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Case Report

Pigmented Paraaxillary Located "Complex" Basal Cell Carcinoma Imitating clinically irritated Melanocytic Lesion - Succesfull Surgical Approach in Bulgarian Patient

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Abstract

BACKGROUND: Basal cell carcinoma (BCC) is the most frequently encountered neoplasm worldwide. While nodular BCC is the most frequent clinical subtype, other forms of BCC, such as superficial, cystic, morpheiform, infiltrative, and pigmented may also be encountered.

CASE PRESENTATION: We present the case of a 67-year-old male with a relatively well-defined infiltrative, pigmented plaque with multiple colours and peripheral growth situated in the right axillary region. The histopathologic examination performed after complete surgical excision of the tumour revealed a complex pigmented BCC with macronodular, fibroepithelioma-like, cystic, focally infiltrative and basosquamous features.

CONCLUSION: Uncommon locations of BCCs in sun-protected areas such as the axillary region require a higher degree of suspicion for diagnosis. The complex histology of the presented case, including subtypes with differing biologic attributes, emphasises the importance of histopathological examination in the diagnosis and therapeutic management of BCC.

Introduction

Basal cell carcinoma (BCC) is the most frequently encountered cutaneous neoplasm worldwide, accounting for approximately 90% of all skin cancers [1], with an incidence of 2,000 cases /100,000 population [2]. Most BCCs develop in individuals with Fitzpatrick photo-types I or II and arise in sun-exposed areas, mostly in the head and neck and less frequently in the trunk and limbs [3, 4]. Less than 4% of all BCCs occur in the genital and perianal

region [5]. It is a slow growing tumour with a 0.5% metastatic rate [6], but with a considerable risk of local invasion and destruction if left untreated.

Several risk factors have been described in the pathogenesis of BCC. Long-term exposure to sunlight or artificial ultraviolet light (UV), especially UVB [7], represents the main BCC- inducing factor. Phenotypic and genetic traits (e.g. inherited diseases or syndromes such as basal cell nevus syndrome (Gorlin-Goltz syndrome), xeroderma pigmentosum, epidermodysplasia verruciformis, albinism, and Gardner's syndrome); a familial history of skin cancer; DNA repair deficiencies leading to chromosomal instability; immunosuppression; exposure to other environmental carcinogenic factors (e.g. arsenic, alkylating agents, polycyclic aromatic hydrocarbons) [8]; accidental or therapeutic exposure to ionizing radiation; and repeated cutaneous trauma have also been designated as important factors in the development of BCCs [3, 9, 10, 11].

A constitutive activation of the sonic hedgehog signalling pathway caused by acquired mutations in the PTCH and SMO genes [11], localised in the basal epidermal cell layer represents the early developmental determinant of BCCs, while other molecular alterations of P53 and melanocortin-1 receptor genes also play essential pathogenic roles [13, 14].

Nodular BCC is considered the most frequent clinical subtype, while other forms (superficial, cystic, morpheaform, infiltrative, pigmented tumours, and others) account for less than 10% of all BCCs [15].

Fibroepithelioma of Pinkus is another distinct BCC subtype, mostly found in the trunk; it can resemble an acrochordon, compound melanocytic nevus, melanoma, seborrheic keratosis, or other benign skin lesions [16].

The clinical diversity of BCCs emphasises the importance of histopathological examination in the diagnosis and therapeutic management of BCC. While nodular BCCs have definite clinical and histopathologic features, the other variants (adenoid, cystic, morpheaform, pigmented and others) may show more complex features and less predictable outcomes.

The differential diagnosis can be challenging; the major risk is that of mistaking BCC for benign, harmless lesions [17] or, on the other hand, for more severe, life threatening malignancies such as melanoma.

Standard surgical excision or Mohs micrographic surgery remain the mainstays of localised BCC treatment. In particular situations of inoperable cases, as in patients with locally advanced, metastatic disease or those with severe comorbidities or immunosuppression, BCCs may be approached with more conservative, nonsurgical methods [18].

The following report depicts an unusual case of BCC in a Bulgarian patient with a pigmented skin lesion localised in the axillary region. Histopathologic examination performed after complete surgical excision revealed the diagnosis of a complex pigmented BCC with macronodular, fibroepithelioma-like, cystic, focally infiltrative, and basosquamous features.

Case report

We report the case of a 67-year-old male who presented to the dermatology department with a skin lesion in the right axillary region that had been gradually growing for the past ten years (Fig. 1a). The lesion had bled two days before presentation but was otherwise asymptomatic. The patient did not report any food, or drug allergies or intolerances and his medical history were unremarkable except for benign prostatic hyperplasia. Clinical examination revealed a relatively well defined, infiltrated plaque with an uneven eroded surface, irregular borders, variegated colours, and peripheral growth in the right axillary region, measuring approximately 1x1.5 cm in greatest diameter (Fig. 1b).

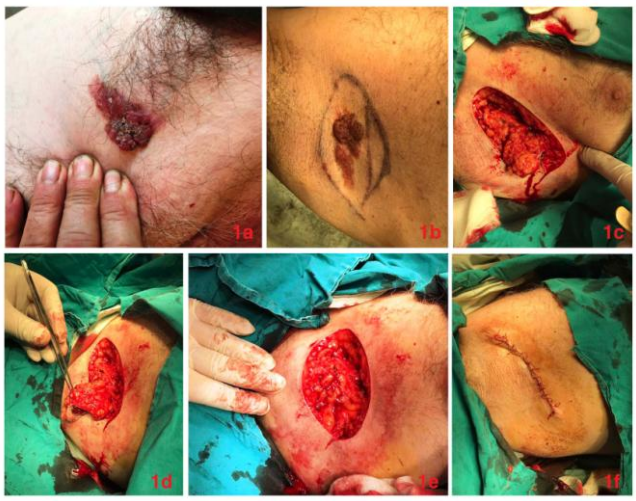

Figure 1: 1a) Clinical appearance of the lesion in the right axillary region; 1b) Preoperative markings showing wide excision margins; 1c) Surgical defect after excision of the lesion; 1d) Further excisional debridement of the subcutaneous fat to ensure complete tumor remova; 1f) Final surgical defect ready for reconstruction; 1f) Primary closure of the defect with interrupted non-absorbable sutures

The differential diagnosis included pigmented BCC, irritated melanocytic nevus, pigmented seborrheic keratosis, benign or malignant adnexal tumours, and melanoma. Paraclinical tests were unremarkable as well, with sinus tachycardia on ECG,

normal abdominal ultrasound, and a chest x-ray showing no visible infiltrations of the lung parenchyma, free costodiaphragmatic recess, and an extended aortic arch. Taking into consideration the history of change and the concern for a possibly aggressive malignant process, the lesion was surgically excised in an elliptical manner with wide margins under local anaesthesia with 2% lidocaine and epinephrine. Primary closure of the defect was achieved (Fig. 1c-f) followed by application of antiseptic ointment dressings. Postsurgical health status was eventless, and the patient was discharged with follow-up instructions. Histological examination revealed a large, complex basal cell carcinoma with several different histopathologic types, including macronodular, fibroepithelioma-like, cystic, focally infiltrative, and basosquamous (Fig. 2 a-h).

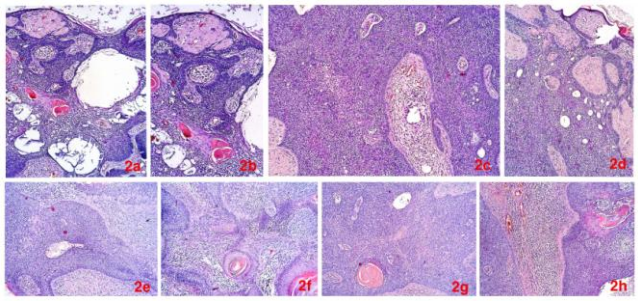

Figure 2: 2a and 2b) These are slightly different views of the same area of the tumour. There are epidermal atrophy and keratin debris above the stratum corneum. The hyalinized papillary dermal material likely represents secondary amyloid formation. The narrow branching cords of basaloid cells extending from the epidermis are reminiscent of fibroepithelioma of Pinkus. Other areas of the tumour show cystic change, and there are islands of keratinization, staining more intensely red, that represent squamoid differentiation within the tumour; 2c) Here, the tumour islands are most consistent with macronodular basal cell carcinoma. They are associated with a cellular, fibrous stroma featuring small vessel proliferation; 2d) The upper ½ of this image displays features of fibroepithelioma of Pinkus; changes in the lower ½ of the image are similar to those in (2c) and are mainly macronodular, with small foci of cystic change. The cellular, fibrotic stroma is evident; 2e) There is a central island of macronodular BCC associated with a cellular fibrotic stroma. The tumor island at the top of the figure (12:00-1:00) shows infiltrative features along its lower edge; 2f) Centrally, there is a distinctly squamoid area, with horn cyst formation (at 6:00) and infiltrative features; this area can be interpreted as a focus of basosquamous carcinoma. Again, there is a cellular, fibrotic stroma with lymphocytic inflammation; 2g) This image shows a macronodular focus of basal cell carcinoma with more subtle squamoid changes and a distinct focus of keratinization (at 7:00); 2h) Islands of macronodular basal cell carcinoma are present at the left and right of the figure. The larger tumour island on the right also shows a squamoid change in its upper portion. Between the two islands is a cellular fibrotic stroma with lymphocytic inflammation.

Many of these types (fibroepithelioma-like, cystic, basosquamous) are indicative of follicular/primary epithelial germ differentiation, while the infiltrative and basosquamous carcinoma areas are associated with more biologically aggressive tumours. The probable amyloid formation seen in Figures 2a and 2b is known to occur in basal cell carcinoma, and derives from degenerated basaloid cells, with modification of keratin filaments into a beta-pleated sheet configuration.

Discussion

Basal cell carcinoma is the most frequent type of skin cancer, and a strong association between its development and long-term sun exposure has been established [19].

However, its development in uncommon locations - such as sun-protected areas - requires a higher degree of suspicion for diagnosis. There exist few reports of axillary BCC cases, with an estimated a prevalence of 0.17%. As of August 2014, there were only 81 cases of axillary BCCs presented in scholarly journals [20]. Cohen observed that these tumours occurred predominantly in Caucasians, without significant BCC-associated risk factors [21]. The histologic sub-types associated with this localisation were mainly superficial or nodular, with an excellent prognosis after complete surgical removal [21]. No case of metastatic spread has been reported. However, the development of axillary tumours in patients with Gorlin-Goltz syndrome emphasises the risk of their inheritance, an important pathogenetic factor that should be thoroughly investigated. Moreover, the report of a linear adamantanoid BCC in the axilla, a sub-type with an increased risk of local invasion and recurrence [22], suggests the need for caution in the diagnosis and management of tumours localised in sun-protected areas.

Because of the wide-ranging clinical differential diagnosis in the presented case, including an array of benign and malignant tumours, histologic evaluation was carried out to determine the correct diagnosis. The peculiarity of our case consisted of its mixed histopathological patterns of macronodular, fibroepithelioma-like, cystic, focally infiltrative, and basosquamous features that have rarely been described in axillary BCCs. Infiltrative and basosquamous carcinomas are considered aggressive tumours, with an increased risk of recurrence and metastases. The treatment approach should focus on surgical excision with free margins to prevent tumour recurrence.

Although the tumour had slowly progressed over the previous ten years, the reason the patient presented for a dermatologic appointment was the acute symptom of bleeding. This reinforces the importance of educational campaigns and dermoscopic screenings for early diagnosis and treatment of skin cancers.

While international reports suggest a worldwide increase in the incidence of non-melanoma skin cancers [23], generally attributed to ultraviolet exposure, it would be useful to study the epidemiology of BCCs that develop in sun-protected areas, to gain more insight into the pathogenesis of this subset of tumours.

In conclusion, uncommon locations of BCCs

in sun-protected areas such as the axillary region require a higher degree of suspicion for diagnosis. The complexity of histopathologic subtypes in the presented case, each with potentially different biologic attributes, emphasises the importance of histopathological examination in the diagnosis and therapeutic management of BCC.

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