International Journal of Research in Medical Sciences
Srinivas T et al. Int J Res Med Sci. 2017 Sep;5(9):3869-3874
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20173659

Original Research Article

Granulomatous dermatosis: histopathological study in a tertiary care hospital

Teerthanath Srinivas[1], Hariprasad S.[2]*

[1]Department of of Pathology, K S Hegde Medical Academy, Deralakatte, Mangalore, Karnataka, India
[2]Department of Surgery, Navodaya Medical College, Mantralayam Road, Navodaya Nagar, Raichur, Karnataka, India

Received: 24 July 2017
Accepted: 28 July 2017

***Correspondence:**
Dr. Hariprasad S.,
E-mail: raohariprasads@yahoo.co.in

ABSTRACT

Background: Granulomatous dermatosis shares the histological finding of granuloma formation; it is usually formed because of the persistence of a non-degradable product of active hypersensitivity. The identical histological picture may be produced by several causes, which pose a diagnostic challenge to dermatopathologist, Present study aims at classifying cutaneous granulomatous dermatosis based on the morphology and aetiology of granulomas, and to highlight its significance for specific clinical diagnosis.
Methods: A retrospective analysis of skin biopsy was done and cases of cutaneous granulomatous lesions diagnosed on histopathological examination were retrieved for a period of 8 years. Clinical data and diagnosis were retrieved from hospital records. Hematoxylin and eosin stained paraffin sections were reviewed. The morphological pattern of granuloma was classified into sarcoidal, necrotizing, necrobiotic and suppurative granulomas and further aetiological evaluation for the granulomatous dermatosis were done using various special stains like Periodic Acid Schiff stain, Fite-Farraco stain, Gomori methenamine silver stain and acid-fast bacilli stain.
Results: A total of 228 cases of cutaneous granulomatous lesion were retrieved; out of these 93cases (40.79%) were sarcoidal granuloma type, 83cases (36.40%) were of suppurative granulomas, 29 cases (12.72%) were of necrobiotic granulomas, 20 cases (8.77%) were necrotizing granuloma and 3 cases (1.32%) had granulomatous dermatitis with vasculitis. Infective aetiology was the commonest cause for granulomatous dermatosis (57.89%), mainly by leprosy, tuberculosis and various fungal infection.
Conclusions: Granulomatous dermatosis has significant overlap in histopathological picture of various granulomatous reactions. Morphology alone is seldom specific and cannot be used as diagnostic tool. It is better understood based adequate clinical data, morphology of granuloma, special stains and laboratory workup in arriving at a etiology specific diagnosis for definitive clinical management.

Keywords: Dermatosis, Granulomas, Infective granulomas, Vasculitis

INTRODUCTION

Granulomatous dermatosis has identical histological pattern may be produced by several causes, and conversely, a single cause may produce several histological patterns.[1] Granuloma was originally thought to represent a neoplastic growth of granulation tissue, "Granuloma" now implies a reactive, nonneoplastic, inflammatory tissue reaction.[2]

Granulomatous inflammation is best defined as special variety of chronic inflammation in which granuloma is formed in response to insoluble, nondegradable or slowly

released antigens.[3,4] According to the current concept, 'granuloma' is defined as a focal chronic inflammatory response to tissue injury, characterized by collection of activated histiocytes, epitheloid cells and multinucleated giant cells that may or may not be trimmed by lymphocytes and/ or show central necrosis.[5] Granulomas may be confluent or discrete; the degree of necrosis is variable ; the cell components differ; and the presence or absence of Schumann bodies and of calcification is distinctive.[6]

Granulomas has been divided into 5 distinctive patterns by Rabinowitz et al, based on the presence or absence of necrosis, necrobiosis, vasculitis and the nature of inflammatory cell infiltrate.[7] Granulomatous dermatosis frequently poses a diagnostic challenge to dermatopathologists due to varied histological pattern, because of which it's difficult to present a completely satisfactory classification of granulomatous dermatosis.[6,7] The present study aims at classifying granulomatous dermatosis based on the morphology and aetiology of granulomas, and to highlight significance of clinical correlation in making specific diagnosis.

METHODS

A retrospective analysis of skin biopsies received in Department of Pathology, K.S. Hegde Medical Academy, Mangalore over a period of from 2007-2014, which were diagnosed as cutaneous granulomatous lesions on histopathological examination were reviewed.

Clinical data and diagnosis were retrieved from hospital records. Hematoxylin and eosin stained paraffin sections were reviewed. The morphological pattern of granuloma was classified into sarcoidal, necrotizing, necrobiotic and suppurative granulomas; and further aetiological evaluation for the granulomatous dermatosis were done using various special stains like Periodic Acid Schiff stain, Fite-Farraco stain, Gomori methenamine silver stain and acid-fast bacilli stain.

RESULTS

A total of 228 cases of cutaneous granulomatous lesions were reviewed, out of these 225 cases (98.68%) had granulomatous dermatitis without vasculitis and 3 cases (1.32%) had granulomatous dermatitis with vasculitis.

Table 1: Morphological patterns of granulomas.

Morphological patterns	Type of granulomas	Number (%)
Granulomatous dermatitis without vasculitis	Sarcoidal	93 (40.79%)
	Suppurative	83 (36.40%)
	Necrobiotic	29 (12.72%)
	Necrotizing	20 (8.77%)
Granulomatous dermatitis with vasculitis		3 (1.32%)
Total		233

Table 2: Classification of cutaneous granulomatous dermatitis based on aetiology.

Aetiology		Number	Percentage (%)
Infections	Mycobacteria	84	57.89%
	Fungi	31	
	Bacteria	12	
	Parasite	05	
Vasculitis		03	1.32%
Immunological		18	7.89%
Foreign body		39	17.11%
Neoplasia		06	2.63%
Miscellaneous		30	13.16%
	Total	228	100%

Granulomatous dermatitis without vasculitis were further classified into 4 categories based on the morphology of granulomas, nature of inflammation, necrosis, and necrobiosis into 1. Sarcoidal granuloma, 2. Suppurative granuloma, 3. Necrobiotic granulomas and 4. Necrotizing granuloma. Sarcoidal granulomas constituted the major type of granulomatous dermatosis, accounting for 40.79% (93cases), followed by suppurative granuloma (83cases (36.40%), Necrobiotic granulomas [29 cases (12.73%)] and necrotizing granuloma [20 cases (8.77%)] (Table 1). Sarcoidal granulomas was constituted predominantly by tuberculoid and borderline tuberculoid leprosy (49 cases),

followed by foreign body granulomas (39 cases), lupus vulgaris (3 cases) and syphilis (2 cases).

Suppurative granuloma was seen due to infection (60 cases), keratin (20 cases), hidradenitis suppurativa (3 cases). Among infectious suppurative granulomas majority of them were by fungi (31 cases) followed by bacteria (24 cases) and parasites (5 cases).

Necrotizing granuloma in absence of suppurative inflammation was seen in 20 cases (8.77%). The only cause retrieved was cutaneous tuberculosis in various clinical patterns like tuberculous verrucous cutis (7 cases), scrofuloderma (11 cases) and erythema induratum (2 cases).

Necrobiotic granuloma with or without palisiding of histiocytes was seen in 29 cases (12.73%), of which rheumatoid nodule was seen in 8cases who had plaques, papules and nodules lesions with predilection to involve skin over joint.

Granuloma with vasculitis contributed a minor group in the study 3 cases (1.32%) which included Wegener's granulomatosis, (2 cases) and allergic granulomatous (1 case).

Granulomatous dermatosis is also being classified based on the etiology under following headings.1. Infectious, 2. Vasculitis, 3. Immunological, 4. foreign body, 5. Neoplastic (Table 2). Among 228 cases, of retrieved granulomatous lesions, 57.89% (132cases) had infective etiology which constituted the largest group. They were categorized into leprosy (47 cases), tuberculosis (37 cases), other bacterial (12 cases) [Actinomycosis (8), Nocardia (4)], fungal (31cases) [Mucormycosis (13), blastomycosis (1), chromomycosis (11), candida (4), Sporotricosis (2)] and parasitic 5 cases [filaria (4), Rhinosporidiosis (1)]. The other cytological categories include vasculitis - 3 cases. Immunological -18 cases (7.89%), foreign body - 39 cases (17.11%), neoplastic - 6 cases (2.63%), and miscellaneous 30 cases (13.16%) which are due to keratin, foreign body, granulomas annulare, granulomas multiforme, necrobiosis lipodica, rosacea, and panniculitis.

DISCUSSION

Granulomatous inflammation is defined as a special variety of chronic inflammation in which the mononuclear phagocyte system cells take the form of macrophages, epithelioid cells and multinucleated giant cells admixed with other cells, especially lymphocytes, plasma cells and fibroblasts. Epithelioid cells are the hallmark of delayed hypersensitivity granulomas, they are mononuclear cells with finely granular eosinophilic cytoplasm, vesicular nuclei, and indistinct cell boundaries which are usually found aggregated into clusters within certain granulomas. Multinucleated giant cells are a regular feature of granulomatous inflammation produced by the fusion of macrophages. The granulomas result from a complex interplay between invading organism or antigen, chemical, drug or other irritant, prolonged antigenaemia, macrophage activity, Th1 cell response, B cell over activity, circulating immune complexes, and a vast array of biological mediators. Giant cell production is stimulated by lymphokines which are said to be immunological mediated. Traditionally inflammatory giant cells have been divided into the Langhan type (tuberculous), in which up to 20 nuclei are distributed centrally or around the periphery of the cell, and the foreign-body type with often very numerous haphazardly arranged nuclei throughout the cytoplasm. There is no fundamental difference between these two cells types, both types are commonly found to coexist in the same lesion and there is no diagnostic significance. Tissue necrosis is due to auto digestion by macrophages enzymes, necrosis may also be produced by the dried toxic action of causative agent and the immune complex in the centre of the lesion. Fibrosis results from Interleukin1, lymphokines and fibronectin that are synthesized by lymphocytes, macrophages play important in fibroblast migration, proliferation and collagen synthesis. Non-immunological, low turnover foreign body type granulomas appear to stimulate least amount of collagen production.[8,9]

It is difficult to present a completely satisfactory classification of granulomatous dermatosis. Based on the pure morphology of granuloma, histopathologists have divided granuloma into "foreign body" and "epitheloid" type depending primarily on the absence or presence of epitheloid cells. An inducing agent is often recognizable in foreign body granuloma, while it's impossible to find in epitheloid lesion. Moreover, the two lesions are said to contain either foreign body or Langhan type of giant cells respectively. This classification was unsatisfactory.[9]

A second classification of granulomas is based on cell kinetics.[9,10] Granulomas are divided into "High turnover" and "Low turnover" granuloma. In high turnover granuloma, there is increased turnover of macrophages, while low turnover granuloma shows little macrophage death and immigration or mitosis. This classification is of considerable theoretical importance.[9-11]

In the present study, granulomatous dermatosis is classified on the morphology of granuloma and its association with vasculitis. The etiological basis of the granulomatous dermatosis has been tried to evaluate with the help of special stains. The granulomatous dermatosis has been broadly divided into two categories: 1. Granuloma with vasculitis 2. Granuloma without vasculitis.[6] Majority of the cases 225 (98.68%) had granulomas without vasculitis and only 3 cases (1.32%) had granulomas with vasculitis.

The granulomatous dermatosis without vasculitis has been subdivided into four categories based on the morphology of granuloma into 1. Sarcoidal type; 2.

Necrobiotic type; 3. Necrotizing type; 4. Suppurative type. Cases with circumscribed epitheloid histiocytes forming circumscribed nodule without necrosis, with scant mononuclear cells with foreign body or Langhan giant cells were classified as sarcoidal granulomas (Figure 1). Necrobiotic granulomas are identified by pale staining collagen fibres, ringed by palisading epitheloid histocytes, lymphocytes and fibroblast (Figure 2). Granulomas with microscopic coagulative necrosis in absence of suppurative inflammation and abscess formation were classified as necrotizing granuloma (Figure 3) and granulomas with acute inflammation and abscess formation were classified as suppurative granuloma (Figure 4).

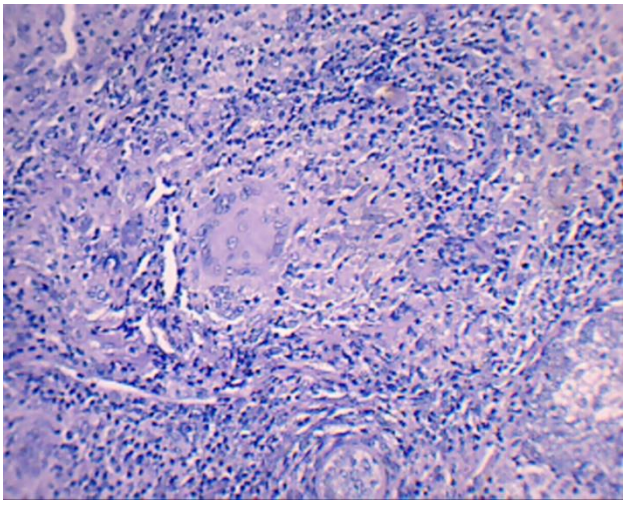

Figure 1: Sarcoidal granulomas containing circumscribed epitheloid histiocytes forming circumscribed nodule without necrosis, scant mononuclear cells and langhan giant cells. (H and E X400).

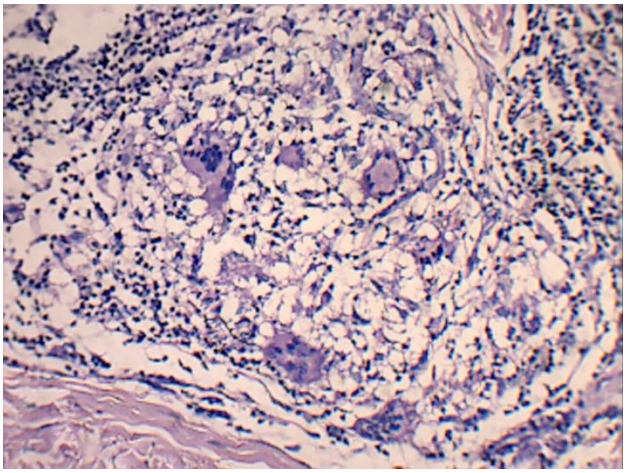

Figure 2: Necrobiotic granulomas containing pale staining collagen fibers, ringed by palisading epitheloid histocytes, lymphocytes and fibroblast. (H and E X400).

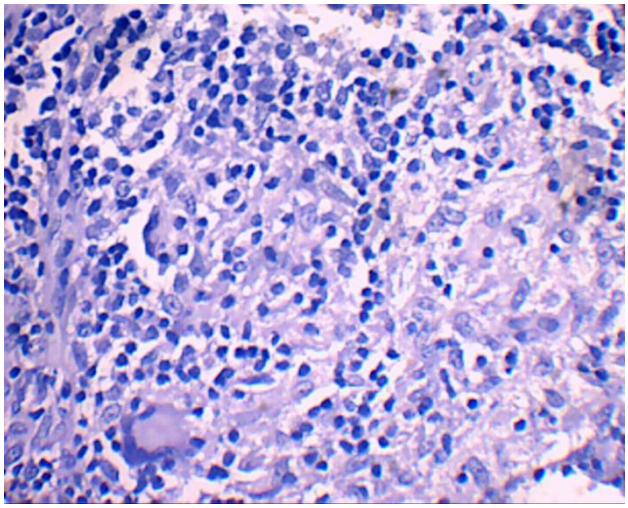

Figure 3: Necrotizing granuloma containing granulomas with microscopic coagulative necrosis in absence of suppurative inflammation and abscess formation. (H and E X400).

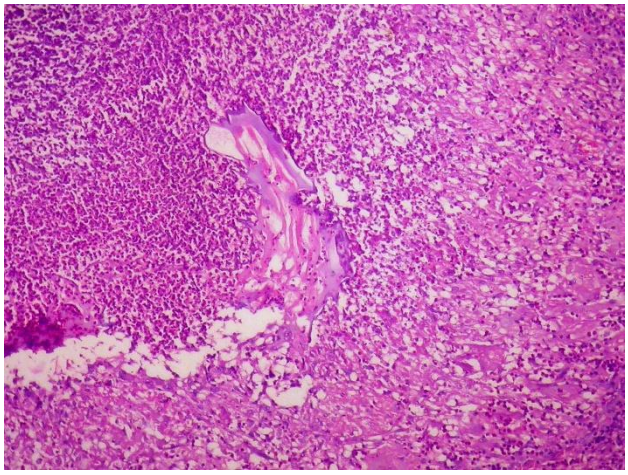

Figure 4: Suppurative granuloma granulomas with acute inflammation and abscess formation around microfilaria. (H and E X400).

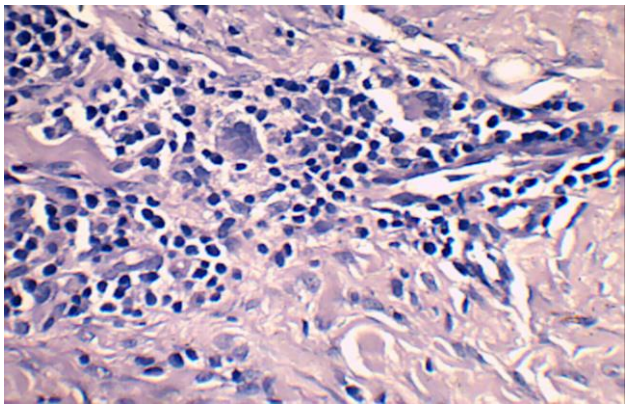

Figure 5: Granulomatous vasculitis containing giant cells. (H and E X400).

Sarcoidal granulomas was the commonest type encountered in the study (40.79%), of which leprosy constituted most cases, followed by foreign body granulomas, lupus and syphilis respectively. Leprosy granulomas needs to be differentiated from sarcoidosis and noncaseating tuberculoid granuloma.[12,13] Location of granuloma around neurovascular bundle, erector pili muscle and adnexa in combination with clinical picture are helpful.[14] Suppurative granuloma is the next frequently (36.40%) encountered followed by Necrobiotic granuloma (12.72%) and necrotizing granulomas (8.77%). Infections were the most common cause for suppurative granuloma which was due to bacteria, fungi, parasites and rest of them were due to foreign body, keratin and hidradenitis suppurativa. Necrotizing granuloma is commonly seen in various clinical patterns cutaneous tuberculosis like tuberculous verrucous cutis, scrofuloderma and erythema induratum. Abdul Mamen and Seneha et al in their studies conducted on cutaneous tuberculosis found lupus vulgaris is the commonest form of cutaneous tuberculosis, while scrofuloderma was prevalent in children.[15,16]

Granuloma with vasculitis contributes a minor group of granulomatous dermatoses. They are characterized by inflammatory cells in the vessel wall, endothelial reaction, thrombus formation and fibrin deposition (Figure 5). There are several vasculitis characterized by sarcoidal, suppurative, necrobiotic, necrotizing primarily extra vascular and cutaneous granuloma. As there are systemic diseases that show overlapping clinical features, skin biopsy is potentially crucial to establish the diagnosis.[17]

Granulomatous dermatosis can also be classified based on the aetiology under following headings: 1. Infectious, 2. Vasculitis 3. Immunological, 4. Foreign body, 5. Neoplastic.[18] Infective aetiology constituted the largest group (57.89%) of granulomatous dermatosis, of which leprosy and tuberculosis constituted the commonest infective agent followed by other bacteria like syphilis, actinomycosis and nocardia. Fungal infections commonly causing dermatosis include chromomycosis, mucormycosis, and candidiasis while filariasis and rhinosporidiosis are the commonest parasitic infestation causing granulomatous dermatosis. Miscellaneous category includes causes which are due to keratin, foreign body, granulomas annulare, granulomas multiforme, necrobiosis lipodica, rosacea, and panniculitis. Infectious granulomatous lesions were predominant in the study done by Bal et al.[14]

CONCLUSION

Granulomas are of differing morphology, which are caused by a wide variety of irritants has led to numerous attempts to classify granulomatous dermatosis. Histological examination alone without clinical history could lead to a misdiagnosis, as there is significant overlap in histopathological picture of various granulomatous reaction. Therefore, morphology alone is not specific and cannot be used as diagnostic tool. Granulomatous dermatosis is better understood based adequate clinical data, laboratory workup, morphology of granuloma and special stains, which will help in arriving at an aetiology specific diagnosis for the proper clinical management.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Zaim MT, Brodell RT, Pokorney DR. Nonneoplastic inflammatory dermatoses: a clinical pathologic correlative approach. Mod Pathol. 1990;3:381-414.
2. Pinkus H, Mehregan AH. A guide to dermatopathology. 3rd ed. New York: Appleton-Century-Crofts; 1981:223.
3. Rabinowitz LO, Zaim MT. A clinicopathologic approach to granulomatous dermatoses. J Am Acad Dermatol. 1996;35(4):588-600.
4. VanFurth R, Thompson J, Gossman AE. The regulation of participation of mononuclear phagocytes in inflammatory responses. In: Glynn LE, Schlumberger HD, editors. Bayer-Symposium VI: experimental models of chronic inflammatory diseases. New York: Springer Verlag; 1977:302-20.
5. Hirish BC, Jhonson WC. Concepts of granulomatous inflammation. Int J Dermatol 1984;23:90-100.
6. James DG. A clinicopathological classification of granulomatous disorders. Postgrad Med J. 2000;76:457-65.
7. Rabinowitz LO, Zaim MT. A clinicopathological approach to granulomatous dermatoses. J Am Acad Dermatol. 1996;35:588-600.
8. Mohan H, Bal A. Non-infectious granulomatous dermatitis: A clinicopathological approach to diagnosis. Indian J Dermatol. 2004;49:1-8.
9. Williams GT, Williams. WJ Granulomatous inflammation- a review. J Clin Pathol. 1983;36:723-33.
10. Spector WG. The macrophage: its origin and role in pathology. Pathobiol Ann. 1974:4:33-64.
11. Spector WG. The granulomatous inflammatory exudate. Int Rev Exp Pathol. 1969;8:1-55.
12. Hirish BC, Jhonson WC. Pathology of granulomatous diseases: Epithelioid granulomas, Part II. Int J Dermatol. 1984;23:306-13.
13. Chakrabarti S, Pal S, Biswas B, Bose K, Pal S, Pathak S. Clinico-pathological study of cutaneous granulomatous lesions- a 5 years experience in a tertiary care hospital in India. Iran J Pathol. 2016;11(1):54-60.
14. Bal A, Mohan H, Dhami GP. Infectious granulomatous dermatitis: A clinico pathological study. Indian J Dermatol. 2006;51:217-20.

15. Bhutto AM, Solangi A, Khaskhely NM, Arakaki H, Nonaka S. Clinical and epidemiological observations of cutaneous tuberculosis in Larkana, Pakistan. Int J Dermatol. 2002;41(3):159-65.
16. Sehgal VN, Srivastava G, Khurana VK, Sharma VK, Bhalla P, Beohar PC. An appraisal of epidemiologic, clinical, bacteriologic, histopathologic, and immunologic parameters in cutaneous tuberculosis. Int J Dermatol. 1987;26(8):521-6.
17. Lie JT. Illustrated histopathologic classification criteria for selected vasculitis syndromes: American College of Rheumatology Subcommittee on classification of vasculitis. Arthritis Rheum. 1990;33:1074-87.
18. Chensue SW, Ward PA. Inflammation. In: Damjanov I, Linder J editors. Anderson's Pathology. 10th ed. Vol 1. London: Mosby; 1996.

Cite this article as: Srinivas T, Hariprasad S. Granulomatous dermatosis: histopathological study in a tertiary care hospital. Int J Res Med Sci 2017;5:3869-74.