Case Report

Cytokeratin Positivity in Secondary Angiosarcoma of Breast: A Diagnostic Pitfall

Abstract

Reappearing breast lump in a known case of breast carcinoma often turns out to be a recurrence of the carcinoma. However, in patients receiving radiotherapy for the disease, possibility of secondary angiosarcoma should also be suspected. Secondary angiosarcoma can pose a challenge in pathological diagnosis especially in small trucut biopsies. Aberrant expression of epithelial marker can also add to the difficulty. In this article, we report a case wherein similar difficulties were faced during the diagnosis.

Keywords: *Angiosarcoma, breast, carcinoma, cytokeratin positivity, secondary*

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Introduction

Angiosarcoma of the breast is rare, accounting for 0.04% of all soft-tissue breast tumors.[1] It can be primary or present as a secondary tumor often the following radiotherapy. Primary angiosarcoma arises in younger women with no known risk factor while secondary angiosarcoma of the breast is more prevalent in older patients with a history of radiation exposure or lymphedema. The relative risk for developing angiosarcoma of the chest and/or breast among women with a history of invasive breast cancer has been estimated to be 11.6%.[2]

Over 200 cases of radiation-induced angiosarcoma of the breast are currently known in literature.[3] Secondary angiosarcoma commonly presents with predominant cutaneous involvement. Only a minority of cases (~7%) present as a palpable mass in the breast.[4]

Angiosarcoma has distinct morphological features with a vasoformative pattern. However, small biopsies may pose a problem due to paucity of diagnostic material combined with a strong differential of carcinoma recurrence, thus making preoperative diagnosis difficult. Aberrant immunoexpression of epithelial markers in angiosarcoma can also mislead toward a diagnosis of breast carcinoma. Both these problems were faced in our case. We hereby report an unusual case of secondary angiosarcoma arising in an irradiated breast as a palpable mass and with aberrant cytokeratin (CK) expression.

Case Report

A 55-year-old female was diagnosed of invasive carcinoma of the right breast in 2010 and managed with breast conservation surgery and local radiotherapy. She presented 6 years later with a lump at surgery site. A trucut biopsy was done which showed fibro-fatty tissue with scattered tumor cells in one corner of the biopsy. The tumor cells were infiltrating the adipose tissue diffusely with vague acini formation [Figure 1a]. Suspecting a recurrence of infiltrating carcinoma, immunohistochemistry (IHC) for CK was done which showed strong positivity in tumor cells [Figure 1b]. A diagnosis suggestive of recurrence of breast carcinoma was rendered following which the patient underwent right-sided mastectomy.

Resected specimen showed an infiltrating lesion in the right breast parenchyma with gray-white and firm cut surface [Figure 2]. Overlying skin was largely normal.

Microscopic examination showed similar malignant tumor cells as seen in biopsy, but with a distinct sinusoidal pattern

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suggesting it to be of vascular origin. Intersecting vascular channels lined by pleomorphic cells were observed. The cells had varied amount of cytoplasm with distinct hyperchromatic nuclei and anisonucleosis [Figure 3a and b].

IHC for CD34, CD31, and CK showed strong positivity in tumor cells [Figure 4]. Therefore, a diagnosis of secondary postradiation epithelioid angiosarcoma was rendered.

Discussion

Reappearing mass in a known case of breast carcinoma is a worrisome sign implying poor prognosis. It proves to be a recurring invasive carcinoma most of the time; however, differential of a secondary malignancy should also be kept in mind. An attempted biopsy or aspirate from a recurring lump in a treated case of breast carcinoma may sometimes be diagnostically challenging due to poor overall yield, especially in cases with diffuse necrosis and fibrosis of the tumor. Scattered malignant looking cells without any specific pattern may render multiple differential diagnoses with relapse of the breast carcinoma being most probable. However, in the setting of previous irradiation, similar to our case, caution must be exercised. It should be kept in mind that irradiated breast is prone to secondary sarcomas with angiosarcoma being the most prevalent.[5] In cases of doubtful morphology, immunostaining with epithelial markers must be done to confirm the suspicion of relapse. A diagnosis of relapse of breast carcinoma can be confidently made on the basis of strong CK expression by tumor cells. However, angiosarcomas, especially of epithelioid type, pose a challenge. They occasionally show positivity for CK and focally for EMA.[6,7]

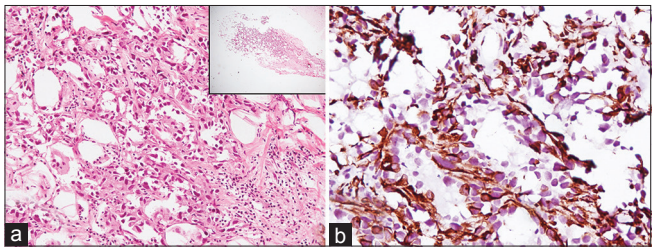

Figure 1: Trucut biopsy of the right breast lump showed scattered tumor cells in fibroadipose tissue, (a, ×200); Inset showing cellularity in the corner of the biopsy, (H and E, ×100). Tumor cells with strong cytokeratin expression, (b, ×400), immunohistochemistry

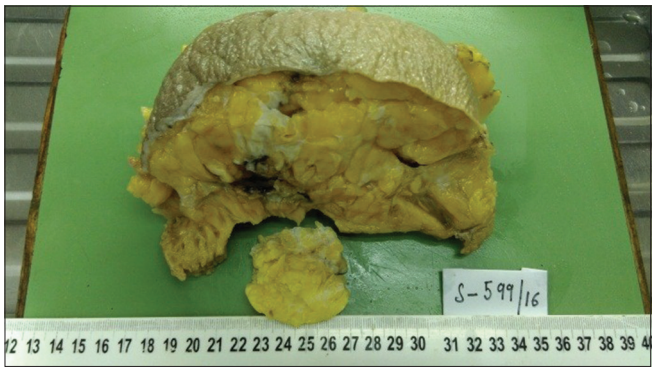

Figure 2: Right mastectomy specimen

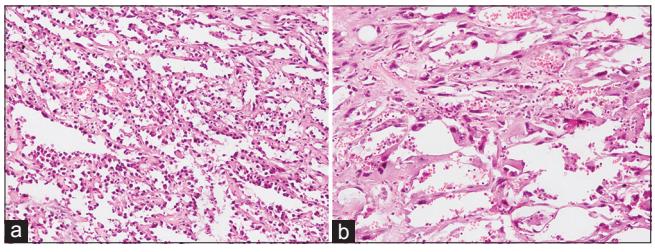

Figure 3: Microscopic examination of resection specimen showed tumor cells arranged in anastomosing vascular channels containing red blood cells, (a, H and E, ×200). Tumor cells are epithelioid to elongated with hyperchromatic nuclei and moderate to abundant eosinophilic cytoplasm, (b, H and E, ×400)

Adding to the difficulty, positivity for estrogen and progesterone receptors have also been reported in secondary angiosarcomas of the breast.[8] Endothelial markers such as factor VIII, CD 34, and CD31 come to rescue in such cases. Angiosarcomas almost always express these markers of vascular differentiation with the exception of rare cases of high grade and poor differentiation. Tumor cells in breast carcinoma do not express endothelial markers. Immunophenotyping of such tumors with conflicting morphology should thus be done with a comprehensive panel including both vascular and epithelial markers. Secondary angiosarcomas are treated with radical surgery with negative resection margins followed by chemotherapy. However, recurrent breast carcinoma is treated by mastectomy followed by neoadjuvant chemotherapy and/or hormonal therapy. The difference in management and evidence of better faring of patients treated for recurrent breast carcinoma as compared to secondary angiosarcoma mandate their distinction by histology and immunophenotyping.

Conclusion

We, therefore, stress that despite rarity, secondary angiosarcoma should be considered as a possibility in cases of suspected recurrence of breast lump. High index of suspicion should be maintained in postradiotherapy cases. When trucut biopsy of the recurrent lump is done, a panel of IHC markers should be applied. It is desirable to include epithelial as well as endothelial markers in such cases to avoid misdiagnosis.

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Nil.

Conflicts of interest

There are no conflicts of interest.

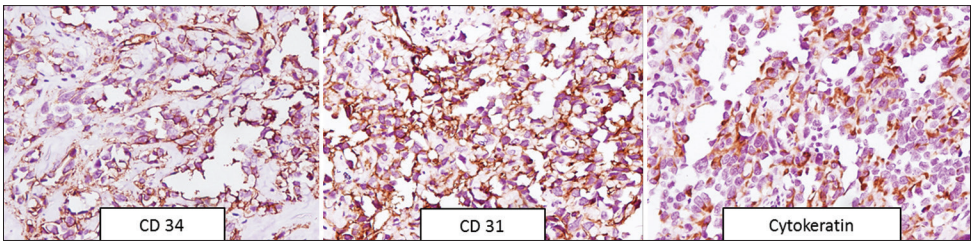

Figure 4: Tumor cells expressed CD34, CD31 and cytokeratin, ×200, immunohistochemistry

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