Case Report

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Basal cell carcinomas of the areola-nipple complex: Case report and review of the literature

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Abstract

Basal cell carcinoma of the areola-nipple complex poses diagnostic and therapeutic challenges due to its rarity and unique anatomical location. This subtype of basal cell carcinoma necessitates meticulous management to address potential recurrence and metastasis. Surgical excision with clear margins remains the cornerstone treatment for basal cell carcinoma of the areola-nipple complex, while alternative modalities such as radiation therapy, Mohs surgery, and systemic therapies may be considered in specific cases. However, optimal management strategies remain contentious, with varying opinions on the necessity of aggressive surgical intervention to minimize recurrence and metastasis risks. Additionally, the absence of standardized diagnostic criteria and treatment guidelines complicates clinical decision-making. Herein, we present a rare case of basal cell carcinoma of the areola-nipple complex in a 47-year-old woman with a notable medical history of hypertension, type 2 diabetes, and untreated psychosis, alongside a family history of breast cancer in her aunt. The patient exhibited a non-regressing ulceration on the right areolar region of the breast, persisting for approximately 10 years and progressively extending over time. Following surgical excision, a favorable post-therapeutic course was observed during follow-up. This case underscores the diagnostic challenges and nuanced management considerations inherent in basal cell carcinoma of the areola-nipple complex, underscoring the imperative for tailored treatment approaches.

Keywords

Basal cell carcinoma, areola-nipple complex, breast, skin cancer

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Introduction

Basal cell carcinoma (BCC) stands as a prevalent skin neoplasm, predominantly observed on sun-exposed regions such as the face, neck, and arms.[1,2] However, BCC affecting the nipple-areola complex (NAC) represents a rare entity, fraught with diagnostic intricacies and therapeutic challenges. The first documented case of BCC of the breast aereolar plate dates back to 1893, and only a few cases have been reported since then.[3] Despite its rarity, the incidence in BCC of the NAC appears to be increasing, as evidenced by recent publications of case reports and reviews.[4,5]

BCC of the breast areolar plate may present with a range of clinical manifestations, including erythematous and scaly cutaneous lesions, as well as ulcerating subareolar masses.[2] However, the location of the lesion can pose diagnostic challenges due to potential confusion with other breast pathologies, such as Paget's disease and melanoma.[6]

We present a rare case of BCC affecting the NAC in a 47-year-old woman.

Case presentation

We report the case of a 47-year-old, smoker female patient with a medical history of hypertension, type 2 diabetes, and untreated psychosis. The patient had a family history of

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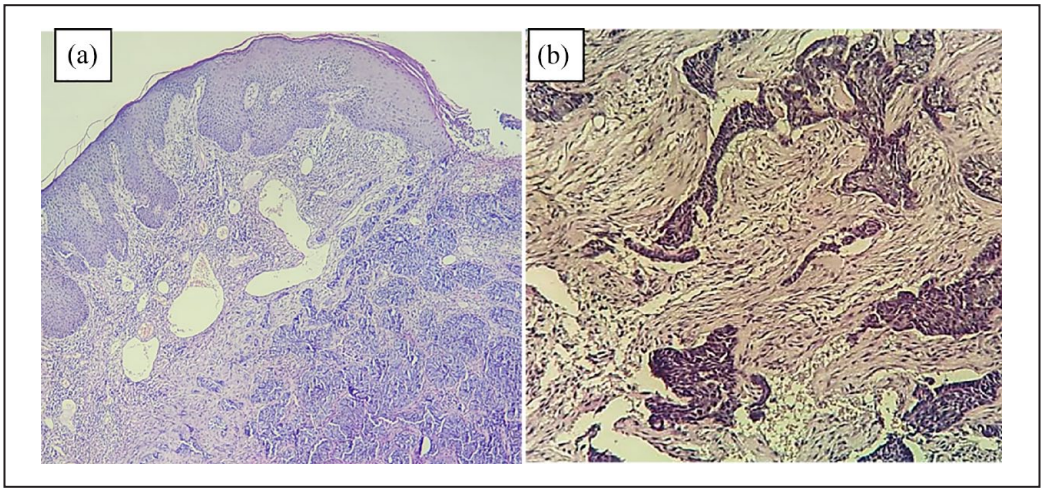

Figure 1. The histological examination after H&E staining reveals: (a) a tumor proliferation arranged in trabeculae and nests, (b) a tumor proliferation arranged in nests and cords of basophilic cells, forming peripheral palisades. Peripheral retraction clefts are also observed.

breast cancer in her aunt. She presented with a non-regressing ulceration on the right areolar region of the breast, without nipple involvement, which had been present for about 10 years and had progressively extended over time. The lesion had several episodes of infection, becoming inflamed, purulent, and bleeding with irritation of the peri-lesional skin, which prompted the patient to seek medical attention. Dermatological examination revealed a well-defined irregularly shaped ulceration, roughly oval, with a budding surface in some areas and fibrino-purulent surface in others, sharp-edged borders, and a surrounding erythematous-violaceous rim. The lesion measured 15 cm in the longest axis. The peri-lesional skin was erythematous, infiltrated, erosive in some areas, and dotted with pustules in others.

Breast tumor origin was ruled out after ultrasound and mammography examinations. Clinical suspicion was focused on Paget's disease, infiltrating BCC, ulcerated pigmented squamous cell carcinoma, or porocarcinoma. A biopsy of the ulcer margins was performed, and histopathological analysis showed a well-demarcated proliferation of tumor lobules with large cells having abundant basophilic cytoplasm and moderately atypical nuclei arranged in a palisading pattern at the periphery. Retraction clefts were observed between the lobules and the adjacent tumor stroma (Figure 1). Immunohistochemical analysis revealed strong and diffuse expression of GATA3, CK5/6, and P63 (Figure 2), with no expression of epithelial menmbrane antigen (EMA), hormone receptors, CK7, CK19, mammaglobin, GCDFP-15, or HER2, leading to a diagnosis of BCC of the areolar plate.

Upon thorough clinical examination and comprehensive imaging studies, there was an absence of axillary lymph node (LN) involvement noted in the patient.

Following the planned surgical intervention for local tumor excision, the patient underwent regular postoperative follow-up appointments, including scanner checks to monitor for any signs of recurrence or complications. Throughout the follow-up period, no recurrence or adverse events were observed, indicating a favorable post-therapeutic course.

Discussion

Skin cancer is the preeminent form of malignancy in humans, representing approximately 50% of all diagnosed cancers. Among these, non-melanoma skin cancers are most prevalent, with BCC being the most common subtype, accounting for 70%–80% of all cases.[2,4,5,7] The emergence of basal cell carcinoma in the nipple and areola complex (BCC-NAC) is exceedingly rare.[8,9] Notably, the incidence of BCC-NAC has risen twofold over the past decade, possibly owing to heightened awareness and advancements in skin cancer detection modalities.[10]

The enhanced incidence of BCC specifically affecting the NAC in males (63.6%) as compared to females (36.4%) has been attributed to their increased chest sun exposure. This gender-based difference in the incidence of BCC of the NAC has been documented in several studies.[11–14] Although ultraviolet (UV) light exposure is the foremost risk factor for BCC development, additional etiological factors such as environmental exposures, immunosuppression, genetic predisposition, injury (burns or trauma), ionizing radiation exposure, light-colored skin, sunburns, arsenic exposure, and previous BCCs at other sites have been implicated.[3]

Contrary to the prevailing notion that BCC is primarily induced by UV radiation exposure, emerging evidence supports the existence of BCC cases that are unrelated to UV radiation. Indeed, the traditional UV-induced pathway remains a significant contributor to BCC development, often associated with sun-exposed skin areas. Nonetheless, a subset of BCC occurrences is discernibly distinct, arising in

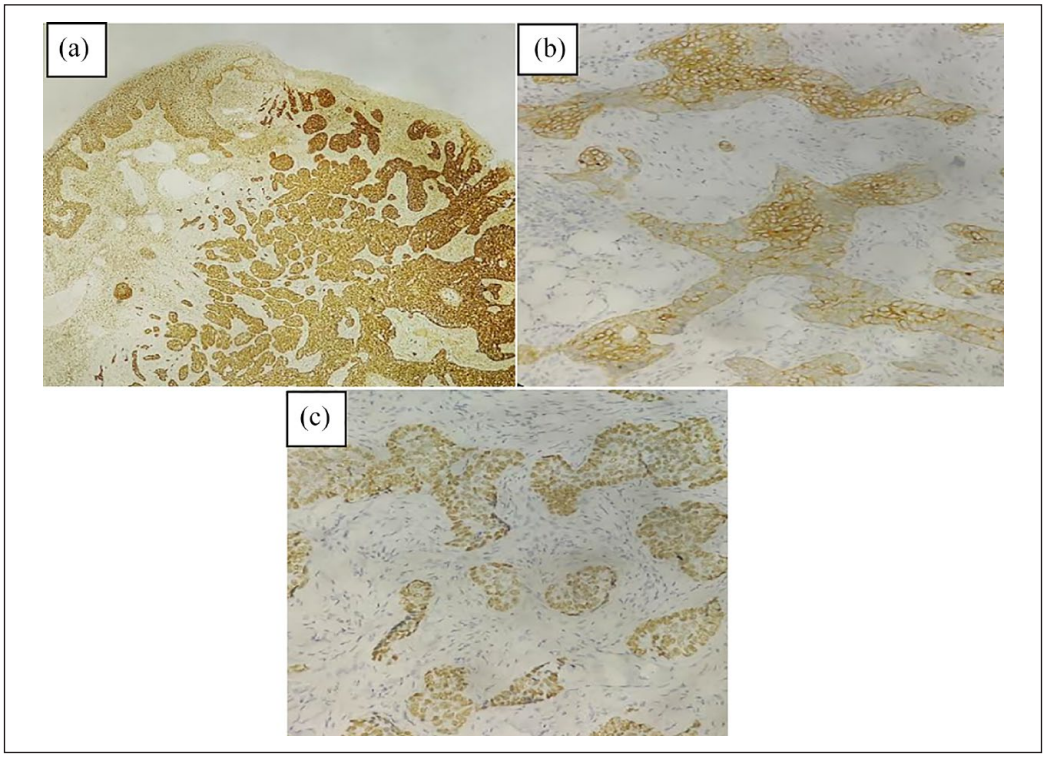

Figure 2. The immunohistochemical examination reveals a strong and diffuse expression of GATA3 (a), CK5/6 (b), and P63 (c).

glandular structures, where the traditional influence of UV radiation may not be as pronounced.[15,16]

BCC-NAC frequently emerges as a de novo lesion.[7] The patient of interest is a female individual with no notable history of sun exposure to the breast, suggesting that this factor does not account for the apparent predilection of BCC for the NAC as observed in males. The patient's history did not reveal any known risk factors for BCC-NAC, with the exception of a family history of breast cancer.

The distinction between BCC at the NAC and Paget disease of the nipple, papilloma of lactiferous ducts, melanoma, invasive ductal carcinoma, Bowen disease, or eczema can pose a formidable challenge to the clinician.[17,18] Nonetheless, histopathological examination of an excisional biopsy specimen typically provides a reliable means of establishing a definitive diagnosis.[14] The presence of proliferative nests of basaloid cells that emanate from the epidermis and extend into the superficial dermis and nipple stroma is sufficient for identifying this pathologic entity. Notably, these nests of tumor cells frequently involve the underlying lactiferous ducts, and a peritumoral cleft can often be observed between the tumor nests and the stroma. Moreover, the presence of melanin pigment in both tumor cells and stromal macrophages may be observed in some cases.[5,6,18]

In the NAC, BCC is considered to behave more aggressively than other anatomical sites, but other nonaggressive histological subtypes exist, and tumor recurrence is uncommon after the successful treatment of the primary cancer.[12,19] In a previous study, a report of 3 out of 31 cases of BCC in the NAC have developed apparent axillary lymphadenopathy with histologically confirmed cases.[12] Takeno et al.[19] found that axillary LN metastasis of BCC was about 11.5% in 26 patients, which was high compared to the rate of 0.01%–0.028% noted by Bruce et al.[20] The likely explanation is that the subareolar plexus is rich in a network of lymphatic capillaries, and this might provide a high potential for metastasis of tumors in this area, hence this relative difference.[3,18,19,20]

The consideration for sentinel lymph node biopsy (SLNB) is substantiated by the documented axillary LN positivity rate of approximately 10%.[19] Although our case did not manifest axillary LN involvement following a thorough clinical examination and comprehensive imaging studies, the rationale for SLNB in analogous cases remains salient. SLNB serves as an invaluable modality for precise disease staging and guiding subsequent therapeutic decisions, particularly in scenarios characterized by a discernible albeit low risk of axillary LN metastasis.[21]

An additional theory for the enhanced metastatic potential in BCC-NAC is based on the increased likelihood of tumor infiltration into the underlying lactiferous ducts and consequent invasion of the deeper soft tissue, which may not occur as frequently in BCCs of other anatomical locations. This greater tendency for infiltration and invasion is postulated to increase the possibility of metastasis.[5,6]

The management of BCC-NAC demands special attention,[4–6] given that large and ulcerated lesions have been associated with an increased risk of metastasis.[5]

Table 1. Clinical case summaries "insights from the literature."

Case.	Age	Sex	Histology	Location	Treatment	Recurrence
Our case	47	Female	Nodular Basal cell carcinoma (BCC)	right areola	Surgical excision	No recurrence
Huang et al.[2]	46	Female	A focal residual BCC in the papillary dermis	right areola	Surgical excision	No recurrence
Chun et al.[3]	60	Male	—	Nipple	—	—
Oram et al.[4]	60	Male	Mixed BCC composed of superficial and micronodular types	Left nipple	Lost to follow up	Lost to follow up
Kalyani et al.[5]	78	Male	Pigmented BCC	Left nipple and areola	Surgical excision	No recurrence
Jung et al.[6]	67	Female	Pigmented BCC	Right areola	Surgical excision	No recurrence
Almeida et al.[8]	77	Male	Superficial and nodular BCC	Right areola	Surgical excision	—
Zhu et al.[13]	47	Female	BCC of the superficial type	Left nipple	Surgical excision	No recurrence

Consequently, extended follow-up periods are advisable to monitor for recurrence and metastasis in patients with BCC-NAC.[6,9] Nonetheless, based on a study that examined reported cases and involved an 8-year follow-up period, it has been suggested that BCC-NAC does not possess a substantially greater malignant potential compared to BCC arising from other anatomical regions.[22] Therefore, while BCC-NAC may require heightened clinical vigilance due to its unique location, it appears to have a similar malignant potential as other BCCs.

The optimal treatment for BCC-NAC is determined by the extent of the tumor and its involvement with anatomical structures, such as LNs and deeper soft tissue.[2,5] The available therapeutic options encompass a range of modalities, including medical treatment, laser therapy, radiotherapy, wide excision, partial mastectomy, Mohs surgery, and simple mastectomy with LN dissection.[7,12,18,19] The choice of treatment modality should be based on a careful evaluation of the tumor's size, location, and the potential for functional and aesthetic outcomes. In addition, consideration should be given to the patient's medical history, overall health status, and individual treatment preferences.

In the present case, there was no evidence of lymphadenopathy or involvement of the lactiferous duct. Furthermore, the margins of the resected tissue were free from the presence of tumor cells. The patient underwent surgical excision and is currently being monitored for 5 months without any complications or adverse events (Table 1).

Given the rich lymphatic flow in the NAC and the relatively high incidence of LN metastasis, sentinel node navigation surgery should be considered in conjunction with local resection as part of the surgical treatment.[4,19]

Conclusion

In conclusion, BCC-NAC is a rare subtype of basal cell carcinoma that arises in the region of the nipple and areola. Due to its unique location, BCC-NAC presents a distinct set of clinical challenges for diagnosis and management. Surgical excision with a clear margin is typically the primary treatment modality for BCC-NAC, and extended follow-up periods are necessary for monitoring the risk of recurrence and metastasis. While the available evidence suggests that BCC-NAC does not exhibit a substantially higher malignant potential than other forms of BCC, careful clinical attention and ongoing surveillance are still crucial in achieving favorable clinical outcomes.

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Author contributions

All authors provided clinical care for the patient. A.M. wrote the manuscript and approved the final version. A.M. and S.B. contributed to the study's conception and design. Data collection was conducted by A.M. and S.B. Histological studies to confirm the histological type were performed by A.M. and L.T. L.T. provided feedback on the manuscript and approved the final version. All authors reviewed and approved the final manuscript.

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Ethics approval

Our institution does not require ethical approval for reporting individual cases.

Informed consent

Written informed consent was obtained from the subject for the publication of the case report.

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