

## Spectrum of granulomatous lesions in a tertiary care hospital

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### Abstract

**Introduction:** Granulomatous lesions comprise a large family of disorders sharing a common histological denominator of formation of granulomas, either immune or non-immune category with tuberculosis being the most common cause in our country.

**Aims and Objectives:** To study the spectrum of granulomatous lesions in a tertiary care hospital, to categorise tuberculous versus non-tuberculous causes and to study the incidence of acid-fast bacilli (AFB) positivity in granulomatous lesions.

**Material and Methods:** This is a retrospective descriptive study of all granulomatous lesions reported over a period of two years from November 2013 to November 2015. All cytology and histopathology cases reported as granulomatous inflammation during this period were taken for this study and, while granulomatous lesions of the skin (Hansens disease) were excluded. Histological findings and acid-fast bacilli staining were then analyzed.

**Result:** In this study, majority of the patients were of 51-60 year age group (30%) followed by 41-50 years (21.42%). The majority of the patients were male (64.28%) followed by females (35.72%). Out of a total of 70 patients, 42.86% (30 cases) showed features of tuberculosis, out of which 7 were positive for Acid-fast bacilli by Ziehl Neelsen stain, and 22 were negative. Out of the 30 cases, 22 showed extensive caseation necrosis. One case of tuberculous lymphadenitis was associated with metastatic ductal carcinomatous deposits in axillary lymph node. 41.42 % showed chronic granulomatous inflammation, 4.29% showed foreign body granulomatous reaction (2 cases of fungal infection and 1 case of gossypiboma). 2.86% showed xanthogranuloma, 1.42% showed Lipogranuloma (chalazion).

**Conclusion:** Tuberculosis is considered first in differential diagnosis of granulomatous diseases, especially in the countries with a high incidence of tuberculosis, but detailed analysis of clinical and ancillary studies are essential to rule out other granulomatous lesions. Exact diagnosis is important for treatment purpose as a lot of granulomatous lesions are treated as tuberculosis on an empirical basis.

**Keywords:** Caseating necrosis, Granulomatous lesions, Xanthogranuloma, Chalazion, Gossypiboma.

### Introduction

Granulomatous lesions comprise a large family of disorders sharing a common histological denominator of formation of granulomas. Granulomas may be confluent or discrete and the degree of necrosis is variable, the cell components may differ, and the presence or absence of features like Schaumann bodies and calcification are distinctive. A clinicopathological analysis provides the most secure foundation. Granulomatous reactions are seen in a wide variety of diseases like infectious diseases, sarcoidosis, Crohn disease, Wegener granulomatosis, rheumatoid arthritis, berylliosis, drug reactions and foreign body granulomas. The common causes of granulomatous inflammation are infective agents such as mycobacteria, fungi, parasites and non-infective causes including sarcoidosis, foreign bodies, Wegener granulomatosis and Crohn disease. Additionally, certain neoplasms are also associated with a granulomatous reaction in the parenchyma such as Hodgkin disease.<sup>1</sup> Differential diagnosis and management demand a good interpretation of clinical findings and histology. Infections are the most common cause of disseminated granulomatous diseases. Some experts regard infection as the root cause of all such disorders but it still remains undetected in some. Advances in molecular diagnostic techniques over the past decade have allowed

identification of causative organisms that were previously unrecognised.<sup>2</sup> The T cell induces interleukin-1 on the macrophage and thereafter a sequence of chemotactic factors promote granulomagenesis. Interferon-gamma increases MHC class II molecule expression on the macrophages, and activated macrophage receptors carry an Fc portion of IgG to potentiate their ability to phagocytose. The end result is the formation of epithelioid granuloma which progress under the impact of transforming growth factor and platelet-derived growth factor towards fibrosis.<sup>3,4</sup> Large family of granulomatous lesions comprise infections, vasculitis, leucocyte oxidase defect, immunological upsets, hypersensitivity, chemicals and neoplasia.<sup>5</sup> Chronic granulomatous disease is being recognized more commonly in adults. Though it is still rare, it has to be excluded in unexplained granulomas or infections in adults.<sup>6</sup>

### Aims and Objectives

- To study the spectrum of granulomatous lesions in a tertiary care hospital and to categorise tuberculous versus non-tuberculous causes.
- To study the incidence of acid-fast bacilli positivity in granulomatous lesions.

## Material and Methods

This is a retrospective descriptive study of all granulomatous lesions reported over a period of two years. All cases reported as granulomatous inflammation in the Department of Pathology, Saveetha Medical College over a period of two years from November 2013 to November 2015 are taken from the archives of cytology and histopathology and analysed, while granulomatous lesions of the skin (Hansens disease) were excluded from the study. A total of 29 FNAC and 41 histopathology cases were included for the study.

## Results

**Table 1: Age-wise distribution of the cases**

Age (Years)	Number of cases	Percentage
<10	2	2.85%
11-20	3	4.28%
21-30	9	12.85%
31-40	13	18.57%
41-50	15	21.42%
51-60	21	30%
>60	7	10%
Total	70	100%

The majority of the patients were from the 51-60 year age group (30%) followed by 41-50 years (21.42%); least common in <10 years (2.85%).

**Table 2: Sex-wise distribution of the cases**

Sex	Number of cases	Percentage
Male	45	64.28%
Female	25	35.72%
Total	70	100%

The majority of the patients were males (64.28%) followed by (35.72%) females.

**Table 3: Distribution of the cases as per the histopathological features**

S. No	Pathological diagnosis	Common pathological features	Number of cases	Percentage
1.	Features suggestive of tuberculosis	Caseating tuberculous lymphadenitis	20	28.57%
		Tuberculous arthritis	1	1.43%
		Necrotizing granulomatous lesion probably tuberculosis	1	1.43%
		Granulomatous lymphadenitis probably tuberculosis	8	11.43%
2.	Chronic granulomatous inflammation	Chronic granulomatous inflammation	29	41.42%
		Chronic granulomatous inflammation with Abscess	4	5.71%
3.	Granuloma with foreign body giant cell reaction	Fungal infection with foreign body granulomatous inflammation	2	2.86%
		Gossypiboma with foreign body granulomatous reaction	1	1.43%
4.	Miscellaneous	Xanthogranulomatous inflammation	2	2.86%
		Lipogranulomatous inflammation	1	1.43%
		Chronic pancreatitis with granulomatous reaction	1	1.43%
Total			70	100%

Out of a total of 70 patients, 42.86% (30 cases) showed features of tuberculosis (which included 20 cases of caseating tuberculous lymphadenitis, 1 case of tuberculous arthritis), out of which 7 were positive for Acid-fast bacilli by Ziehl Neelsen stain, and 22 were negative. Out of the 30 cases, 22 showed extensive caseation necrosis and the remaining 8 showed caseation necrosis focally. In one case with clinical diagnosis of carcinoma breast with axillary lymph node metastasis, Modified radical mastectomy was performed which on histopathology showed invasive ductal carcinoma and out of 8 axillary lymph nodes, 2 showed metastatic carcinomatous deposits of ductal carcinoma, 2 showed caseating tuberculous lymphadenitis and the remaining 4 showed features of reactive lymphadenitis.

41.42% showed chronic granulomatous inflammation, 4.29% showed foreign body granulomatous reaction (which included 2 cases of fungal infection and 1 case of gossypiboma (due to gauze fiber) presenting clinically as a pyocele). 2.86% showed xanthogranuloma, 1.42% showed Lipogranuloma (chalazion). One case of fibroadenoma breast showed areas of infarction with xanthogranulomatous reaction.

**Table 4: Histopathological diagnosis, special stains in correlation with the initial clinical diagnosis**

S. No	Histopathological Diagnosis		Frequency	AFB		PAS		GMS		Initial Clinical Diagnosis (No of cases)
				+	-	+	-	+	-	
1.	Features suggestive of tuberculosis	Caseating tuberculous lymphadenitis	19	6	13		1		1	Tuberculous lymphadenitis (12) Lymphoma (3) Cold abscess (1) Axillary swelling (1) Implantation dermoid (1) Submandibular swelling (1)
		Caseating tuberculous lymphadenitis with metastatic carcinomatous deposits	1		1					Carcinoma breast metastasis to axillary lymph nodes (1)
		Tuberculous arthritis	1	1	0		1		1	Tuberculous arthritis (1)
		Necrotizing granulomatous lesion probably tuberculosis	1		1					Paravertebral mass (1)
		Granulomatous lymphadenitis probably tuberculosis	8		7					Tuberculous lymphadenitis (6) Preauricular swelling (1) Dermoid cyst (1)
2.	Chronic granulomatous inflammation	Chronic granulomatous inflammation	29		12		4		2	Tuberculous lymphadenitis (12) Suppurative lymphadenitis (2) Breast lump (2) Breast abscess (1) Spinal tuberculosis (1) Suprasternal swelling (1) Sebaceous cyst (1) Abscess (1) Lumbar spondylosis (1) Forearm swelling (1) Submandibular swelling (1) Parotid swelling (1) Mucosal irregularities at lower end of rectum (1) Fistula in ano (1) BPH (1) Rheumatoid arthritis (1)
		Chronic granulomatous inflammation with Abscess	4		3					Tuberculous lymphadenitis (3) Submandibular swelling (1)
3.	Granuloma with foreign body giant cell reaction	Fungal infection with foreign body granulomatous inflammation	2		2	2		2		Implantation dermoid (1) Swelling Back (1)
		Gossypiboma with foreign body granulomatous reaction	1		1		1		1	Pyocele (1)

4.	Miscellaneous	Xanthogranulomatous inflammation	2		1		1		1	Breast abscess (1) Fibroadenoma breast (1)
		Lipogranulomatous inflammation	1							Chalazion (1)
		Chronic pancreatitis with granulomatous reaction	1		1					Chronic pancreatitis (1)
Total			70	7	42	2	8	2	8	

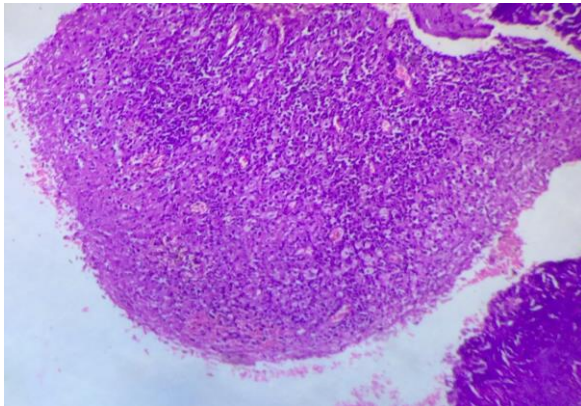


Fig. 1: Xanthogranulomatous inflammation breast

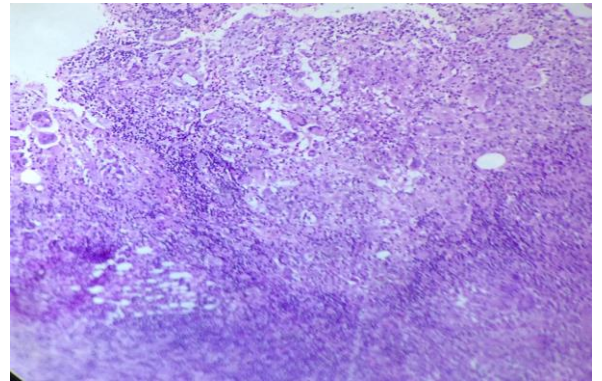


Fig. 4: Granulomatous mastitis

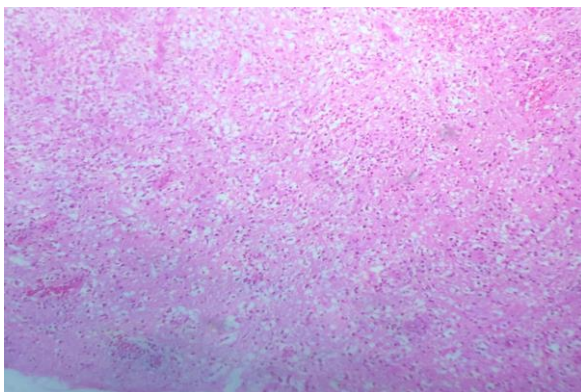


Fig. 2: Lipogranuloma (Chalazion)

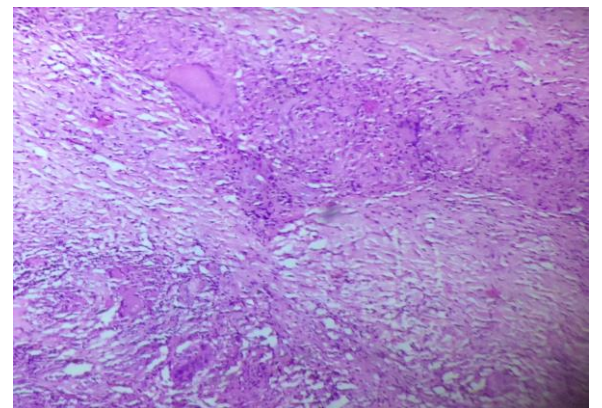


Fig. 5: Granulomatous inflammation wrist

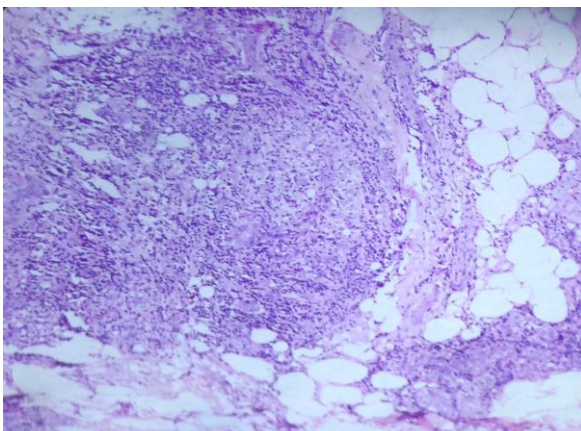


Fig. 3: Granulomatous mastitis

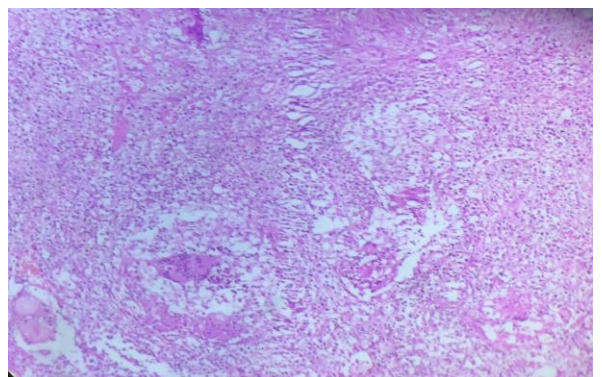
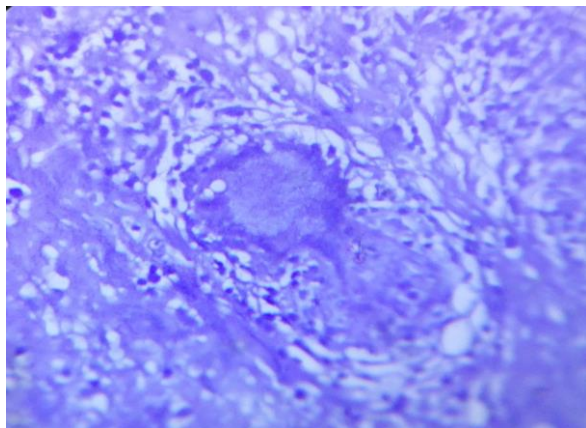
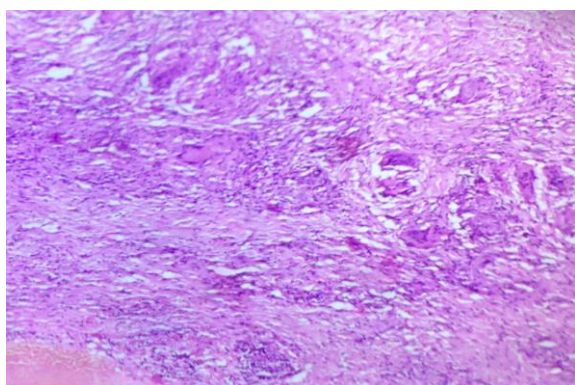


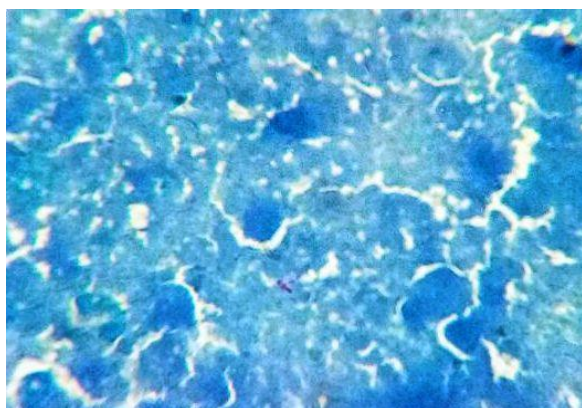
Fig. 6: Granulomatous inflammation prostate



**Fig. 7: Foreign body granuloma**



**Fig. 8: Tuberculous granuloma**



**Fig. 9: Caseous necrosis with Acid Fast Bacilli positivity**

### Discussion

In this study, the majority of the patients were from 51-60 year age group (30%) followed by 41-50 years (21.42%); 31-40-18.57%; 21-30-12.85%; >60-10.00%; 11-20-4.28%; <10-2.85%. The majority of the patients were males (64.28%).

Out of a total of 70 patients, 30 cases (42.86%) showed features of tuberculosis, out of which 7 were positive for Acid-fast bacilli and 22 were negative. 41.42% showed chronic granulomatous inflammation, 4.29% showed foreign body granulomatous reaction (which included 2 cases of fungal infection which was

confirmed by staining with PAS and GMS stains and 1 case of gossypiboma (due to gauze fiber) presenting clinically as a pyocele). 2.86% showed xanthogranuloma, 1.42% showed Lipogranuloma (chalazion).

Ziehl-Neelsen stain for acid-fast bacilli is positive only in around one-third to one-fourth of the cases with confirmed tuberculosis infection. Detection of tuberculosis, especially in the tissue slides is still based on the histological characteristics of granuloma, which has several differential diagnoses each having different treatments. Ziehl-Neelsen staining has low sensitivity, especially in tissue sections and requires the presence of intact tubercle bacilli.<sup>7,8</sup>

In this study, out of 84.28% of cases suggestive of tuberculosis and only granulomatous inflammation, 19% of cases showed AFB positivity by Ziehl-Neelsen staining and 81% were AFB negative. In a study by Abdurehman et al, from a total of 60 specimens examined by Ziehl-Neelsen staining technique, acid-fast bacilli was microscopically identified and confirmed in 37 (61.7%) of the nodal tissue biopsies. The bacilli in the tissues were scanty and were seen in the granulomas associated mainly within the epithelioid cells as well as in the caseation necrotic areas. The Acid fast bacilli seen were fragmented or beaded rods present inside the cells or outside near the cell.<sup>9</sup> Considering the limitations in sensitivity and specificity of Ziehl-Neelsen staining for mycobacterial detection, mycobacterial culture, and molecular and serological techniques, histomorphological analysis appears to be the only important and feasible technique for the diagnosis of tuberculosis in some patients.<sup>10,11,12</sup>

### Conclusion

Tuberculosis is considered firstly in the differential diagnosis of granulomatous diseases, especially in the countries with a high incidence of tuberculosis, but it is always required to confirm by detailed analysis of clinical and ancillary studies to rule out other granulomatous diseases. Tuberculosis must always be excluded in spite of cases not showing AFB positivity, as exact diagnosis is important for the treatment purpose.

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