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A Study on Histopathological Features of Granulomatous Lesions of Skin

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Abstract

Introduction: The morphologic pattern in the various granulomatous diseases may be sufficiently different, to allow reasonably accurate diagnosis by an experienced pathologist, however there are so many atypical presentations, that it is always necessary to identify the specific etiologic agent by special stains for organisms, by culture methods and by serological studies to exclude an infectious cause. *Methodology:* The clinical assessment of the patients were done by the Dermatologists. The skin biopsies were taken from the most prominent lesion or from the anaesthetic area depending on clinical diagnosis. *Results:* Leprosy formed the largest population, of the total 58 cases were Leprosy. The next in frequency was fungal granulomas. Out of the total 13 cases, in 9 cases (69.2%), a diagnosis of chromoblhomycosis was made, in one case the diagnosis was Histoplasmosis (7.7%). *Conclusion:* A detailed evaluation of good H&E stained sections could offer many diagnostic points for the accurate aetiological classification

Key words: Granulomatous; Histopathology; Leprosy.

Introduction

Granulomatous inflammation is a distinctive pattern of chronic inflammatory reaction in which the predominant cell type is an activated macrophage with a modified epithelial-like (epithelioid) appearance. Recognition of the granulomatous pattern in a skin biopsy specimen is important because of the limited number of possible conditions that cause it and the significance of the diagnosis associated with the lesion [1]. A granuloma is a microscopic aggregation of macrophages that are transformed into epithelium-like cells, usually surrounded by a collar or mononuclear leucocytes principally lymphocytes and occasionally plasma cells. Granulomatous dermatitis is defined as a predominantly dermal, chronic inflammatory reaction in which formed granulomas are present. Conditions in which there is a diffuse infiltration of histiocytes within the dermis, such as lepromatous leprosy are not included in this reaction pattern [2].

It is difficult to present a completely satisfactory classification of the granulomatous reaction. Five histological types of granulomas can be identified on the basis of the constituent cells and other changes within the granulomas as — sacoidal,luberculoid, necrobiotic, suppurative and foreign body.

The morphologic pattern in the various granulomatous diseases may be sufficiently different, to allow reasonably accurate diagnosis by an experienced pathologist, however there are so many atypical presentations, that it is always necessary to identify the specific etiologic agent by special stains for organisms (eg., acid fast stains for mycobacterium), by culture methods (eg., in fungal causes) and by serological studies (eg. in syphilis) to exclude an infectious cause. There have been considerable advances made in the understanding of the formation and maintenance of granulomas in tissue reaction and the roles played by B and T lymphocytes and cytokines. The different types of multinucleate giant cells seen in grahulomas may simply reflect the types of cytokines being produced by the component cells.

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This new information has not so far been shown to be useful in routine diagnostic problems. Polymerase chain reaction (PCk) have proved useful in detecting in fectioills agents in tissue sections, particularly mycobacterial species [3,4].

Methodology

The biopsy material for the study was obtained from the Department of Dermatology, Medical College. Ninety-four cases showing a granulomatous reaction pattern in the skin biopsy were selected. These patients are clinically suspected of having granulomatous and non-granulomatous lesions. The duration of their illness varied from months to years and the patients belonged to a wide age range. The clinical assessment of the patients were done by the Dermatologists. The skin biopsies were taken from the most prominent lesion or from the anaesthetic area depending on clinical diagnosis. Both scalpel and punch biopsy specimens are included in the study. Specimens were fixed in 10% formalin for 7-8 hours and are processed. Sections of about 41.tm thickness were taken and stained with H & E.

These sections were subjected to microscopic examination and the study of the epidermis, dermis, dermal appendages, arteries and nerve bundles were carried out.

Results

Age of the patients ranged from 13 years to 85 years, with a mean age of 76.7 years. Out of the 94 patients, 63 were males and 31 were females.

Considering the distribution of aetiological factors — leprosy comprised the largest group coming up to 61.7% of the total number of cases. Tuberculosis

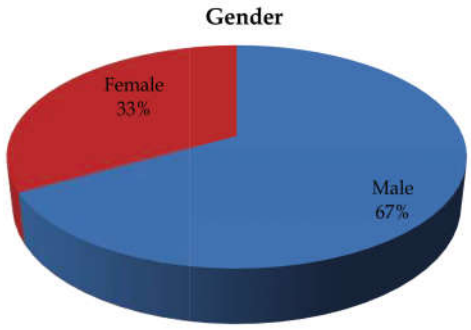

Fig. 1: Gender distribution

comprised 11.7% and fungal comprised 13.8%. The remaining was of diverse aetiology which comprised 12.7%.

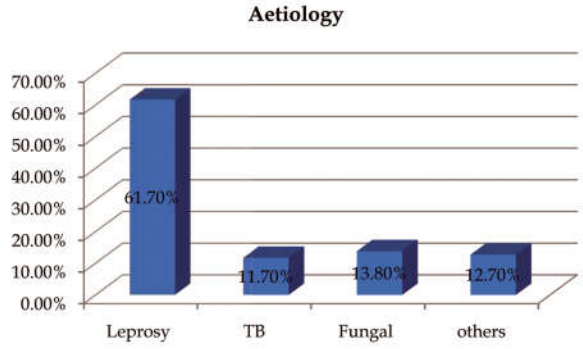

Fig. 2: Aetiology distribution

Leprosy formed the largest population, Of the total 58 cases were Leprosy. The next in frequency was fungal granulomas. Out of the total 13 cases, in 9 cases (69.2%), a diagnosis of chromoblhomycosis was made, in one case the diagnosis was Histoplasmosis (7.7%). Rest of the 3 cases (23%) failed to show any fungal hyphae or spores and the diagnosis was given as suppurative granulomas suggestive of fungal aetiology Considering cutaneous tuberculosis, of the total 11 cases, lupus vulgaris (LV) comprised 7 cases (63.6%) and the rest were of tuberculosis verucosa cutis (TBVC) (36.3%).

Table 1: Fungal Granulomas

Fungal granuloma	Chomoblasto-mycosis	Histoplasmosis	Others
Total: 13	9	1	3

Table 2: Miscellaneous

Miscellaneous (d)	Number	Percent
Granuloma anulare	6	50
Foreign body reaction	3	25
Rheumatoid nodule	2	16.6
Parasitic granuloma	1	8.3
Total	12	

In the miscellaneous group, of the 12 cases, 6 cases were of granuloma anulare (50%), 3 cases were of foreign body granulomatous reaction(25%), 2 cases (16.6%) were of rheumatoid nodule and 1 case (8.3%) was of parasitic granuloma.

Discussion

This study was intended to analyze the histological features ingranulomatous lesions of the skin. The study was based 'mainly on a detailedmorphological analysis of skin biopsies with the use of the relevant special stains. It was hoped that this would pick up a recognizable aetiological factor in most, notif all the cases.

The features suggestive of the aetiology were well marked in many cases.Special stains were shown to be complementary in determining the aetiology.The various causes of cutaenous granulomas in this series as judged by thehistopathological features and is considered under four categoriesa,b, c and d.

In a similar study [5], the total number of cutaneous granulomas was 78, with minimum number of leprosycases (56.7%) followed by cutaneous tuberculosis, sarcoidosis, necrobiosislipodica, granuloma anulare, syphilis, mycotie granuloma and jumenilexanthogranuloma which constituted 1.25% each.

In the present study, out of the 94 patients the aetiological distribution wasalmost similar, but the number of fungal granulomas formed an outstanding ûgureconstituting 12.1%.

In 35% cases, the granulomas were of fungal aetiology coming second infrequency. As mentioned earlier this constituted a high ûgure comparing tosimilar studies and the disparity may be related to the high prevalence ofagricultural workers in the locality. Chromoblastomycosis which constituted 69.2% of the fungal granulomas; andpercutaneous inoculation of the fungus is the most widely accepted mode ofinjection.

Chromoblastomycosis is a chronic fungal infection of the skin andsubcutaneous tissues caused by demaliaceous fungi. All the cases were presentedas vermcous lesions and in most of them ven-ucous carcinoma was a clinicaldifferential diagnosis. Duration of the lesions ranged from 1-14 years and the most frequent site affected was the lower leg and foot.

One was a case of repeat biopsy, previous biopsy report was a Lupusvulgaris, but the patient failed to respond to anti-tuberculous regimen and a repeatbiopsy was taken.

According to Caplan RM (1988) [6] epiderrnoid carcinoma can arise inextensive chromoblastomycosis. If not diagnosed earlier, chromoblastomycosis can have a chronic evolutional course. By Minottoet al [7], chronicchromoblastomycosis can pose many problems such as difûculty in managingtherapy because of the recmdescent character of the disease, potential associationwith the growth of epidermal carcinoma in affected regions, and poor quality oflife and work incapacity to the patient.

In a study of 51 cases of chromoblastomycosis in Mexico by Bonifaz A et al [8] the principal aetiologic agent isolated was Fonsecaeapedrosi (90%). In our set up histopathological detection of sclerotic bodies was taken as conûrmatory andcultural isolation of the fungus was not attempted in most of the cases.

In one case the diagnosis was Histoplasma-capsulatiom. The patient was a 60 year old male when presented with multiple ulcers of duration ranging from 6months to 2 years. Ulcers were present on the angle of the mouth, dorsal aspect ofthe tongue and over the prepuce.

Tissue smears were negative for LD and Donovan bodies. We received biopsies from lesion on the angle of mouth and from tongue- Skin biopsy showed a chronicgranulomatous reaction with multiple rounded bodies inside the histiocytes. Thesespores were positive for PAS and Methenamine silver. Biopsy from the tongueulcer also showed a similar picture. A diagnosis of chronic disseminatedhistoplasmosis was made and the patient put on Itraconazole 300 mg/ day. Heresponded well with healing of the ulcers within 4 weeks. From review of literature, the largest endemic focus of histoplasmosis is inthe central eastern United States, it is a rare disease in India.

In the pre-AIDS era disseminated histoplasmosis was rare and thecutaneous manifestations thereof were reported infrequently. According to Goodwin[9], before the advent of HIV, disseminated histoplasmosis developed in only in 50,000 infections and was usually found ininfants, in patients with lymphoma or in those receiving immunosuppressivetreatment. Now it is the most common opportunistic infection in AIDS patientsliving in highly endemic areas .

Goodwin Jr et al [9] observed that cases with mild degrees of parasitizationpresents as chronic disseminated disease with multiple focal destructive lesionsand the response to treatment is generally good.

The number of patients belonging to this histopathological category was l 1.7%. In this study the diagnostic features of cutaneous tuberculosis included aproliferative reaction of the epidermis with areas of ulceration, presence of nearlyconûuent granulomas throughout the dermis and occasionally caseous necrosis inthe granulomas. Absence of nerve involvement proved a helpful feature todifferentiate from tuberculoid leprosy. Also there was signiûcant

increase indermal ûbrosis with increase in reticulin particularly in cases of long duration.

Nirmala V et al (1977) [10] suggests that the most important differentiatingfeatyure of cutaneous tuberculosis was a proliferative reaction of the epidermiswith absent nerve destruction.

According to Lever (l997) [11], the secondary epidermal changes in lupusvulgaris ranges from atrophy, ulceration, acanthosis or pseudoepitheliomatous hyperplasia. In the case of TBVC, the changes were more consistent and showedonly hyperkeratosis, acanthosis and papillomatosis; no epidermal atrophy wasobserved in these cases. .

In this study, all the cases of TBVC showed hyperplastic changes in theepidermis. The epidermal changes in lupus vulgaris vary from atrophy andulceration to hyperplasia.

Conclusion

Cutaneous granulomas can be of varied aetiology. Hence the task lies on the 'Dermatopathologist' to confirm and classify granulomas accurately for institution of proper therapy.

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