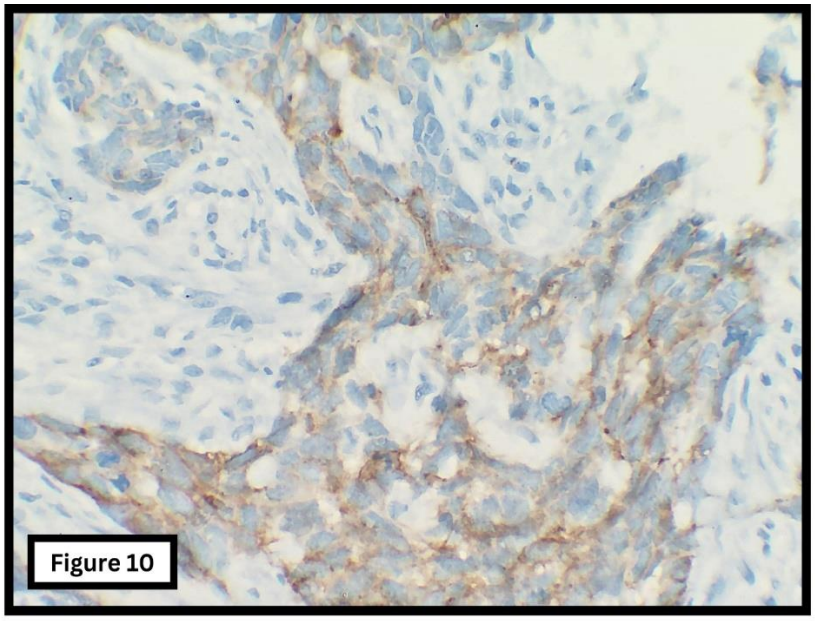

Figure 10. BerEp4 Showing Positive Membranous Staining Pattern in the Tumour Cells

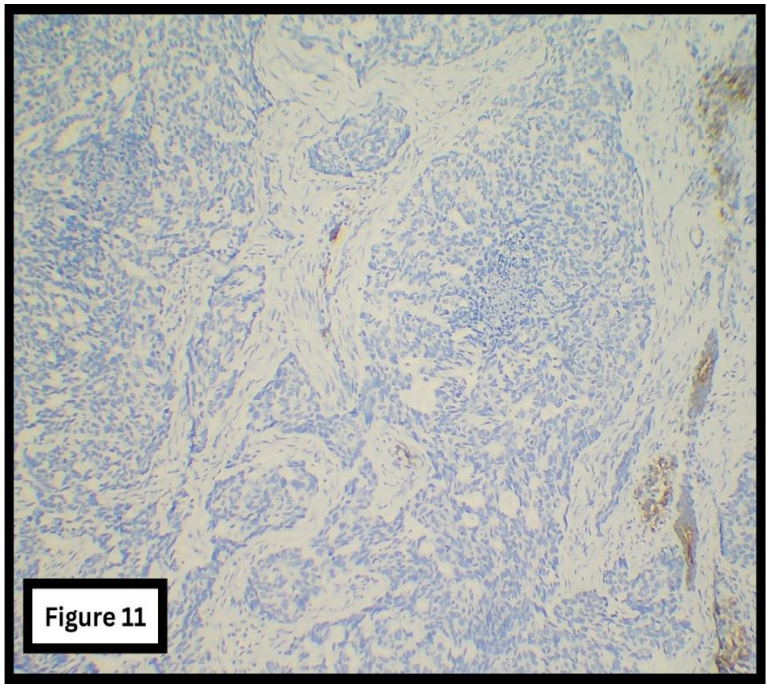

Figure 11. EMA Showing Negative Staining Pattern in Tumour Cells

Discussion

Basosquamous cell carcinoma (BSC) formerly known as metatypical carcinoma, is a rare type of epithelial skin tumour, Most authors consider it a rare variant or subtype of basal cell carcinoma (BCC) [1]. Metatypical Basal carcinoma is a rare cutaneous aggressive tumour that is mostly located in the cranial and cervical region, mainly the upper half of the face over the nasal and periorbital region.

Basosquamous Cell Carcinoma accounts for 4.8% of all Nonmelanoma Cutaneous Malignancies which is predominantly seen in males [1, 2, 3, 4]. Usually, it presents in the 6th to 8th decade with an average age of 70 years of life. Due to its rarity and clinical resemblances distinguishing BSC from BCC is highly challenging. If not nearly impossible based on clinical features alone 1 [6, 7]. The conclusive diagnosis relies on histopathological

assessment and a set of Immunohistochemistry markers.

BSCC often has infiltrative growth patterns invading the dermis and even invading the subcutaneous tissue. This contributes to its aggressive pattern and for its potential chance of recurrence. It has a metastatic rate of 5-8.4%.

The etiology for BSC is mostly of chronic UV rays' exposure, in patients with Fitzpatrick skin types I-II and in recent times it is believed that it presents as BCC initially then with genetic alterations it develops into BSC characterized by squamous differentiation. The genetic alterations include the majority of PTCH1, SMO gene mutations and other gene mutations including MYCN, PPP6C, GRIN2A, CSMD3, DCC, PREX2, APC, PTEN, PIK3CA & ARIDIA [4, 14, 15].

Basosquamous Cell Carcinoma (BSCC) presents with histopathological features of both BCC and SCC[12]. The BCC component includes basaloid cells with small cytoplasm and large, pale, uniform nuclei. The SCC component includes squamous cells with moderate to large amounts of cytoplasm, large vesicular nuclei, prominent nucleoli and increased mitosis. Basaloid cells along with atypical squamous cells, and cellular fibrotic stroma are seen. These tumours typically have transition zones where Basaloid morphology blends with squamoid morphology where tumour islets coexist [13, 14]. A large nest of tumour cells will be surrounded by a desmoplastic stromal reaction.

To further refine the diagnosis immunohistochemical analysis utilizing markers such as BER EP4 and EMA are done. BerEP4 stains BCC elements and EMA stains SCC elements [1, 2, 3]. They provide accurate characteristics of tumours.

The primary management of BSCC is early surgical-wide local excision of the tumour or MOHS micrographic surgery with a tumour-free margin [11, 18, 19]. In patients suspected to have lymph node metastasis, a Sentinel lymph node biopsy is to be done. This helps in further staging and planning of treatment. The use of frozen section analysis during surgery can help confirm the absence of residual tumour cells in the excised margins. Thus, reducing the chances of local recurrence.

It is important to note that the local recurrence rate following surgical excision of a BSC tumour is high ranging between 12.1% to 45.7%. In patients with a high risk of disease relapse, patients may need further treatment in the form of Radiotherapy [5, 8, 9]. Factors contributing to this increased risk include positive excision margins, deep tumour invasion, nodal involvement as well as perineural or intravascular spread [10].

Regular and vigilant follow-up is necessary in the post-treatment phase to monitor for any signs of disease recurrence [Figure 12]. Early detection of recurrence of the disease and appropriate treatment can reduce the burden of disease and death of the patient.

Figure 12. Six-Month Post-Operative Image of The Patient (Lateral View Showing Healthy Scar)

Figure 13. Six-Month Post-Operative Image of the Patient (Anterior view showing healthy scar)

Conclusion

Due to its rarity and clinical similarities, it is difficult to differentiate and diagnose basosquamous cell carcinoma from basal cell carcinoma clinically. Basosquamous cell carcinoma exhibits an increased risk of metastasis and recurrence. As there is an increase in the incidence of Basosquamous cell carcinoma [3, 4]. It is important to arrive at a definitive diagnosis as early as possible and perform surgical excision of the tumour with tumour-free margins. Also, confirm the diagnosis by doing a proper histopathological and immunohistochemical analysis. Patients should be followed up at regular intervals [Figure 13] to reduce the disease burden and death of those patients in future.

Conflict of Interest

There is no conflict of interest.

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