GAVIN PUBLISHERS

OPEN ACCESS

Annals of Case Reports

Lin MS, et al. Ann Case Report 6: 632.

DOI: 10.29011/2574-7754.100632

Case Report

# Post-Biopsy Granulomatous Reaction Mimicking Ductal Carcinoma in Situ: Report of 2 Cases

**Michelle S. Lin, Mary R. Schwartz, Hazel L. Awalt, Jae Y. Ro***

Department of Pathology and Genomic Medicine, Houston Methodist Hospital, Weill Medical College of Cornell University, Houston, TX, USA

***Corresponding author:** Jae Y. Ro MD PhD, Department of Pathology and Genomic Medicine, Houston Methodist Hospital, Weill Medical College of Cornell University, 6565 Fannin Street, Houston, TX 77030, USA

**Citation:** Lin MS, Schwartz MR, Awalt HL, Ro JY. (2021) Post-Biopsy Granulomatous Reaction Mimicking Ductal Carcinoma in Situ: Report of 2 Cases. Ann Case Report 6: 632. DOI: 10.29011/2574-7754.100632

**Received Date:** 11 February, 2021; **Accepted Date**: 19 February, 2021; **Published Date:** 25 February, 2021

## Abstract

Granulomatous lesions in the breast are uncommon, have a variety of etiologies, and may mimic malignancies on clinical, radiologic, and histopathologic examination. We present two cases of post-biopsy granulomatous reaction mimicking ductal carcinoma in situ (DCIS): in a 67-year-old female who underwent mastectomy for DCIS and a 73-year-old female with a history of invasive ductal carcinoma who underwent excisional biopsy for an incompletely excised radial scar. On microscopic examination, the area of the previous biopsy sites contained a circumscribed proliferation of epithelioid cells surrounding collections of acellular pale eosinophilic material, resembling DCIS with comedo necrosis. Immunohistochemical staining demonstrated that the epithelioid cells were immunoreactive for CD68 and negative for cytokeratin (AE1/AE3). There was absent expression of the myoepithelial markers p63 and smooth muscle myosin heavy chain around the cells. The light microscopic and immunohistochemical findings were supportive of a granulomatous process rather than DCIS. These cases demonstrate an unusual presentation of exuberant biopsy site-related granulomatous reaction morphologically mimicking DCIS, and underscore the need for careful histopathologic examination with ancillary immunohistochemical testing in distinguishing granulomatous processes from malignancies.

**Keywords:** Ductal carcinoma in situ, Granuloma, Breast, Immunohistochemistry

## Introduction

Granulomatous processes in the breast can resemble malignancies, both clinically and histologically. We describe two cases of unusually florid biopsy-related foreign body granulomatous reaction mimicking ductal carcinoma in situ (DCIS). We discuss common biopsy site-related changes in the breast, etiologies of granulomatous inflammation in the breast, and pitfalls in the interpretation of granulomatous lesions, especially in the setting of malignancy.

## Case Report

The first case (Case 1) arose in a 67-year-old female who was found to have a 1.6 cm area of heterogeneous grouped calcifications in the left breast on screening mammogram. She underwent stereotactic-guided core needle biopsies, which demonstrated high-grade ductal DCIS with clinging architectural pattern and comedo necrosis. She subsequently underwent left nipple-sparing mastectomy. Microscopic examination demonstrated high-grade DCIS with solid and clinging architecture and central comedo necrosis, spanning 1.8 cm in extent (Figure 1A). The second case (Case 2) arose in a 73-year-old female with a history of invasive ductal carcinoma of the left breast, who was found to have a focal architectural distortion within the upper inner right breast on diagnostic mammogram. She underwent stereotactic-guided core needle biopsies, which demonstrated an incompletely excised radial scar with no atypical hyperplasia or malignancy. Wire-guided excisional biopsy was then performed. Microscopic examination showed a small focus of residual radial scar adjacent to the previous biopsy site. In both cases, in the area of the previous biopsy site, there was a complex, well-demarcated proliferation of epithelioid cells with increased cytologic atypia, surrounding collections of amorphous, pale eosinophilic material superficially resembling comedo necrosis (Figure 1B, Figure 3). To further characterize the epithelioid proliferation, immunohistochemical stains for AE1/AE3 (Agilent Technologies, Santa Clara, CA, 1:200 dilution) and CD68 (Leica Microsystems, Buffalo Grove, IL, prediluted) were performed. The epithelioid cells were negative for cytokeratin using the AE1/AE3 antibody and positive for CD68,

consistent with a granulomatous reaction (Figure 2A-B, Figure 4A-B). Further stains for smooth muscle myosin heavy chain (Leica Microsystems, Buffalo Grove, IL, prediluted) and p63 (Leica Microsystems, Buffalo Grove, IL, prediluted) were negative, indicating lack of a myoepithelial layer in this focus and further supporting interpretation as granulomatous reaction rather than an intraductal process (Figure 2C-D, Figure 4C-D).

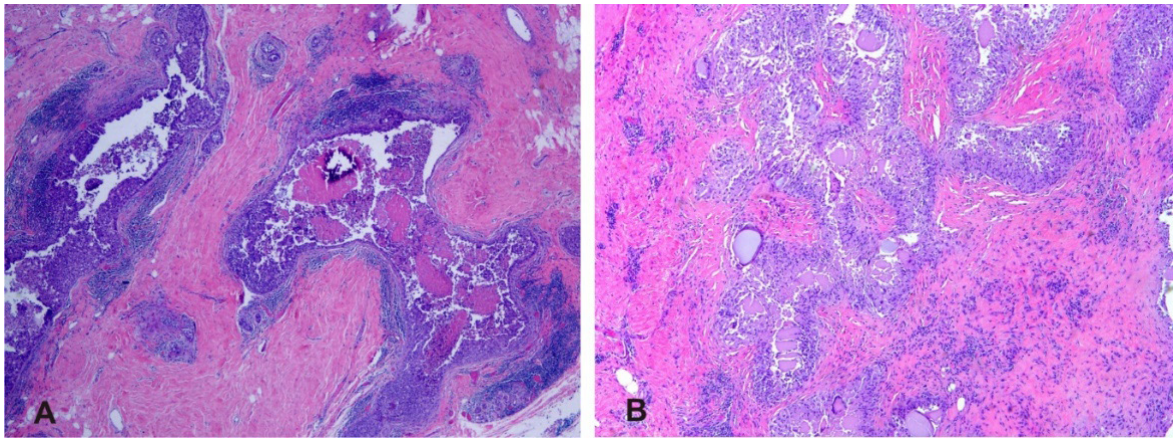


**Figure 1:** Microscopic examination of Case 1 demonstrating high-grade DCIS with comedo necrosis (A) and an adjacent granulomatous reaction, characterized by well-demarcated proliferation of epithelioid cells surrounding acellular pale eosinophilic material (B).

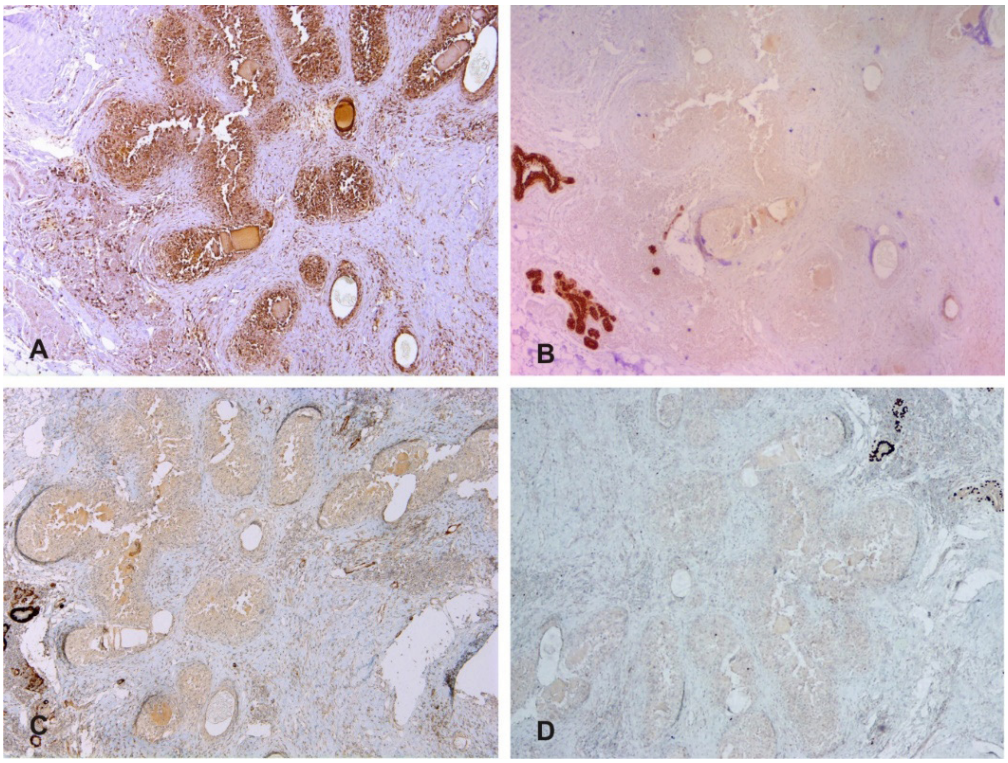


**Figure 2:** Immunohistochemical staining of Case 1 demonstrating positivity for CD68 (A), negativity for AE1/AE3 (B), and lack of smooth muscle myosin heavy chain (C) and p63 (D) immunoreactivity in the granulomatous reaction.

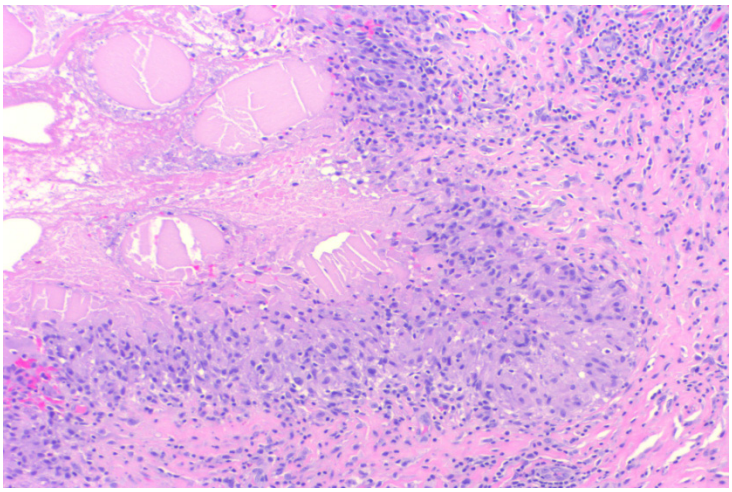

**Figure 3:** Microscopic examination of Case 2 demonstrating a proliferation of epithelioid cells surrounding pale eosinophilic material.

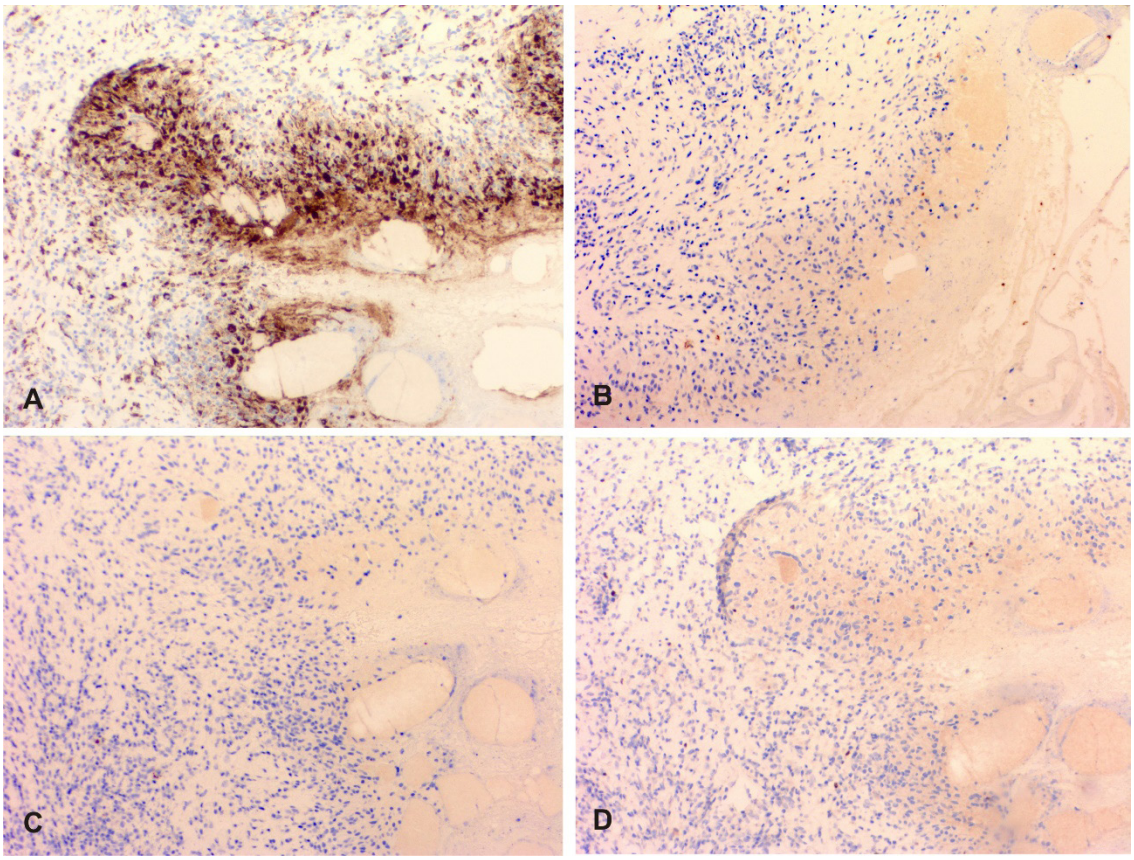


**Figure 4:** Immunohistochemical staining of Case 2 demonstrating positivity for CD68 (A), negativity for AE1/AE3 (B), and lack of smooth muscle myosin heavy chain (C) and p63 (D) immunoreactivity in the epithelioid proliferation.

## Discussion

Our cases demonstrated an unusually extensive granulomatous inflammation at the previous biopsy site morphologically resembling DCIS. Biopsy site changes in the breast typically include hemorrhage, fat necrosis, granulation tissue, and fibrous parenchymal scars [1,2]. Polymer or hydrogel marking devices placed during biopsies often induce a histiocytic and foreign body multinucleated giant cell reaction; well-formed granulomas are seen in a small minority (5%) of cases [3]. Many other biopsy site-related changes can also raise a differential of carcinoma. These include atypical small duct-like structures within granulation or fibrous tissue, artifactual displacement of epithelial cells into the surrounding stroma or vascular spaces, and squamous metaplasia of ductal-lobular units [1,2]. To the best of our knowledge, granulomatous reaction at a biopsy site mimicking malignancy has not been previously documented in the literature.

The etiologies of granulomatous inflammation in the breast are broad. In addition to biopsy marking devices, many other foreign materials such as silicone, paraffin, suture material, and cholesterol may also produce a granulomatous reaction in the breast [4,5]. Mycobacterial, fungal, and parasitic infections are also classically associated with formation of granulomas, which may be necrotizing [4,6]. Cystic neutrophilic granulomatous mastitis (CNGM) refers to a unique form of mastitis caused by Corynebacterium infection, and is usually characterized histologically by lobulocentric granulomas, sometimes with central cystic spaces lined by neutrophils [7]. Granulomatous lobular mastitis (also known as idiopathic granulomatous mastitis) can show similar histologic features to CNGM, with lobulocentric non-necrotizing granulomas often containing neutrophils, but is not related to Corynebacterium infection and usually does not contain the central cystic spaces seen in CNGM [6,8]. Sarcoidosis can rarely involve the breast and usually produces non-lobulocentric, non-necrotizing granulomas within the breast stroma [2,4].

Of note, all of the above-mentioned granulomatous processes can present as distinct masses which may mimic malignancy, both clinically and radiographically. Furthermore, while uncommon, granulomatous inflammation associated with invasive carcinoma has been well-documented in the literature [9-11]. In these instances, the granulomas were usually non-caseating (although cases of necrobiotic granulomas have also been described), present in the lymph nodes draining the carcinoma (with or without metastasis) or the adjacent stroma, and postulated to derive from an abnormal host immune response to the tumor [11,12]. Coyne et al. also described two cases of microinvasive carcinoma with associated granulomatous stromal response, and proposed that the presence of granulomatous reaction could facilitate the identification of microinvasion in these cases [13]. While rare cases of concurrent CNGM and DCIS have been described, no association between granulomatous inflammation and DCIS has otherwise been documented in the literature [14].

Our cases demonstrate florid granulomatous reaction surrounding amorphous eosinophilic material at the previous biopsy site mimicking DCIS; in the first case, this reaction in particular produced a striking resemblance to adjacent high-grade DCIS with comedo necrosis elsewhere in the mastectomy. While more well-known mimickers of DCIS include florid usual ductal hyperplasia, atypical ductal hyperplasia, lobular carcinoma in situ, and invasive carcinoma; this case illustrates the potential for granulomatous inflammation to mimic DCIS as well [15]. Here, the use of immunohistochemistry was instrumental in facilitating the differentiation of these two entities. In conclusion, to avoid misinterpretation of post-biopsy granulomatous reaction as a neoplastic process, careful histopathologic examination as well as judicious utilization of immunohistochemical stains including epithelial, myoepithelial, and histiocytic markers is recommended.

## Acknowledgements

The authors would like to thank Ms. Heather McConnell and Dr. Sasha Pejerrey for their excellent editorial assistance.

### Conflicts of Interest

The authors have no conflicts of interest to declare.

## References

1. Layfield LJ, Frazier S, Schanzmeyer E (2015) Histomorphologic features of biopsy sites following excisional and core needle biopsies of the breast. The Breast Journal 21: 370-376.
2. Schnitt SJ, Collins LC (2018) Biopsy Interpretation of the Breast, 3rd ed. Wolters Kluwer, Philadelphia.
3. Guarda LA, Tran TA (2005) The pathology of breast biopsy site marking devices. The American Journal of Surgical Pathology 29: 814-819.
4. Illman JE, Terra SB, Clapp AJ, Hunt KN, Fazzio RT, et al (2018) Granulomatous diseases of the breast and axilla: radiological findings with pathological correlation. Insights into Imaging 9: 59-71.
5. Tez S, Sen M, Yenidünya S, Tez M (2009) Foreign body granuloma: a mimic of breast carcinoma. Bratisl Lek Listy 110: 366-367.
6. Seo HR, Na KY, Yim HE, Kim TH, Kang DK, et al (2012) Differential diagnosis in idiopathic granulomatous mastitis and tuberculous mastitis. Journal of Breast Cancer 15: 111-118.
7. Renshaw AA, Derhagopian RP, Gould EW. (2011) Cystic neutrophilic granulomatous mastitis: an underappreciated pattern strongly associated with gram-positive bacilli. American Journal of Clinical Pathology 136: 424-427.
8. Lacambra M, Thai T, Lam CC, Alex MC, Pham HT, et al (2011) Granulomatous mastitis: the histological differentials. Journal of Clinical Pathology 64: 405-411.
9. Oberman HA (1987) Invasive carcinoma of the breast with granulomatous response. American Journal of Clinical Pathology 88: 718-721.

10. Alujević A, Jurić G, Separović V, Kruslin B (1997) Invasive breast carcinoma with granulomatous stromal response. Zentralblatt fur Gynakologie, 119: 343-345.

11. Alalshee T, Hamed T, Shafi SM (2014) Granulomatous reaction associated with breast carcinoma: A report of two cases. Saudi Journal of Medicine and Medical Sciences 2: 120-122.

12. Coyne JD (2005) Necrobiotic palisading granulomas associated with breast carcinoma. Journal of Clinical Pathology 58: 1290-1293.

13. Coyne J, Haboubi NY (1992) Micro□invasive breast carcinoma with granulomatous stromal response. Histopathology 20: 184-185.

14. Oddó D, Domínguez F, Gómez N, Méndez GP, Navarro ME (2019) Granulomatous lobular mastitis associated with ductal carcinoma in situ of the breast. SAGE Open Medical Case Reports 7.

15. Johnson NB, Collins LC (2012) Less common variants and mimics of DCIS. Surgical Pathology Clinics 5: 529-544.