

Research Article

Granulomatous reaction - a histopathological study: a retrospective and prospective study of 5 years

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Received: 23 November 2014

Accepted: 8 December 2014

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ABSTRACT

Background: The present study was done to investigate the prevalence of granulomatous infection among the patients. The study was conducted from the time period of July 2008 to June 2013. The study was conducted at the histopathology laboratory, pathology department, P. D. U. government medical college, Rajkot (Gujarat, India).

Methods: In the present study, total 300 cases were studied. Specimens for study were received from various departments like surgery, ENT, medicine, pediatrics etc. from July 2008 to June 2013. The sections of these specimens were taken & slides were prepared by staining with Hematoxylin & Eosin (H&E) for microscopic examination.

Results: In present study, most the common granulomatous reaction was tuberculosis and majority of cases were found in among young Hindu males specially in the lower socioeconomical class of rural areas.

Conclusion: Our study confirms that the most common granulomatous reaction is tuberculosis, mainly found in skin and more common among the population of lower socioeconomic class & rural population, signifying increasing incidence of granulomatous infection. The present study is a comprehensive comparative study of granulomatous reactions done in correlation with the age, sex, involved sites and clinical profile of the patients. This information is valuable in policy formation for the control & specific treatment and outcome of granulomatous infection.

INTRODUCTION

Granulomatous inflammation was recognized as a distinct entity in the early nineteenth century and has been of continuing interest since then.^{1,2} Yet, granulomatous reaction remains enigmatic. Granulomatous inflammation is a distinctive pattern of chronic inflammation that is encountered in a limited number of infectious and non-infectious conditions.^{3,4} Recognition of granulomatous pattern on histopathology and finding the etiology in a biopsy specimen is very important for specific treatment and outcome of the disease.⁴

The granulomatous inflammatory response is ubiquitous in pathology, being a manifestation of many infective, toxic, allergic, autoimmune and neoplastic diseases and also conditions of unknown etiology.⁵ A knowledge of

the basic pathophysiology of this distinctive tissue reaction is therefore of fundamental importance in the understanding many disease processes.^{4,5} Over the past few decade advances in molecular diagnostic techniques have allowed identification of organisms involved in granulomatous diseases that previously were of unknown etiology.⁶

However, good clinical history, a close histological examination and a clinicopathological correlation is essential in making a final diagnosis. By combining all the available information, one should be able to arrive at a reasonable differential diagnosis on which to proceed. However in a minority of the cases, it will not be possible to make a definitive diagnosis, even with all the clinical information being available. The histopathological

examination of various granulomatous reactions is must to reach a definite diagnosis.

Hence, in the present study we aimed at studying the spectrum of granulomatous reaction, morphological findings of granulomas & finding the etiology of all granulomatous lesions on tissue biopsy sent for histopathological examination and compare them with other studies. We have also included the autopsy specimens, thus including the end stages of granulomatous diseases. Special stains are being used to reach at the diagnosis and for confirmation of exact cause of granulomatous reaction.

METHODS

The histopathological study of various granulomatous reactions was carried out in histopathology laboratory of department of pathology, PDU government medical college and hospital, Rajkot over a period of 5 years from July 2008 to June 2013.

Most of the patients' specimens for histopathological study in our institute are coming from clinical department O.P.D.'s/wards mainly. The specimens for the histopathological study were obtained by incisional skin biopsies, excisional biopsies, resections & other surgical procedures done by clinicians, dermatologists & surgeons, along with the autopsies obtained from forensic department as well as those received from outside. A histopathological study of total 300 cases of granulomatous lesions was done.

For histopathological examination, the specimens were received in 10% formalin. The received specimens have been fixed in 10% formalin and kept overnight. After passing the tissue dehydration in graded alcohol for 6 hours each in three changes, clearing is done with two changes of xylene for hours each. Followed by this, impregnation and embedding in paraffin were done, blocks were prepared and 5µ sections were cut.

Then, the sections were stained with hematoxylin and eosin, dried and mounted in DPX and then microscopy was done.

The cases diagnosed as granulomas from all the sites, on hematoxylin and eosin stained sections were selected. Special stains like Ziehl Neelsen, Fite Faraco, Periodic Acid Schiff, were used whenever required. The relevant clinical details and laboratory investigations were collected from the hospital case sheet.

RESULTS

The present retrospective and prospective study, conducted from July 2008 to June 2013, a time period of 5 years included a total of 300 cases and the study was carried out in histopathology section, department of pathology, P. D. U. government medical college and

hospital, Rajkot. These cases were further studied and analysed in correlation with the clinicopathological profile and various histopathological findings.

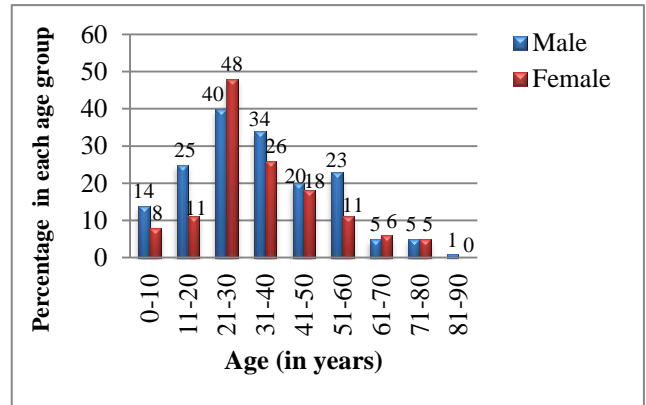


Figure 1: Distribution of granulomatous reaction according to age and sex.

Table 1: Distribution of granulomatous reaction cases according to religion.

Religion	No of cases	Percentage
Hindu	262	87.33%
Others	38	12.67%
Total	300	100%

As per the availability of information about the patient's education, occupation, income and residential status, majority patients in present study belonged to lower socioeconomic status with 248 (82.67%) cases and patient with higher socioeconomic status were 52 (17.33%) respectively. The patients coming from peripheral rural areas included 221 (73.67%) cases while those from urban population were 79 (26.33%) respectively. Data procured here are as per availability.

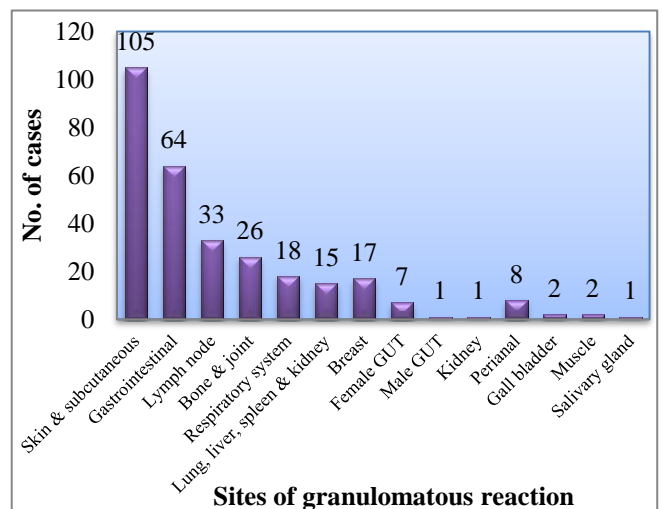


Figure 2: Distribution of granulomatous reactions according to site of presentation.

Table 2: Etiology based distribution of granulomatous reaction.

Causes of granuloma	No. of cases	Percentage
Tuberculosis	169	56.33%
Leprosy	53	17.67%
Foreign body granuloma	38	12.67%
Fungal	04	01.33%
Actinomycosis	01	00.33%
E. histolytica	01	00.33%
Unknown etiology	34	11.34%
Total	300	100%

Table 3: Distribution of granulomatous reaction based on caseation necrosis.

Morphology	No. of cases	Percentage
Caseating granuloma	164	54.67%
Non-caseating granuloma	136	45.33%
Total	300	100%

In the present study, Tuberculosis was the only cause for caseation necrosis in the granulomatous reaction.

The non-caseating granulomas comprised of atypical mycobacterium, BCG adenitis, foreign body granulomas, leprosy, fungal and other causes.

Table 4: Ziehl Neelsen staining for demonstration of Acid Fast Bacilli in Tuberculous granulomas.

Ziehl Neelsen stain	No. of cases	Percentage
Positive	35	20.71%
Negative	134	79.29%
Total	169	100%

Table 5: Fite Faraco staining for demonstration of Leprae bacilli in leprosy.

Fite Faraco stain	No. of cases	Percentage
Positive	11	20.75%
Negative	42	79.25%
Total	53	100%

DISCUSSION

In the present study 300 cases over a period of 5 years, from July 2008 to June 2013 were studied which included Histopathology specimens, biopsies and autopsies. Histopathology remains a time-tested tool for establishing a correct diagnosis like in many other diseases pertaining to various organ systems of the body.^{4,7}

Age and sex

The age range of the patient varied from as young as 4 months to 85 years.

Table 6: Comparison of age wise distribution of granulomatous reaction in the present study with other studies.

Age (year)	Present study (July 2008 - June 2013)		Harish S. Permi et al. (2012) ⁴		Jayashree et al (2011) ⁸	
	No. of cases	Percentage	No. of cases	Percentage	No. of cases	Percentage
0-10	22	07.33%	11	04.00%	10	5.88%
11-20	36	12.00%	31	11.40%	26	15.29%
21-30	88	29.33%	65	23.60%	46	27.06%
31-40	60	20.00%	50	18.16%	35	20.59%
41-50	38	12.67%	41	14.90%	30	17.65%
51-60	34	11.33%	51	18.52%	15	08.82%
61-70	11	03.67%	24	08.70%	08	04.71%
71-80	10	03.34%	01	00.36%	00	00.00%
81-90	01	00.33%	01	00.36%	00	00.00%
Total	300		275		170	

Majority of the patients were in the age group 21-30 years (29.33%), closely followed by 31-40 years (20.00%). Similar findings were recorded by Harish S. Permi et al.,⁴ Jayashree et al.⁸ on 170 cases of granulomatous reaction and Gautam et al.⁹

In the present study, males (55.67%) were affected more commonly than the females (44.33%) with male to female ratio of 1.25:1. Similar findings were reported by other studies.

Table 7: Shows comparison of male to female ratio of present study with other studies.

Study	No. of cases	Male to female ratio
Present study	300	1.25:1
Harish et al. ⁴	275	1.09:1
Jayashree et al. ⁸	170	1.18:1
Gautam et al. ⁹	106	1.7:1

Table 8: Comparison of various sites of presentation of granulomatous reaction in the present study with other studies.

Sites	Present study (July 2008 - June 2013) n (%)	Harish et al. ⁴ (2012) n (%)	Jayashree et al. ⁸ (2011) n (%)
Skin and subcutaneous tissue	105 (35.00)	68 (24.72)	53 (49.53)
Gastrointestinal tract	64 (21.33)	22 (8.00)	11 (10.28)
Lymph node	33 (11.00)	59 (21.46)	31 (28.97)
Respiratory system	32 (10.67)	26 (9.46)	29 (27.10)
Bones and joint	26 (8.67)	50 (18.18)	13 (12.14)

Table 9: Comparison of causes of granulomatous reaction in the present study with other studies.

Causes of granuloma	Present study (300 cases)	Harish et al. ⁴ (275 cases)	Jayashree et al. ⁸ (170 cases)
Tuberculosis	56.33%	47.26%	49.41%
Leprosy	17.67%	12.72%	17.65%
Foreign body granuloma	12.67%	8.36%	14.12%
Fungal	01.33%	8.73%	5.88%
Actinomycosis	00.33%	1.45%	1.18%
Parasite	00.33%	1.45%	-
Unknown etiology	11.34%	8.00%	-
Rhinoscleroma	-	5.10%	11.76%
Tumour	-	5.83%	-
Others	-	1.10%	-

The overall Acid Fast Bacilli (AFB) positivity of 20.71% (35 cases out of 169 cases) is similar to other published data.

Table 10: Showing the comparison of results of Ziehl Neelsen stain in Tuberculosis for demonstration of Acid Fast Bacilli in the present study with other studies.

Studies	Ziehl Neelsen stain		Total
	Positive	Negative	
Present study	35 (20.71%)	134 (79.29%)	169
Harish et al. ⁴	27 (20.76%)	103 (79.23%)	130
Jayashree et al. ⁸	19 (22.62%)	65 (77.38%)	84
Krishnaswamy H et al. ¹¹	91 (71.09%)	37 (28.90%)	128
P. Jayalakshmi et al. ¹²	29 (49.15%)	30 (50.84%)	59

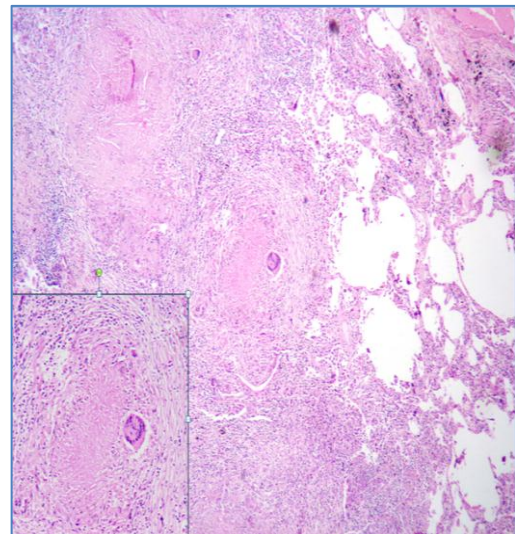


Figure 3: Koch's inflammation of lung (4x) with inset showing caseating granuloma and Langhans giant cell (10x).

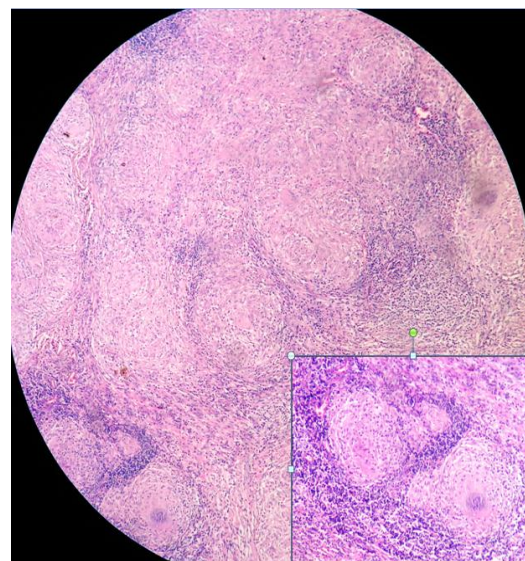


Figure 4: Koch's lymphadenitis (10x) with inset showing caseating granuloma.

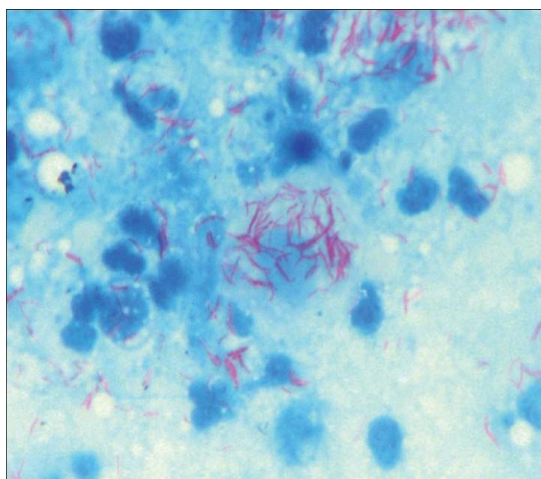


Figure 5: Acid fast bacilli with Ziehl Neelsen Stain positive (100 + 5x).

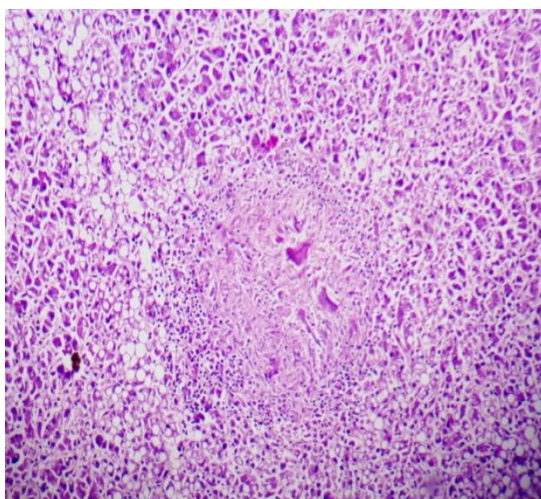


Figure 6: Hepatitictuberculous granulomatous reaction (10 + 3x).

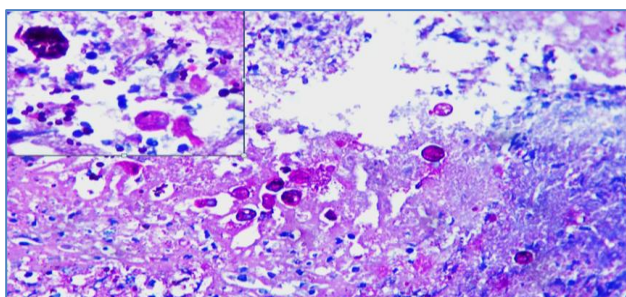


Figure 7: Histolytica with foreign body granuloma showing PAS positivity (10 + 3x) with inset showing E. histolytica (40x).

CONCLUSION

We studied 300 cases of granulomatous reaction. Whose detailed history and microscopic examination was done and the findings were as follows:

- Maximum numbers of granulomatous reaction cases were detected in age group of 21-30 years with 88 (29.33%). Most are Hindu Males with Male to Female ratio was 1.25: 1 respectively.
- Granulomatous reaction was more common among lower socioeconomic status with 248 (82.67%) and patients belonged to patient from rural areas.
- Most commonly skin and subcutaneous tissue was the site affected by granulomatous reaction followed by gastrointestinal tract and lymph node respectively and Tuberculosis was found to be the most common etiology.
- The overall rate of AFB positivity with ZiehlNeelsen stain in tuberculosis was found to be 20.71%.
- The most common histomorphological feature in granulomatous reaction was epithelioid granuloma with caseous necrosis of which tuberculosis was the causative agent.
- Most common cause of fungal granulomatous reaction was Madura mycosis.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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DOI: 10.5455/2320-6012.ijrms20150136

Cite this article as: Babaria KR, Agravat AH, Dhruva GA. Granulomatous reaction - a histopathological study: a retrospective and prospective study of 5 years. *Int J Res Med Sci* 2015;3:201-6.