

“A HISTOPATHOLOGICAL STUDY OF GRANULOMAS WITH CLINICAL CORRELATION”

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Abstract

Introduction: A localised collection of immune cells that develops in reaction to a chronic inflammatory stimulation is called a granuloma.^[1] During the second wave of COVID-19, granulomas were particularly essential diagnostic features in diseases such as tuberculosis, leprosy, and mucormycosis. This study examines the clinical correlation and histological assessment of granulomatous lesions in a tertiary care setting in Eluru, Andhra Pradesh.

Materials and Methods: A retrospective study was conducted from January 2019 to December 2021. Specimens from granulomatous lesions across various departments were analyzed. Hematoxylin & Eosin (H&E), Ziehl-Neelsen (ZN) stain for Acid-Fast Bacilli, and Periodic Acid-Schiff (PAS) stain were used for Histopathological examination. Data analysis was done using SPSS version 20.

Results: Out of 4100 biopsies, 40 cases (1%) were identified as granulomatous lesions. Tuberculosis accounted for the highest incidence (55%), followed by leprosy (17.5%) and mucormycosis (15%). The cervical and supraclavicular lymph nodes were the most common site of lesions (22.5%). The study also noted a male preponderance (55%), with the 51–60 years age group being the most affected (27.5%).

Conclusion: Granulomatous inflammation remains a significant diagnostic challenge, particularly in tuberculosis. The majority of granulomatous lesions were of tuberculous etiology. The study underscores the importance of histopathological evaluation in the early diagnosis and management of granulomatous diseases, especially in the wake of the COVID-19 pandemic.

Keywords: Granulomas, Tuberculosis, Histopathology, Mucormycosis, Leprosy.

Introduction:

A localised collection of immune cells that develops in reaction to a chronic inflammatory stimulation is called a granuloma. Mature macrophages are characterised by their compact organisation, which may or may not be connected to other types of inflammatory cells. Granuloma production can be caused by a variety of stimuli, both viral and non-infectious. There are certain situations, like sarcoidosis, where the trigger is yet unknown. Numerous fungal infections, parasites like schistosomiasis, and bacteria like Mycobacteria are examples of infectious stimuli. Triggers that are not infectious include neoplasia, autoimmune diseases, and foreign objects like sutures.^[1]

Granulomas in sarcoidosis rarely exhibit central necrosis or caseation of the granuloma; nevertheless, this is a common finding in TB and other pathogen-driven granulomas. It is generally accepted that *M. tuberculosis* thrives in necrosis and uses it to propagate its progeny, despite the fact that the actual cause of necrosis is uncertain.^[2,3,4] It is common to refer to the histiocytes in granulomas as "epithelioid." Unlike conventional histiocytes, which have round, oval, or kidney bean-shaped nuclei and well-defined cell boundaries, epithelioid histiocytes have elongated, sole-shaped nuclei.^[5] Surgical pathologists most frequently find granulomas in the skin and subcutaneous tissues, lymph nodes, and lungs.^[6]

Among all the infectious causes of granulomas, tuberculosis bears the highest incidence rate, with World Health Organization (WHO) statistics for 2022 giving an estimated incidence figure of 2.8 million cases for India out of a global incidence of 10.6 million cases.^[7]

Granulomas are quite commonly noted and are an essential part of diagnosis in tuberculosis, leprosy, and mucormycosis cases, which were dramatically increased during the second wave of COVID-19. This project focusses on the histopathological evaluation of granulomatous inflammatory lesions with various etiologies associated with clinical correlation and also to find the frequency of granulomatous lesions in comparison with other studies.

Materials and Methods:

This retrospective study was conducted at a tertiary care center in Eluru district, focusing on patients who visited, consulted, and were treated there. The study included all biopsies reported as granulomatous lesions in the Department of Pathology during a three-year period from January 2019 to December 2021. Patients who provided consent for the study were included, while inadequate or improperly fixed specimens and those who did not give consent were excluded. Fresh specimens were submitted in sterile, properly labeled containers filled with formalin, and after tissue processing, embedding, and sectioning using a microtome, staining was performed. Hematoxylin & Eosin (H&E) staining was done for all sections, and special stains like Ziehl-Neelsen (AFB) and Periodic acid-Schiff (PAS) were used as needed. The data was entered into Microsoft Excel 2010 and analyzed using SPSS Trial Version 29, with quantitative variables expressed as means and frequencies as percentages. The study was conducted with approval from the Institutional Ethics Committee, ensuring confidentiality of individual data collected.

Results :

Out of 4100 total biopsies in a 3 year period from Jan 2019 to Dec 2021, 40 cases were reported as granulomatous inflammatory cases due to various etiological factors. Granulomatous inflammation in cervical lymph nodes is the commonest site followed by skin, abdomen and inguinal lymph nodes in present study.

Table 1: Distribution of study group population according to location of the lesion

Site	No of Cases	%
Intestine	4	10

Joints	2	5
Cervical and Supraclavicular lymph node	9	22.5
Inguinal Lymph node	4	10
Ear	3	7.5
Brain	2	5
Respiratory system	4	10
Skin	7	17.5
Frontal and Sphenoidal Sinuses	1	2.5
Breast	1	2.5
Kidney	2	5
Male genital system	1	2.5

Table 2: Age wise categorization of cases

Age	No of Cases	%
10-20 Years	5	12.5
21-30 Years	4	10
31 - 40 Years	8	20
41-50 Years	8	20
51-60 Years	11	27.5
61-70 Years	1	2.5
71- 80 Years	3	7.5

There was wide range of age group involvement in the study, of which 51 to 60 years age group showed a greater number of cases comprising of 27.5% (table 2). The minimum age of patient was 11 years and maximum age was 80 years in present study.

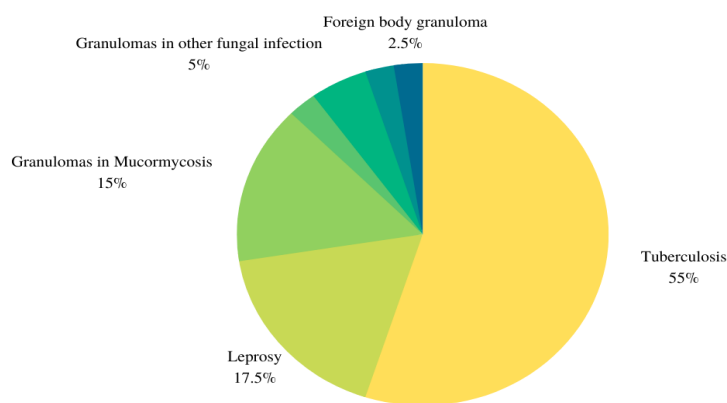
Table 3: Gender Distribution in Study group

Gender	No of Cases	%

Male	17	42.5
Female	23	57.5

The present study observed female predominant granulomatous lesions comprising of 23 cases (57.5%) followed by 17 cases (42.5%) of male patients (Table 3).

Image 1: Pie chart showing etiological causes granulomatous inflammation.



The present study shows highest number of cases with tuberculous etiology comprising of 22 cases (55%), followed by 7 cases (17.5%) of leprosy and later is granulomas associated with mucormycosis during covid period with 6 cases (15%). All the cases of tuberculous etiology were confirmed by ZN stain and few of them were also confirmed with CBNAAT with a tiny aspirate material sent in normal saline. The granulomas due to fungal infections were confirmed using PAS stain which identifies the fungal filaments.

Image 2: Tuberculous granulomatous inflammation in a cervical lymph node.

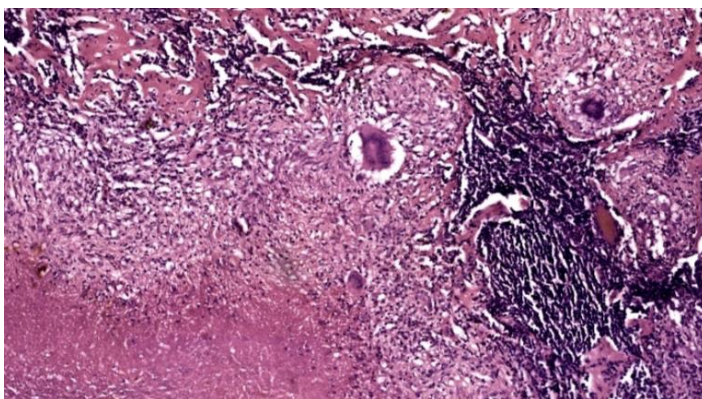
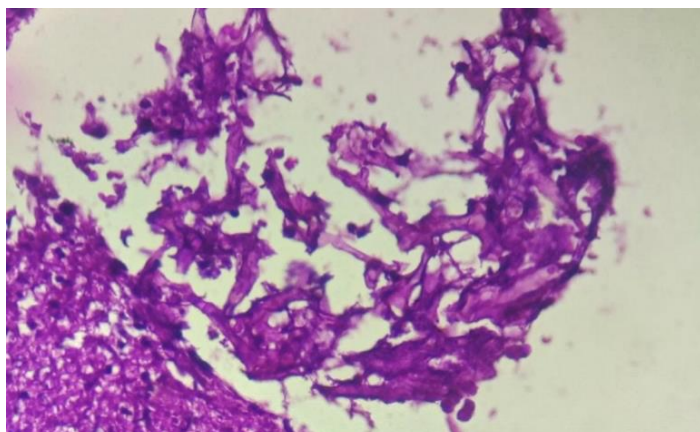


Image 3: PAS stain for fungal hyphae in granulomatous lesion.



Discussion

In this study, granulomatous lesions were common in 51-60 yrs age group. The present study showed male preponderance, correlating to other similar studies. J Pawale et al study^[8], Adhikari RC et al study^[9] also had similar percentage, showing male preponderance and correlating to present study.

Table 4: Comparison of gender distribution of granulomas in various studies.

Study	Male	Female
J Pawale et.al	54.12%	45.88%
H S Permi et.al	52.36%	47.64%
Adhikari R C et.al	54.54%	45.46%
Present Study	42.5%	57.5%

H.S. Permi et.al study^[10] showed increase in leprosy associated granulomas followed by fungal infections which correlated to the present study. However, the present study showed increase in mucormycosis infection associated with granulomas, due to the increase in the incidence of these cases during the second wave of COVID-19 in India.

Table 5: Comparison of etiology of granulomas

Etiology of granuloma	H S Permi et.al	Adhikari R C et.al	Present study
Tuberculosis	47.26%	61.9%	55%
Leprosy	12.72%	0.5%	17.5%

Granulomas in Mucormycosis	-	-	15%
Xanthogranulomatous lesion	-	-	2.5%
Granulomas other Fungal Infection (Aspergillosis)	8.73%	3.1%	5%
Cholesterol Granuloma	-	-	2.5%
Foreign body granuloma	8.36%	1.7%	2.5%
Abscess with Granulomatous Infection of unknown etiology	8.00%	28.9%	-
Tumor with granuloma	5.83%	0.2%	-
Rhinoscleroma	5.10%	-	-
Actinomycosis	1.45%	-	-
Parasites	1.45%	0.7%	-
Rheumatoid arthritis	1.10%	-	-
Sarcoidosis	-	0.5%	-
Catscratch disease	-	0.5%	-
Chron's disease	-	0.5%	-
Leishmaniasis	-	0.5%	-
Chalazion	-	0.2%	-
Toxoplasmosis	-	0.7%	-

H S Permi et.al study^[10] and Adhikari R C et.al study^[9] has a greater number of cases with tuberculous etiology similar to the present study. A prevalence rate of 86% of tuberculosis is seen in Andhra Pradesh according to annual TB report 2022, which correlates with the study as leading cause of granulomas.

In case of Tuberculosis, gaining a better understanding of the factors that promote or limit tuberculosis will contribute significantly to the development of new diagnostics and means of prevention and treatment of tuberculosis. Identification of granulomas is also helpful in differentiating intestinal tuberculosis from its differential diagnosis because it has clinical symptoms that can mimic a variety of diseases and hence called the great mimicker.

Table 6: Comparison of lesion site in various studies.

Site of lesion	H S Permi et.al	Adhikari R C et.al	Present study
Gastrointestinal tract	8%	5.5%	10%
Bones and joints	18.2%	11.5%	5%
Lymph node	21.5%	41.1%	32.5%
Ear	-	-	7.5%
Brain	0.72%	0.2%	5%
Respiratory system	9.46%	7.7%	10%
Skin	24.7%	22%	17.5%
Frontal and Sphenoidal Sinuses	-	-	2.5%
MGT	3.64%	1.4%	2.5%
Urinary system	-	2.4%	5%
FGT	2.55%	2.4%	-
Pericardium	-	2.2%	-
Oral cavity	2.8%	0.7%	-
Breast	-	0.5%	2.5%
Eye and ocular adnexae	-	1.4%	-
Omentum	-	1.0%	-

Skin and subcutaneous tissue were the most common site in HS Permi et.al study^[10] and J Pawale et.al study^[8] when compared to the present study which shows cervical lymph node as the commonest site, corresponding to Adhikari et.al study^[9].

Conclusion

The histopathological features were consistent with maximum number of tuberculosis cases which is followed by leprosy and mucormycosis. The majority of patients in this study are between the age of 51 to 60 years and showed male predominance. The most common site in this study is found to be cervical lymph nodes followed by skin & subcutaneous tissue. Granulomatous infections present challenges to scientific enquiries and clinical management. The existing literature suggests that the unstable balance between bacterial virulence and host immunity determines the pathological features of infections related to these diseases.

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