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Case Report

When a skin lesion imitates a metastatic breast cancer: a diagnostic pitfall

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ABSTRACT

Adenocarcinoma involving the skin presents a diagnostic challenge, as it may represent either a rare primary cutaneous adnexal malignancy or cutaneous metastasis from an internal primary, most commonly breast carcinoma. We report the case of a 77-year-old female with a scalp lesion excised for presumed squamous cell carcinoma (SCC), with an immunohistochemical profile raising concern for metastatic breast carcinoma. Despite a strong family history of breast cancer, comprehensive systemic investigation with various imaging modalities, tumour markers, and screening mammograph identified no primary malignancy. Surgical re-excision was performed to achieve clear margins, and final histopathology demonstrated a small residual focus of adenocarcinoma with negative margins. In the absence of an identifiable visceral primary, findings were most consistent with primary cutaneous adnexal adenocarcinoma. This case emphasises the importance of a multidisciplinary approach and supports complete surgical excision with margin clearance as definitive management when metastatic disease is excluded.

Keywords: Primary adnexal adenocarcinoma, Cutaneous metastases, Breast cancer

INTRODUCTION

Adenocarcinoma involving the skin presents a significant diagnostic challenge because its clinical and histopathologic features can arise from either primary cutaneous adnexal structures or metastatic spread from internal malignancies. Primary cutaneous adenocarcinomas, including those of sweat or sebaceous gland origin, are rare entities.

However, the skin may also be a site for secondary involvement by malignancies such as breast, gastrointestinal, pancreaticobiliary, or lung adenocarcinoma.[1-3] These may represent the first clinical manifestation of an underlying visceral cancer such as an otherwise occult breast carcinoma.[4]

Distinguishing between primary and metastatic disease is essential, as the correct classification directly influences staging, therapeutic decision-making, and prognosis. Clinical appearance of the lesions alone is insufficient for accurate diagnosis, evaluation requires a multimodal approach that integrates histopathologic analysis, immunohistochemical profiling, and a thorough review of the patient's medical and oncologic history.[4,5]

This case report discusses the diagnostic considerations and investigative pathway involved in differentiating primary cutaneous adenocarcinoma from metastatic disease. By detailing a presentation concerning for metastatic breast cancer, it highlights the importance of a systematic and multidisciplinary approach when assessing adenocarcinoma within the skin and contributes

to the growing literature aimed at refining diagnostic accuracy in these challenging scenarios.

CASE REPORT

We present a case of a 77-year-old female patient who was referred to our hospital's general surgical clinic for consideration of a re-excision of a scalp lesion with histology suggestive of metastatic adenocarcinoma.

The patient initially presented in the community with a lesion macroscopically suggestive and biopsy proven to be a SCC on the vertex of the scalp. At the time of planned excision, a small nodule was noted just posterior to the SCC which was also excised (Figure 1). The histology demonstrated adenocarcinoma, with the tumour involving peripheral and deep margins of the specimen. Immunoprofiling was thought to be potentially compatible with a breast primary, with positive anticytokeratin monoclonal antibodies (AE1/AE3), cytokeratin 7 (CK7) immunotype, moderate nuclear staining with GATA-binding protein 3 (GATA3).

Figure 1: Nodular skin lesion on scalp vertex, marked circumferentially.

Of significance to note, the patient had a strong familial history for breast cancer with two first-degree relatives and one second-degree relative previously diagnosed. However, there had been no suggestion of positive breast cancer genes including for BReast CAncer (BRCA) gene. As such, the patient had been participating in two-yearly ultrasound and mammogram breast screening, with the most recent being four-months prior to this presentation. No lesions were detected, with breast imaging reporting and data system (BI-RADS) category 1. Additionally, on examination in the clinic there were no palpable breast lesions or abnormalities noted, with no associated cervical or axillary lymphadenopathy.

The patient was referred for a positron emission tomography/computer tomography (PET/CT) scan to assess for physiological uptake that could identify a primary source of malignancy including breast, gastrointestinal, or pancreaticobiliary tract. There was low-grade metabolism at the scalp vertex, but no primary source or other evidence of metastatic disease identified. A breast magnetic resonance imaging (MRI) was also performed and did not identify any suspicious enhancing breast lesions.

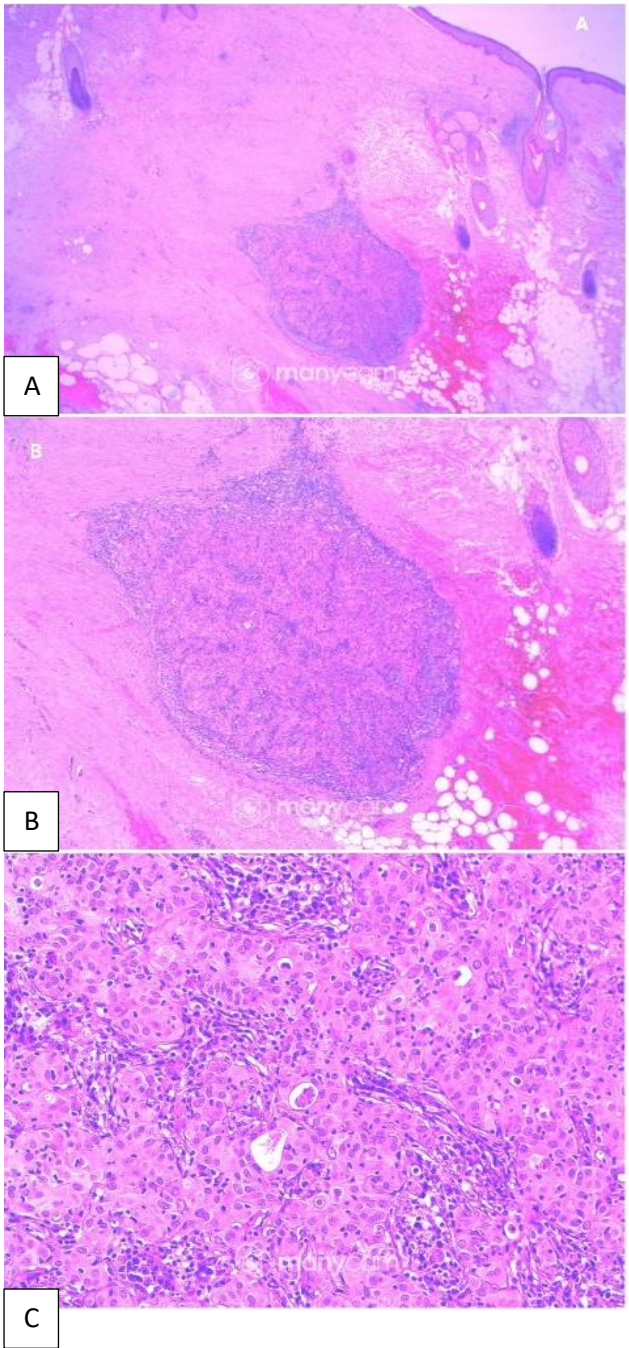
Cancer antigen (CA) 125, CA 15-3, CA 19-9, carcino embryonic antigen (CEA), and serum alpha-foetoprotein (ALP) were all negative.

This case was discussed at the local breast cancer multidisciplinary meeting with the recommendation being for operative re-excision. An elliptical excision over the lesion was performed, to ensure adequate deep and peripheral margins based on pre-site markings. A transpositional flap was created to facilitate wound closure. The patient was discharged on the same day of the procedure without complication.

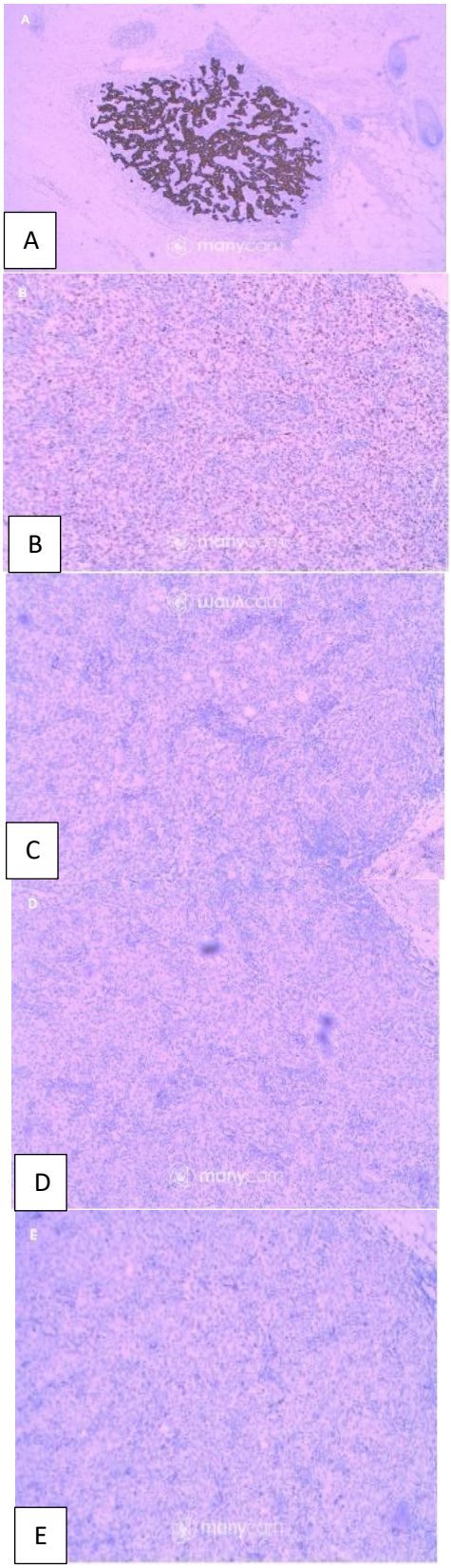
At the one-week post-operative follow up, the wound was healing well without any dehiscence (Figure 2). Re-excision histopathology demonstrated a small focus of residual adenocarcinoma from original excision, with clear margins: 1.3 mm from deep and at least 2.7 mm from radial margins (Figure 3 A-C). Immunohistochemistry profiling showed strong staining with CK7, moderate nuclear staining with GATA3, and minor staining with tumour protein 63 (p63). Additionally, there was no staining in the tumour of estrogen receptor (ER), progesterone receptor (PR), or SRY-box 10 (SOX10). In the context of negative breast and PET screening, the immunohistochemical profile was favoured to be compatible with a primary cutaneous adnexal adenocarcinoma.

Figure 2: One-week wound review following re-excision of scalp lesion with transpositional flap.

The case referred for discussion at the local Skin Cancer Multidisciplinary Meeting for consideration of adjuvant treatment. The consensus was that given margins were clear on re-excision and no other primary site was identified, that this was most likely primary adnexal adenocarcinoma and there was no role for adjuvant chemotherapy or radiotherapy. The patient was encouraged to continue breast surveillance screening, and she was also referred for an outpatient colonoscopy, which did not identify any abnormalities.



Figures 3 (A-C): Haematoxylin and eosin stains of skin lesion. (A) Low power view showing tumour within the dermis with adjacent scar tissue from previous excision, (B) Medium power view showing the tumour focus, (C) High power view of the tumour highlighting glands confirming adenocarcinoma.



Figures 4 (A-E): Immunohistochemical staining of skin lesion. (A) Positive CK7 which is not specific to primary site, (B) GATA3 staining with a small number of cells positive and can be seen in various tumour types, (C) ER status negative, (D) PR status negative, (E) SOX-10 stain negative.

DISCUSSION

Adenocarcinoma involving the skin is an uncommon finding and presents a significant diagnostic and management challenge. The principal difficulty lies in distinguishing primary cutaneous adenocarcinoma from cutaneous metastasis of an internal malignancy, as both entities may demonstrate overlapping clinical, histopathologic, and immunohistochemical features. Accurate classification is essential, as it directly determines surgical intent, the role of adjuvant therapy, and long-term surveillance strategies.[1,5,6]

Primary cutaneous adenocarcinomas are rare malignant neoplasms arising from eccrine, apocrine, sebaceous, or follicular structures and account for a small fraction of non-melanoma skin cancers.[7] They most frequently occur in elderly patients and commonly involve the head and neck region, including the scalp.[8] In contrast, cutaneous metastases to scalp, while well described, are uncommon and typically occur in setting of known systemic malignancy, most often breast carcinoma in women.[9]

Histopathologic evaluation and immunohistochemical profiling are central to diagnosis. However, no single marker reliably differentiates primary from metastatic adenocarcinoma. CK7 positivity is present in many epithelial malignancies, including both breast carcinoma, adnexal tumours, and lung, upper gastrointestinal, and pancreatic limiting its specificity. GATA3 has been widely used as a marker of breast epithelial differentiation, and its staining is usually very diffuse in breast cancer.[10,11] However, this is non-specific and it is now recognised to be expressed in a proportion of primary cutaneous adnexal carcinomas, particularly those with apocrine differentiation.[12] Consequently, contemporary diagnostic algorithms recommend the use of multi-marker panels and correlation with clinical and radiologic findings rather than reliance on isolated immunohistochemical results.[13]

In this case, the initial immunoprofile raised concern for metastatic breast carcinoma, prompting comprehensive systemic investigation. The absence of detectable visceral malignancy on PET/CT and breast MRI significantly reduced the likelihood of metastatic disease. From a management standpoint, exclusion of a systemic primary is a prerequisite before assigning a diagnosis of primary cutaneous adenocarcinoma, as this diagnosis is considered one of exclusion.[14]

Surgical excision with histologically clear margins remains the cornerstone of management for primary cutaneous adnexal adenocarcinoma.[15] In cases where margins are involved or close, current literature supports further surgical re-excision as the preferred next step, provided this is anatomically and functionally feasible.[15,16] Several retrospective series have demonstrated significantly higher rates of local recurrence in patients with positive margins, emphasising the importance of achieving complete excision.[17,18] When re-excision is not possible due to anatomical constraints, particularly in the head and neck region, or when repeated surgery would result in unacceptable morbidity, adjuvant radiotherapy is recommended to improve local control.[19,20] The role of systemic therapy in primary cutaneous adenocarcinoma remains ill-defined and is generally reserved for high-risk features such as positive margins, perineural invasion, unresectable disease, or nodal involvement.[17,20] Given the absence of such features in this patient, multidisciplinary consensus appropriately favoured observation following complete excision. This approach is consistent with reported outcomes in surgical series, where margin-negative resection alone has been associated with favourable local control.[18,19]

Surveillance following resection of primary cutaneous adnexal adenocarcinoma is not standardised due to the rarity of the disease. Most authors recommend regular clinical follow-up with focused skin and regional lymph node examination, particularly during the first two to three years when recurrence risk is highest.[21,22] In cases where the initial differential included metastatic disease, continued surveillance for occult internal malignancy is prudent. In this patient, ongoing breast screening and age-appropriate gastrointestinal surveillance were recommended, aligning with risk-adapted follow-up principles described in the literature.[23]

CONCLUSION

Primary cutaneous adenocarcinoma is a rare malignancy requiring careful diagnostic evaluation to exclude metastatic disease. Management is centred on complete surgical excision with clear margins, supported by multidisciplinary assessment. When systemic malignancy is excluded and margins are negative, surgery alone is often sufficient, with structured clinical surveillance forming the basis of ongoing management. This case highlights the importance of integrating pathology, imaging, and surgical principles to guide appropriate treatment and follow-up in cutaneous adenocarcinoma.

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