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Spectrum of Granulomatous Skin Lesions- A Dermato-Pathological Perspective

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ABSTRACT

Granulomatous dermal lesions pose a diagnostic challenge, since several causes can produce an identical histologic picture and, conversely, a single cause may produce varied histologic pattern. The aim of this study is to analyze the spectrum of various etiologies involved in granulomatous skin diseases and their clinicopathological correlation. Cases of granulomatous lesions reported over last one year on histopathological and cytological examination were reviewed along with special stains. A total of 20 cases of different etiologies were taken for study including infectious and non-infectious underlying causes. Out of the 20 dermal granulomatous lesions studied, 12 cases (60.0%) were bacterial, 1 case (5%) each of fungal and associated with malignancy and 6 cases (30%) due to non-infectious etiology like granuloma annulare and foreign body associated were recorded. Amongst the bacterial granulomatous lesions, predominance of Mycobacterium leprae was seen, 6 cases (40%). The varied presentation of Hansen's disease in our study included 4 cases (20%) of tuberculoid leprosy and 2 cases (10%) each of lepromatous leprosy and borderline tuberculoid leprosy. Three cases (15%) of cutaneous tuberculosis seen in our study and were typified as lupus vulgaris, 2 cases (10%) and a single case (5%) of tuberculosa verrucosa cutis. One case, (5%) of Klebsiella rhinoscleromatis was also seen. Skin biopsies help in arriving at a conclusive diagnosis, if aided by a proper clinical history and examination and assisted by special stains, culture of organisms, PCR and immunoflourescence.

Key Words: Skin, Granulomatous lesions, Biopsy.

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INTRODUCTION

Chronic granulomatous disease represents a group of genetic disorders in which impaired intracellular microbial killing by phagocytes leads to recurrent bacterial and fungal infections and granuloma formation. Cutaneous disease occurs in 60% to 70% of cases. The granulomatous reaction can be defined as a distinctive inflammatory response characterized by the presence of granulomas, which are relatively discrete collections of epithelioid histiocytes with variable numbers of admixed multinucleated giant cells and chronic inflammatory cells.[1] According to Dorland, the term "granulomatous" was expressed initially by Virchow to describe a tumor-like mass or nodule of granulation tissue.[2]

Granulomatous skin lesions often present as a diagnostic challenge to dermatopathologists due to various modes of presentation and identical histological picture. The occurrence of different types of granulomatous lesions of the skin varies according to the geographical location. This is a comparative clinical and histologic study of different granulomatous lesions of the skin in our geographical location.

CASE SUMMARY

Case 1:

A 35 year male farmer presented with pain and irregular shaped plaque measuring 4x6cms, with pus discharge on dorsum of the right foot since the last 1year. There was inconclusive family history, with no history of immunodeficiency or constitutional symptoms of tuberculosis. On histopathology, pseudo-epitheliomatous hyperplasia of the epithelium with hyperkeratosis and acanthosis, with diffuse tuberculoid caseating granulomas with histiocytes and Langhan's giant cells in papillary and reticular dermis was seen. Acid fast stain (AFS) showed 3+ positivity. A final diagnosis of **Tuberculosis Verrucosa Cutis** was made.(Figure 1)

Figure 1: Tuberculosis Verrucosa Cutis:

Grossly an irregular shaped plaque measuring 4x6cms, with pus discharge on dorsum of right foot. On HPE diffuse tuberculoid caseating granulomas with histiocytes and Langhan's giant cells in papillary and reticular dermis. Hematoxylin and Eosin x 40 X.

Case 2:

A 40 year male presented with a papule on the lower lip, with surface ulceration, hanging edges and pale floor since 10 months. Family history and constitutional symptoms were not contributory. On HPE acanthotic stratified squamous epithelium with surface ulceration and dense lympho-plasmacytic infiltrate in the underlying dermis, with well-defined caseating epithelioid granulomas and Langhan's giant cells was seen. A final diagnosis of **Lupus Vulgaris** was made.(Figure 2)

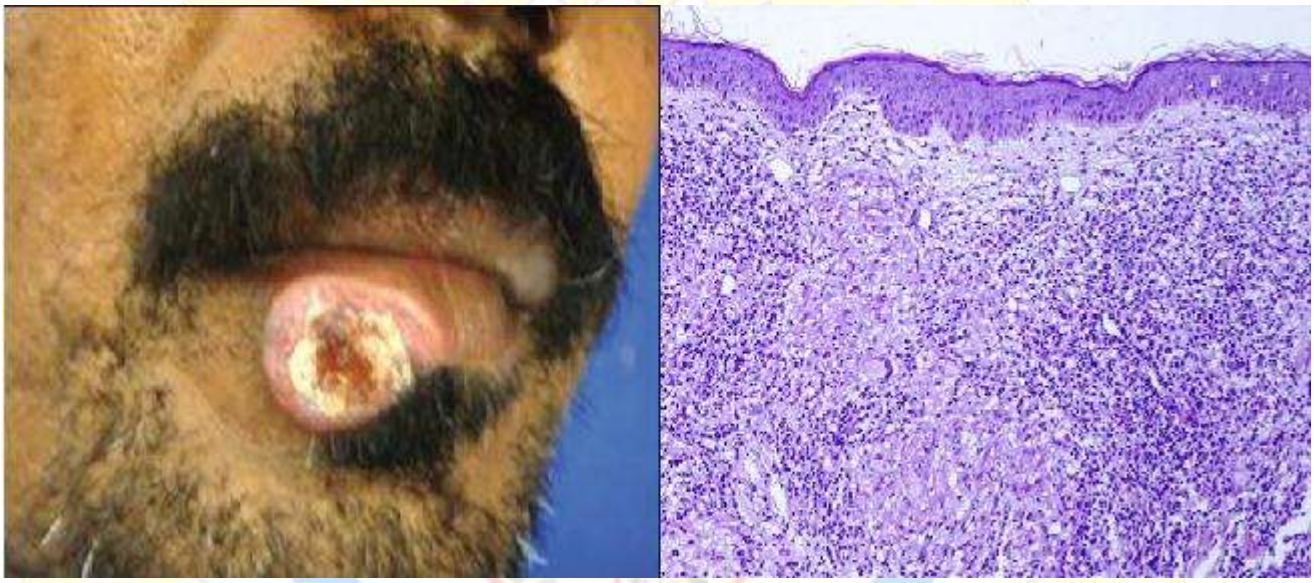

Figure 2: Lupus Vulgaris: Grossly a papule on lower lip, with surface ulceration, hanging edges and pale floor. On HPE dense lympho-plasmacytic infiltrate in underlying dermis with well defined caseating epithelioid granulomas and Langhan's giant cells seen. Hematoxylin and Eosin x 40 X.

Case 3:

A 30 year female had multiple macules, and hypopigmented spots with ill-defined borders on the upper back. On HPE a thinned out stratified squamous epithelium with underlying grenz zone of normal collagen, with a mixed inflammatory infiltrate, with foamy macrophages mostly perineural and around skin appendages without granulomas was seen. AFS was 5+ and a final diagnosis of **Lepromatous Leprosy** was given.(Figure 3)

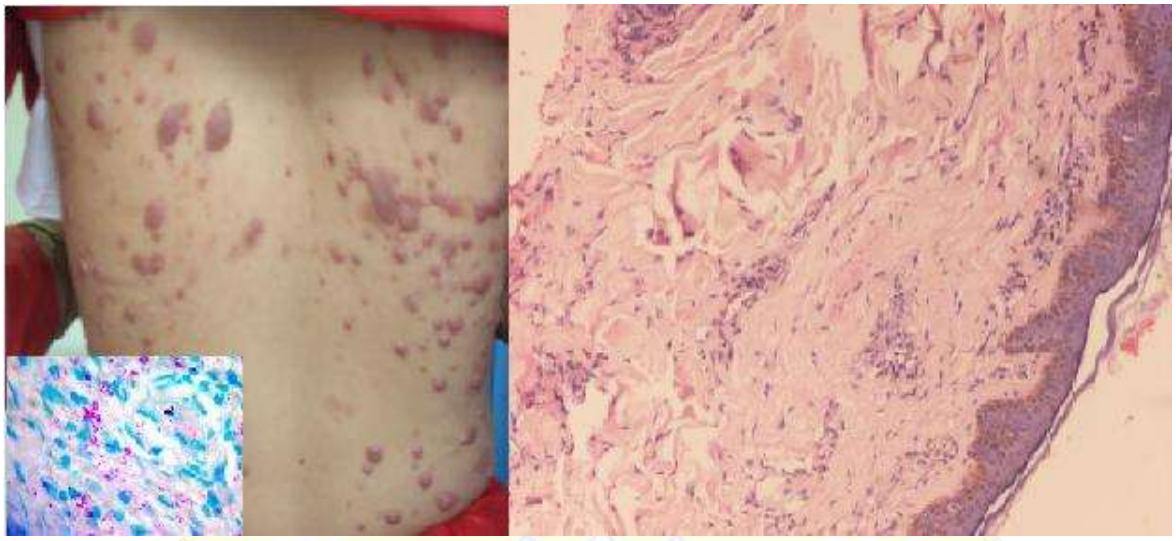

Figure 3: Lepromatous Leprosy:

Grossly, multiple macules, and hypopigmented spots with ill-defined borders on the back. On HPE, Grenz zone of normal collagen seen with a mixed inflammatory infiltrate, with foamy macrophages mostly perineural and around skin appendages without granulomas seen with AFB positivity of 5+. Hematoxylin and Eosin x 40 X.

Case 4:

A 80 year male presented with large raised erythematous plaques with well-defined borders on the right leg and buttock with numbness in both legs since 4 months. On HPE, large epithelioid cell granulomas around neurovascular bundles and dense peripheral lymphocytic infiltrate was seen. On AFS, bacterial index was 1+, thus diagnosed as **Tuberculoid Leprosy.** (Figure 4)

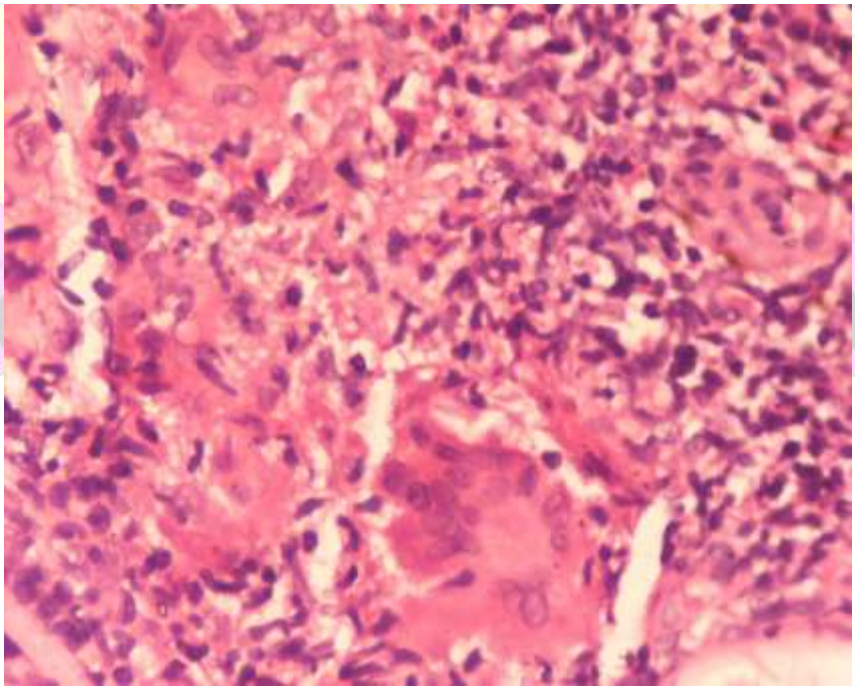

Figure 4: Tuberculoid Leprosy:

Microscopically, tissue section shows large epithelioid cell granulomas around neurovascular bundles and dense peripheral lymphocytic infiltration. Hematoxylin and Eosin x 40 X.

Case 5:

A 25 year male presented with a nodule with fistula formation at ankle since last 5 months. On HPE of the skin nodule, well demarcated granulomas with central abscess formation and black colored grains containing pigmented hyphae was seen in the subcutaneous tissue, which was highlighted on reticulin stain. A final diagnosis of **Actinomycosis** was made. (Figure 5)

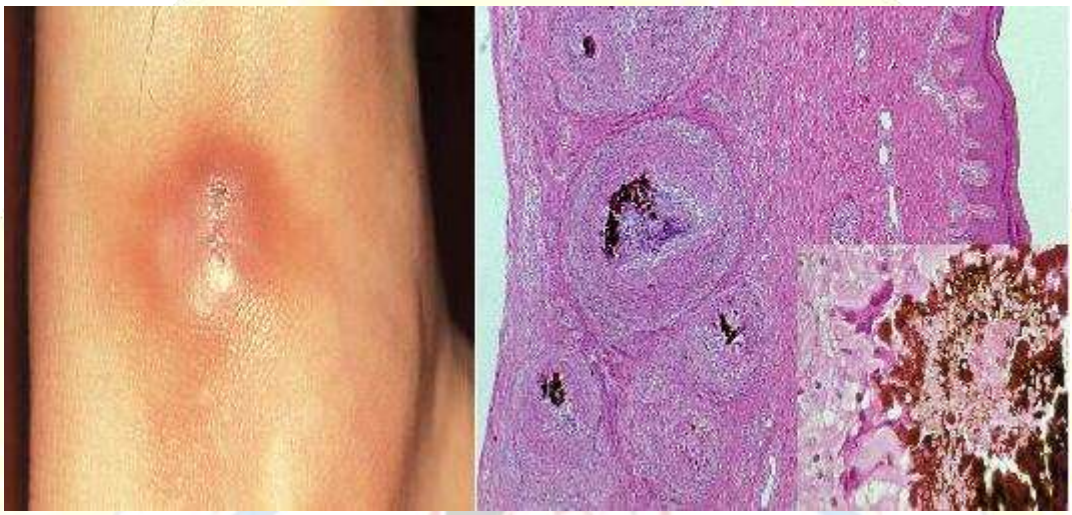

Figure 5; Actinomycosis:

Grossly a nodule with fistula formation at ankle. On HPE of skin nodule well demarcated granulomas with central abscess formation and black colored grains containing pigmented hyphae seen in subcutaneous tissue. Hematoxylin and Eosin x 40 X. seen, with few foreign body giant cell granulomas. Hematoxylin and Eosin x 40 X.

Case 6:

A 63 year female presented with small asymptomatic papules on dorsum of hand with ring like arrangement since 5 months. On HPE, abundant histiocytes and few lymphocytes with slight palisading around increased mucin in full thickness dermis was seen, with the diagnosis of **Granuloma Annulare.** (Figure 6)

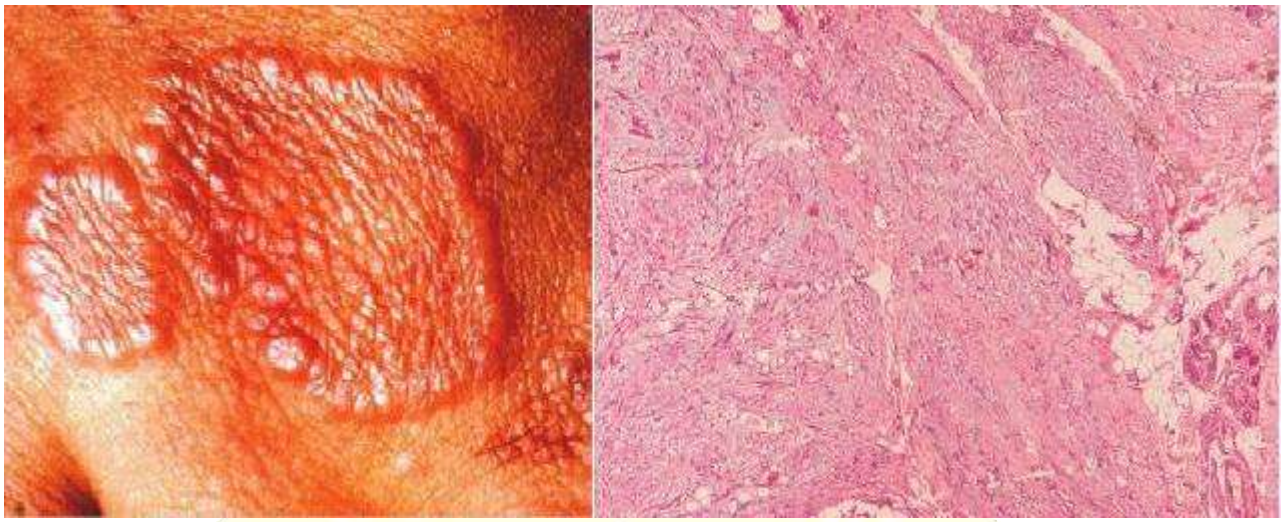

Figure 6: Granuloma Annulare:

Grossly small asymptomatic papules on dorsum of hand with ring like arrangement. On HPE abundant histiocytes and few lymphocytes with slight palisading around increased mucin in full thickness dermis seen. Hematoxylin and Eosin x 40 X.

Case 7:

A 22 year female had a supranasal mass with some narrowing of nasal passage for 3 months. On HPE of the mass, nodular granulomas rich in plasma cells, lymphocytes and foamy histiocytes were seen, with few foreign body giant cell granulomas. It was diagnosed as **Rhinoscleroma with granulomatous inflammation.** (Figure 7)

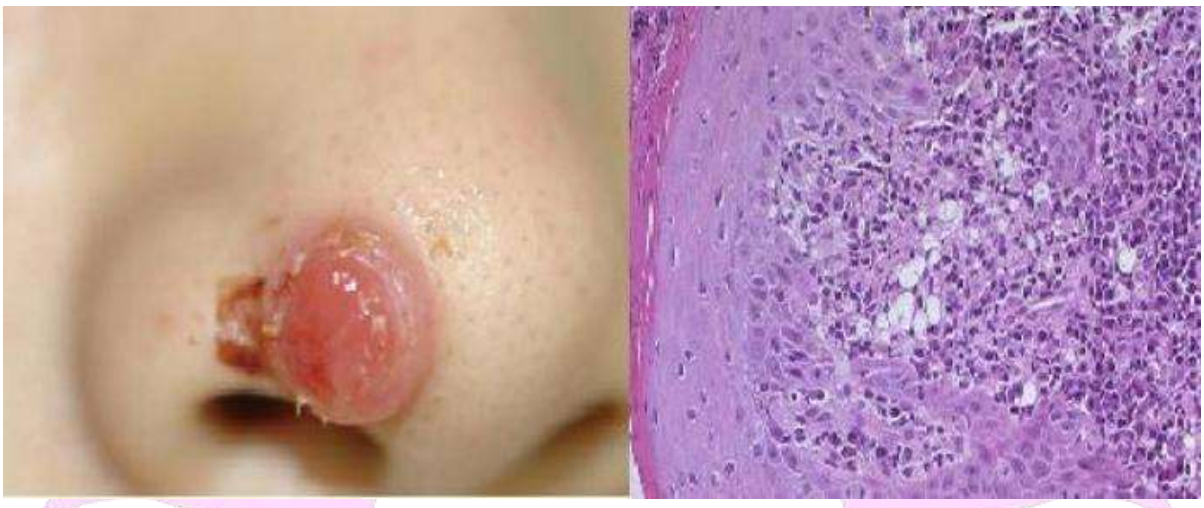

Figure 7: Rhinoscleroma with granulomatous inflammation:

Grossly, a supranasal mass with some narrowing of nasal passage. On HPE of skin biopsy, nodular granulomas rich in plasma cells, lymphocytes and foamy histiocytes

DISCUSSION

Granulomatous reactions in the skin develop as an immune system response to an antigen, in which epithelioid macrophages and various inflammatory and immune cells congregate, often surrounded by fibrosis or a lymphocyte cuff.[3,4] They are classified as infectious or non-

infectious, based upon the presence or absence of an infectious pathogen that serves as the inciting antigen. However, for many of these conditions, we have a poor understanding of the inciting antigen, which may range from infectious to drugs, or result from innate host pathology, like connective tissue disease, vasculitis or cancers.[4,5]

A granuloma is a focal compact collection of inflammatory cells, mononuclear cells predominating, usually as a result of the persistence of a non-degradable product and of active cell mediated hypersensitivity. There is a complex interplay between invading organism or prolonged antigenaemia, macrophage activity, a Th1 cell response, B cell overactivity and a vast array of biological mediators.[5,6] Differential diagnosis and management demand a skilful interpretation of clinical findings and pathological evidence.

Various infectious and non-infectious granulomatous dermatoses are frequent among the population of northern India.[7,8] Definitive etiological diagnosis is important for their management. Histopathology is a gold standard tool for correct diagnosis of various granulomatous skin lesions. Microscopically, wide spectrum of histopathological features of different granulomatous lesions was observed in the present study. We classified the lesions based on histo-morphology and etiology of the granulomatous diseases.

Infectious granulomatous disorders are straightforward in that a microorganism can be identified for a relatively straightforward diagnosis and treatment, while non-infectious diseases are often more difficult to identify and treat. While many granulomatous responses have traditionally been regarded as non-infectious, it is important to acknowledge the proposed role for infection in the etiology of several of these conditions that are regarded as 'non-infectious' granulomatous disorders, such as a slow-growing infection, a post-infectious immunologic response, or presentation of granulomatous disease in the setting of infection.[8,9] Further, it is also possible that these diseases represent a cutaneous expression of infective states mediated by the immune system.[9,10]

Non-infectious granulomatous disorders encompass a challenging group of diseases both in terms of their diagnosis and in counseling patients regarding their prognosis, in addition to the possible systemic co-morbidities they may subsequently encounter.[10] An important source of this challenge is the clinical and histologic overlap among these conditions, with the potential for misdiagnosis.[10,11] Importantly, several of these conditions can present both clinically and histologically with a variety of phenotypes, such as sarcoidosis, which has been noted to clinically and histologically resemble several of the other cutaneous granulomatous disorders.[11,12]

CONCLUSION

The cutaneous manifestations of chronic granulomatous disease encompass a variety of infections and inflammatory lesions. Diagnostic and therapeutic problems may arise because of difficulty in isolating a causative organism. The characteristic pigmented macrophages of visceral granulomas can also be found in skin lesions. Granulomatous skin lesions have varied modes of presentation. A classical clinical picture may not always be present, posing a diagnostic challenge. Skin biopsies help in arriving at a conclusive diagnosis, if aided by a proper clinical history and examination and assisted by special stains, culture of organisms, PCR and immunoflourescence.

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