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Granulomatous Lesions: An Experience in a Tertiary Care Hospital

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Abstract

Background: Chronic inflammation is often marked by granuloma formation. This is a diagnostic sign of a plethora of lesions. Individual entities have their respective and unique presentation and hence the need to accurately identify the etiology of individual granulomatous lesion. This has a direct relationship with treatment protocols and hence patient morbidity. With this study we try to understand the various clinical settings and presentations in all the granulomatous lesions encountered in our Department of Pathology, Histopathology, in a year. *Materials and Method:* Retrospective study of cases diagnosed as granulomatous lesions throughout the body received over a period of 1 year from January 2015 to December 2015. All the lesions reported on histopathology were studied for individual characteristics and etiology with the help of special stains wherever required. *Result:* Fourty cases of granulomatous lesions were studied at Department of Pathology, Krishna Institute of Medical Sciences, Karad, Maharashtra, India. Most commonly affected age group was 3rd decade and females being most commonly affected with 29 cases (72.50%). Lymph node was the most commonly affected site with 19 cases (47.50%) with tuberculosis predominating the etiologies in 18 cases (45%). Other conditions noted were Leprosy, Fungal infections and Inflammatory conditions. *Conclusion:* Tuberculosis is the predominant etiological factor behind granulomatous lesions throughout the body, most commonly affecting lymph nodes. Most commonly granulomatous lesion encountered in skin is Leprosy. Fungal infections had considerable share in granulomatous lesions affecting predominantly the head and neck region.

Keyword: Granuloma; Tuberculosis; Organs; Stains.

Introduction

Granulomas are seen in various clinical settings and are a special type of chronic inflammation. The various causes range from toxic, allergic, infective, autoimmune and neoplastic to unknown etiologies [1]. Granulomatous inflammation can affect virtually every organ frequently encountered sites are the skin, subcutaneous tissue, lymph nodes and lungs [2].

Granulomatous inflammation implies chronic inflammation which is marked by epithelioid cell proliferation with/without central caseation surrounded by zone of lymphocytes, histiocytes with / without presence of giant cells [3]. Giant cell could be of Langhan, Foreign body, Touton or Tumor giant cells. Granulomatous inflammation can be encountered in numerous infective and non-infective conditions.

Materials and Method

The present study was a one year retrospective, cross sectional, analytical study undertaken in Department of Pathology, Krishna Institute of Medical Sciences Karad, Maharashtra, India. Study period was from January 2015 to December 2015. All the biopsies and specimen which were received from various departments at department of histopathology, Krishna Institute of Medical Sciences, Karad were studied. 40

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cases of granulomatous lesions were undertaken. Various sites such as lymph node, skin, bone, intestine, nasal cavity, auditory canal, testis, tonsil, muscle were affected of which lymph node was the most commonly affected organ

All the biopsyspecimens were processed according to standard technique and were sectioned and stained with routine H&E stain. Special stainssuch as 5% and 20% Zielh- Neelsen stain and Periodic Acid Schiff were employed wherever deemed necessary. Clinical history, (physical examination) was obtained from patient file or through direct patient examination.

Result

Fourty cases of granulomatous lesions were encountered throughout the body with various organs affected. The most common affected sites were, lymph node with 19 cases (47.5%) followed by skin with 6 cases (15%), breast with 4 cases (10%). Intestine was also involved seen in 3 cases (7.5%), bone in 2 cases (5%) and tonsil, tubo-ovarian mass, testis, nasal cavity, auditory canal and tendon / muscle were involved in 1 case each (Table 1).

Most commonly affected age group was from 21-30 years followed by 31-40 years with 13 cases (32.5%) & 10 (25.0%) cases respectively (Table 2). Youngest patient was a 13 years old female who had necrotising granulomatous lymphadenitis. Oldest patient was a 75 years female with granulomatous inflammation in bone.

Females were most affected with 29 cases out of 40 cases (72.5%) with a Male: Female ratio 1:2.6 (Table 3). Among etiologies, tuberculosis was most common causative agent with 18 cases (45.0%) followed by Leprosy with 5 cases that is 12.5% of etiologies. Fungal infections also had a significant share with 3 cases (7.5%) of which 2 (5.0%) of Mucormycosis and single case of Actinomycosis (Table 4).

We had single case of tonsilar Actinomycosis and Rhinoscleroma, however in 3 cases the etiology of granuloma remained elusive.Intestine was affected in 3 cases in which 2 were of inflammatory bowel disease and with 1 case of ulcerative colitis and other being in determiant which showed features of both ulcerative colitis and chron's disease and 1 case of tuberculosis. 6 cases showed granulomas having foreign type of giant cell.

We employed special stains like 5%, 20% ZN and PAS whenever required.

Table 1: Showing site distribution among all granulomatous lesions

Site	No. of cases	Percentage
Lymph node	19	47.5%
Intestine	03	7.5%
Bone	02	5%
Tonsil	01	2.5%
Breast	04	10%
Tubo-ovarian mass	01	2.5%
Testis	01	2.5%
Nasal cavity	01	2.5%
Auditory canal	01	2.5%
Muscle/ Tendon	01	2.5%
Skin	06	15%
Total	40	100%

Table 2: Showing age wise distribution among all granulomatous lesion

Age	No. of cases	Prcentage
11-20	05	12.5%
21-30	13	32.5%
31-40	10	25%
41-50	6	5%
51-60	4	10%
>61	2	5%
Total	40	100%

Table 3: Showing sex wise distribution among all granulomatous lesions

Male	Female	M:F ratio
11(27.50%)	29(72.25%)	1.26

Table 4: Etiological distribution among all granulomatous lesions

Causes	No. of Cases	Percentage
Tuberculosis	18	45%
Leprosy	05	12.5%
Foreign body reaction	06	15%
Unknown etiology	03	7.5%
Rhinosclerosis	01	2.5%
Actinomycosis	01	2.5%
Mucormycosis	02	5%
Inflammatory bowel disease	02	5%
Kikuchi Fujimoto disease	02	5%
Total	40	100%

Table 5: Showing special staining positivity

Special stain	5% ZN	20% ZN	PAS
Positive	05	18	03
Negative	11	03	12
Total	16	21	15

Discussion

Granulomatous infection is a type of chronic inflammation that is seen in various conditions which could be infective, allergic, autoimmune or malignant. Many a time the lesion could be idiopathic [1]. Granuloma is focally chronic inflammatory lesions which are manifested as means of defending host from persistent exogenous or endogenous irritants [1].

Causes of granuloma include bacterial,fungal,, viral ,helminthic, foreign body induced etc. [4], Granulomas classified as epitheliod, histiocytic foreign body , necrobiotic palisading and inflammatory [5].

Few epitheliod granulomas are necrotizing while others show suppuration. Absolute diagnosis of individual granulomas for etiology can be done by ancillary studies like special stains (Ziehl-Neelsen, Periodic Acid Schiff, Grocott- Methamine- Silver), real time PCR insitu hybridisation. However in cases which still remain unexplained clinical history and clinicopathological correlation is essential to make final diagnosis.

Mechanism of Action

The provocative agents of granulomatous inflammation are to a larger extent nondegradable by acute inflammatory cells. The combined action of polymononeuclear cells,non-activated macrophages and chemical mediators released by them are unable to digest completely and eradicate the offending agent [6]. For the degradation of these agents activated macrophages are required which are formed by CD4+ T cells. These cells secrete Interleukin, Interferon, Tumor necrotic factor, Lymphotoxins for transformation of macrophages and formation of epithelioid cells and / or giant cells.

We had 40 cases granulomatous lesions distributed through the body. Lymph node was most common site with maximum number of cases, 19 comprising 47.5% cases followed by skin with 6 cases (15%). There were 4 cases (10%) of breast lesions, 3 (7.5%) of intestine and 2 bone granulomatous lesion. There was one case each of tonsil, tubo ovarian mass, testis, nasal cavity, auditory canal and tendon.

Of all the cases, various infectious and non infectious causes were diagnosed. In our study there was no case of malignancy causing granuloma. Among infective causes we came across bacterial and fungal lesions. We also had inflammatory condition in 2 cases. Tuberculosis as expected in this part of India was the most common etiologywith 18 cases (45%) followed by foreign body granuloma which were seen in 6 cases (15%). Leprosy was third most common etiology with 5 cases comprising of 12.5% cases. There were 2 cases of inflammatory bowel diseasewith 1 case of ulcerative colitis and other being indeterminant which displayed features of both ulcerative colitis and chron's disease. In this case, histiocytic type granulomas were noted along with partial involvement of bowel with inflammatory cells. We had 3 cases of fungal infection in which 2 were of mucormycosis which was noted in lymph node and lesion of skin (Table 1) Broad aseptate occasionally wide angle branching hypae along with epitheliod type granuloma formation were noted which were confirmed on PAS stain. Two cases of Kikuchi-Fujimoto disease were noted which showed classical necrotizing pattern. A single case of tonsillar actinomycosis was also seen.

We had single case of rhinoscleroma which revealed plasma cells, Mikulicz cell and inflammatory cell in the nasal cavity. Of the 4 cases of breast lesions, 1 case revealed epitheliod type granuloma which on 20% ZN stain showed acid fast bacilli. One showed foreign

body type giant cell reaction and etiology in 2 cases could not be identified even performing PAS and ZN stain.

2 cases of bone were noted in our study of which one was diagnosed as tuberculous osteomyelitis while other showed foreign body reaction. We had one case of tuboovarian mass with tuberculosis as etiology in our study which showed epitheliod granuloma with suppuration. Fungal infections were most commonly observed having histiocytic characteristics in their granulomas.We had a single case of actinomycosis which was an incidental finding in tonsillectomy specimen.

Of 19 cases of lymph node 13 were affected by tuberculosis and showed epitheliod granulomas. On ZN stain all the 13 cases showed numerous acid fast bacilli. 2 cases were of Kikuchi-Fujimoto disease, 3 cases showed foreign body type granulomas. A single case of mucormycosis was confirmed on PAS stain was also noted (Table 5).

Skin was involved in 6 cases comprising of 50% cases of which majority that is 5 cases (12.5%) were diagnosed as leprosy. 5% of ZN stain was employed to visualize the lepra bacilli. Of the 5 cases, 3 cases were of tuberculoid leprosy, 1 was borderline tuberculoid and 1 was lepromatous leprosy. However, our study was not in concordance to present literature which favour borderline tubercuoid leprosy as the prominent lesion [7,8,9]. A case of granulomatous orchitis which on 20% ZN staining revealed acid fast bacilli.

The most commonly affected age group was the 3rd decade and the females being worst affected. Our study showed concordance of age most commonly affected with studies such as Permi HS et al and Pawale JS et al [10,11]. However, males are the most commonly affected according to literature [10,11]. In our study females were most commonly affected with 29 cases (72.5%) out of 40 cases, affecting a Male: Female ratio of 1:2.6, which was new finding.

Special stains can be very helpful in pinpointing an exact diagnosis when coupled with ideally stained H&E sections (Table 5).

ZN stain demonstrated acid fast bacilli in 62.16% cases which was in concordance with study by Krishnaswamy H et al, who showed positivity of 71% [12]. High suspicion index and selection of cases for special stains could have also lead to this high incidence.

Conclusion

Granulomatous lesions are most commonly seen in third decade of life and affecting most commonly females as seen in our study. Special stains coupled with H&E and ancillary techniques such as real time PCR and FISH can prove to be powerful diagnostic triad for accurate diagnosis of granulomatous lesions. Tuberculosis is the most common cause of granulomatous inflammation followed by leprosy. Fungal infections also play an active role in granuloma formation. Accurate diagnosis of individual entities is of prime importance as treatment protocols differ for different etiologies.

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