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Original Article

Histopathological Review and Distribution of Granulomatous Inflammatory Disorders in Makurdi, North Central Nigeria

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ABSTRACT

Granulomatous inflammation is a pattern of chronic inflammation characterized by the presence of granulomas consisting of microscopic aggregates of macrophages transformed into epithelioid cells surrounding by a collar of lymphocytes and occasioned plasma cells. The study aimed to determine the distribution by tissue site, of all the granulomatous inflammatory disorders diagnosed at Benue State University Teaching Hospital (BSUTH), Makurdi over a 5-year period. It was a retrospective review of 236 histologically confirmed cases of granulomatous lesions seen from March 2013 to February 2018 diagnosed on hematoxylin and eosin stains with further analysis after staining with Ziehl-Neelsen (ZN), Periodic Acid Schiff (PAS) and Gomori Methenamine Silver (GMS) special stains. A total of two hundred and thirty-six cases of granulomatous inflammatory disorders were diagnosed, analysed and categorized based on the tissue site. The most common sites were cervical lymph nodes, appendix, skin, testicular tissues etc with the eyelid been the least common site.

Keyword: Granulomatous, Inflammation, Lymph node

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INTRODUCTION

Granulomatous inflammation is a distinctive and well-recognized pattern of chronic inflammation characterized by granulomas, which are foci of microscopic aggregates of macrophages transforming into epithelioid cells surrounded by fibroblastic collar, lymphocytes and occasional plasma cells with or without features of necrosis.[1,2] In this pattern of injurious response, which may occur in all tissues, the activated macrophage appears as an epithelioid cell with a round to oval nuclei and abundant granular eosinophilic cytoplasm. They may also coalesce to form multinucleated giant cells.[3] The aetiology of granulomatous disorders are broadly classified into infections, autoimmune, toxic, allergies, neoplastic, foreign body, fungal, helminthic, bacterial, and unknown causes.[4,5] The pathogenesis of granulomas is hinged on the production of mediators from

activated macrophages, especially interferon-gamma (INF–γ) from myeloid precursors maturing into monocytes in the peripheral circulation[6] When recruited into tissues are called histiocytes, stellate cells, microglia cells, alveolar macrophages and activated via the innate immune response, release chemokines and cytokines (TNF, IL-1, IL-6, IL-17, and INF gamma), which gives the cell the characteristic epithelioid cell and giant cells which are the components of granulomas.[2,7]

Classification of granulomas is based on aetiology, bacterial, metal-induced, fungal, viral, chlamydial, cat-scratch fever, lymphogranuloma venereum, helminthic, foreign body, and unknown causes [7,8] morphologic classification is based on Epithelioid, Histiocytic, foreign body, necrobiotic/palisading, and mixed inflammatory cells.[9]

MATERIALS AND METHODS

This was a 5-year retrospective review of 236 histologically confirmed cases of all granulomatous lesions diagnosed from March 2013 to February 2018 on hematoxylin and eosin stains. The tissues were further analyzed after staining them with Ziehl-Neelsen (ZN), Periodic Acid Schiff (PAS) and Gomori Methenamine Silver (GMS) special stains. In addition, the clinical history and other information were collected from the medical records.

RESULTS

Within the five year period under review, 236 granulomatous lesions were diagnosed in the Anatomical Pathology Department of BSUTH Makurdi. The patient's median age, presenting with granulomatous lesions, was 39 years. The majority of patients (39.0%) were in the age group of 40-49 years, males predominate with a male to female ratio of 2.2:1 (Table 1).

The majority of granulomas were seen in the lymph nodes (41.5%), followed by the appendix (14.8%) and skin (11.9%). Other sites were the testicles, fallopian tube, bladder, ovary, colon, peritoneum, breast, eyelid, and nose (Table 2).

Table 1: Age and Sex Distribution of all the Patients

Age (Years)	Male N (%)	Female N (%)	Total Percentage N (%)
0-9	5 (3.1)	2 (2.7)	7 (3.0)
10-19	12 (7.4)	8 (10.8)	20 (8.5)
20-29	25 (15.4)	10 (13.5)	35 (14.8)
30-39	30 (18.5)	10 (13.5)	40 (16.9)
40-49	62 (38.3)	30 (40.5)	92 (39.0)
50-59	10 (6.2)	5 (6.8)	15 (6.4)
60-69	13 (8.0)	5 (6.8)	18 (7.6)
≥70	5 (3.1)	4 (5.4)	9 (3.8)
Total	**162 (100.0)**	**74 (100.0)**	**236 (100.0)**

Table 2: Site of distribution of granuloma

S/No.	Site of Granuloma	Number of Cases	Percentage (%)
1	Lymph Nodes	98	41.5
2	Appendix	35	14.8
3	Skin biopsy	28	11.9
4	Testicles	22	9.3
5	Fallopian Tube	14	5.9
6	Bladder	10	4.2
7	Ovary	9	3.8
8	Colon	7	3.0
9	Peritoneum	6	2.5
10	Breast	3	1.3
11	Eyelid	2	0.8
12	Nose	2	0.8
	Total	**236**	**100.0**

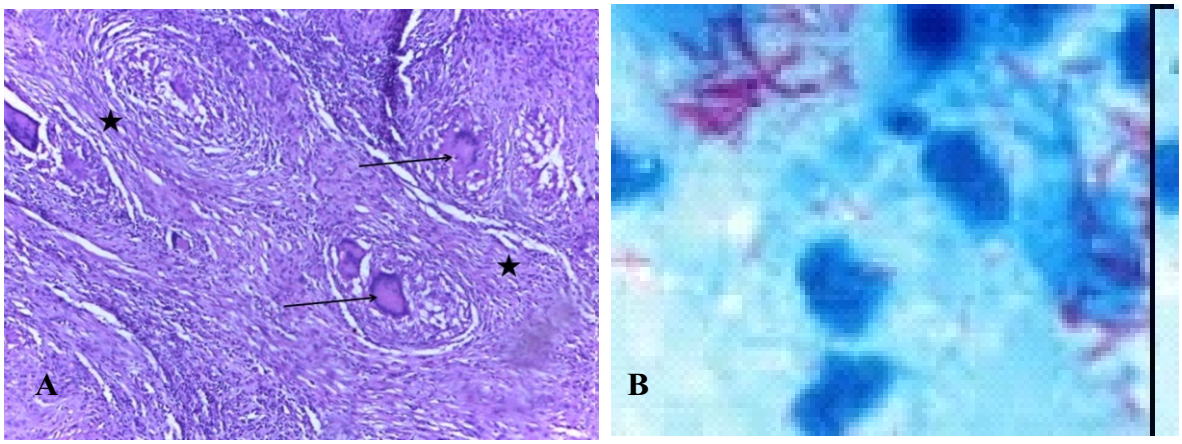

Figure:1 Lymph Node with granuloma. A, Photomicrograph of lymph node at a medium magnification shows chronic granulomatous inflammation with a partly effacement of the nodal architecture. Majorly, noncaseating granulomatous infiltrate with vague foci of necrosis are seen. Granulomas are discrete and variable in size and shape, and they are composed of epithelioid histiocytes with abundant eosinophilic cytoplasm and oval nuclei containing a small central nucleolus. Some Langhans giant cells are apparent, and areas of sclerosis are livid. *Haematoxylin and eosin, x 10 objective magnification.* ***B,*** *Photomicrograph of an FNAC ZN-stained slide from the same patient, demonstrating numerous AFB-positive cocci.*

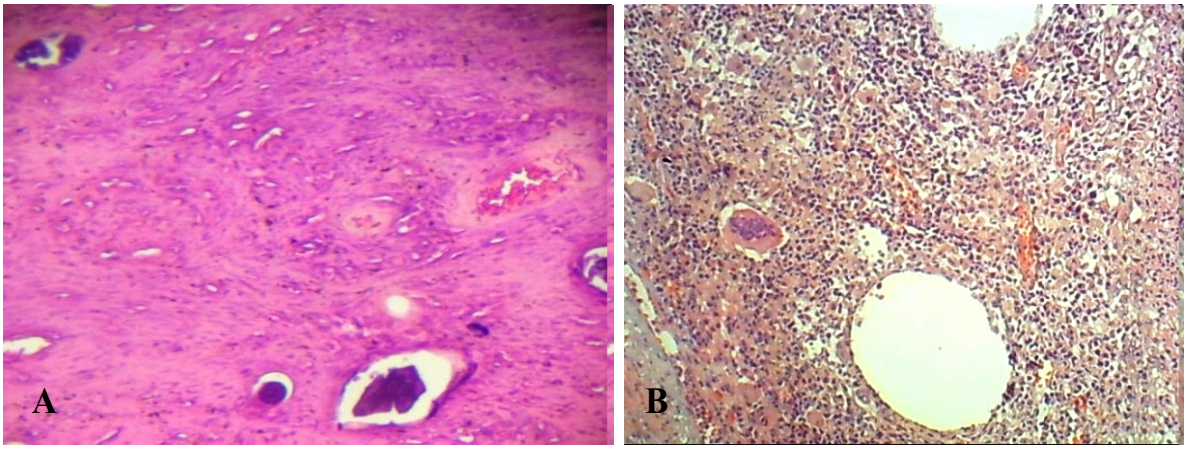

Figure: 2 Chronic Granulomatous Inflammation. A, Low-power view is showing a Fallopian tube harbouring ova of Schistosome in a chronic granulomatous inflammatory background. **B,** Vermiform appendix tissue with **widespread chronic granuloma admixed with pus cells.**

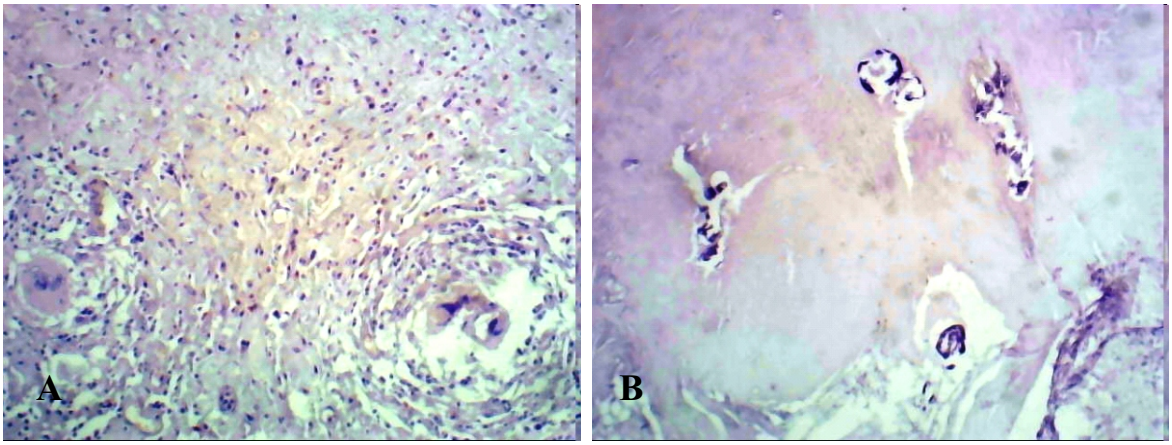

Figure 3 Schistosomiasis involving the Appendix and Ovary. A, Vermiform appendix with foci of granuloma with associated multinucleated giant cells of the foreign-body type. **B,** Fallopian tube from a 23-year old patient with ova of Schistosoma in a sclerosed background.

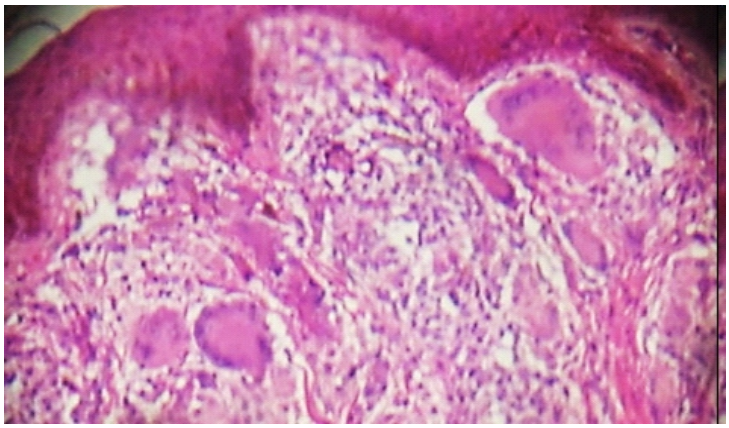

FIGURE 4 Skin tissue biopsy with inflammatory and granulomatous inflammation composed of multinucleated giant cells mainly of the Langhan-type; the granuloma are located within the superficial and deep dermis in a patient with Lupus vulgaris.

DISCUSSION

Granulomatous inflammation is a recognized pattern of chronic inflammation characterized by granulomas with microscopic aggregates of macrophages transformed into epithelioid cells surrounded by a collar of fibroblasts, lymphocytes and plasma cells.[10] In the study, granulomatous lesions were common in the fourth decade of life, with male predominance (Table1) corresponding with studies in other parts of the world.[11]

The most typical site of granulomas in this study was the lymph node, followed by the appendix, skin, testes, and fallopian tube (Table 2).

The rare causes of granulomas in this study were breast, eyelid, and nose (Table 2). Epithelioid granulomas were the most common type of granulomas, followed by foreign body type granuloma (Fig. 1). This finding is also in conformity with other studies in the world. [3,12,13]

A case report by Civelli *et al*. from California, United States of America (USA) about a right testicular mass in a 41-year-old Hispanic male who underwent right orchidectomy due to clinical suspicion of testicular malignancy. A histologic examination of the lesion revealed a granulomatous inflammation without any evidence of neoplasia. However, the patient subsequently developed a left testicular swelling, and after extensive work evaluation, a diagnosis of tuberculous epididymal orchitis was made. The patient was evaluated, treated with anti-tuberculous medications and recovered.[10] However, in our study, there were 22 similar cases of granulomatous orchitis (9.3%) out of a total of 236 patients with granulomatous inflammatory disorders diagnosed in our centre (Table 2). All these cases were caused by tuberculosis with acid-fast bacilli demonstrated using ZN stain.

In another case report, Sekulic Simona and Sekulic Miroslav from Columbia University Irving Center, New York, USA, reported two rare cases of non-caseating granulomas on the cardiac mitral valve of 1,043 cardiac valves excised in the institution.[11] Pathologic examinations of both patients revealed non-granulomatous inflammations with lymphocytes, plasma cells, epithelioid cells, and multinucleated giant cells. However, other laboratory investigations failed to yield any infectious agents or foreign body material. It appears as though no case of granulomas involving the heart in our institution has been reported in the works of literature.[11] The unusual sites affected by granulomatous disorders in our study include breast, eyelid, and ovary, which make up a total of 14 cases (Ovary – 9; breast – 3; and eyelid – 2).

A retrospective study done in Egypt by El-Khalawany *et al*. on the number of infectious granulomas of the skin diagnosed from 2004 to 2010 revealed a total of 233 cases with tuberculosis consisting the largest group (40.8%), followed by leprosy (31.7%) and leishmaniasis (15.9%).[15] Our study only evaluated tuberculosis using the Ziehl-Neelsen stain. In addition, granulomas involving the skin made up a total of 28 cases (11.9%) out of 236.

In North-Western Nigeria, a retrospective study by Sanusi and Bello on 1,123 appendectomy specimens received over 15 years in the Department of Histopathology, Aminu Kano University Teaching Hospital revealed 36 cases of schistosomal appendicitis constituting 3.2% of all the specimens.[16] This finding is similar to our study, with the appendiceal samples comprising the second-largest group of the organ affected by granuloma after lymph node. A total of 35 cases of schistosomal appendicitis were found in our study with a frequency of 14.8% (see Table 2). Other sites that were also affected by schistosomiasis, according to our research, included the fallopian tubes and bladder, which represented 5.9% and 4.2% of specimens, respectively.

A study in South-Eastern Nigeria by Ukekwe *et al*. on 1,180 lymph node biopsies received over 15 years showed 172 cases of tuberculous lymphadenitis, with 23 cases occurring in HIV-positive patients. In addition, acid-fast bacilli were demonstrated in 26 patients using Ziehl-Neelsen stain[17] Lymph node samples formed the largest group of specimens received in our study for granulomatous disorders. There were 98 cases of granulomatous diseases of the lymph node in our study with a frequency of 41.5%. The retroviral disease status of patients from which these biopsies were obtained was not ascertained.

CONCLUSION

Granulomatous inflammatory disorders are still a common disease conditions that affects multiple organs and tissues and affect more males than females. Tuberculosis still accounts for a significant portion of these disorders and can be demonstrated using the Ziehl-Neelsen stain. Understanding the patterns as well as pathologic features of these conditions is crucial for accurate diagnosis.

REFERENCES

1. Sunitha K, Macha Y, Marde S, Kumar M, Bansal A, Bitra S. Granulomatous Lesions in Head and Neck Region. IOSR (IOSR-JDMS) 2017; 16(10).
2. Shah KK, Pritt BS, Alexander MP. Histopathologic Review of Granulomatous Inflammation. Journ. Clin Tuber. 2017; 7: 1-12.
3. Kumar SN, Prasad TS, Parameswaran A, Jayanandan M. Granuloma with Langhans Giant Cells: An Overview. Joun Oral Maxillofpathol 2013; 17(3): 420-3 DO/:/0.4103/0973/0973-029X.125211.
4. Kushwah A, Bhattarai N, Koirala A. A Histopathological Study of Granulomatous Lesions. Journpathol Nepal 2018;8(2): 1341-1345 DO/:/03/26/Jpn.V8;2,20863.
5. Henrickson SE, Jongco AM, Thomson KF, Garabedian EK, Thomsen IP. Noninfectious Manifestations and Complications of Chronic Granulomatous Disease. J. pacel Infect Dis Soc. 2018;4(1): 518-S24.
6. Arnold DE, Heimall JR. A Review of Chronic Granulomatous Disease. Adv Ther 2017; 34:2543-57. DO/10.1007/S12325-017-0636-2.
7. Romero TB, Montiel JL, Fernandez G, Valecillo A. Role of Cytokines and other Factors Involved in the Mycobacterium Tuberculosis Infection. World J Immunol. 2015;5(1):16-50.
8. Garg S, Das A, Gulati N, Sinha M. Granulomatous Inflammation by Candida Presenting as a Hard Subcutaneous Nodule: A Rare Case Report with Review of Literature. Ind J Pathol&Microbiol 2020;63(4): 640-41.
9. Gulia SP, Lavanya M, Archana V, Kumar SPA, Selvi K. Histomorphological Analysis of Granulomative Lesion in a Teaching Hosptial Puducherry. Internal J Curr Res and Rev 2015; 7(9): 78-84.
10. (McAdam AJ **:** *Chronic Inflammation,* In: *Robbins and Cotran Pathologic Basis of Disease:* Saunders Elsevier, Philadelphia**, 2010:** pages 53 – 57)
11. Civelli VF, Heidari A, Valdez MC, Narang VK & Johnson RH. A case of testicular granulomatous inflammation mistaken for malignancy: tuberculosis identified post orchiectomy. Journal of Investigative Medicine High Impact Case Reports 2020;8:1 – 3. DOI: 10.1177/2324709620938947.
12. H J van der Rhee, C P van der Burgh-de Winter, W T Daems**,** The differentiation of monocytes into macrophages, epithelioid cells, and multinucleated giant cells in subcutaneous granulomas. Cell Tissue Res. 1979 Apr 12;197(3):355-78. DOI: 10.1007/BF00233563
13. Adams DO. The granulomatous inflammatory process.A review. Am J Pathol 1976;84:164-191 [PubMed]
14. Pichler Sekulic S &Sekulic M. Case report: Isolated and focal non-necrotizing granulomatous inflammation of the mitral valves: A report of two cases. Front Cardiovasc Med 2021;8:615707. doi: 10.3389/fcvm.2021.615707.
15. El-Khalawany M, Meraag I, Eassa B & El-Naby HH. Clinicopathologic features and the practice of diagnosing infectious cutaneous granulomas in Egypt. International Journal of Infectious Diseases 2011;e620 – e626.
16. Sanusi HM, Bello U. Histopathological analysis of schistosomal appendicitis in Kano North-Western Nigeria. Indian J Pathol Oncol 2021;8(2):267 – 270.
17. Ukekwe FI, Olusina DB, Banjo A, Akinde OR, Nzegwu MA, Okafor OC, et al. Tuberculous lymphadenitis in South-Eastern Nigeria; A 15 years histopathologic review (2000 – 2014). Ann Med Health Sci Res 2016;6:44 – 9.