International Journal of Pathology; 2004; 2(1):31-34

Chronic Granulomatous Inflammatory Disorders of Skin at a Tertiary Care Hospital in Islamabad

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A retrospective study was carried out to evaluate skin diseases associated with Chronic Granulomatous Inflammation at Pakistan Institute of Medical Sciences (PIMS) over a period of six months. There were a total of 249 skin biopsies in this period, among which 14.8 % cases were diagnosed as lesions associated with chronic granulomatous inflammation. Among these cutaneous leishmaniasis constituted 56.7% of cases while cutaneous tuberculosis was diagnosed in 14.9%. Sarcoidosis, Syphilis and Granuloma annulare constituted a small number of cases.

Key words: Chronic granulomatous inflammation, Cutaneous Leishmaniasis, Cutaneous Tuberculosis, Lupus vulgaris, Scrofuloderma, Tuberculosis vericosa cutis, Sarcoidosis, Syphilis, Granuloma annulare.

Introduction

Chronic granulomatous inflammation is a type IV hypersensitivity reaction. A variety of agents, exogenous and endogenous may induce this type of chronic inflammation.[1, 2] These are quite common in South Asian countries mostly due to high prevalence of tuberculosis and leishmaniasis. Tuberculosis used to be the leading cause of chronic granulomatous inflammation of the skin. However due to recent political turmoil in Afghanistan which has also affected neighboring Pakistan due to rapid movements of immigrants and goods between the two countries, leishmaniasis has taken over tuberculosis as the single most common cause in Pakistan. Tuberculosis still remains as the leading cause of Chronic Granulomatous inflammation affecting organs other than skin.

The objective of the study was to find out the frequency of varieties of dermatology diseases associated with chronic granulomatous inflammatory inflammation at Pakistan Institute of Medical Sciences (PIMS).

Patients and Methods

Inclusion Criteria: All dermatology cases diagnosed to have diseases associated with chronic granulomatous inflammation on skin biopsies at PIMS. Cases of both genders and all ages were included.

Exclusion Criteria: All skin biopsies not showing lesions associated with Chronic Granulomatous Inflammation and the referred biopsies from other hospitals were excluded.

A weekly joint meeting of Pathology and Dermatology is held every Friday in the Department of Pathology at Pakistan Institute of Medical Sciences (PIMS). All cases of skin biopsies are thoroughly discussed in this joint Multihead microscopic session with overhead TV monitor. Case histories are presented along with digital images of the patient when available. Occasionally patients themselves are examined during the conference. The slides are reviewed and relevant microscopic pictures of interesting cases are simultaneously saved in the computer. The diagnoses are arrived after thorough debate and discussion on all individual cases. In this study, all cases of skin diseases associated with Chronic Granulomatous Inflammation were selected during six months starting from 13th October 2003 to 13th April, 2004. These cases were then tabulated according to the final diagnosis. It should be noted that review of the cases were made when a particular patient did not respond to the initial treatment. For example a case suspected of tuberculosis if did not respond to antituberculous treatment, review of the slides in next Friday meeting may favor leishmaniasis as most likely diagnosis. This switch of clinical impression in light of skin biopsy did occur occasionally in borderline cases. The patient is then

started on anti leishmanial treatment to which he usually responded. Thus the final diagnoses were based on joint dermato-pathology meetings as well as in a few borderline cases on clinical trials after the diagnosis.

As Granulomatous lesions may show a very wide spectrum of microscopic changes, the diagnosis was not based on identification of a well-developed granuolma. Many a times frank tuberculosis is not associated with well formed granulomas. As a matter of fact numerous polymorph leukocytes constituting a purulent exudates is seen in fulminant lesions of tuberculosis in both initial and recurrent lesions. Occasionally only caseation necrosis or only a few epithelioid cells are seen. Therefore instead of well-defined granulomas, all diseases associated with granulomas were included in this study.

Results

Two hundred and forty nine dermato-histopathology reports were given during this period, out of which diseases associated with chronic granulomatous inflammation accounted for 37 cases. (Fig. 1)

Breakup of cases of chronic granulomatous inflammation has been depicted in table 1.

The results clearly showed overwhelming majority of cases of leishmaniasis, accounted for over half the cases. Tuberculosis constituted nearly 20% of cases. Other diseases constituted only a small number of cases.

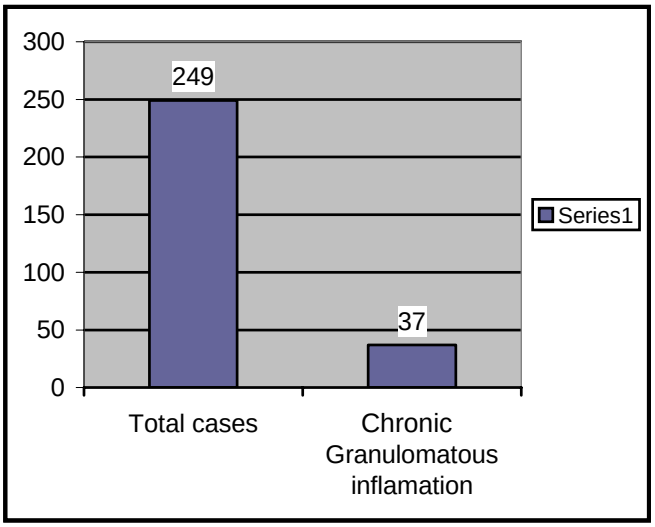

Figure 1: Number of Granulomatous Inflammation in Total Skin Biopsies.

Discussion

Chronic granulomatous inflammation is a Type IV hypersensitivity reaction. Well-defined granulomas are comprised of clusters of plump rather cohesive macrophages known as epithelioid cells. The nuclei of these cells are faintly and delicately stained with hematoxylin.[1, 2]

Table 1

Lesions	No of Cases	% age
Cutaneous leishmaniasis	21	56.7
Lupus vulgaris	5	13.5
Scrofuloderma	1	2.7
Tuber.vericosa cutis	1	2.7
Sarcoidosis	3	8.1
Syphlis	1	2.7
Deep mycosis	1	2.7
Ch.granulomat.inflam. (Non Specific)	2	5.4
Granuloma annulare	2	5.4

The cytoplasm is faintly eosinophilic. Usually lymphocytes are seen in the periphery of the collections of the epithelioid cells. Multinucleated giant cells of Langhans type are frequently seen in Tuberculosis, Sarcoidosis and occasionally in leishmaniasis.[3] Foreign body giant cells with rather more central and widely spread nuclei are seen in fungal and foreign body granulomas. However both types of giant cells can be seen in either type of lesion. Giant cells containing darkedly stained "sclerotic" nuclei along with dense fibrosis is frequently seen in fungal infection. On the other hand sarcoid granulomas are usually more tightly woven and lack lymphocytes giving an impression of bare or naked granulomas. At times the giant cells may show some inclusion bodies, microorganism or particles of ingested microorganism. Granulomas have been divided in the following categories; Foreign body granulomas, infectious granulomas, immunogenic granulomas and granulomas associated with tissue injury. Most foreign body granulomas are "primary irritant granulomas, and in only a few instances do

they form on the basis of a specific sensitization.

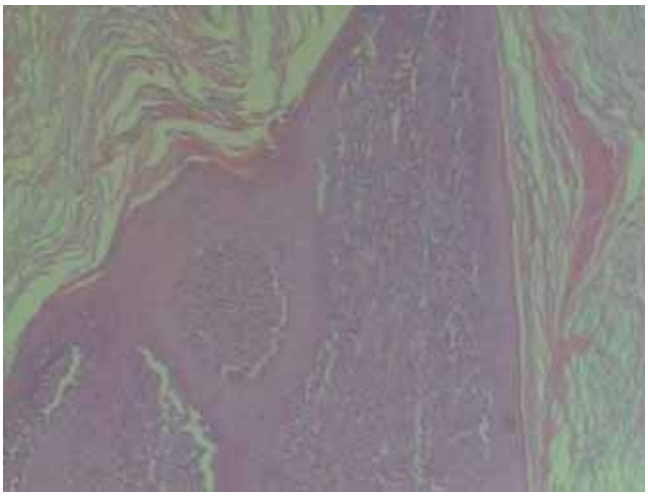

Fig. 2: Hyperkeratosis and Verrucous Growth in Lieshmaniasis (H & E & 100)

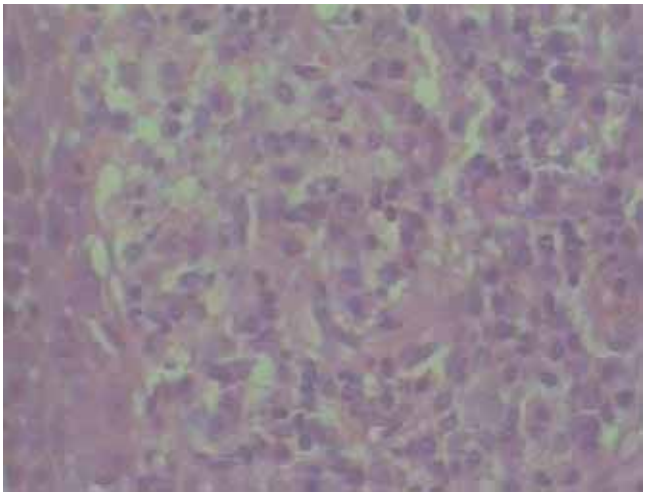

Fig. 3: Numerous Plasma Cells in Leishmaniasis (H & E & 400)

Fig. 4: Cutaneous Leishmaniasis in An Afghan Refugee.

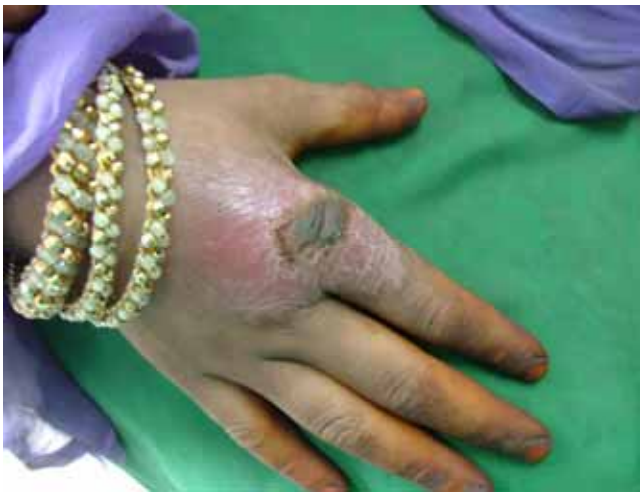

Fig. 5: Cutaneous Leishmaniasis, A Scabbed Erythematous Plaque on Hand.

Infectious granulomas, which develop without sensitization to the microorganism, show numerous microorganisms in the macrophages without the development of epithelioid cells. These infectious granulomas are seen in granuolma inguinale, acute leishmaniasis, and lepromatous leprosy. In immunogenic granulomas, in which sensitization to microorganism has taken place, many epithelioid cells are present but only a few microorganism are seen, occur in chronic leishmaniasis, tuberculoid leprosy, tertiary syphilis and the re-infection type of tuberculosis.[4] The sarcoidosis may also be classified as a type of immunogenic granuolma even though delayed hypersensitivity reactions are depressed.[5] Among the granulomas associated with tissue injury are necrobiosis lipoidica and granuloma annulare.

The histopathology of leishmaniasis varies with factors such as etiological factors, time of evolution, secondary infection, location of lesion, previous treatment and the host immune response in the skin.[1, 2] The initial papular lesions show a dermal nodular or diffuse infiltrate made up of lymphocytes and numerous plasma cells with vacuolated subepidermal macrophages containing abundant amastigotes (Fig. 2 & 3). This is associated with scab formation, acanthosis and papillary hyperplasia. The

older ulcerated lesions reveal a characteristic diffuse granulomatous inflammatory pattern with scattered epithelioid cells, ill defined granulomas and occasionally well defined granulomas. Giant cells are absent or infrequent. However on occasions both well developed giant cells and LT bodies are seen simultaneously. No caseation necrosis is seen. Dust like particles of karyorrehxis and fibrinoid material at times may make it very difficult to separate leishmaniasis from tuberculosis. Amastigotes are hard to find at this stage. Culture and therapeutic trial may be necessary in a few cases to arrive at the final diagnosis.

Laboratory data of cases of last six months shows that cutaneous lieshmaniasis is seen in 56.7% of histological cases and tuberclosis of skin is seen in 18.9% of cases. Cutaneous leishmaniasis affected all ages mainly including children and adults It occurs on exposed parts of the body (Figure 4 & 5). None of them were diagnosed as generalized cutaneous lieshmaniasis or visceral lieshmaniasis. Most of the patients belonged to the people of kachi abadi and refugees. Afghan refugees are generally aware of the nature of the lesion and call it “saldana” i.e. a papule lasting for a year. It responds to antimony injections and heals with depressed scarring.

Tuberculosis of the skin used to be the most common cause of chronic granulomatous inflammation around two years back but now trends are changing and cutaneous lieshmaniasis is at a rapid rise.

This rise of the disease could be due to rapid shift and movement of large number of refugees from Afghanistan to Pakistan after war. In our series there were few cases in which cause of granuloma could not be determined despite special stains etc

The other forms of granulomas are associated with specific tissue changes for example syphilis is associated with endarteritis oblitrans. The granuloma annulare is associated with collagen degeneration. These granulomas are generally ill defined and palisading.

Conclusion

We examined 249 cases of skin biopsies out of which 37 were skin diseases associated with Chronic Granulomatous Inflammation. This constituted 15% of the total skin biopsies. Cutaneous leishmaniasis (56.7%) was the most common disease associated with granulomatous inflammation followed by tuberculosis (18.9%). Political and demographic turmoil had brought considerable changes in the disease pattern. With transport of goods and immigration of the population the vector of leishmaniasis have arrived in Pakistan in large numbers affecting the local population. A wide spectrum of granulomatous responses are seen which keep changing with times. At times granulomas could be quite subtle. Tuberculosis for example may present with suppurative type of acute inflammatory cell infiltrate with very few epithelioid cells. Clinical correlation along with time sequence and tendency toward fibrous must be kept in mind while interpreting granulomas.

References

1. David Elder, Rosalie E, Christine J, Bernett J. Lever’s Histopathology of the skin. 1996; p 60-61.
2. John H, Arnold O, Niel P. Textbook of peadiatric dermatology. volume 1, p 516-517, 2002.
3. Berman JD. Human leishmaniasis: clinical, diagnostic and chemotherapeutic developments in the last ten years. Clin. infec. dis 1997;24:648-703
4. Epstien WL; Cutaneous granulomas.Int.J.Dermatol. 1977; 16: 574-579.
5. Hogan DJ. Localized granuloma Anulare. J. Ama. Acad. Dermatol. 1984;10:1068-9