

Significant Eosinophilic Infiltrate of the Breast

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Citation

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Abstract

Background: Prominent tissue eosinophilic infiltrate is encountered in a number of inflammatory states, particularly in allergic diseases, parasitic infection, collagen diseases and hematological malignancies. We searched for significant or prominent eosinophilic infiltrates of the breast in benign and malignant diseases. **Methods:** All breast cases reported in our institution during the period of 1999-2008 were reviewed for significant or prominent eosinophilic infiltrate. **Results:** Eight cases were identified. Four cases diagnosed as granulomatous mastitis, one eosinophilic mastitis, two ductal carcinomas and one gynecomastia. **Conclusion:** Significant eosinophilic infiltrate was identified mainly in cases of mastitis and rarely in breast carcinomas. Although eosinophils can degranulate and release toxic inhibiting factors into tumors, they are uncommonly encountered in breast carcinomas.

INTRODUCTION

Eosinophils are considered as pleiotropic multifunctional leukocytes. They are involved in the initiation and propagation of diverse inflammatory responses, and act as modulators of innate and adaptive immunity^{1,2,3}. They can be detected in a variety of healthy tissue, although their functions are not well defined⁴. Eosinophils are detected in many types of human cancers, including hematological tumors such as Hodgkin's lymphoma, T cell lymphoma and variety of solid tumors⁵. Although the presence or absence of eosinophils within specific tumors may have no major influence on the prognosis of the disease, they appear to play an important role in host interaction within the tumor. Eosinophils may promote angiogenesis and connective tissue formation⁶. In addition, tissue eosinophilia provides some interesting clues into the pathologic process, particularly with regard to the production of cytokines. This study focuses on the significant eosinophilic infiltrate of the breast in benign and malignant diseases.

MATERIALS AND METHODS

The computer-based archival records of the Department of Pathology, McMaster Medical Centre, Hamilton, Ontario, Canada, were searched for breast cases with eosinophilic infiltrates reported during the period

1999 – 2008. Cases with prominent or significant eosinophilic infiltrates were selected. These include four

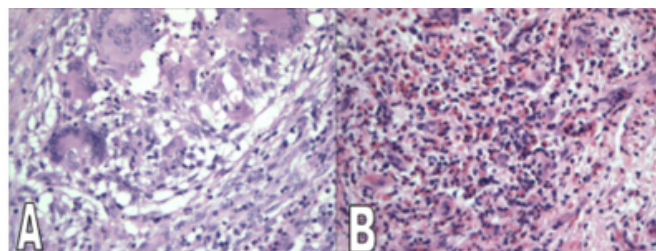
cases of granulomatous mastitis, one eosinophilic mastitis, two ductal carcinomas and one case of gynecomastia. Ten cases of scattered or sparse eosinophilic infiltrates were excluded from this study.

RESULTS

All cases of idiopathic granulomatous mastitis, clinically presented with palpable breast lesions that were suggestive of malignancy. Pathological examination revealed a mixed inflammatory infiltrate with distortion of the breast lobules. The infiltrate was composed of lymphocytes, plasma cells, varying numbers of giant cells Fig 1(A) and heavy eosinophilic infiltrate Fig 1(B).

Figure 1

Fig 1 (A) Granulomatous mastitis Fig 1(B) with heavy eosinophilic infiltrate (H&E stain with original magnification x 200)

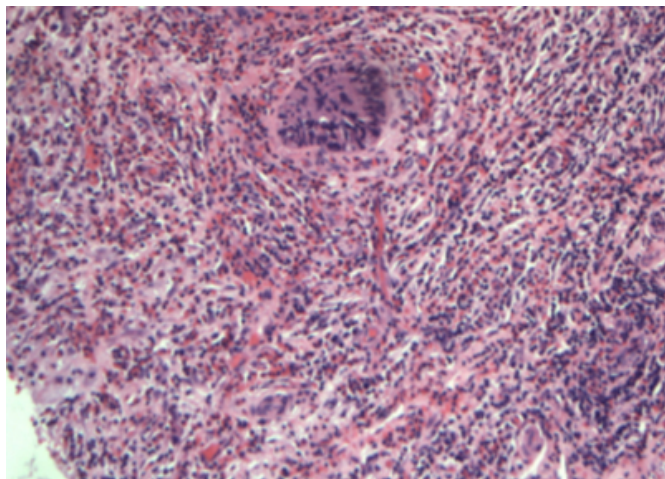


Special stains for fungi and mycobacteria were negative. Microbial cultures were also reported as negative. Eosinophilic mastitis was diagnosed on a core biopsy from a

patient with a clinical presentation of a slightly tender mass lesion in the left breast, which was present for few months. The microscopic examination revealed a hyperplastic ductal epithelium with cellular atypia and heavy eosinophilic infiltrate Fig 2.

Figure 2

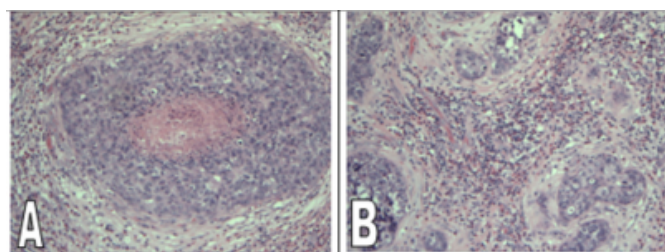
Fig 2 Eosinophilic mastitis with atypical ductal cellular changes (H&E stain with original magnification x 100)



No prior significant past medical history obtained in this case. The other two cases were ductal carcinoma in situ and invasive ductal carcinoma. Both showed significant eosinophilic infiltrates Fig 3 (A) and (B).

Figure 3

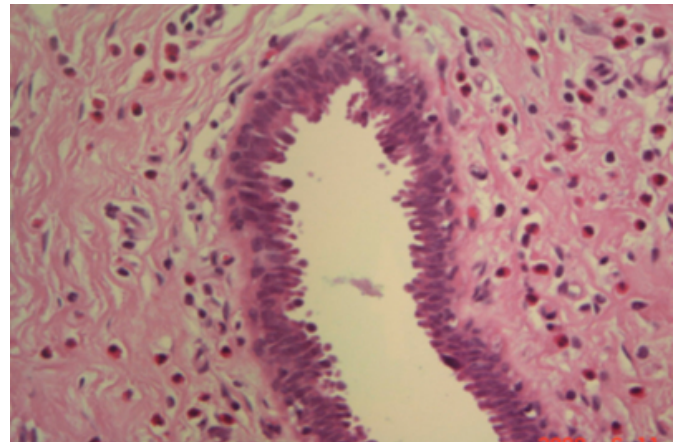
Fig 3(A) Ductal carcinoma in situ with heavy eosinophilic infiltrate (H&E original magnification x100) Fig 3(B) Infiltrating carcinoma with heavy eosinophilic infiltrate (H&E original magnification x100)



Prominent periductal fibrosis was an evident feature of ductal carcinoma in situ. The last case was a male who presented with bilateral breast enlargement. The resection specimen showed features of classical gynaecomastia with significant eosinophilic infiltrate Fig 4.

Figure 4

Fig 4 Gynaecomastia with significant eosinophilic infiltrate (H&E stain with original magnification x 100)



Clinical history failed to reveal any obvious etiology such as drug or collagen vascular disease, which could account for the eosinophilic infiltrate.

DISCUSSION

Prominent blood and tissue eosinophilia is detected in a number of inflammatory conditions, particularly allergic diseases¹. Eosinophils are a source of numerous cytokines and growth factors, thus in principle, they can display both pro-inflammatory and anti inflammatory activities as well as immunoregulatory function. Recruitment and activation of eosinophils has been studied intensely in allergic diseases²³. The production of eosinophils requires three cytokines: interleukin-5, interleukin-3, and granulocyte-macrophage colony-stimulating factor. Cells destined for the eosinophilic lineage, display high-affinity receptors for interleukin-5, which is a specific differentiation factor for eosinophils. A monoclonal population of T cells lurks behind the eosinophils. These T cells are activated, display abnormal combinations of surface markers, and produce large amounts of interleukin-5, which is the presumed cause of the eosinophilia. In rare instances, lymphoma or leukemia cells overproduce interleukin-5, thereby evoking hypereosinophilia⁷⁸. Both eosinophils and mast cells have been found to be associated with chronic fibrotic conditions with different etiologies. Eosinophils can modulate fibroblast properties by other growth factors⁹. They have been documented to be elevated in peripheral blood and/or to infiltrate the tissue in some malignant disorders⁵. The degranulation of eosinophils in tumor and tumor stroma was reported, and the presence of Charcot-Leyden crystals was identified by electron microscopic studies on gastric carcinoma and pancreatic tumors¹⁰¹¹. In addition,

eosinophils have been found to play a role in angiogenesis, a process that plays a central role in cancer pathology and embryogenesis⁶. Recent studies have focused on the relationship between tumor and eosinophilic infiltrate more than the relationship between tumor and peripheral blood eosinophilia. Some studies claimed tissue or blood eosinophilia is correlated with significantly better prognosis¹², while others find no significant prognostic value⁵. Eosinophil-rich squamous cell carcinoma of the oral cavity, although associated with metastatic involvement of cervical lymph node, seems to pursue a less aggressive course if compared with ordinary squamous cell carcinoma¹³.

Earlier studies claimed that high peripheral lymphocytes and eosinophils enhance the patient's ability to fight breast cancer¹². This study focuses on significant eosinophilic infiltrates of breast tissue from resected tumor and non-tumor pathology. Despite the fact that some human cancers are associated with eosinophilic infiltrates, we identified very few cases of breast ductal carcinoma with such significant eosinophilic infiltrate. The infiltrates seem to be associated with periductal fibrosis and ductal obliteration in ductal carcinoma in-situ. In contrast, we identified significant eosinophilic infiltrates in granulomatous mastitis. This is a rare disease of unclear etiology; however, correlation with breast-feeding, use of oral contraceptives and autoimmune etiologies were suggested¹³. In mammography and sonography these show nodular opacities and hypoechoic nodules¹⁵. Pathologically, they are characterized by granulomatous lobulitis with mixed infiltrates of lymphocytes, plasma cells, giant cells and eosinophils. Granulomatous mastitis is a heterogeneous group of diseases with an adverse clinical picture. The response to steroid or immune suppression supports a strong autoimmune etiology.

Eosinophilic mastitis is an extremely rare condition characterized by heavy eosinophilic infiltrates around ducts and lobules with no known peripheral eosinophilia¹⁶. Atypical ductal hyperplasia and mitotic activity is commonly encountered in this condition. The pathogenesis is unknown, but it could reflect a local reaction to intraluminal substances. The presence of heavy eosinophilic infiltrates in this entity may represent a form of allergic reaction. Local excision is recommended to exclude an underlying malignant disease. Rarely these lesions may reoccur following surgery¹⁶.

Gynaecomastia reflects a mammary response to absolute or

relative hyperoestrogenism. Medications that have estrogen-like activity, or that adversely affect testosterone levels, may also lead to gynaecomastia. Gonadal dysfunction, neoplasm and systemic diseases, drugs such as spironolactone, digitalis, cimetidine, phenothiazine and thiazide are possible causes¹⁸. Our patient was in good general health and was not on any medications. No peripheral eosinophilia was identified. The reason for eosinophilic infiltrate in this case remains obscure.

CONCLUSION

Significant eosinophilic infiltrate of mammary inflammatory and tumor pathologies was the focus of this study. Despite the fact that eosinophils may degranulate and release toxic inhibiting factors into tumors, they are rarely seen in breast carcinoma and are more commonly seen in inflammatory conditions of the breast.

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