CASE REPORT

REVISED Case Report: A Pathological Odyssey in Primary Cutaneous Apocrine Carcinoma [version 3; peer review: 2 approved, 1 approved with reservations]

Previously titled: Case Report: An in-depth look into apocrine carcinoma of the axilla - a rare case presentation.

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Abstract

Apocrine carcinoma is an extremely rare malignant cutaneous neoplasm that usually arises in areas with a high density of apocrine glands. Diagnosis can be challenging as tumours share histological and immunophenotypic characteristics with them. At first evaluation, the disease is often assumed to be benign. There have been approximately 100 reports of apocrine neoplasms in the literature.

A 48-year-old male presented with a right axillary mass which increased in size over a period of 2 years. The patient was reported to have had ayurvedic therapy, but his swelling remained unchanged. Axillary lymph nodes were palpable. USG axilla suggested a well-defined fungating solid isoechoic lesion. USG neck did not reveal any abnormality. The mass was surgically excised as a whole by removing the overlying skin with margins and lymph node excision. The patient was diagnosed with primary apocrine carcinoma after surgical excision. The differentials include adenocarcinoma of breast and prostate and apocrine adenoma. There are no established standards for the care of this form of carcinoma due to its rarity and the absence of clinical studies. A literature evaluation and further reporting will aid in developing diagnostic standards and the most efficient treatment options.

Open Peer Review

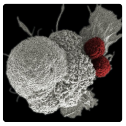
Approval Status ✓ ? ✓

	1	2	3
version 3 (revision) 08 Nov 2023	✓ view		✓ view
version 2 (revision) 27 Sep 2023		? view	
version 1 10 Jul 2023	? view		

1. **Rehan Zahid**, The University of Iowa Healthcare, Iowa City, USA
2. **Nour Kibbi**, Stanford University School of Medicine, Palo Alto, USA
3. **Dr. Ashwinkumar Barsagade**, Andaman and Nicobar Islands Institute of Medical sciences, Port Blair, India

Any reports and responses or comments on the article can be found at the end of the article.

Keywords
Apocrine carcinoma, Axillary mass, rare presentation, apocrine neoplasms, solid lesion, lymph node excision, malignant, surgical excision.



This article is included in the Oncology gateway.

This article is included in the Datta Meghe Institute of Higher Education and Research collection.

Corresponding author: Dr. Suhit Naseri (drsuhitnaseri@gmail.com)

Author roles: Naseri DS: Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Resources, Writing – Original Draft Preparation, Writing – Review & Editing; **Shukla S**: Conceptualization, Project Administration, Supervision, Validation, Visualization; **Acharya DS**: Supervision; **Vagha S**: Supervision, Validation

Competing interests: No competing interests were disclosed.

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First published: 10 Jul 2023, **12**:803 https://doi.org/10.12688/f1000research.135154.1

REVISED **Amendments from Version 2**

Revisions in response to the reviewer's comments include:

Modification of the title.
Inclusion of further literature.
An elaboration on the Tru-Cut biopsy. (Added in Notes to Reviewers).
A clarification on the rationale behind the surgical margin range. (Added in Notes to Reviewers).
Proper placement of abbreviations.

Any further responses from the reviewers can be found at the end of the article

Introduction

Apocrine carcinoma of the axilla is a seldom-seen form of breast cancer that originates in the axillary sweat glands. This disease has been reported to be an invasive ductal carcinoma subtype, the most prevalent form of breast cancer among women. From a surgical perspective, apocrine carcinoma of the axilla may present as a palpable mass or a non-palpable abnormality on imaging studies, such as mammography or ultrasound. Treatment typically involves surgical excision of the tumor with clear margins, which may be followed by radiation therapy and/or systemic chemotherapy depending on the stage and biology of the cancer. From a pathological standpoint, Large, pleomorphic cells with an abundance of eosinophilic cytoplasm and prominent nucleoli are seen in axillary apocrine carcinomas. Apocrine carcinoma of the axilla is uncommon, but it can still be a clinically relevant diagnosis that has to be treated promptly and effectively to provide the patient the best chance of survival.

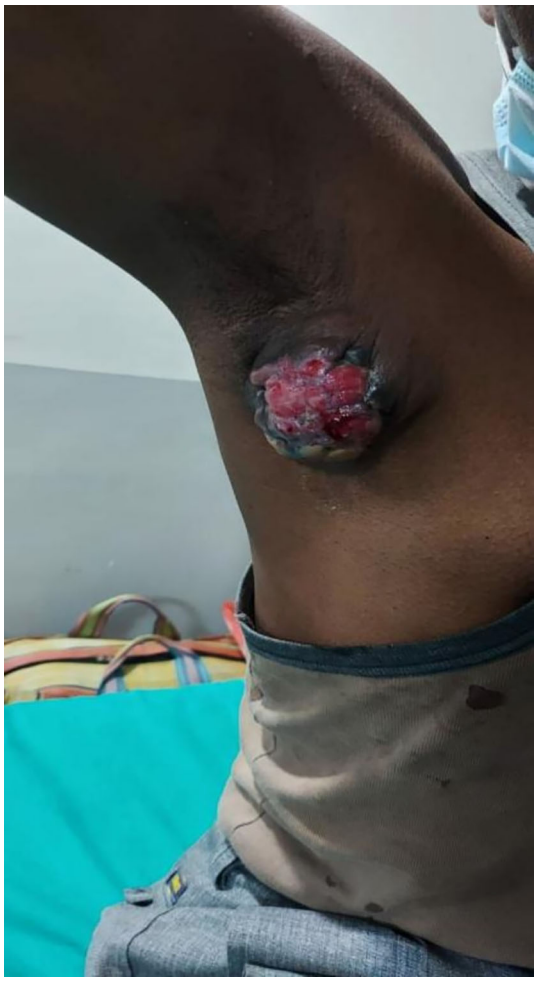

Figure 1. Clinical image of right axillary mass with inflammation.

Case report

In 2022, a male aged 48, hailing from South Asian origins and employed as a carpenter, visited the surgery department due to the presence of a lump (Figure 1) in the axilla. The patient initially discovered a painless, indurated nodule in their right axilla around a year back. Over time, this nodule increased in size until the time of their presentation that is the size of 8 × 8 × 2.3 cm. The patient attempted ayurvedic treatment for a year, but the lesion continued to progress. On local examination, signs included inflammation of the skin covering the area, occasional discharge of a serosanguinous nature, and mild pain in the affected axilla. The patient did not experience any constitutional symptoms such as fever, weight loss, night sweats, or loss of appetite. The patient had no family history of malignancy. A physical evaluation and Ultrasonography (USG) for both breasts did not find any abnormalities. USG of the right axilla suggested a well-defined solid isoechoic lesion with multiple microcalcifications with prominent vascularity. Additionally, the patient had a preexisting condition of hypertension and was taking antihypertensive medications. Patient revealed his past habit of smoking bidi once a day. He did not consume alcohol.

A Tru Cut Biopsy was carried out which revealed cells showing moderate amount of eosinophillic to pale vaccuolated cytoplasm, Eccentric nuclei showing mild hyperchromasia and significant mitotic activity. Another population of cells seen with squamoid feature intervening the stroma showing desmoplastic reaction. Biopsy findings were suggestive of Malignancy of Adnexal origin.

Patient underwent wide local excision of the right axillary lesion with right axillary lymphadenectomy up to level III was carried out. A sufficient clearance margin of 1 - 1.5 cm was taken, and primary closure of defect was achieved.

Seven axillary lymph nodes were isolated, the largest lymph node was measured to be 4×2×1.5 cm.

Grossly (Figure 2), the tumour mass was white, firm in consistency and measured 4×4×3.5 cm. On the cut section, solid, homogenous blackish areas were identified with the involvement of overlying skin.

Microscopically, sections from superior, anterior and posterior margins showed unremarkable squamous lining epithelium with unremarkable deeper tissue and adnexal structure with few distended ducts of histopathology. Section from the inferior margin (Figure 3) was positive for infiltration by malignant epithelial cells. Sections also show fibro-collagenous

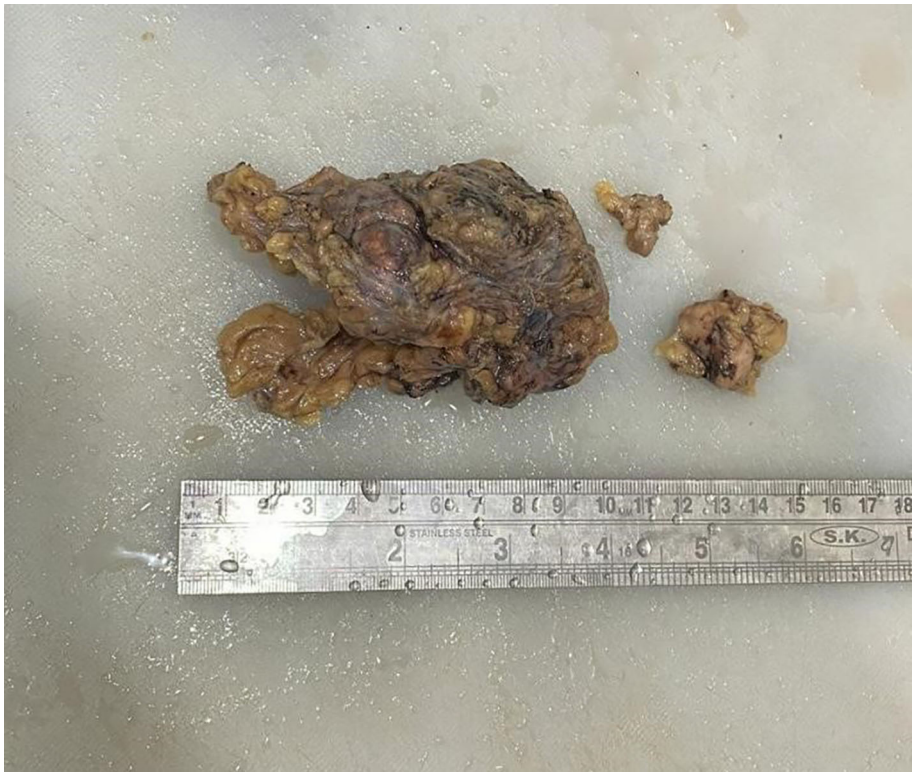

Figure 2. Gross image of excised specimen of axillary mass with a lymph node.

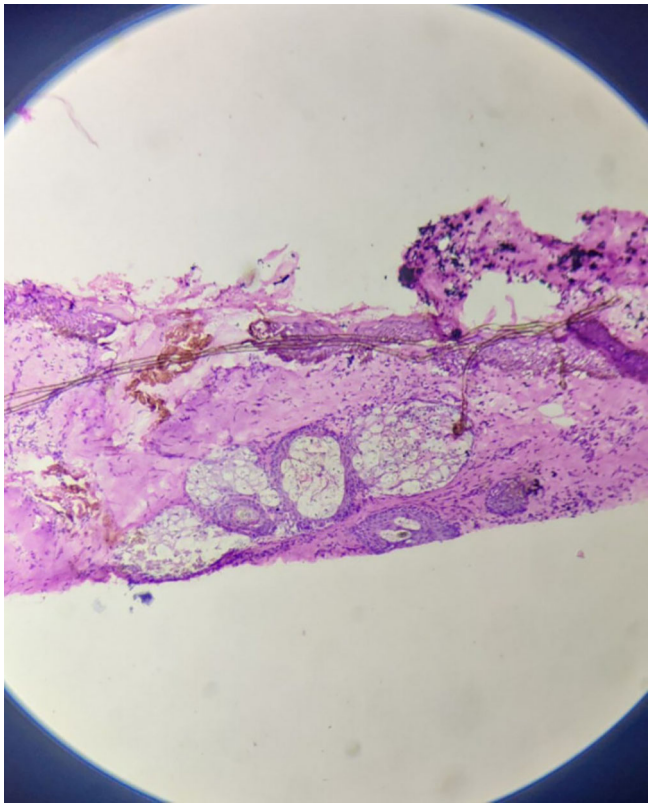

Figure 3. **High power view of inferior surgical margin on frozen section – positive for infiltration by malignant cells.**

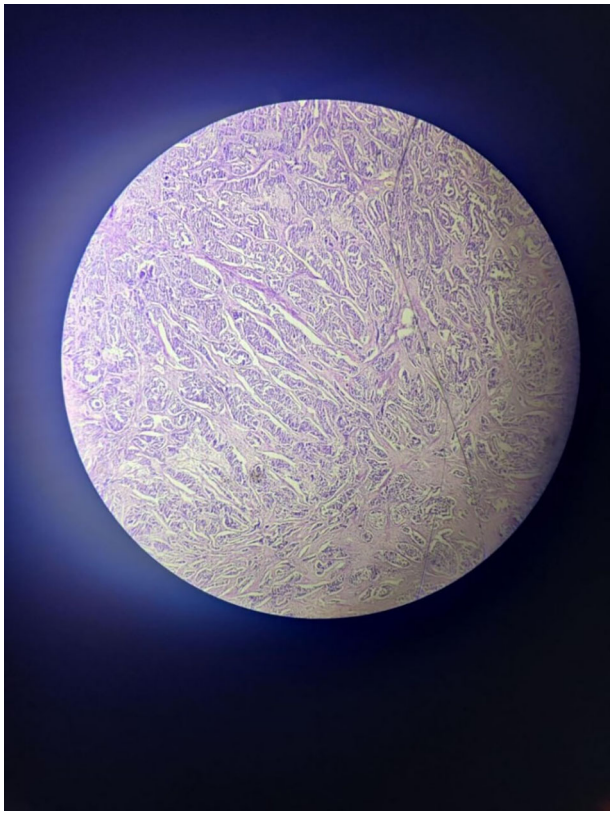

Figure 4. **Tumor mass – scanner.**

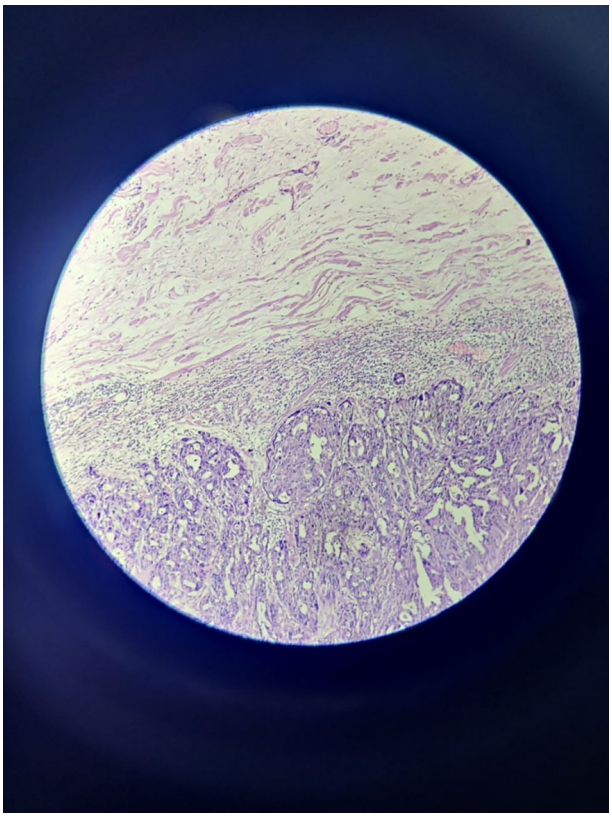

Figure 5. **Tumor mass 10× – low power view.**

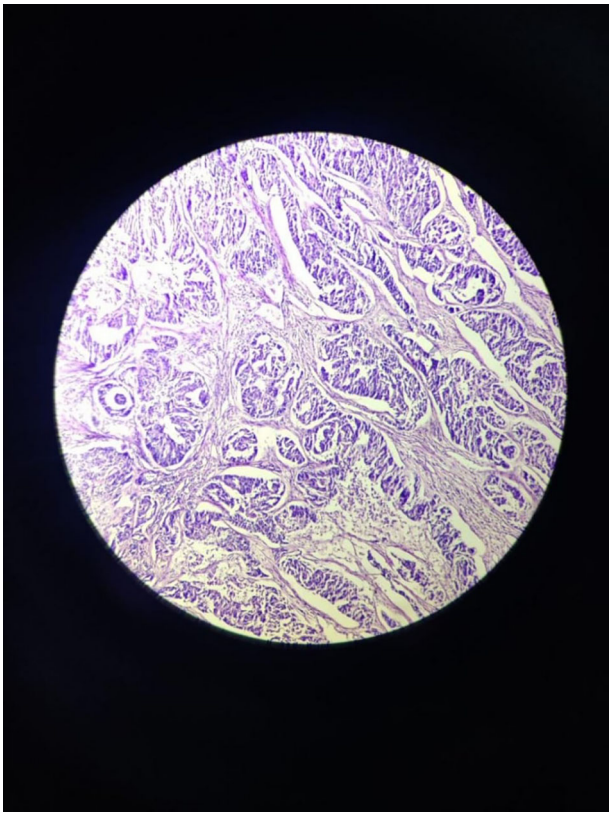

Figure 6. **Tumor mass - 40× – high power view.**

areas with minimal scattered inflammatory infiltrate. Sections from the tumour were also positive for perineural and lymphovascular invasion.

Section from all seven lymph nodes shows histopathological features suggestive of metastatic deposits of epithelial malignancy.

The epidermis is visible in some portions of the tumour, which has a dermis with mostly papillary cystic architecture. Focal inflammation with numerous benign apocrine glands were noted.

The tumour with papillary architecture (Figures 4–6) was found to have fibrovascular cores lined by eosinophilic epithelial cells. The patient's recuperation after surgery proceeded without any complications. The patient's case was discussed in the hospital's interdisciplinary tumour board and he was considered for adjuvant radiotherapy. Considering the metastatic involvement in the lymph nodes and to exclude the possibility of distant metastasis, a comprehensive whole-body Positron emission tomography–computed tomography (PET-CT) scan was performed, revealing no signs of distant metastatic spread.

A thorough follow-up plan was advised to the patient, but he did not follow through.

Discussion

Apocrine carcinoma is an extremely uncommon adnexal malignancy with limited data on histologic prognostic factors and patient outcomes.[1] The axilla and adjacent medial upper arm are the most typical sites for apocrine carcinoma.[2] The tumour, which derives from pleuripotent adenexal cells capable of eccrine and follicular development, had first been discovered by Goldstein in 1982.[3] Reddish-purple subcutaneous nodules and solid or cystic masses are common characteristics of these tumours. Skin ulceration may be a comorbid condition, and they are frequently locally advanced when diagnosed. This tumour has a sluggish rate of growth, is locally invasive, and has the potential to spread to nearby lymph nodes, the lungs, the liver, the bone, and the brain.[4] When metastasis occurs, it occurs by lymphatic and hematogenous spread.[4] At the time of diagnosis, lymph node metastases were present in over fifty per cent of all reported individuals suffering from apocrine carcinoma, it is critical to consider the choice for SLN (sentinel lymph node) biopsy plus localised lymph node dissection. While there is still debate about the diagnostic criteria for apocrine carcinoma, decapitation secretion within eosinophilic epithelial cells is seen as an important confirmation of apocrine differentiation. If the SLN is positive, axillary lymphadenectomy ought to be performed. The recommended treatment for these lesions is wide local excision.[5] Apocrine gland carcinomas and eccrine carcinomas are the two primary subtypes of sweat gland carcinomas. Apocrine carcinomas appear as hard, rubbery, cystic, solitary or numerous, non-tender masses with red to purple overlaying skin. Eccrine gland carcinomas lack distinguishing clinical characteristics, rendering gross examination diagnosis nearly difficult. They often only affect older individuals and present as quasi-tender, subcutaneous nodules.[6] Although the tumour often arises de novo, it can potentially result from previously present benign tumours like apocrine hyperplasia or apocrine adenoma.[7] Several studies have shown that utilising CD15 and lysozyme staining can assist differentiate Apocrine malignancy from Eccrine malignancy. Furthermore, the presence of androgen receptors has been found to be closely linked to Apocrine carcinoma. In immunohistochemical analysis, several stains may be utilised to assist in determining the diagnosis of Apocrine carcinoma. 1,5 Cytokeratin AE1/AE3, CAM5.2, epithelial membrane antigen (EMA), smooth muscle antigen (SMA), periodic acid-Schiff positive with diastase resistance, and GCDFP-15 are all beneficial in confirming the diagnosis.[8] Wide local excision is the preferred method of management of primary cutaneous ductal apocrine carcinoma. In addition to excision, chemotherapy as well as radiotherapy have been utilised, but they haven't significantly reduced mortality or morbidity among patients with either localised or metastatic disease. The total number of reported instances and the amount of follow-up data that currently exists, both seem insufficient for determining the prognosis. Therefore, there is a need for further case accumulation.

Conclusion

The rare tumour referred to as apocrine carcinoma has a characteristic but non-specific histological appearance. For determining the prognosis and formulating particular therapy recommendations, the reported cases and follow-up data appear to be insufficient. Hence, additional cases needs to be collected.

Consent

Written informed consent for publication of their clinical details and clinical images was obtained from the patient.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

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Publisher Full Text

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Publisher Full Text

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PubMed Abstract | Publisher Full Text | Free Full Text

Open Peer Review

Current Peer Review Status: ✔ ? ✔

Version 3

Reviewer Report 13 June 2024

https://doi.org/10.5256/f1000research.158522.r271478

✔ **Dr. Ashwinkumar Barsagade**
Andaman and Nicobar Islands Institute of Medical sciences, Port Blair, India

This is a well written case report of rare malignancy, primary cutaneous apocrine carcinoma. the clinical findings, diagnostic workup including pathological findings and treatment are reported in detail. the case report in its discussion emphasizes the difficulties in recognizing and controlling this cancer due its rarity and inadequate prognostic data. The focus on the importance of incorporating apocrine carcinoma in the differential diagnosis of axillary tumors is helpful.

Is the background of the case's history and progression described in sufficient detail?
Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Yes

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Cytopathology and Histopathology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 30 November 2023

https://doi.org/10.5256/f1000research.158522.r221655

Rehan Zahid
Plastic Surgery, The University of Iowa Healthcare, Iowa City, IA, USA

I have reviewed the revisions. You can change the status to Approved. One thing I wasn't able to access was the list of references.

Is the background of the case's history and progression described in sufficient detail?
Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Yes

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 2

Reviewer Report 03 October 2023

https://doi.org/10.5256/f1000research.156396.r202439

Nour Kibbi

Stanford University School of Medicine, Palo Alto, California, USA

This is a case report describing a rare presentation of a rare neoplasm. The authors should rename this as a primary cutaneous apocrine carcinoma since an invasive ductal breast carcinoma could not be found. The novelty of the case is not entirely clear and the authors might consider completing a literature review to determine what this case adds to the existing literature on this rare tumor.

Regarding language, the report is a bit wordy at times and would benefit from further editing for brevity and consistency. The histopathological images provided are not of adequate quality and would benefit from retaking with a camera attached to the microscope. There are abbreviations used without being spelled out, such as USG. It is also not clear what a Tru Cut biopsy is. The surgical margin is indicated as a range and it is not clear why.

Is the background of the case's history and progression described in sufficient detail?
Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Yes

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Rare tumors

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 03 Nov 2023

Dr. Suhit Naseri

The authors should rename this as a primary cutaneous apocrine carcinoma since an invasive ductal breast carcinoma could not be found.
- Modification of the title is done.

The novelty of the case is not entirely clear and the authors might consider completing a literature review to determine what this case adds to the existing literature on this rare tumor.
- Inclusion of further literature has been done.

Regarding language, the report is a bit wordy at times and would benefit from further editing for brevity and consistency.
- The required language corrections have been implemented.

The histopathological images provided are not of adequate quality and would benefit from retaking with a camera attached to the microscope.
- Regrettably, due to the unavailability of the necessary resources, it is not feasible to retake the images.

There are abbreviations used without being spelled out, such as USG. It is also not clear what a Tru Cut biopsy is. The surgical margin is indicated as a range and it is not clear why.
- Proper placement of abbreviations.
- A Tru-Cut, also known as a Tru-Cut biopsy, is a medical procedure used to obtain a small core of tissue from a specific area of the body for diagnostic purposes.
- The surgical margin is expressed as a range to account for variations in tumor size and shape.

Competing Interests: None.

Version 1

Reviewer Report 24 August 2023

https://doi.org/10.5256/f1000research.148257.r192585

?

Rehan Zahid
Plastic Surgery, The University of Iowa Healthcare, Iowa City, IA, USA

I appreciate the authors for presenting this rare carcinoma. The authors have duly noted the lack of literature of such rare cases which makes it even more important to provide as much detail as possible when presenting this case.

I suggest starting with elaborating the presentation. Progression of disease including a timeline and more details of the history and physical findings. Rephrase the first sentence of the case report section.

Emphasize on the treatment plan. Was a biopsy done to confirm the diagnosis before the final excision? If it was planned as an excisional biopsy before being identified as a carcinoma then was a wide local excision carried out? Or planned? Especially with a positive inferior margin. Please

clarify the surgical treatment that the patient underwent including lymph node dissection.

What were the surgical sequelae post excision? Was the defect closed primarily and was there any post surgical complication including wound healing delays or ulcerative margins? Although the patient was lost to follow up, it would be beneficial to provide as much data as available in terms of the outcome. It helps to identify the progression of disease and overall prognosis.

Was any other work up planned to check for metastatic disease?

Finally the authors should reflect on the findings of this case report and how it contributes to the existing literature on apocrine carcinoma. I feel there is more information that could be provided to contribute to the already scarce existing literature. Although it may not be practically feasible in many instances but all efforts should be made to pursue the patient for follow up and determine outcome of the disease.

Is the background of the case's history and progression described in sufficient detail?
Partly

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
No

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Partly

Is the case presented with sufficient detail to be useful for other practitioners?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Plastic and Reconstructive Surgery

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 21 Sep 2023

Dr. Suhit Naseri

1. Progression of disease including a timeline and more details of the history and physical findings.

In 2022, a male aged 48, hailing from South Asian origins and employed as a carpenter, visited the surgery department due to the presence of a lump (Figure 1) in the axilla. The patient initially discovered a painless, indurated nodule in their right axilla around a year

back. Over time, this nodule increased in size until the time of their presentation that is the size of 8 x 8 x 2.3 cm. The patient attempted ayurvedic treatment for a year, but the lesion continued to progress. On local examination, signs included inflammation of the skin covering the area, occasional discharge of a serosanguinous nature, and mild pain in the affected axilla. The patient did not experience any constitutional symptoms such as fever, weight loss, night sweats, or loss of appetite. The patient had no family history of malignancy. A physical evaluation and USG for both breasts did not find any abnormalities. USG of the right axilla suggested a well-defined solid isoechoic lesion with multiple microcalcifications with prominent vascularity. Additionally, the patient had a preexisting condition of hypertension and was taking antihypertensive medications. Patient revealed his past habit of smoking bidi once a day. He did not consume alcohol.

2. Emphasize on the treatment plan. Was a biopsy done to confirm the diagnosis before the final excision? If it was planned as an excisional biopsy before being identified as a carcinoma then was a wide local excision carried out? Or planned? Especially with a positive inferior margin. Please clarify the surgical treatment that the patient underwent including lymph node dissection.

A Tru Cut Biopsy was carried out which revealed cells showing moderate amount of eosinophillic to pale vaccuolated cytoplasm, Eccentric nuclei showing mild hyperchromasia and significant mitotic activity. Another population of cells seen with squamoid feature intervening the stroma showing desmoplastic reaction. Biopsy findings were suggestive of Malignancy of Adnexal origin.
Patient underwent wide local excision of the right axillary lesion with right axillary lymphadenectomy up to level III was carried out.

3. What were the surgical sequelae post excision? The patient's recuperation after surgery proceeded without any complications.Was the defect closed primarily and was there any post surgical complication including wound healing delays or ulcerative margins?

A sufficient clearance margin of 1-1.5 cm was taken, and primary closure of defect was achieved. The patient's recuperation after surgery proceeded without any complications.

4. Was any other work up planned to check for metastatic disease?

Considering the metastatic involvement in the lymph nodes and to exclude the possibility of distant metastasis, a comprehensive whole-body PET-CT scan was performed, revealing no signs of distant metastatic spread.

Competing Interests: No competing interests.