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ORIGINAL RESEARCH

Histopathological study of granulomatous mastitis

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ABSTRACT
Idiopathic granulomatous mastitis (IGM) is a rare, benign breast disease without a clearly known etiology. It was first described by Kessler and Wolloch in 1972, hundreds of cases have been reported from all over the world. It is characterised by inflammation without necrosis. It has to be differentiated from simple mastitis and inflammatory carcinoma clinically and histological differentiation is of greater significance. There is no definitive classifications, scoring systems or certitudes. Mastitis can however also affect males and non-breastfeeding women. The aim of this study is to define a few causative factors related to the occurrence of the disease, which may aid in early diagnosis and treatment. We retrospectively analyzed the clinical, radiological and morphological features of 36 cases diagnosed as GM by histopathological study. In this study we attempted to describe the detailed clinical and histomorphological features, diagnostic clues for various specific and idiopathic GM.

Keywords: Idiopathic granulomatous mastitis, surgery.

INTRODUCTION

Idiopathic granulomatous mastitis (IGM), also known as granular lobar mastitis, is a rare, benign breast disease without a definitive etiology. Granulomatous mastitis (GM) mimics breast carcinoma clinically and radiologically and present as nipple discharge, orange peel sign and irregular masses. Granulomatous mastitis (GM) is characterized histopathologically by granulomatous inflammation in lobulocentric distribution with sparinginterlobular stroma[1].GM etiologically can be divided into two groups; idiopathic and specific. Specific causes include foreign body reaction, sarcoidosis, vasculitis,infectious causes such as tuberculosis, cat scratch disease, fungalinflammation, and corynebacteria infection. Factors associated with idiopathic GM includes Gestation, oral contraceptive therapy, diabetes mellitus, smoking, autoimmunity[2,3]. The definitive diagnosis can be arrived by histopathological examination tissue biopsy sample. Treatment modality depends on the etiology, extent of the lesion, and skin changes with fistula/abscess formation. The idiopathic form of GM is problematic for clinicians and surgeons in terms of the diagnosis and treatment strategy[2,3,4,5,6,7,8]. GM is an uncommon benign breast pathology which included a wide range of conditions. Thus it is completely crucial to differentiate between two principle types of GM, namely specific granulomatous mastitis which is of secondary nature and emerges as a phenomenon after certain defined reasons, as well as the idiopathic granulomatous mastit (IGM), which usually affects women of childbearing years with an incidence ranging from 0. 44 and 1. suggested that in their study, ductal CA accounts for only 6% of total breast biopsy specimens[9,10]. Thus, first described by Kessler and Wollock[1] in 1972, IGM is both a diagnostic and therapeutic dilemma. Various manifestations are seen in IGM which resembles breast carcinomas. Generally, IGM is characterised by a unilateral palpable breast lump with later skin changes with or without LN enlargement. Biopsy is very important in the diagnosis and treatment of granulomatous mastitis, and therefore, histopathological examination must be performed. This entails the examination of breast tissue biopsies under the microscope to look for the typical granulomas which are round indurated nodules that are made up of macrophages. These granulomas

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and the exclusion of infectious pathogens consisting of bacteria, fungi and parasite help in differentiating granulomatous mastitis and other diseases and cancers. In this study we attempted to describe the detailed clinical and histomorphological features, diagnostic clues for various specific and idiopathic GM.

OBJECTIVES

The main objective of the study is to find the histopathological analysis of granulomatous mastitis.

Methodology of the study

This histopathological study was conducted to analyze and evaluate the features of granulomatous mastitis in a cohort of patients. Breast tissue samples were obtained from 36 female patients presenting with symptoms suggestive of granulomatous mastitis, such as painful breast lumps, abscesses, or sinus formation.

Inclusion Criteria

- Female patients of reproductive age
- Clinically diagnosed with granulomatous mastitis based on presenting symptoms
- Tissue samples adequate for histopathological examination

Exclusion Criteria

- Patients with a prior history of breast cancer or other breast diseases
- Insufficient or poor-quality tissue samples

Histopathological Examination

The collected breast tissue samples were fixed in 10% formalin, embedded in paraffin, and sectioned at 4-5 microns. These sections were then stained with Hematoxylin and Eosin (H&E) for routine histopathological examination. Additional special stains, such as Ziehl-Neelsen, Periodic Acid-Schiff (PAS), and Gram stain, were employed to identify any infectious agents.The stained tissue sections were examined under a light microscope by two independent pathologists. The presence of granulomas, giant cells, caseous necrosis, and any other histopathological features were recorded. Special attention was given to identifying etiological agents like bacteria, fungi, and parasites.Data on patient demographics, clinical presentation, histopathological findings, and the presence of infectious agents were collected and systematically recorded.

Data analysis

Statistical analysis was performed to determine the prevalence of different histopathological features and to correlate these findings with clinical data.

RESULTS

The study analyzed 36 cases with an age range of 21-52 years. Clinical features included a mass in all cases (36/36), nipple induration in 4 cases, and pain or tenderness in 19 cases. Circumscription was well circumscribed in 16 cases and ill circumscribed in 20 cases. Ultrasound findings showed 20 cases with hypoechoic features and 16 with mixed echogenicity; circumscription on ultrasound matched the clinical assessment, with 16 well circumscribed and 20 ill circumscribed.

Table 01: Demographic data of patients

Variables	Values-36
Age range	21- 52yrs
Bilateralility	3cases
Lactational history	4cases
clinical features	Mass-36/36 nipple induration-4/36 pain/tenderness-19/36
Circumscription	weel circumscribed-16/36 ill circumscribed-20/36
USG	hypoechoic- 20/36 mixed exhogenicity-16/36 well circumscribed-16/36 ill circumscribed-20/36

Microabscess formation was observed in 6 cases, while caseous necrosis was present in 12 cases. Neutrophilic cysts were found in 4 cases, and eosinophilic infiltration was noted in 2 cases. Interlobular inflammation occurred in 5 cases. Additionally, fat necrosis, ductal ectasia, and lactational changes were each identified in 2 cases.

Table 02: Histopathological Evaluation

Microabscess formation	6
Caseous necrosis	12
Neutrophilic cysts	4
Eosinophilic infiltration	2
Interlobular inflammation	5
Fat necrosis	3
Ductal ectasia	2
Lactational changes	2

Histopathological diagnosis

- Tubercular- 16 (AFB +ve 14, AFB-ve 02)
- Fat necrosis- 08 (Traumatic- 06, atraumatic- 02)
- Papilloma- 04
- Sillicone granuloma- 02
- Eosinophilic granuloma-02
- Idiopathic granuloma- 02
- Sarcoid granulomatous mastitis- 01
- Fungal granulomatous mastitis-01

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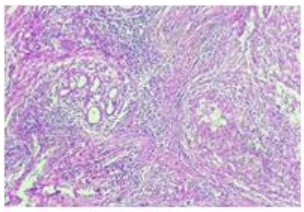

Fig 1: Shows lobulocentric and

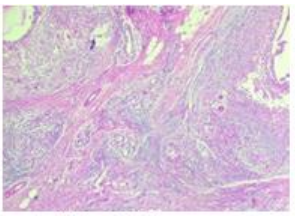

Fig 2: Shows lobulocentric

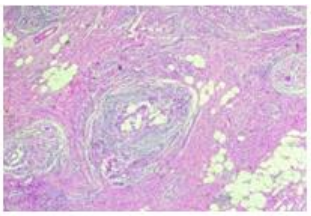

Fig. 3: Highpower view of fig. 10 showing

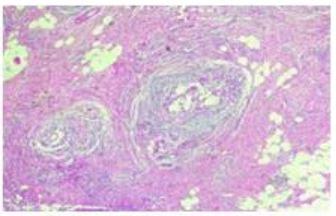

Fig. 4: Shows highpower view of lobulocentric

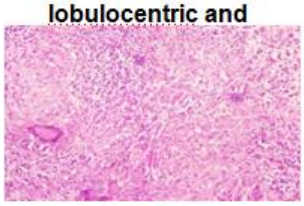

Fig 5: Shows epitheloid

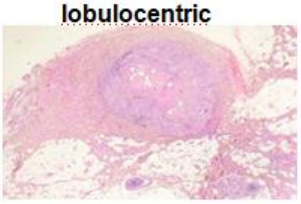

Fig. 6: Shows TB granuloma

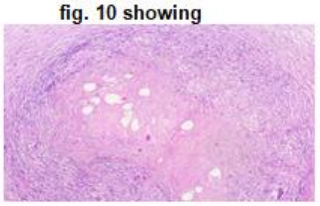

Fig. 7: Shows high power view of fig 3.

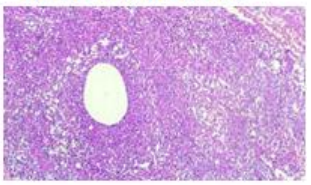

Fig. 8: Shows idiopathic granulomatous mastitis

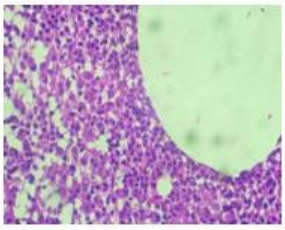

Fig 9: High power view of fig 3, showing the cystic cavity and lining showing histiocytic and granulomatous inflammation

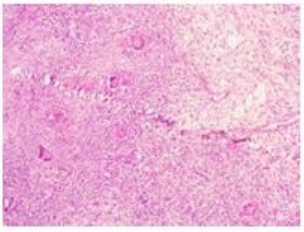

Fig. 10: Shows epitheloid granuloma with giant cells

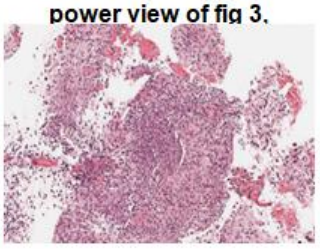

Fig. 11: Shows low power view of sarcoid granuloma

Fig. 12: Shows sarcoid granuloma showing giant cell with inclusions

Fig. 13: Sarcoid granuloma (naked granuloma)

Fig. 14: Shows high power view of sarcoid granuloma

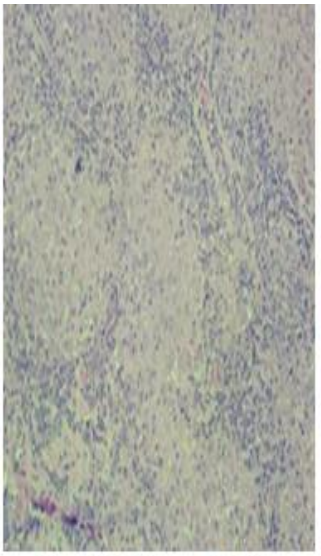

Fig. 15: Shows high power view of sarcoid granuloma

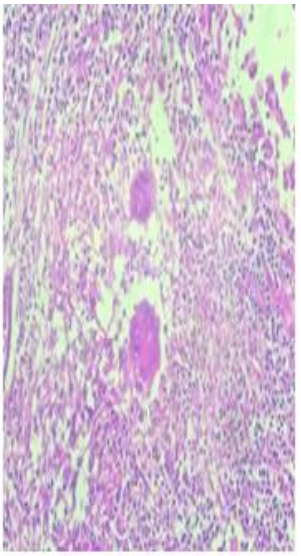

Fig. 16: Shows foreign body giant cell granuloma

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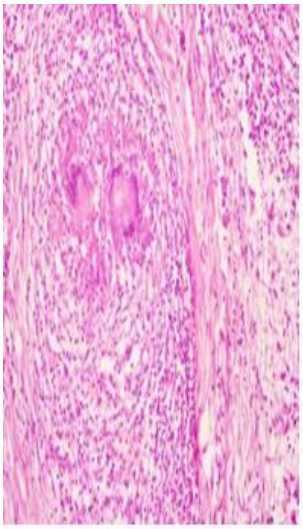

Fig. 17: Shows high power view of foreign body giant cell granuloma

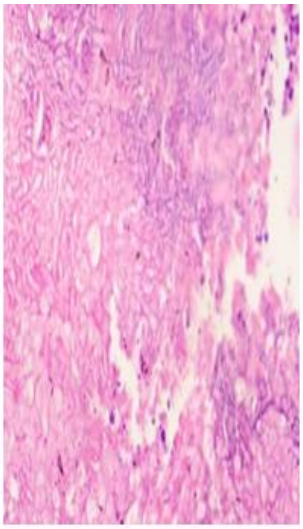

Fig. 18: Shows fungal granuloma showing fungal hyphae, septate branching of aspergillus hyphae

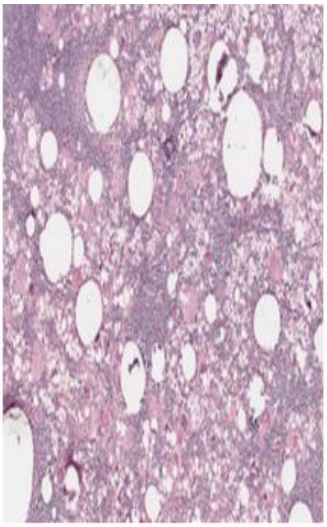

Fig 19: Showing fatty spaces with multiple fat necrosis

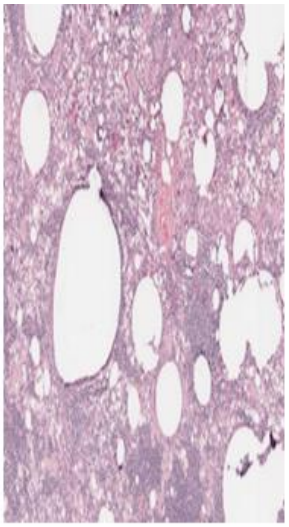

Fig. 20: Showing fatty spaces with multiple fat necrosis, necrotic cells engulfed by giant cells

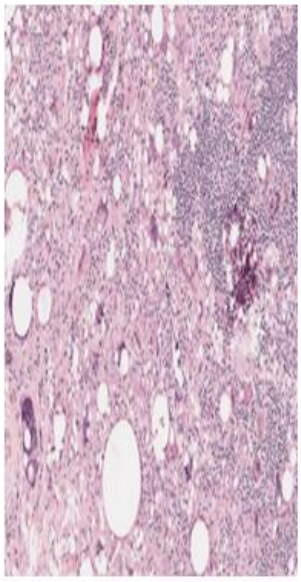

Fig. 21: Showing fatty spaces with multiple fat necrosis, necrotic cells engulfed by giant cells

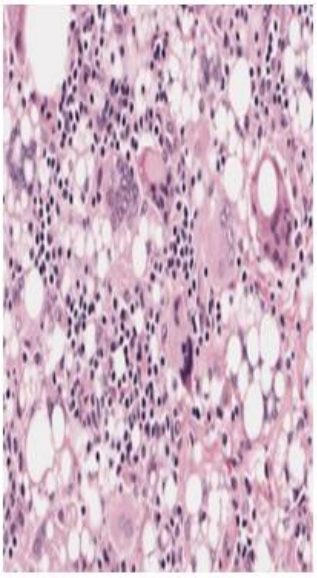

Fig. 22: Showing fatty spaces with multiple fat necrosis, necrotic cells engulfed by giant cells

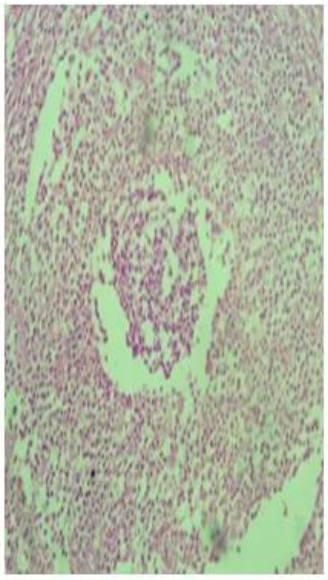

Fig. 23: Shows eosinophilic granuloma

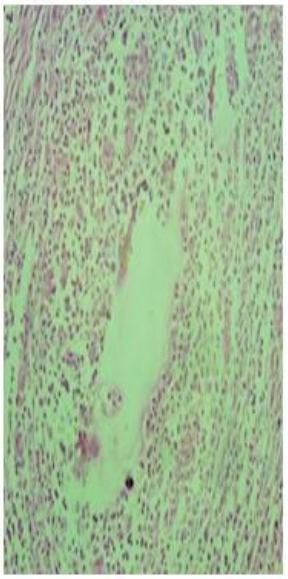

Fig. 24: Shows high power image of eosinophilic granuloma

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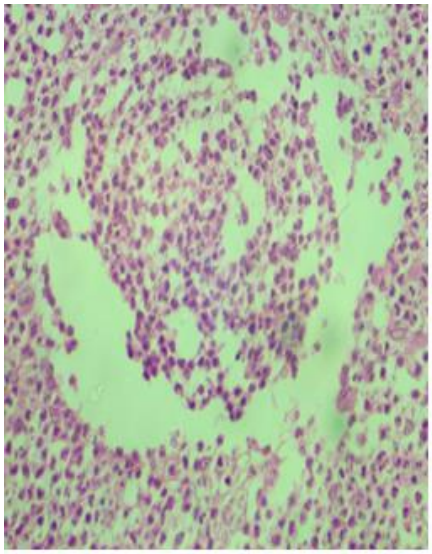

Fig. 25: Shows high power image of eosinophilic granuloma

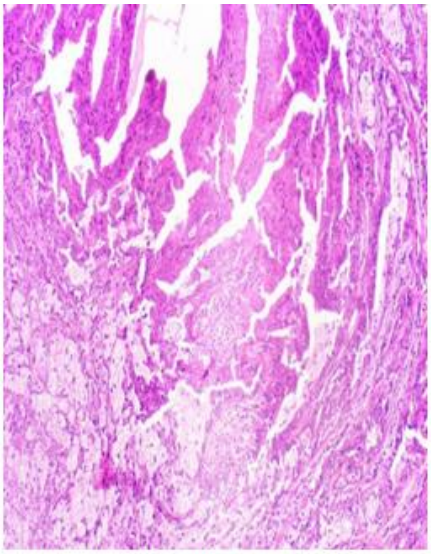

Fig. 26: Shows ductal papilloma with granulomatous mastitis

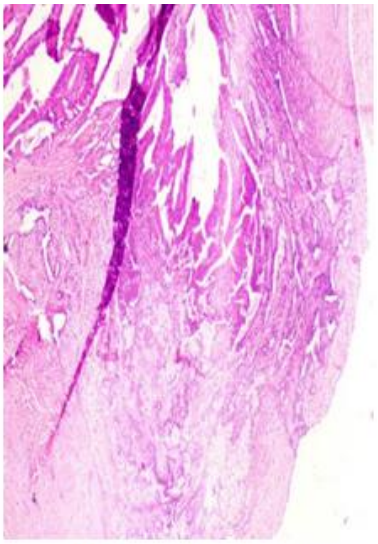

Fig. 27: Shows ductal papilloma with granulomatous mastitis

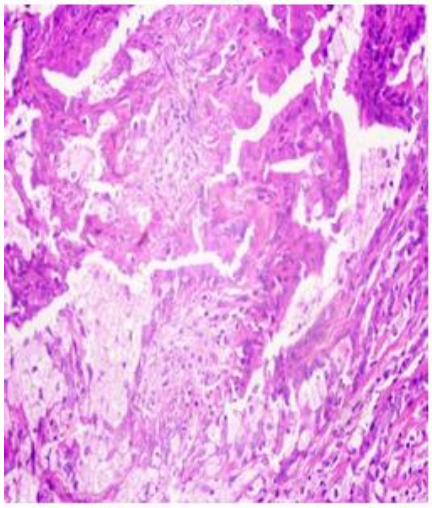

Fig. 28: High power image of ductal papilloma with granulomatous mastitis, showing chronic inflammatory infiltrate and foamy histiocytes

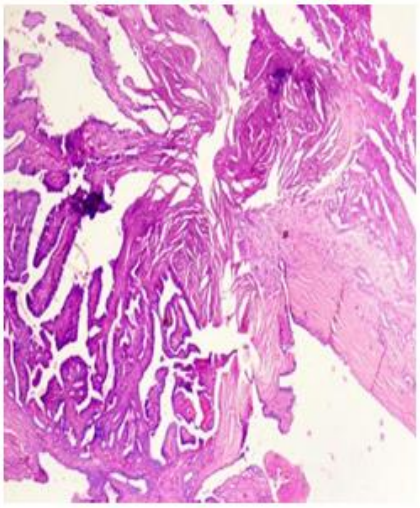

Fig. 29: Shows ductal papilloma with granulomatous mastitis

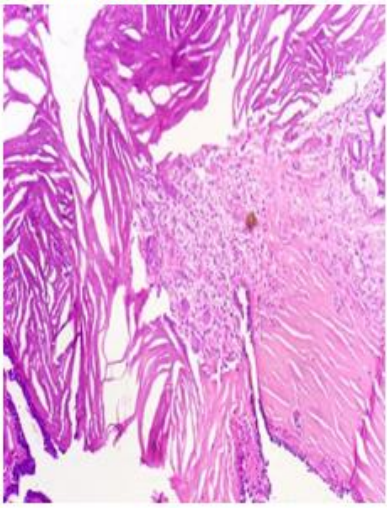

Fig. 30: Ductal papilloma with granulomatous mastitis

DISCUSSION

The etiology of granulomatous mastitis is quite elusive in most cases, and it presents as a diagnostic dilemma. Mycobacterial, fungal, parasitic disease, sarcoidosis, IgG4 related sclerosing disease and autoimmune diseases can involve the breast and show a granulomatous pattern[11,12,13,14,15,16,17,18,19]. Also squamous metaplasia of lactiferous ducts (SMOLD), foreign body reaction and fat necrosis should be thought of in differential diagnosis. In case of granulomatous lobar mastitis, the granulomas being located deeply in breast parenchyma, FNAB has a lower sensitivity as compared to core needle biopsies, as the later can be used to make a definitive diagnosis, while the former may rule out malignancy[20]. Both incisional and excisional biopsies are helpful to identify the localisation of the granuloma, and for architectural evaluation. In case of fat necrosis, the lipid laden foamy histiocytes are diagnostic, besides the clinical history. In case of extensive foreign body giant cell reaction, the classic features may not be visualised. Cystic neutrophilic granulomatous mastitis (CNGM) is characterised by lobulocentric mixed inflammatory infiltrate composed of lymphocytes, neutrophils and multinucleated giant cells; central round cystic spaces (lipid vacuoles) rimmed by neutrophils and a cuff of epitheloid histiocytes. Central lipid spaces surrounded by neutrophils are not specific for CNGM, and should be investigated for fungal, mycobacterial and other bacterial organisms[21]. Tuberculous mastitis affects ducts, rather than lobules and is composed of necrotising or non-necrotising granulomas. EZN staining, culture or PCR can be used for establishing the diagnosis[22,23].Eosinophils are rare in the mammary gland in breast carcinoma as well. They are more commonly seen in inflammatory

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conditions of the breast. Eosinophilic mastitis is an extremely rare condition characterised by heavy eosinophilic infiltrates around the ducts and lobules. Most of them are accompanied with hypereosinophilic syndromes, as per literature[24]. Though sarcoidosis typically is rare in pregnancy, those occurring in pregnancy, probably are breast sarcoidosis[25,26]. Patients with idiopathic granulomatous mastitis present with a breast mass that is initially difficult to differentiate from breast carcinoma, for which imaging studies must be done.Inflammation in IGM starts around lobules, with disease progression, duct lumens and interstitium are involved. The treatment of granulomatous mastitis is complete resection, or open biopsy with corticosteroid theraupy. Immunosupressive agents such as methotrexate, azathioprine, leflunomide, cyclophosphamide, thalidomide, anti-inflammatory antimicrobial agents such as antimalarials and tetracycline derivatives may also be used[27,28].

CONCLUSION

Granulomatous mastitis is quite distressing for both patient and the treating physician. Currently, there is no consensus on the etiology, classification and severity of the disease. Due to lack of classification system for GM, its very hard for the treating physician to stratify patients according to recurrence risk, and to make an appropriate decision on the treatment modality. This study may help future studies to establish a definitive classification for the disease, which would have a positive impact on the treatment and outcome.We should try to establish a definitive scoring system, the treatment can then be designed in a precise manner.Low risk patients can be treated medically, whereas high risk ones can be directly referred for surgical treatment without wasting time by medical means.

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