



CLINOPATHOLOGICAL STUDY OF GRANULOMATOUS LESIONS AT TERTIARY CARE CENTRE (A STUDY OF 155 CASES).

Pathology

Dr. Noopur K. Bansal

MBBS, MD Pathology, Senior Resident, Department of Pathology, B. J. Medical College and Civil Hospital, Asarwa, Ahmedabad- 380016, Gujarat, India.

Dr. Hetal S. Patel*

MBBS, MD Pathology, Senior Resident, Department of Pathology, B. J. Medical College and Civil Hospital, Asarwa, Ahmedabad- 380016, Gujarat, India. *Corresponding Author

ABSTRACT

INTRODUCTION Granuloma is a focus of chronic inflammation consisting of microscopic aggregation of macrophages that are transformed into epithelial like cells, surrounded by a collar of lymphocytes and occasionally plasma cells. It is characterised by focal collections of macrophages, epithelioid cells and multinucleated giant cells. It is response to infectious or non-infectious injurious stimuli. Fate of granuloma can be either necrosis or fibrosis depends on immune reactions

AIMS & OBJECTIVES

- To find out the etiology incidence of granulomatous lesions.
- To study the histopathology of granulomatous lesions.
- To correlate the clinical findings and laboratory findings with histopathological findings.
- To compare age and sex wise distribution

MATERIAL AND METHODS:

Cases received from June 2017 to December 2019, All biopsies received in Histopathology section from various departments of Our hospital included for this study. During this period total 155 cases of Granulomatous lesions were found and their Clinical details, laboratory parameters and histopathology were studied. The data was retrieved from computerised software laboratory information system (LIS). **RESULTS:** In present study, out of 155 cases most common cause of Granuloma was Tuberculosis seen in 100(64.51%) cases followed by Foreign body granuloma in 30(19.35%) cases, Leprosy in 10(6.45%) cases, Fungal granuloma in 7(4.52%) cases, Tumor associated granuloma in 5(3.23%) and Granuloma of unknown etiology in 3(1.94%) cases. GIT was the commonest site followed by Skin. In Granulomatous lesions, the most common clinical feature was pain in 80 cases (51.61%) and fever was in 64 cases (41.29%) followed by Swelling 55 cases (35.48%). **CONCLUSIONS:** Granuloma are the commonest lesions that the pathologist come across in routine practice. In order to treat these lesions, definitive diagnosis by the demonstration of the etiological agent is essential, which will bear an impact on patient management and outcome. Histopathological examination of granulomatous lesions helped us to find exact etiology of granuloma. Cooperation between the clinician and pathologist is more important, if the patient is to derive the greatest benefit.

KEYWORDS

Granulomatous lesion, Giant cells, Macrophages.

INTRODUCTION:

Granulomatous lesions are seen in high incidence. Tuberculosis is most common granulomatous lesion seen in our country. It comprises a large bunch of pathology. Diagnosis of these lesions according to etiology with high accuracy rate is important for management of patient.

Granulomatous inflammation is a form of chronic inflammation characterized by collections of activated macrophages, often with T lymphocytes, and sometimes associated with central necrosis.¹ It is also defined as a special type of chronic inflammation characterised by focal collections of macrophages, epithelioid cells and multinucleated giant cells.² The granulomatous inflammatory response is ubiquitous in pathology, being a manifestation of many infections, toxic, allergic, autoimmune and neoplastic diseases, vasculitis, immunological aberrations, leucocyte oxidase deficiency, hypersensitivity, chemicals and also conditions of unknown etiology.

The provocative agents of granulomatous inflammation appear to be nondegradable by both neutrophils and non-active macrophages. The actions of polymorphonuclear leucocytes, non-activated macrophages and chemical mediators which are associated with the tissue injury are insufficient to completely digest and eradicate the offending agents. For such degradation, the action of transformed macrophages which are formed with the help of the CD+T cells is required. The CD+T cells secrete various mediators such as IL2, IFa, TN and lymphotoxin for the transformation of macrophages into epithelioid and giant cells, which are the components of granuloma. The steps in infection are the following:

- Entry into macrophages.
- Replication in macrophages.
- Recognized by innate immune receptors.
- The TH1 response.
- TH1-mediated macrophage activation and killing of bacteria.
- Granulomatous inflammation and tissue damage.³

In granulomas associated with certain infectious organisms (most classically *Mycobacterium tuberculosis*), a combination of hypoxia and free radical-mediated injury leads to a central zone of necrosis. Grossly, this has a granular, cheesy appearance and is therefore called caseous necrosis.⁴

Fate of granuloma can be either necrosis or fibrosis depends on immune reactions. Necrosis causes death of involved tissue. Fibrosis causes permanent tissue damage even after causative agent has been eliminated.

Classification of granuloma based on etiology:

- Infection
 - *Mycobacteria*
 - Fungi
 - Bacteria
 - Protozoa
 - Spirochetes
- Vasculitis
- Immunological aberrations
- Leucocyte oxidase defect
- Hypersensitivity pneumonitis
- Chemicals
- Neoplasia
- Miscellaneous
 - Granuloma Annulare
 - Buruli ulcer
 - Granulomatous Rosacea

Classification based on morphologic criteria:

- Necrotising
 - Caseating granuloma
 - Suppurative granuloma
- Non-necrotising
 - Epithelioid (Non-caseating) granuloma
 - Foreign body granuloma
 - Sarcoid granuloma
 - Histiocytic granuloma

MATERIAL AND METHODS:

Cases received from June 2017 to December 2019, All biopsies received in Histopathology section from various departments of Our hospital included for this study.

The biopsies of the cases which were diagnosed as granulomas from all the sites, on haematoxylin and eosin stained sections were selected. Special stains like ZN were used whenever required. The relevant clinical findings and lab investigation details were collected by a personal interview and the examination of the patient, or from the hospital case sheets and integral server system. Patients were investigated with routine laboratory investigations like complete blood picture (CBC) by automated Cell Counter, erythrocyte sedimentation rate (ESR) by Westergren's Method,

Specimens sent to the histopathology section are fixed, processed, stained and reported.

ETHICAL CONSIDERATIONS:

All procedures performed were in accordance with the ethical standards of the institution.

OBSERVATION AND RESULTS:

In the present study of 155 cases, 64.5% cases were of Tuberculosis, 19.35% cases were diagnosed as Foreign body granuloma, 6.45% cases of Leprosy, 4.52% cases were diagnosed as Fungal granuloma, 3.23% cases as Tumor associated granuloma and 1.94% cases were diagnosed as Granuloma of Unknown etiology. Majority of the patients were seen in Age Group of 20-29 years in 25.16% cases. Males are affected in 90 cases (58%) whereas females are affected in 65 cases (42%). Male to Female ratio is 1.38 :1. The most common site to be affected is GIT (29.03%) followed by Skin (18.07%). The least common affected site are Oral Cavity, Salivary Gland, Spleen and Kidney (0.64% each). Cases of Tuberculosis of soft tissue include Gluteal abscess, Thigh swelling and Chest wall abscess.

Table-1 Laboratory Investigations in patients with Granulomatous Lesions

Parameters	Tuberculosis	Leprosy	Foreign body granuloma	Fungal granuloma	Tumor associated granuloma	Granuloma of unknown etiology	total	Percentage
Hb(g/dl)	<12	77	8	18	5	3	112	72.20%
	≥ 12	23	2	12	2	2	43	27.80%
Total leucocyte count(/cumm)	<4000	15	0	0	0	0	15	9.60%
	4000-11000	82	9	15	5	4	117	75.50%
	>11000	3	1	15	2	1	23	14.90%
ESR(mm/1 hr)	≤20	35	5	28	5	1	77	49.70%
	>20	65	5	2	2	4	78	50.30%

Table-2 Morphology of Granuloma

S. No.	Types of Granuloma	No. Of Cases	Percentage
1	Epithelioid (Non-caseating) granuloma	58	37.42%
2	Caseating granuloma	44	28.38%
3	Foreign body granuloma	33	21%
4	ill-defined granuloma	19	12.26%
5	Histiocytic granuloma	1	0.64%
	Total	155	100.00%

Table 3 Comparison of incidence of various types of granulomatous diseases on histo-pathological study with other studies

Types of Granulomatous Diseases	Jayashreepawal et al(2011) ⁵	Harish S. Permit et al (2012) ⁶	Vaidehi Patel et al (2013) ⁷	Present Study (2019)
Tuberculosis	49%	47%	82%	64.51%
Leprosy	18%	13%	7%	6.45%
Foreign body granuloma	8%	8%	2%	19.35%
Parasitic Granuloma	-	4%	1%	-
Fungal granuloma	6%	9%	4%	4.52%
Actinomycosis	1%	1%	-	-
Tumor associated granuloma	-	6%	-	3.23%
Rhinoscleroma	12%	5%	-	-

In Granulomatous Lesions the most common clinical feature was the pain which was seen in 51.6% cases, followed by Fever in 41.3% cases, followed by Weight loss in 34.8%. In cases which were histopathologically diagnosed as tuberculosis, the clinical feature were Pain (56%), Fever (51%), Weight loss (38%) and Swelling (33%). In Foreign body granuloma, the common clinical feature was pain (56.67%) followed by Weight loss (13.33%) and Swelling (30%). In Leprosy, the common clinical feature was skin lesion (100%) and numbness (60%). In Fungal Granuloma, the common clinical feature was swelling (100%) followed by pus discharge (28%) and pain (28%).

Foreign body granuloma was observed in 19.35% cases. Most common agent were Tattoo Granuloma and Suture granuloma (23.33% each) followed by Hydatid cyst and Epidermoid cyst (10% each), Cholesterol granuloma (6.67%) and Xanthoma & Majocchi granuloma (3.33% each). Other cases of Foreign body granuloma were because of non-specific inflammation of GIT & Joint.

Fungal granuloma was observed in 4.52% cases where the etiological agent was identified. Most common agent was Maduramycosis of foot in 5 cases (71.42%) followed by Aspergillosis in nasal cavity & ear in 2 cases (28.58%).

Granuloma of unknown etiology was observed in 3 cases where the etiological agent was identified. One case was of Crohn's disease and 2nd case was of Granuloma Annulare and 3rd case was of Granulomatous mastitis. Granulomatous response to tumor was seen in 5 cases where each case belongs to Seminoma, Langerhans histiocytosis, Infiltrative ductal carcinoma, Hodgkins lymphoma and Non hodgkin's lymphoma. A various haematological parameters such as Haemoglobin, Total Leucocyte count, ESR were studied and results are given on table No. 1.

Morphological pattern wise distribution is given in Table No 2.

Granuloma of unknown etiology	6%	8%	5%	1.94%

SUMMARY & CONCLUSION:

Present study was carried out in 155 cases of granulomatous lesions of all age groups.

- Out of 155 cases, 65 females and 90 males. The M:F ratio was 1.38:1.
- Maximum number of cases observed was in third decade (20-29 years) followed by forth decade (30-39) and fifth decade (40-49 years)
- GIT was the commonest site followed by Skin.
- In Tuberculosis, the most common clinical presentation was pain in 56 cases (56%), followed by fever in 51 cases (51%)
- In Granulomatous lesions, the most common clinical feature was pain in 80 cases (51.61%) and fever was in 64 cases (41.29%) followed by Swelling 55 cases (35.48%).
- In 112 cases (72.25%) of Granulomatous lesions the Haemoglobin was < 12 gm/dl, in 117 cases (75.48%) total leucocyte count was in normal range of 4000-11000 /cumm and ESR was more than 20 mm/hr in 78 cases (50.32%).
- Most common cause of Granuloma was Tuberculosis seen in 100(64.51%) cases followed by Foreign body granuloma in 30(19.35%) cases, Leprosy in 10(6.45%) cases, Fungal granuloma in 7(4.52%) cases, Tumor associated granuloma in 5(3.23%) and Granuloma of unknown etiology in 3(1.94%) cases.
- Among foreign body Granuloma most common was Tattoo & Suture Granuloma in 7 cases (23.33%).
- Among tumor associated Granuloma most common was lymphoma.

- Out of 155 cases, definite etiological diagnosis of granuloma was made in 152 cases (98.06%).

We conclude that Granuloma are the commonest lesions that the pathologist come across in routine practice. In order to treat these lesions, definitive diagnosis by the demonstration of the etiological agent is essential, which will bear an impact on patient management and outcome. Histopathological examination of granulomatous lesions helped us to find exact etiology of granuloma. Clinical features and laboratory investigations assisted the histopathological study to find out the etiology of granulomatous lesions. Granulomatous lesions have diversity of presentation, so the clinical judgement alone cannot always be relied upon to identify the exact cause in every case. It is here that Histopathology acts as one of the most valuable tests to find out the etiology of lesion.

Thus, histopathological evaluation of biopsies along with clinical features and laboratory investigations, definite etiological diagnosis of most of granulomatous lesions could be made. Cooperation between the clinician and pathologist is more important, if the patient is to derive the greatest benefit.

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