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ORIGINAL RESEARCH ARTICLE

Study of Granulomatous Lesions at Various Sites-An Ambispective Study.

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Abstract

Background: Granulomatous inflammation is a chronic inflammatory response characterized by the formation of granulomas, which can occur in response to various infectious and non-infectious stimuli. This study aimed to evaluate the histopathological spectrum, age and gender distribution, and site-wise occurrence of granulomatous lesions.

Methods: This ambispective study analyzed 60 histopathological confirmed cases of granulomatous inflammation over a definite period. Data regarding patient age, gender, and site of the lesion were collected and analyzed.

Conclusion: Granulomatous inflammation is most frequently observed in lymph nodes and breast tissue, particularly in middle-aged females. Tuberculosis is likely the predominant cause in endemic regions. Histopathological study remains crucial in the diagnostic approach to granulomatous conditions.

Results: The most affected age group was 51–60 years (33.3%), with a female predominance (68.3%). The most common site was lymph nodes (68.3%), followed by breast tissue (16.6%) and appendix (5%). Rare sites included the ileocecal junction, endometrium, omentum, testis, gallbladder, and prostate (each 1.6%).

Key words: Granulomatous inflammation, histopathology, tuberculosis, lymphadenitis, mastitis, ambispective study.

1 | INTRODUCTION

Granulomatous inflammation is a distinct and chronic type of inflammatory response, characterized by the collection of activated macrophages, often transforming into epithelioid cells and forming granulomas. (1–4) This type of reaction typically occurs when the immune system attempts to isolate and contain substances supposed as foreign but difficult to eradicate. Granulomas may be infectious commonly caused by agents such as Mycobacterium tuberculosis, fungi, and certain parasites or non-infectious, resulting from conditions like sarcoidosis, Crohn's disease, and foreign body reactions. (2, 5, 6)

The granuloma may be necrotizing, nonnecrotizing, suppurative, diffuse or foreign body type with a broad spectrum of etiologies within each category. Granulomas may also contain additional cells such as neutrophils, eosinophils and fibroblasts, which can provide a clue to the etiology of the granuloma. This pattern of injury response occurs in all age groups and within all tissue sites. (7, 8)

Among the various causes, tuberculosis remains the most frequent etiology of granulomatous inflam-

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mation in developing countries, where it continues to be a major public health challenge. While pulmonary tuberculosis is more common, extrapulmonary involvement often presents as granulomatous lesions at various anatomical sites, including lymph nodes, breast, gastrointestinal tract, genitourinary tract, and others. The diagnosis of such lesions can be challenging due to their variable clinical presentations and overlapping features with malignancies or other inflammatory conditions. (3, 7, 9)

Central necrosis may also help determine the cause of the granuloma; infectious granulomas tend to have central necrosis, termed necrotizing granulomas. (5) Tuberculosis is the most common classical example of necrotizing granuloma, whereas sarcoidosis is the characteristic of non‑ necrotizing granuloma. Fungal infections and parasitic infestation usually have a suppurative granuloma. (3, 5)

Histopathological examination plays a pivotal role in the definitive diagnosis of granulomatous inflammation. It not only confirms the presence of granulomas but also helps differentiate between infectious and non-infectious causes based on cellular patterns, necrosis, and the presence of organisms. However, establishing the precise etiology often requires correlation with clinical, radiological, and microbiological findings. (4, 6, 7)

Ancillary studies like special stains (Ziehl-Neelsen, Grocott methamine silver), (10, 11) real-time PCR, In situ hybridization can be performed to find the cause of granuloma. However, some granulomas remain unexplained even with ancillary studies and in these instances, good clinical history and clinicopathological correlation are essential in making a final diagnosis. (12, 13) (14, 15)

This study was undertaken as an ambispective analysis to evaluate the histopathological spectrum of granulomatous lesions across various anatomical sites (16) . The aim was to identify the common sites, age and gender distribution, and relative frequency of these lesions, thereby contributing to improved diagnostic accuracy and patient management, particularly in tuberculosis-endemic regions. (17)

Objectives:

•To identify and analyse the different types of granulomatous lesions occurring at various anatomical sites.

• To assess the demographic distribution (age, gender, etc.) of patients presenting with granulomatous lesions.

2 | MATERIALS AND METHODS

Study design: An Ambispective study (Retroprospective and Prospective).

Study Setting: Attars diagnostic laboratory, Kalaburagi.

Data collection period: 1st January 2020 to 31st December 2024 (5 years)

Sample size: 60 cases

This This was an Ambispective study (Retrospective and Prospective) conducted in Attars diagnostic laboratory, Kalaburagi, for a period of 5 years. The study material included a total of 60 Biopsy proven granulomatous lesions in any tissue spec- imens between January 2020 and December 2024 were included in the study. Data were extracted using medical records of these patients, which is maintained in the laboratory registers. Both retro- spective cases from archived records and prospective cases received during the study period were included. Relevant demographic data including age, gender, and site of lesion were obtained from histopathol- ogy requisition forms and patient records. All tissue specimens were fixed in 10% neutral buffered for- malin, processed routinely, and stained with Hema- toxylin and Eosin (H&E). Special stains such as Ziehl–Neelsen (ZN) for acid-fast bacilli and Peri- odic Acid–Schiff (PAS) for fungi were performed in selected cases where needed. (18, 19)

Inclusion Criteria:

• All cases showing granulomatous inflammation on histopathological examination.

• Specimens from biopsy or excision samples.

• Sufficient tissue available for microscopic analysis.

Exclusion Criteria

• Inadequate tissue or poorly preserved specimens.

STATISTICAL ANALYSIS: Data was compiled using Microsoft Excel and results were expressed in terms of frequency and percentage. Descrip-

tive statistics were used to analyze the age distribution, gender ratio, and anatomical site involvement. (20, 21)

3 | RESULTS AND ANALYSIS

During the 5 year period, 60 patients with granulomatous pathology were evaluated retrospectively and prospectively. The tissues/organs that were most commonly biopsied were lymph node, breast, appendix etc.

Table 1. Age-wise distribution of the cases

Age (Years)	Number of cases	Percentage
<10	1	1.6%
11-20	3	5%
21-30	7	11.6%
31-40	11	18.3%
41-50	14	23.3%
51-60	20	33.3%
>60	04	6.6%
Total	**60**	**100%**

The age of patients ranged from under 10 years to over 60 years. The most affected age group was 51–60 years, comprising 20 cases (33.3%), followed by 41–50 years with 14 cases (23.3%), and 31–40 years with 11 cases (18.3%). The least affected group was children under 10 years, with only 1 case (1.6%).This indicates a predominance of granulomatous lesions in the middle-aged population. (22–25)

Table 2. Gender-wise distribution of the cases

Gender	Number of cases	Percentage
Male	19	31.6%
Female	41	68.3%
Total	**60**	**100%**

Our study showed Female cases: 41 (68.3%) and Male cases: 19 (31.6%). This shows female predominance, with a male-to-female ratio of approximately 1:2.1.

Table 3. Histopathological diagnosis of granulomas at various sites

Sl.No	Histopathological Diagnosis/Site	Total no: of cases	Percentage(%)
01	Chronic granulomatous lymphadenitis	41	68.3%
02	Chronic granulomatous mastitis	10	16.6%
03	Tuberculous appendicitis	03	5%
04	Granulomatous inflammation (ileocecal junction)	01	1.6%
05	Granulomatous endometrium	01	1.6%
06	Granulomatous omentum	01	1.6%
07	Granulomatous orchitis	01	1.6%
08	Granulomatous cholecystitis	01	1.6%
09	Granulomatous prostatitis	01	1.6%
	Total	**60**	**100%**

The above table summarizes the distribution of 60 granuloma cases based on their location: The most common anatomical site was the lymph nodes, with 41 cases (68.3%), consistent with chronic granu-

lomatous lymphadenitis, likely of tubercular etiology.Figure 1

The second most common site was the breast, accounting for 10 cases (16.6%), representing chronic granulomatous mastitis. Tuberculous appendicitis accounts for 3 cases (5%). Rare Sites (each with 1 case, 1.6% each): granulomatous inflammation (ileocecal junction), granulomatous endometrium Figures 2 and 3 granulomatous omentum, granulomatous orchitis, granulomatous cholecystitis and granulomatous prostatitis. The vast majority of granuloma cases are found in lymph nodes and breast tissue. Other sites are rarely affected.

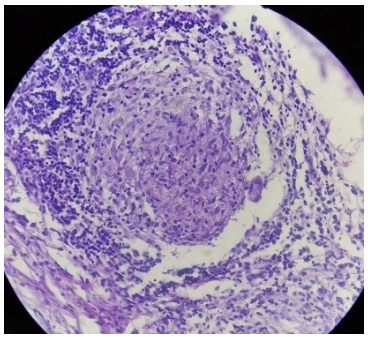

Fig. 1: Microscopy of granulomatous lymphadenitis showing a well formed granuloma with lymphocytes at the periphery.

4 | DISCUSSION:

Granulomatous inflammation is a distinct pattern of chronic inflammation characterized by the formation of granulomas, which are organized collections of epithelioid histiocytes, often with multinucleated giant cells and lymphocytes. This ambispective study aimed to analyze the frequency, age and gender distribution, and histopathological patterns of granulomatous lesions across various anatomical sites.

In our study of 60 histopathologically confirmed granulomatous lesions, the most affected age group was 51–60 years (33.3%), followed by 41–50 years (23.3%) and 31–40 years (18.3%). These findings suggest that granulomatous conditions are more prevalent in middle-aged individuals, possibly due to cumulative environmental exposures, declining immune surveillance, or delayed diagnosis. Very few cases were observed in children (<10 years) and adolescents (11–20 years), indicating lower susceptibility in younger populations.

Females accounted for 68.3% of the cases, significantly outnumbering males (31.6%). This female predominance might be partially explained by the high frequency of chronic granulomatous mastitis in our cohort (16.6% of all cases). Similar gender-based patterns have been reported in previous studies, especially in regions where tubercular mastitis is relatively common. Hormonal, anatomical, and immunological factors may contribute to this gender disparity.

The most common histopathological diagnosis was chronic granulomatous lymphadenitis (68.3%), aligning with findings from studies conducted in tuberculosis-endemic regions. Tuberculous lymphadenitis is a well-known extrapulmonary manifestation of tuberculosis, particularly in developing countries. The high incidence in this study further reinforces the need for robust public health interventions targeting tuberculosis detection and management.

Chronic granulomatous mastitis (16.6%) was the second most frequent diagnosis. Although consid-

Fig. 2: Gross specimen of uterocervix showing irregular and nodular external surface with cut section showing endometrial cavity filled with cheesy, friable, yellowish-white material.

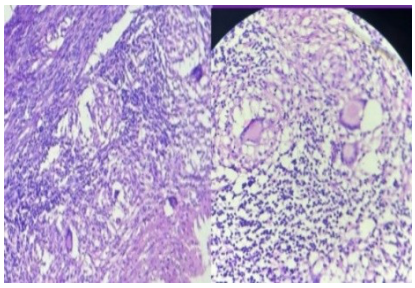

Fig. 3: Microphotograph of endometrium showing numerous epithelioid cell granulomas with Langhan's giant cells along with foci of central caseous necrosis.

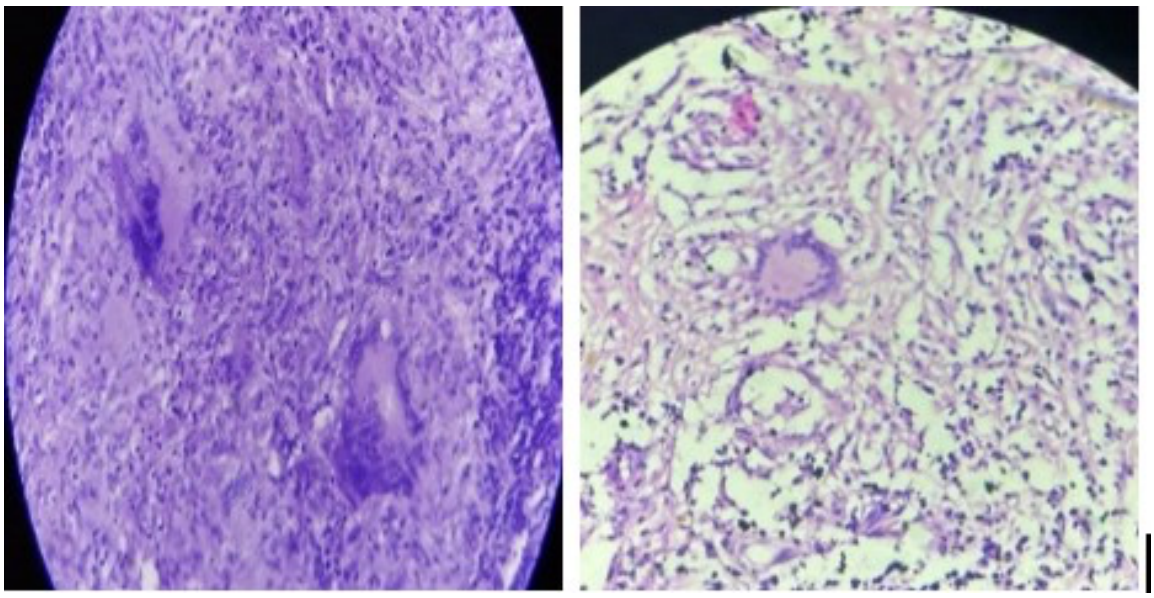

Fig. 4: Microscopyof granulomatous inflammation with multiple epithelioid cell granulomas,multinucleated Langhan's giant cells along with rim of lymphocytes.

ered rare in Western literature, its incidence is relatively higher in developing nations, often mimicking carcinoma clinically and radiologically. Early histopathological diagnosis is thus crucial to prevent misdiagnosis and overtreatment.

Less common sites of granulomatous inflammation in this study included the appendix (5%), ileocecal junction Figure 4 , endometrium, omentum, orchitis, cholecystitis, and prostate (each accounting for 1.6%). The diversity of anatomical involvement highlights the wide-ranging clinical presentations of granulomatous diseases and underlines the importance of histopathology in establishing a definitive diagnosis.

The majority of the lesions studied are likely tubercular in etiology, although microbiological confirmation was beyond the scope of this histopathological study. Nevertheless, in endemic settings, a high index of suspicion for tuberculosis is warranted when granulomatous inflammation is observed, especially in lymph nodes and breast tissue.

Table 4. Comparison of Age Distribution with OtherStudies

Study	Most Common Age Group	% Cases in Peak Group
Present Study (n=60)	51–60 years	33.3%
Adhikari et al., 2013	21–30 years	32%
Permi et al., 2012	20–40 years	45%
Talwar & Sah, 2011	21–40 years	48%
Al-Kandari et al., 2008	31–40 years	29%

In the present study, granulomatous lesions were most commonly seen in the 51–60 years age group, whereas many other studies such as those by Adhikari et al. (2013), Permi et al. (2012), and Talwar & Sah (2011) reported a younger age predominance (20–40 years). This difference could be attributed to regional variations, patient referral patterns, and late presentation in our cohort. The finding highlights the importance of considering granulomatous pathology even in older patients, especially in tuberculosis-endemic regions.

Our study showed a female predominance (68.3%), which correlates with Chander et al. (2016) and Illman et al. (2018), but differs from Adhikari et al. (2013), where males were slightly more affected. The higher female representation in our series is largely due to the significant number of chronic granulomatous mastitis cases, which is inherently a female condition.

Consistent with most published series, our study found lymph nodes as the most common site (68.3%), followed by the breast (16.6%) and appendix (5%). These figures are comparable to Permi et al. (2012) and Talwar & Sah (2011), who also reported a predominance of lymph node involvement. The breast was the second most affected organ, similar to Al-Kandari et al. (2008). Interestingly, our series also documented rare sites like endometrium, omentum, gallbladder, prostate, and testis, highlighting the wide anatomical spectrum of granulomatous pathology. This reaffirms the diagnostic role of histopathology in unexpected organ involvement.

In our study, necrotizing granulomas were the predominant type (~70%), strongly suggesting tubercular etiology, which aligns with reports from tuberculosis-endemic regions where necrotizing granulomas account for 60–80% of cases. Non-necrotizing granulomas were rare and could represent sarcoidosis or idiopathic causes, while suppurative granulomas were uncommon, typically associated with fungal or parasitic infections. Foreign body granulomas were also rare, consistent with global literature. This pattern emphasizes tuberculosis as the leading cause of granulomatous inflammation in our

Table 5. Comparison of Gender Distribution with Other Studies

Study	Male (%)	Female (%)	Remarks
Present Study	31.6%	68.3%	Female predominance
Chander et al., 2016	42%	58%	Slight female predominance
Adhikari et al., 2013	55%	45%	Male predominance
Illman et al., 2018	40%	60%	Higher mastitis cases in females

Table 6. Site-wise Distribution Compared with Other Studies

Study	Lymph Node	Breast	Appendix	Other Rare Sites
Present Study	68.3%	16.6%	5%	Endometrium, omentum, testis, gallbladder, prostate
Permi et al., 2012	65%	12%	6%	Bone, skin, intestine
Adhikari et al., 2013	60%	10%	8%	Liver, spleen
Talwar & Sah, 2011	70%	8%	4%	CNS, GI tract
Al-Kandari et al., 2008	62%	15%	7%	Others (rare)

Table 7. Histopathological Patterns of Granulomatous Inflammation

Pattern	Present Study (%)	Range in Literature (%)
Necrotizing (tubercular)	Majority (~70%)	60–80%
Non-necrotizing (sarcoid-like)	Few	10–20%
Suppurative	Rare	5–10%
Foreign body granulomas	Rare (<2%)	2–5%

study.

5 | CONCLUSION:

Granulomatous inflammation, particularly due to tuberculosis, remains a significant diagnostic entity in developing countries. Lymph nodes and breast tissue are the most commonly affected sites, and common among the middle-aged females. Histopathological examination continues to be a cornerstone in diagnosing granulomatous lesions, guiding further clinical and microbiological workup. Early diagnosis and appropriate treatment can significantly improve patient outcomes, especially in tuberculosis-endemic regions.

Conflict of Interest: Nil.

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