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Original research article

To analyze different granulomatous lesions frequency and aetiology: an observational study

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Abstract

Aim: to analyze different granulomatous lesions and to find the frequency and etiology of all granulomatous lesions.

Materials and Methods: The present Observational study was conducted in the Department of pathology, Anugrah Narayan Magadh Medical College, Gaya, Bihar, India for one year. We include 100 cases of skin biopsies after histopathological confirmation of granulomatous lesions.

Results: Among 80 cases were studied in which male predominance was noted with 46(57.5%) cases and females constituted 34(42.5%) case providing M:F ratio of 1.4:1. Most of the patients were noted in age group of 20 to 30 years i.e 30(37.5%) cases followed by 17(21.25%) case in 30 to 40 years. 83.75% of cases were seen below 50 years of age in our study. Infectious granulomatous dermatoses were very common, only 1.25% cases of sarcoidosis was found. Most cases of infectious dermatoses were noted in 20 to 30years comprising 30(37.5%) cases. Leprosy remained the significant causative reason for infectious granulomatous dermatoses succeeded by tuberculosis of skin. Borderline tuberculoid leprosy was found to be predominant, constituting 22 (27.5%) cases followed by indeterminate 17(21.25%) and lepromatous leprosy had 15(18.75%) cases, tuberculoid leprosy 15(18.75%) case and 6(7.5%) of borderline lepromatous. Lupus vulgaris constituted 2 cases (2.5%) and only 1 (1.25%) case of sarcoidosis was found.

Conclusion: Histopathology is still a gold standard tool in classification of granulomatous lesions and with support of special stains we can arrive at exact etiology to meet out appropriate treatment.

Keywords: Granuloma, histopathology, special stains, etiology.

Introduction

Granulomas are focal chronic inflammatory response characterized by a collection of activated histiocytes and multinucleate giant cells that may or may not have a cuff of surrounding lymphocytes or show necrosis. Granulomas occurring in the skin have numerous etiologies and accordingly variable clinico-pathological presentations. The etiologies range from infections like tuberculosis, leprosy, fungal infections to other causes like foreign body, sarcoidosis, necrobiosis and drug reactions. Thus, an etiological classification is unsatisfactory. Based on the histology, granulomas can be classified into seven types, namely Sarcoidal, Tuberculoid, Suppurative, Necrobiotic (Palisaded), Foreign body, Xanthogranuloma and Miscellaneous.[1] Many conditions described within this group may show only non-specific changes in the early or late resolving stage.[1]The granulomatous inflammatory response is a manifestation of many infective, toxic, allergic, autoimmune, neoplasm and conditions of unknown aetiology. A knowledge of the basic pathophysiology of this distinctive tissue reaction is therefore of fundamental importance in the understanding many disease processes.[2] The provocative agents of granulomatous inflammation appear to

be non degradable 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 CD4+T cells is required. The CD4+T cells secrete various mediators such as IL2, IFγ, TNF and lymphotoxin for the transformation of the macrophages into epithelioid cells and giant cells, which are the components of granulomas.[2] Etiological classification of granulomas based on the aetiology: 1. Bacterial 2. Metal induced 3. Fungal 4. Viral / Chlamydial a. Cat scratch fever b. Lymphogranuloma venerum 5. Helminthic 6. Foreign body type 7. Unknown cause.[3] Classification based on the morphologic criteria: 1. Epithelioid 2. Histiocytic 3.Foreign body 4 Necrobiotic / Palisading Mixed inflammatory.[4] Recognisation of the granulomatous pattern in a biopsy specimen is important because of the limited number of possible conditions that cause it and the significance of the diagnosis associated with it. Granulomatous inflammations are a common and intriguing problem. The arrival at a proper diagnosis is mandatory, so that the appropriate treatment can be meted out. Histopathology is a tool which can be used for establishing a correct diagnosis like in many other diseases, pertaining to the various organ systems of the body.[5] 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. A rational histological diagnostic approach to granulomatous inflammation is also not present without its problems. Special stains may also be required to reach a diagnosis. In a small percentage of cases, no definitive diagnosis can be given, other than that of granulomatous inflammation.[5] The morphologic pattern in the various granulomatous diseases may be sufficiently different to allow reasonable accurate diagnosis by the pathologist. Hence the present study was undertaken to find the frequency and etiology of granulomatous lesions and to compare with other studies. The histological appearances will also depend on the stage of the disease process and treatment status. Fully developed granulomas with sheets of epithelioid histiocytes and giant cells are easily recognized, but more subtle lesions containing a few epithelioid histiocytes still qualify as granulomatous lesions.

Material and Methods

The present Observational study was conducted in the Department of pathology, Anugrah Narayan Magadh Medical college, Gaya, Bihar, India for 1 year, after taking the approval of the protocol review committee and institutional ethics committee.

Methodology

Total80 cutaneous lesion biopsies showing granuloma formation and Skin lesions having granuloma formation histopathologically were include in the study. Cases without any granuloma formation and inadequate biopsies were excluded from the study.

All the granulomatous lesions on tissue biopsy sent for histopathological examination were included in the study. Detailed clinical data was obtained and noted in a structured proforma. This was to obtain information on age, sex, religion, site and distribution of lesion, duration of disease, presence of systemic illness, immunosuppressed status and whether prior FNAC was done or not. The specimen received was fixed in 10% formalin for at least 24 hours and then subjected to histopathological processing and examination. The tissues were placed in tissue teks and processed in the histokinette after processing, the sections were embedded in paraffin and blocks were made. 5 micrometer sections were cut from the blocks and put into

albuminized slides. The sections were then stained with hematoxylin and eosin stain and microscopic examination was done. The slides were reviewed by pathologist and diagnosis was made.

Results

Among 80 cases were studied in which male predominance was noted with 46(57.5%) cases and females constituted 34(42.5%) case providing M:F ratio of1.4:1. Most of the patients were noted in age group of 20 to 30 years i.e 30(37.5%) cases followed by 17(21.25%) case in 30 to 40 years. 83.75% of cases were seen below 50 years of age in our study. Infectious granulomatous dermatoses were very common, only 1.25% cases of sarcoidosis were found. Most cases of infectious dermatoses were noted in 20to 30years comprising 30(37.5%) cases. Leprosy remained the significant causative reason for infectious granulomatous dermatoses succeeded by tuberculosis of skin. Borderline tuberculoid leprosy was found to be predominant, constituting 22 (27.5%) cases followed by indeterminate 17(21.25%) and lepromatous leprosy had 15(18.75%) cases, tuberculoid leprosy 15(18.75%) case and 6(7.5%) of borderline lepromatous. Lupus vulgaris constituted 2 cases (2.5%) and only 1 (1.25%) case of sarcoidosis was found.

Table 1: Sex distribution of patients

Sex	N=80	Percentage
Male	46	57.5
Female	34	42.5

Table 2: Age distribution of patients

Age (years)	Number of cases	Percentage
Below 20	9	11.25
20 -30	30	37.5
30-40	17	21.25
40-50	11	13.75
50-60	6	7.5
60-70	5	6.25
Above 70	2	2.5

Table 3: Etiology of granulomatous skin lesion

Disease	Number of cases	Percentage
Indeterminate	17	21.25
Tuberculoid Leprosy	15	18.75
Borderline Tuberculoid	22	27.5
Borderline Lepromatous	6	7.5
Lepromatous Leprosy	15	18.75
Fungal granuloma	2	2.5
Lupus Vulgaris	2	2.5
Sarcoidosis	1	1.25

Discussion

Cutaneous granulomas are commonly encountered in skin clinics and pose considerable amount of diagnostic dilemma to the dermatologist. Skin biopsy helps confirm a granulomatous reaction and further may point towards a diagnosis in many cases. However, histology alone may also not be sufficient in many cases and other adjunctive tests may be essential to come to a final diagnosis.

Granulomas are the commonest lesions that the pathologists come across in routine practice. In order to treat these lesions, definitive diagnosis by the demonstration of the aetiological agent is essential, which will bear an impact on the patient management and outcome.[6] Fully developed granulomas with sheets of epithelioid histiocytes and giant cells are easily recognized, but more subtle lesions containing a few epithelioid histiocytes still qualify as granulomatous. It is difficult to present a completely satisfactory classification of the granulomatous reaction. Many conditions classified as granulomatous lesions may show only non-specific changes in the early evolution of the inflammatory process and in a late or resolving stage show fibrosis and non-specific changes without granulomas.[7]

Granuloma formation is due to type IV hypersensitivity reaction elicited by infectious and non infectious antigen. Granulomatous dermatoses are common in North India with overlapping clinical presentations. So, it becomes important to catch the definitive etiological diagnosis for their treatment.[8] Histopathology plays a pivotal role for confirmatory diagnosis like in several diseases of other system of the body.[9] The distribution of granulomatous dematoses varies widely according to geographic location. Very less number of studies done on the infectious granulomatous dermatoses, showing broad statistical variation for several lesions. This study is comparable to Gautam et al,[10] Pawale et al,[11] and Dhar et al[12] in finding of predominance of male in granulomatous skin lesion 46(57.5%) cases and females constituted 34(42.5%) case providing M:F ratio of 1.4:1. Infectious granulomatous dermatoses were commonest in this study which is similar with the study by Bal et al.[13,14] Commonest site of the skin lesions was upper extremity which is comparable with the study done by Gautam et al[7] but not with Zafar et al[15] in which most lesion were found in head and neck region. Present study shows Tuberculoid Leprosy as the commonest etiological diagnosis 15(18.75%) cases. Mh El Khalwary et al[8] concluded 40.8% cases showing cutaneous tuberculosis followed by 31.7% case of leprosy. Rubina Qureshi et al[14] concluded cutaneous leishmaniasis 56.7% as the leading cause of granulomatous dermatoses followed by 13.5% case of lupus vulgaris. Bal et al[13] and Potekar et al[16] concluded leprosy as a leading cause of cutaneous granulomatous disease. The observations in this study are similar with the findings of studies by Bal et al[13] and Potekar et al[16] done in India. In our study the commonest subtype of leprosy was found to be borderline tuberculoid 22(27.5%) cases which is comparable with the findings of Gautam et al[10] 46.7% cases, Bal et al[13] 55.2% cases and Chakrabarti[17] et al 57.94% cases. On Morphology non-caseating granulomas were found in all the tuberculoid as well as in borderline tuberculoid leprosy which were same as granulomas in tuberculosis and sarcoidosis. Strong positivity noted in all cases for lepromatous leprosy on Fite Faraco stain. Borderline tuberculoid leprosy show positivity in 1 cases for Fite Faraco stain but none in tuberculoid leprosy. Granulomatous infiltration of nerve bundle, arrector pili muscle and adnexa along with proper clinical findings were helpful in the diagnosis of tuberculoid and borderline tuberculoid leprosy. Cutaneous tuberculosis was the second commonest granulomatous dermatoses in this study, 2(2.5%) cases were diagnosed as lupus vulgaris were found to be negative on Ziehl Neelsen stain. Bal et al [12] found 5% positivity Z-N staining in cases of Lupus vulgaris. Z-N staining is specific for acid fast bacilli, still its positivity is low and varies with different studies. The present study did not reveal any case of cutaneous leishmaniasis. Rubina et al[14] found 56.7% cases in Pakistan. In this study 1.25% cases was reported as cutaneous sarcoidosis based on epithelioid cell granuloma without caseastion and presence of inflammatory cells or Langhans giant cells. In this study there was 1 (1.25%) case of sarcoidosis somewhat similar to reported by Gautam et al[10] 1.88%. In the present study 2(2.5%) cases of fungal granuloma was noted similar to Potekar et al.[16] Different studies reported fungal cutaneous granuloma in span of 2.7%to 3.3%.[17,18]

Conclusion

Histopathology is still a gold standard tool in classification of granulomatous lesions and with support of special stains we can arrive at exact etiology to meet out appropriate treatment.

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