

Case Report

Cystic neutrophilic granulomatous mastitis: Two cases of unusual histological breast entity

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Abstract

Cystic neutrophilic granulomatous mastitis (CNGM) is a newly recognized entity that occurs in parous reproductive-aged or lactating women presented with mastitis and can mimic with malignancy. Most of the cases of CNGM are idiopathic and some cases associated with Gram-positive lipophilic *Corynebacterium* species. Here, we present two cases of CNGM in which patients presented with painful breast lump. Interdisciplinary approach may help in accurate diagnosis and optimal patient management of these subtype of mastitis.

Keywords: Breast lesion, cystic, giant cells, granulomatous, neutrophilic infiltrates

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INTRODUCTION

Inflammatory conditions of the breast are mostly encountered in lactating females and presented with painful breast lump and erythema.^[1] Granulomatous mastitis is an uncommon subtype of chronic benign inflammation that occurs in women of reproductive age from a variety of causes including infections (bacterial, fungal, and mycobacterial), sarcoidosis, and autoimmune diseases.^[2]

Granulomatous mastitis with no specific etiology is known as idiopathic granulomatous mastitis or granulomatous lobular mastitis (GLM), despite extensive clinical, pathological, and microbiological studies.^[3,4] D'Alfonso *et al*,^[5] in 2015 reported cystic neutrophilic granulomatous mastitis with presence of *Corynebacterium bacilli* within the cystic spaces. These bacteria are not easily identified in hematoxylin and eosin-stained slides because the number

is very low and limited to cystic spaces, and microbiological identification is easy on Gram stain.^[5] Recently, a new entity called cystic neutrophilic granulomatous mastitis (CNGM) is described which is characterized by the presence of cystic spaces consistent with dissolved lipid and surrounded by neutrophils, histiocytes, multinucleated giant cells, and granulomas. Some *Corynebacterium* species are lipophilic and grow very poorly in laboratory and require special culture media and prolong incubation period.^[6]

Taylor *et al*,^[7] in 2003 reported a strong relationship between GLM and *Corynebacterium* infection in 14 cases out of 34 cases of breast abscesses of different histological pattern, in which bacilli were confined to empty spaces surrounded by neutrophils within the granuloma. This pattern was defined as CNGM. Patients are often febrile and may have a leukocytosis.^[7] Here, we describe the clinicopathological features of two cases of CNGM which

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were clinically presented with painful breast lump and importance of recognizing this entity.

CASE STUDY

Case 1

A 27-year-old nonlactating female presented with left-sided painful breast lump for 8 months. On examination, it was tender and erythematous lump and clinically suspected as fibroadenosis. On ultrasonography, there was well-defined irregular-walled heterogenous, hypochoic lesion at 12 O' clock position with fluid filled content suggestive of abscess. Excision was done and the specimen was sent for histopathological examination.

On microscopic examination, tissue was densely infiltrated by mixed inflammatory cells and few giant cells and granuloma. There were few cystic spaces that were surrounded by neutrophils and histiocytes, plasma cells, and occasional giant cells [Figure 1]. Inflammatory infiltrates were also noted in fibroconnective stroma and adipose tissue. Few benign ducts were embedded in dense collection of inflammatory infiltrates [Figure 2]. Special stains including PAS, AFB and Gram stain on formalin-fixed paraffin-embedded tissue section were negative for fungal and acid-fast bacilli. Gram-positive bacilli were also not identified in cystic spaces on Gram staining; it may be due to low bacterial count. Because of characteristic histological findings, diagnosis of CNGM was made.

Case 2

A 27-year-old female presented with painful breast lump. Radiological finding was suggestive of fibroadenosis. Microscopic features showed benign breast parenchyma, ducts surrounded by lymphoplasmacytic

infiltrates [Figure 3]. Cystic spaces were also identified surrounded by epithelioid cell granuloma and many giant cells admixed with neutrophils [Figure 4]. Special stains including PAS, AFB, and Gram stain were performed on formalin-fixed paraffin-embedded tissue section, and these were negative for fungal and acid-fast bacilli and Gram-positive bacilli.

On the basis of specific histological finding, CNGM was made as a diagnosis.

DISCUSSION

Cystic neutrophilic granulomatous mastitis (CNGM) is an uncommon form of granulomatous inflammation. The differential diagnosis of granulomatous mastitis includes various infectious etiologies, sarcoidosis, and reaction to exogenous materials. CNGM cases have also been described in nulliparous women with hyperprolactinemia. It is also hypothesized that women who are unable to breastfeed from one breast (due to nipple inversion or pain) may have stasis of lipid-rich milk secretion inside the breast which may predispose to develop CNGM.^[8,9]

Histological features are characteristic of chronic neutrophilic granulomatous mastitis. Affected patient presents with a palpable breast lump that may show sign and symptoms of either inflammation (erythema, pain, sinus tract) or malignancy (hard lump, nipple inversion, and lymphadenopathy). Some patients may also present with complaints of nipple discharge.^[9]

Imaging findings may be worrisome and can mimic to malignancy. Histologically, CNGM is a granulomatous inflammation with lobulocentric distribution that often

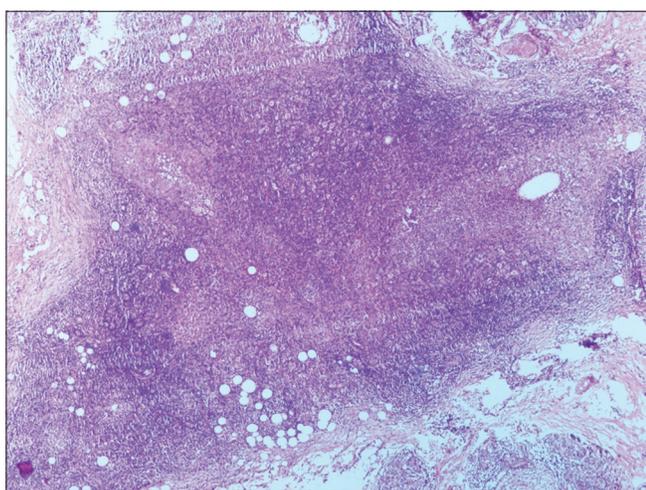


Figure 1: Expanse of inflammatory infiltrates obliterating the normal lobular architecture with cyst formation in the upper right (H and E stain, x40, Case 1)

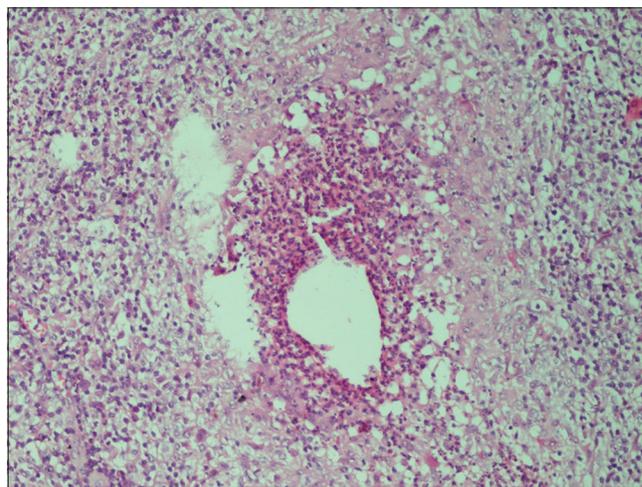


Figure 2: Cystic spaces rimmed by neutrophils and histiocytes (H and E stain, x200, Case 2)

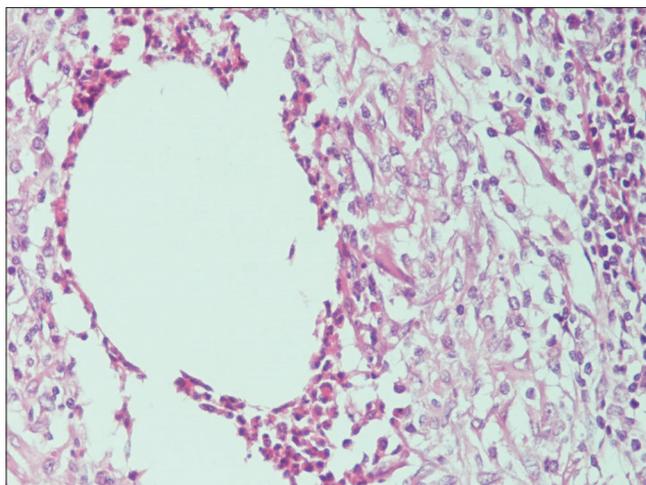


Figure 3: Cystic spaces rimmed by mononuclear cells and clusters of histiocytes (H and E stain, ×400, Case 1)

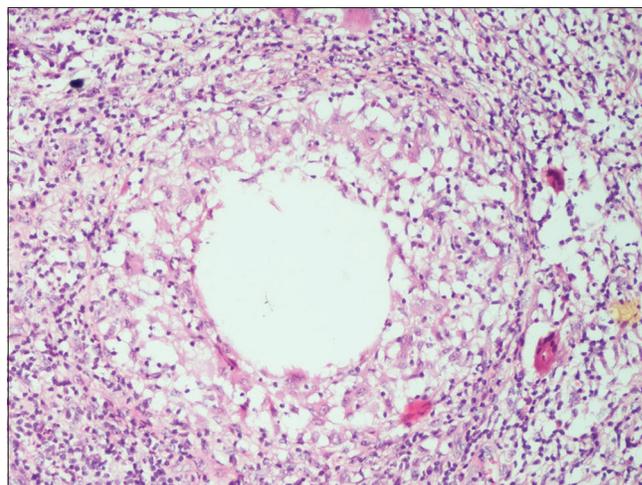


Figure 4: Cystic spaces surrounded by neutrophils, histiocytes, plasma cells, and giant cells (H and E stain, ×40, Case 2)

contains neutrophils and micro-abscess formation similar finding like idiopathic granulomatous mastitis. Wang *et al.*^[9] also identified mix population of bacilli such as *Corynebacterium bovis* and *Staphylococcus* together in a case of CNGM. 16S rDNA PCR and DNA sequencing may be helpful in identifying the causative organism.^[9] It differs from CNGM in having empty “cystic spaces” formation secondary due to dissolved lipid. These spaces are rimmed by neutrophils that are surrounded by histiocytes, lymphocytes, plasma cells, and Langhans type of giant cells forming granuloma. These cystic spaces are not present in all granuloma. Rod-like bacterial structure may be identified within some of the cystic spaces and never present outside of the vacuoles. Often, the number of bacilli is very low in these cystic spaces.^[10]

Corynebacterium spp. is the most common bacteria associated with CNGM in previously reported cases of CNGM and in textbooks.^[11] These bacilli may be identified on the basis of morphology because of their characteristic “coryneform” features and also referred as “diphtheroid.” *Corynebacterium kroppenstedii* is the most frequently isolated lipophilic *Corynebacterium* in previously reported cases of CNGM. Special stains should be performed in all cases of granulomatous mastitis to rule out other causes of granulomas. Due to low number of bacterial DNA in the cystic spaces, the sensitivity of the test may be low when performed on formalin-fixed paraffin-embedded tissue blocks.^[11]

Because of the presence of specific histological findings and low number of bacterial DNA in the cystic spaces, *Corynebacterium* should be considered in a suppurative background with granuloma formation even without the presence of bacteria. GLM and CNGM are chronic and

recurring inflammatory conditions with complications which can lead to abscess and sinus formation. Patients are usually treated with a combination of antimicrobials, corticosteroids, and surgery.^[11]

CONCLUSION

We present a unique form of granulomatous inflammation which has specific histological features and associated with diphtheroid bacilli. CNGM cases are difficult to distinguish from malignant cases on the basis of clinical and radiological findings, without histopathological examination. Despite strong association with CNGM, the number of *Corynebacterium* spp. tends to be low, difficult to identify histologically and microbiologically, and difficult to grow on culture. The rarity of the CNGM cases warrants increased awareness about this entity and interdisciplinary communication for accurate diagnosis, optimal management, and reduced morbidity.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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