

# Imprint cytology of non-specific granulomatous mastitis

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## Summary

Non-specific granulomatous mastitis (NSGM) is a tumor-like inflammatory condition involving breast lobules. Its recognition is of great significance because of clinical masquerade to invasive carcinoma. A 25-year-old woman developed a palpable breast lump with clinical and mammographic findings suggestive of malignancy. Touch imprint cytology of the excised lump was consistent with a granulomatous inflammation while histopathological examination documented a NSGM with central necrosis. Clinical, radiologic and laboratory testing failed to identify any specific causative agent.

**Key words:** Tumor-like breast lesion; Touch imprint cytology; Mammography; Granulomatous mastitis.

## Introduction

Granulomatous inflammatory process of the breast is uncommon. It is composed of epithelioid histiocytes, Langhans-type giant cells and chronic inflammatory cells in lobular areas of the breast [1]. Hematogenous spread is exceedingly rare and occurs mainly in tuberculosis. Viral and fungal infections are also infrequent [2]. Its recognition is of great significance because of clinical and mammographic mimicry to carcinoma [3]. The diagnosis of non-specific (or idiopathic) granulomatous mastitis (NSGM) is one of exclusion, when no infectious causative agent can be detected, locally or systemically. NSGM was first described by Kessler and Wolloch [4]. Since first described a total of 65 cases had been reported by 1994 in the English-language literature, with a few more case reports published up to present day [5]. The etiology of NSGM is unknown and remains debatable. Kessler and Wolloch [4], noting the similarities between granulomatous thyroiditis and orchitis, postulated an autoimmune pathogenesis of the disease, with an antigen-antibody reaction being involved in the promotion of NSGM. Some authors suggested that a process of squamous metaplasia might be initiating the foreign-body reaction by producing keratin products, triggering off the onset of the disease. Oral contraceptive use and pituitary prolactinomas were proposed to be the chemical inducers of squamous metaplasia [6].

In the past, failure to obtain a histologic diagnosis has resulted in mastectomy or radiotherapy, based on the clinical impression of carcinoma. The optimal therapy for NSGM has not yet been established, and treatment options range from simple steroid therapy to surgical excision of the breast lump [5].

Fine needle aspiration cytology (FNA) has been extensively evaluated as a means of NSGM diagnosis, providing that a conservative therapy will follow. However, its

usefulness remains debatable due to a high false-negative rate (13.2%) and to the danger of a hidden malignancy [7].

Very few reports have been published concerning imprint cytology as an adjunct in the diagnosis of NSGM [8]. However, we believe that, since surgical lumpectomy is the most accepted form of therapy in cases of NSGM due to clinical similarity with carcinoma, imprint cytology (perhaps additionally to frozen section) could provide the surgeon with hallmarks concerning interpretation of the disease and manipulation of the patient, inside the operating room.

In the present work, we describe the cytologic features of NSGM diagnosed in a young female, as found on imprint smears, and compare them with the histologic profile of the lesion.

## Case Report

A 25-year-old female with a lump in the outer half of her right breast was admitted to the University Department of Obstetrics and Gynecology, Alexandroupolis Regional Hospital. On clinical examination, the lump was discrete and mobile and there were two ulcerated areas on the overlying skin. It was moderately hard and there were small palpable axillary lymph nodes on the same side.

The patient had a 2-year-old child who had been breast-fed for eight months. Lactation had been discontinued about 14 months before initiation of the lesion. There was no history of oral contraceptive use. The patient's medical history was free of any pathologic condition, except for chronic asthmatic bronchitis.

Mammography showed diffuse increased asymmetric density of fibroglandular tissue within the supralateral aspect of the right breast (Figure 1). No discrete masses, spicules or suspicious microcalcifications were seen. Ultrasound examination revealed a large oval hypoechoic mass connecting to three tubular hypoechoic lesions, as well as the presence of axillary lymph node enlargement. The chest X-ray was normal and the tuberculin (purified protein derivative) skin test was negative. Clinical and laboratory control did not reveal any signs of systemic infection.

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Figure 1. — Diffuse increased asymmetric density of fibroglandular tissue within the supralateral aspect of the right breast.

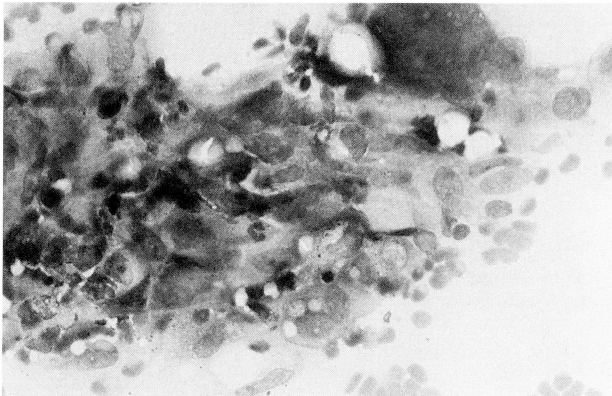


Figure 2. — Epithelioid cells, imprint cytology, Giemsa quick $\times 40$ .

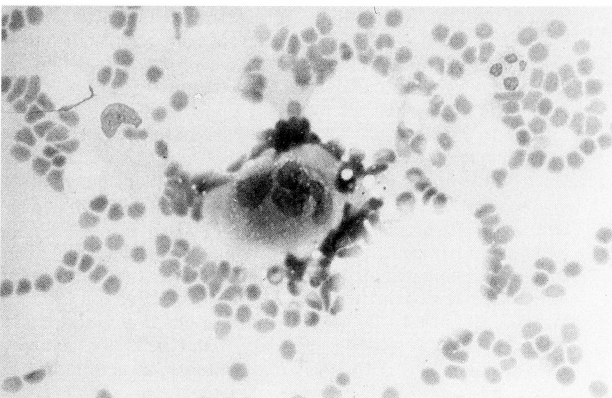


Figure 3. — Langerhans' type giant cell, imprint cytology, Pap $\times 40$ .

The patient underwent surgical lumpectomy. Frozen section biopsy was negative for malignancy. During operation, imprint cytology was performed and findings were indicative of a granulomatous lesion of the breast. Since no infectious microbial, viral or fungal agent was detected, the diagnosis of NSGM was established. Fresh material from the surgical specimen was submitted for microbiologic workup, including bacterial (aerobic and anaerobic), mycobacterial and fungal cultures, which did not reveal any infection. Cultures for fungi and mycobacteria were considered negative after six weeks' incubation. Histopathologic examination of the surgical specimen and performance of special histologic stains confirmed the diagnosis. Following her surgery and subsequent dismissal from the hospital, the patient was sub-

mitted to close follow-up. The surgical wound healed completely five weeks after surgery. The patient did not receive any medication postsurgically and there has been no recurrence of the disease up to now (1.5 years after treatment).

#### *Cytologic findings*

The surgical specimen was submitted to multiple incisions and six slides were prepared; the passes being especially focused on the most suspicious areas. Two smears were stained with the Giemsa quick set without previous fixation. One smear was cytospray-fixed and subsequently stained with the Papanicolaou method. The rest were kept for special stains. Epithelioid cells and multinucleated cells of Langerhans' type were observed (Figures 2, 3). Tight clusters of ductal epithelial cells, naked nuclei of myoepithelial cells inbetween or scattered throughout the smear and chronic inflammatory cells were also found. PAS and methenamine silver stains were negative for acid-fast organisms. The report was negative for malignancy and all features were consistent with granulomatous mastitis.

#### *Histopathologic findings*

The surgical specimen was fixed in buffered formaldehyde, embedded in paraffin, cut in 4  $\mu$ m sections and stained with hematoxylin-eosin (H&E), Gram, PAS, and Ziehl-Neelsen. Histopathologic examination showed multiple epithelioid granulomas, occasional granulomas with central abscess formation, and large dilated vascular spaces in the overlying epidermis with an intense perivascular inflammatory cell infiltration (Figures 4, 5). The granulomatous reaction was confined mainly

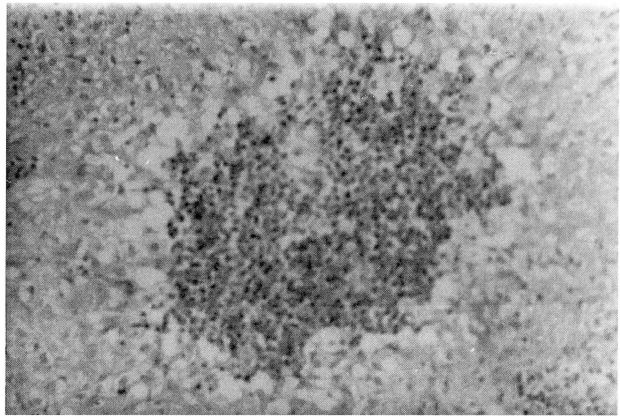


Figure 4. — Epithelioid granuloma, tissue section H&E $\times 40$ .

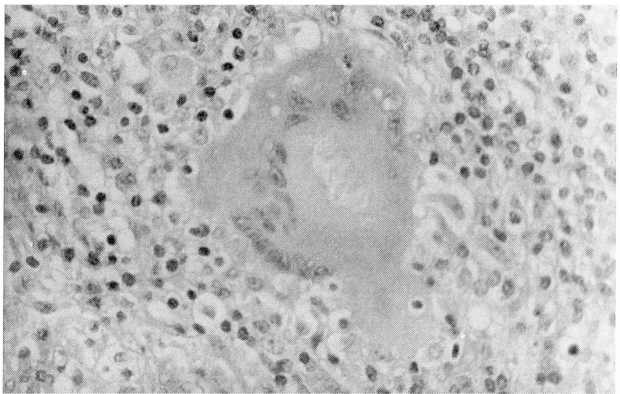


Figure 5. — Langerhans' giant cell, tissue section H&E $\times 40$ .

to the breast lobules. Caseation was not noted. All special stains were negative for acid-fast bacilli, fungi or bacteria. A diagnosis of NSGM was established.

## Discussion

When facing a breast cytologic pattern presenting epithelioid granulomas and multinucleated giant cells, the cytopathologist could establish the cytologic diagnosis of granulomatous lesion of the breast. Nevertheless, this uncommitted diagnosis includes a wide variety of different pathologic entities: NSGM, specific infections (mycobacterium tuberculosis, fungi, parasites), duct ectasia/periductal mastitis, plasma cell mastitis, sarcoidosis and vasculitis.

Radiographically, mammographic findings of granulomatous mastitis, in the literature, have been described as normal or as a suspicious mass or a mass suspected of being malignant [4, 9, 10]. In our case the mammography showed diffuse increased asymmetric density. Various sonographic features have been described. Han *et al.* [11] described granulomatous mastitis as multiple clustered, often continuous tubular hypoechoic lesions that are sometimes associated with a large hypoechoic mass. Additionally, Van Ongeval *et al.* [10], presented a case of granulomatous mastitis, in which the sonographic appearance was as an inhomogenous, irregular hypoechoic lesion with focal posterior shadowing.

A question that arises concerns the performance of cytology in the qualification of a granulomatous lesion of the breast and in the disqualification of other pathologic entities suspected, especially breast carcinoma [3]. Some authors suggest that a positive diagnosis of malignancy by FNA is reliable in establishing the diagnosis and planning the treatment of breast cancer [7], but there are much less published studies concerning imprint cytology [8]. In the present case report, the cytologic findings are similar to the ones reported in other studies revealed from aspiration cytology [3, 6], as well as to others revealed from imprint cytology leading to the same diagnosis [8]. Furthermore, we believe that imprint cytology would provide many fewer pitfalls than FNA, since imprints are taken directly, under visual control. A second question concerns the usefulness of cytology alone in the differential diagnosis between the different types of granulomatous lesions of the breast. Some authors suggest that confident categorization of granulomatous breast lesions should be based more on architectural and topographical criteria than on cytologic features. They believe that such criteria cannot be properly evaluated in smears [3]. Some others suggest that cytologic patterns provide enough information for differentiating granulomatous lesions of the breast [8]. Especially for NSGM, they believe that the typical cellular smear composed of preeminently inflammatory cells, mainly lymphocytes, associated with epithelioid histiocytes along with Langhans'-type giant cells, provides characteristic cellular features that may allow its interpretation [12].

Some of the most commonly accepted features, which are of great help in the cytologic differentiation of NSGM from other granulomatous lesions of the breast, are summarized below [8].

Abundance of neutrophils, a consistent feature in NSGM, is a rarity in tuberculous mastitis. Acid-fast stains are negative for mycobacteria in NSGM.

Fungal mastitis can be accurately diagnosed by demonstration of fungi with special stains of the smears.

In nonmycobacterial infections, such as pyogenic abscesses, Langhans-type cells and epithelioid cells do not seem to occur.

In fat necrosis, the presence of abundant foamy cells is a classic feature, whereas in NSGM foamy cells are seen only occasionally. In addition, epithelial cells, which are usually present in NSGM, are not seen in fat necrosis.

In sarcoidosis, smears show epithelioid cells with abundant lymphocytes without neutrophils or necrosis.

In conclusion, we believe that imprint cytology, like FNAC, provides characteristic enough features for the diagnosis of NSGM. Moreover, imprint cytology performed inside the operating room in cases of granulomatous processes of the breast can help the surgeon in a rapid approach and treatment modalities of the disease, especially due to the reduced number of frozen sections requested by the histopathology department.

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## References

- [1] Going J. J., Anderson T. J., Wilkinson S., Chetty U.: "Granulomatous lobular mastitis". *J. Clin. Pathol.*, 1987, 40, 535.
- [2] Koss L. G., Woyke S., Olszewski W.: "The breast". In: "Aspiration Biopsy. Cytologic Interpretation and Histologic Bases". Second Edition. New York, Igaku Shoin Inc., 1992, 141.
- [3] Parra D. M., Santos M. N., Guerrero B. M., Solano J. G., Guimain C. C. H., Guillermo M. P.: "Utility of fine needle aspiration in the diagnosis of granulomatous lesions of the breast". *Diagn. Cytopathol.*, 1997, 17, 108.
- [4] Kessler E., Wolloch Y.: "Granulomatous mastitis: a lesion clinically simulating carcinoma". *Am. J. Clin. Pathol.*, 1972, 58, 642.
- [5] Donn W., Rebbeck P., Wilson C., Gilks B.: "Idiopathic granulomatous mastitis. A report of three cases and review of the literature". *Arch. Pathol. Lab. Med.*, 1994, 118, 822.
- [6] Macanish S., Greenberg M., Barraclough B., Pacey F.: "Fine needle aspiration cytology of granulomatous mastitis. Report of a case and review of the literature". *Acta Cytol.*, 1990, 34, 39.
- [7] Willis S., Ramzy I.: "Analysis of false results in a series of 835 fine needle aspirates of breast lesions". *Acta Cytol.*, 1995, 39, 858.
- [8] Kumarasinghe M. P.: "Cytology of granulomatous mastitis". *Acta Cytol.*, 1997, 41, 727.
- [9] Jorgensen M. B., Nielsen D. M.: "Diagnosis and treatment of granulomatous mastitis". *Am. J. Med.*, 1992, 93, 97.
- [10] Van Ongeval C., Schaepen T., Van Steen A., Baert L. A., Moerman P.: "Idiopathic granulomatous mastitis". *Eur. Radiol.*, 1997, 7, 1010.
- [11] Boo-Kyung H., Yeon Hyeon C., Jeong Mi P. *et al.*: "Granulomatous mastitis: Mammographic and sonographic appearances". *Am. J. Rad.*, 1999, 173, 317.
- [12] Kobayashi T. K., Sugihara H., Kato M., Watanabe S.: "Cytologic features of granulomatous mastitis. Report of a case with fine needle aspiration cytology and immunohistochemical findings". *Acta Cytol.*, 1998, 42, 716.

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