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Original Research Article

The histopathological approach to granulomatous skin lesions

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ABSTRACT

Introduction: Granulomatous inflammation of skin and subcutaneous tissue are common in India. An identical histological picture is produced by several causes. Present study aims at classifying infectious granulomas based on histomorphology and special staining and developing a proper approach for making a specific etiological diagnosis.
Aims: To classify the granulomatous dermatitis and a simple diagnostic histological approach has been worked out based on morphology of granuloma, presence of caseous necrosis, palisading necrosis, location of the granuloma and use of special stains.
Materials and Methods: A prospective study of skin biopsies with granulomatous inflammation over a period of 2 years is done. Histologically lesions were divided into six subtypes:-Tuberculoid, foreign body type, histoid, necrobiotic, suppurative and sarcoidal type. On basis of morphological features and special staining each type was further subclassified and a specific diagnosis was given.
Results: Among 580 skin biopsies, 175 cases (30.17%) were of granulomatous skin lesions. On histopathological typing Tuberculoid type of granuloma was the most common type (62/175 cases, 35.43%) of which leprosy (40/62 cases, 64.52%) was the commonest etiology identified. Infections form an important etiology of granulomatous skin inflammation (120/175 cases, 68.57%) of which leprosy (82/120 cases, 68.33%) is the leading etiology in our study.
Conclusion: Adequate clinical work-up in combination with pathological resources help in correctly approaching a granulomatous skin lesion and reaching a specific etiologic diagnosis.

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1. Introduction

Granulomatous inflammation is a distinctive pattern of chronic inflammation due to tissue reaction against various organic and inorganic antigens, which are often resistant to be eliminated.[1] Granulomatous dermatitis frequently poses a diagnostic challenge to dermatopathologists, since an identical histologic picture is produced by several causes and conversely a single cause may produce varied histologic patterns.[2] However, good clinical history, histopathological examination and clinicopathological correlation is mandatory in arriving at a proper diagnosis so that appropriate treatment can be meted out.[3] Our study aimed at classifying the granulomatous dermatitis and a simple diagnostic histological approach has been worked out based on morphology of granuloma, presence of caseous necrosis, palisading necrosis, location of the granuloma and use of special stains.

2. Materials and Methods

The histopathological study of granulomatous dermatitis was carried out in histopathology department of Pathology, over a period of 2 years from May 2017 to April 2019. Most of the patient's specimen for histopathological study in our institute were received from OPD and indoor patients from Skin, ENT, Orthopaedics and Surgery departments after incisional and excisional skin biopsies and other surgical

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procedures after taking written informed consent. This study was conducted with the permission of the institutional ethics committee and required procedures were performed according to the declaration of Helsinki. A study of total 580 cases of skin lesions was done.

For histopathological examination, specimens were received in 10% formalin. In histopathology department specimens were processed and sections were stained by Haematoxylin and Eosin (H&E) stain. Special stains like Ziehl Neelson (ZN), Periodic acid Schiff (PAS), Fite Faraco, and Giemsa stain were used wherever required. The relevant clinical details and laboratory investigations were collected from the hospital records.

The cases diagnosed as granulomatous dermatitis were subclassified according to histomorphology into six types: 1) Tuberculoid, 2)Foreign body, 3) Suppurative, 4) Histoid, 5) Necrobiotic and 6) Sarcoidal type.

3. Results

On the basis of histomorphological features out of total 580 cases, 175 cases (30.17%) were diagnosed as granulomatous lesions. These 175 cases were then subclassified. Most common type was Tuberculoid type (62/175 cases, 35.43%), followed by Foreign body type (51/175 cases, 29.14%), Histoid type (42/175 cases, 24%), Suppurative type (16/175 cases, 9.14%), Necrobiotic type (03/175 cases, 1.71%) and Sarcoidal type (01/175 cases,0.57%).

Table 1: Demonstrate the morphological types of granuloma

S. No.	Types of Granulomatous lesion	Number	percentage (%)
1	Tuberculoid type	62	35.43
2	Foreign body type	51	29.14
3	Histoid type	42	24.00
4	Suppurative type	16	9.14
5	Necrobiotic type	03	1.71
6	Sarcoidal type	01	0.57
	Total	175	100

Among Tuberculoid type majority of cases i.e. 40 out of 62 cases, 64.52% were of leprosy (Tuberculoid leprosy 21/40 cases, 52.50%; Borderline tuberculoid leprosy 17/40 cases,42.50%; Borderline borderline leprosy 02/40,5.0% cases), followed by 21 cases,33.87% of skin tuberculosis (Lupus vulgaris 17/21cases, 80.95%; Scrofuloderma 02/21 cases, 9.52%; and Tuberculosis verruca cutis 02/21 cases 9.52%). In 1 out of 62 cases (1.61%) combination of necrosis, giant cells and macrophages were present, forming tuberculoid granulomas in dermis. This case was positive on PAS staining, indicating Fungal etiology.

Among the 51 cases of Foreign body type granulomas 42 cases, 82.35% were secondary to Ruptured epidermal inclusion cyst, 04 cases, 7.84% were secondary to leakage of keratinous contents from Pilomatricoma and in 05 cases, 9.80% granuloma was formed secondary to Foreign substance like horn and suture material.

Among the 42 cases of Histoid type granulomas, we identified 17 cases, 40.48% of Lepromatous leprosy followed by 15 cases, 35.71% of Borderline lepromatous leprosy; 8 cases, 19.05% of Erythrma nodosum leprosum and 2 cases, 4.76% of Indeterminate leprosy.

In the present study we diagnosed 16 cases of Suppurative granulomas, while 12 cases (75%)were secondary to fungal infections which was confirmed by their PAS positivity, 4 cases (25%) of suppurative granulomas revealed parasite and increase in number of eosinophils.

Three cases of Necrobiotic granulomas were identified which comprise of Granuloma annulare (1/3 cases, 33.33%) and of Rheumatoid skin nodules (2/3 cases, 66.67%).

One case of Sarcoidosis was diagnosed by morphology and special staining and was classified into sarcoidal type of granulomatous lesion.

A total of 175 cases of granulomatous dermatitis were identified, of which 120 cases (68.57%) were categorized in infectious granulomatous dermatitis and 55 cases (31.43%) into non-infectious dermatitis. The age of patients ranged from 10years to 75 years. Male (99/175) to female (76/175) ratio is 1.3: 1

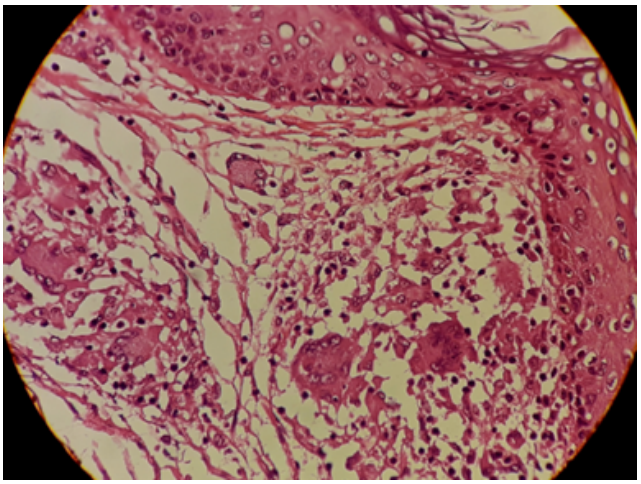

Fig. 1: Photomicrograph of Tuberculoid leprosy showing tuberculoid granulomas infiltrating into epidermis. (H/E, 400X)

4. Discussion

Granulomatous inflammation of skin comprises a spectrum of diseases sharing the common denominator of granuloma formation.[4] A granuloma is a collection of mononuclear cells usually as a result of type IV hypersensitivity reaction in response to an antigen or persistence of non-degradable product.[1]

Granulomatous diseases have been previously classified on the basis of pathophysiology, etiology, immunology and

Table 2: Demonstrate the morphological types of Tuberculoid granuloma(62/175 cases)

S. No	Types		Number	Percentage (%)
1	Leprosy		40	
		Tuberculoid leprosy	21	52.50
		Borderline tuberculoid leprosy	17	42.50
		Borderline borderline leprosy	02	05.0
2	Tuberculosis		21	
		Lupus vulgaris	17	80.95
		Scrofuloderma	02	09.52
		Tuberculosis verruca cutis	02	09.52
3	Fungal	Histoplasmosis	01	01.61

Table 3: Demonstrate the morphological types of Foreign body granulomas (51/175 cases)

S. No	Types	Number	Percentage (%)
1	Ruptured epidermal inclusion cyst	42	82.35
2	Pilomatricoma	04	07.84
3	Others (non-biodegradable material)	05	09.80

Table 4: Demonstrate the morphological types of Histoid type granulomas (42/175 cases)

S. No	Type	Number	Percentage (%)
1	Lepromatous leprosy	17	40.48
2	Borderline lepromatous leprosy	15	35.71
3	Erythema nodosumleprosum	08	19.05
4	Indeterminate leprosy	02	04.76

Table 5: Demonstrate the etiology of granulomatous dermatitis

S. No	Type	Subtypes	Number	Percentage %)
	Infectious		120/175	68.57
1		Tuberculosis	21/120	17.50
2		Leprosy	82/120	68.33
3		Fungal	13/120	10.83
4		Parasitic	04/120	03.33
	Non-infectious		55/175	31.43
1		Ruptured epidermal inclusion cyst	42/55	76.36
2		Pilomatricoma	04/55	7.27
3		Granuloma annulare	01/55	1.82
4		Horn/suture	05/55	9.09
5		Rheumatoid nodule	02/55	3.64
6		Sarcoidosis	01/55	1.82

Table 6: Demonstrate the distribution of granulomatous dermatitis according to age of patients

S. No	Age group (years)	Number	Percentage (%)
1	0-10	04	02.28
2	11-20	38	21.71
3	21-30	41	23.43
4	31-40	48	27.43
5	41-50	25	14.29
6	51-60	13	07.43
7	61-70	04	02.28
8	>70	02	01.14
	Total	175	

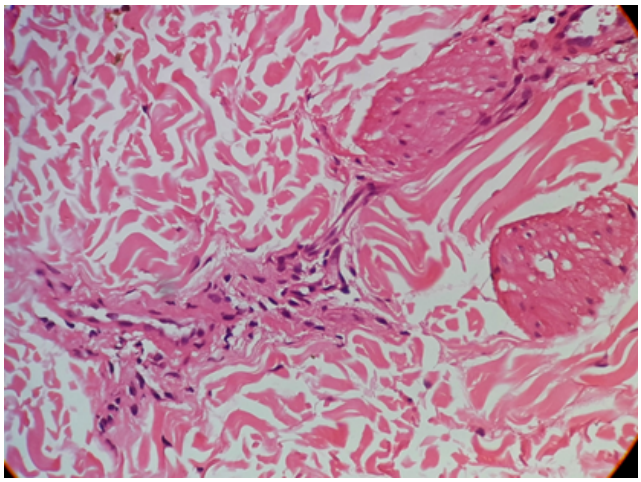

Fig. 2: Photomicrograph of Borderline tuberculoid leprosy showing tuberculoid granuloma in dermis involving neurovascular plexus. (H/E, 400X)

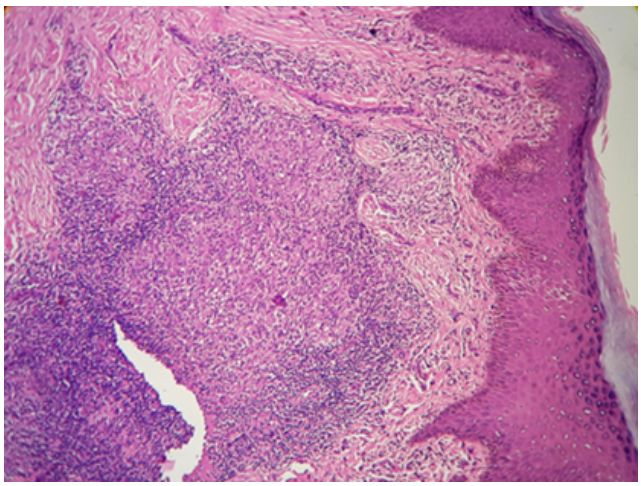

Fig. 3: Photomicrograph of Lupus vulgaris showing tuberculoid granuloma in dermis with slight necrosis. (H/E, 100X)

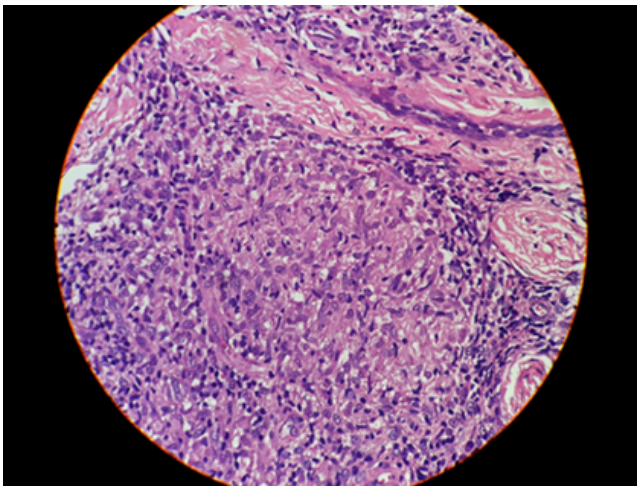

Fig. 4: Photomicrograph of Lupus vulgaris showing tuberculoid granuloma with predominant epithelioid cell component and slight necrosis. (H/E, 400X)

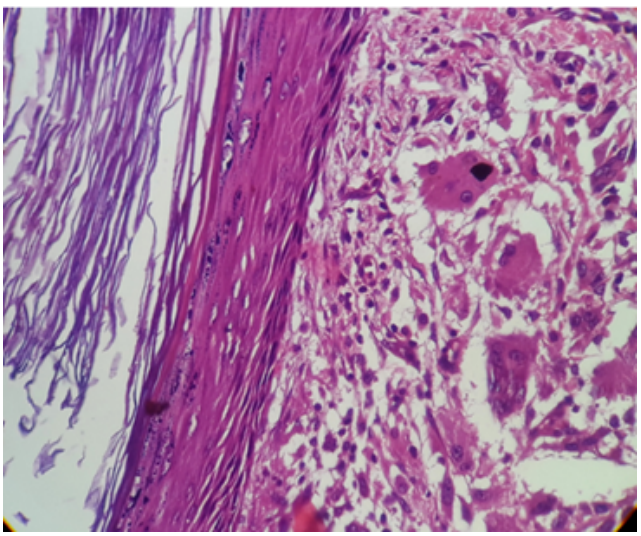

Fig. 5: Photomicrograph of Ruptured inclusion cyst revealing foreign body type granuloma. (H/E 400X)

morphology. In the present study granulomatous dermatitis was classified using combination of histopathological findings and special staining.

Six histological types of granulomas were identified on the basis of the constituent cells and other changes within the granuloma: 1) Tuberculoid, 2) Foreign body type, 3) Suppurative, 4) Histoid, 5) Necrobiotic, 6) Sarcoidal.

Among tuberculoid type granuloma an attempt has been made to identify characteristic pattern of involvement among Tuberculosis verruca cutis, Lupus vulgaris, Scrofuloderma, Tuberculoid leprosy, Borderline tuberculoid leprosy and few fungal granulomas. Granuloma in Tuberculoid leprosy and Borderline tuberculoid leprosy are seen along the neurovascular bundles and superficial vascular plexus whereas granuloma of Tuberculosis verruca cutis, Lupus vulgaris, Scrofuloderma and fungal granulomas, usually involve full thickness of the dermis. Granulomas of Borderline tuberculoid leprosy donot infiltrate into the epidermis where as granulomas of Tuberculoid leprosy are seen infiltrating the epidermis.[5]

We further subdivided tuberculoid granulomas based on cell component predominantly epithelioid cells. In Tuberculosis verruca cutis and Lupus vulgaris epithelioid cells are present in fair number where as in fungal granulomas number of epithelioid cells are scant to absent.[5] Predominantly epithelioid cell granulomas with moderate necrosis were diagnosed as Tuberculosis verruca cutis and those with slight or absent necrosis were diagnosed as Lupus vulgaris. Scant or absent epithelioid cell granulomas were

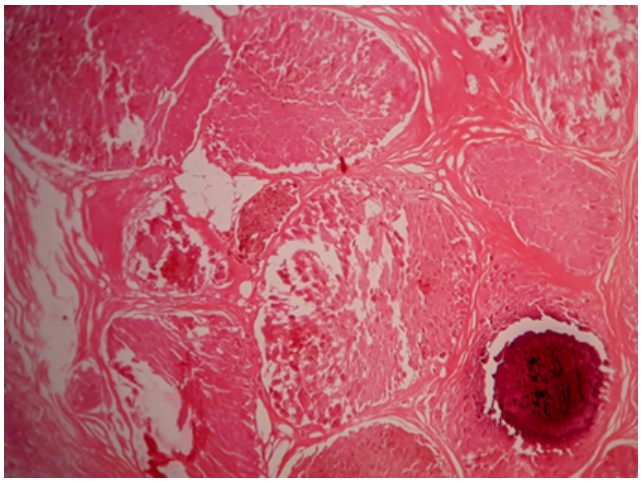

Fig. 6: Photomicrograph of Pilomatricoma revealing foreign body type granuloma. (H/E 100X)

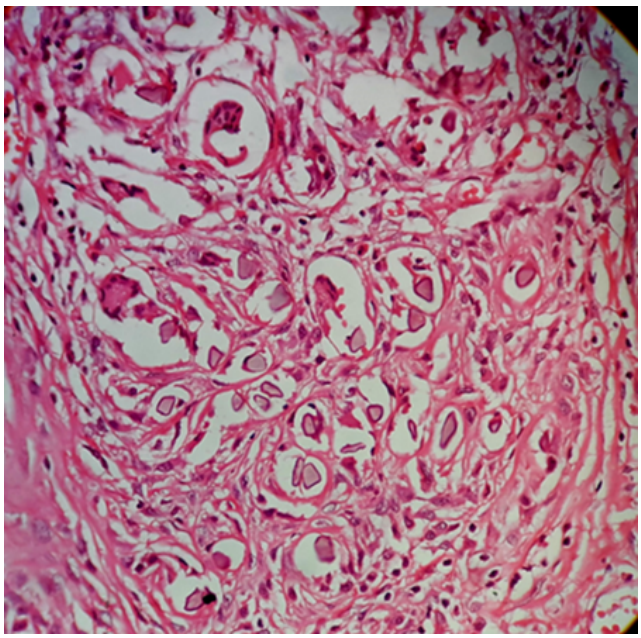

Fig. 7: Photomicrograph showing foreign body type granuloma.secondary to suture material (H/E 400X)

of fungal origin as proved by PAS stain.

ZN staining revealed presence of acid fast bacilli in Tuberculosis verruca cutis while in cases of Lupus vulgaris bacteria were present in small number or absent. FiteFaracostaining revealed scanty bacilli in Borderline tuberculoid leprosy. Bacilli were absent in case of Tuberculoid leprosy.[5]

The sex distribution pattern revealed that most of the patients were males (56.57%) which is in concordance with study of AmanjitBal et al[2] and Ashkakodnani et al[6].The age distribution pattern revealed that maximum cases were in the age range of 31-40 years in contrast to the study of

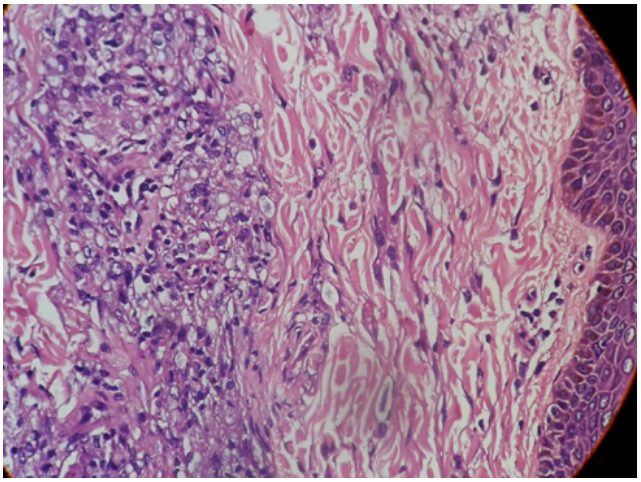

Fig. 8: Photomicrograph of Lepromatous Leprosy showing Histoid type granuloma revealing collection of foamy macrophages and plasma cells. (H/E, 100X)

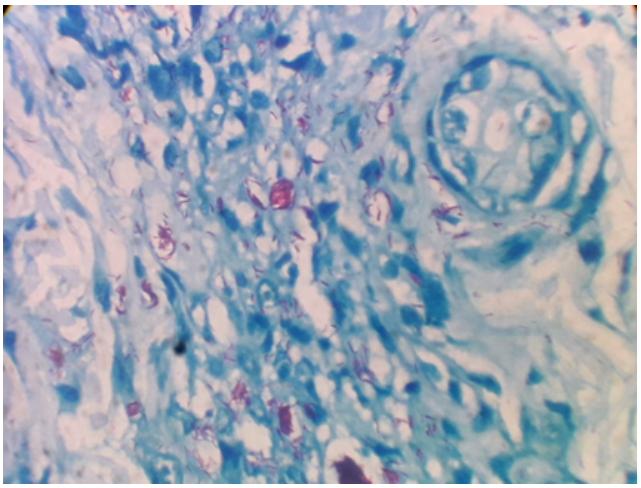

Fig. 9: Photomicrograph of Lepromatous leprosy showing presence of Acid Fast Bacilli (Fite Faraco, 1000X)

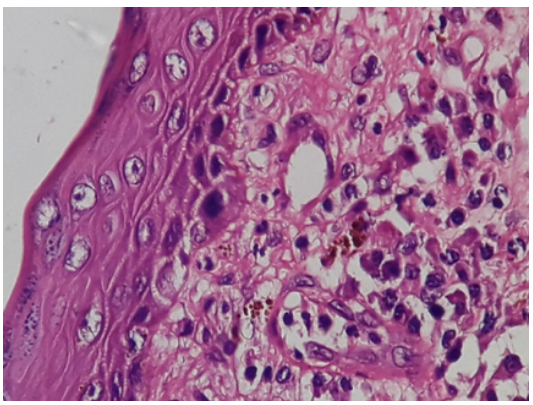

Fig. 10: Photomicrographof Chromobalstomycosis showing suppurative granuloma and presence of copper pennies. (H/E, 400 X)

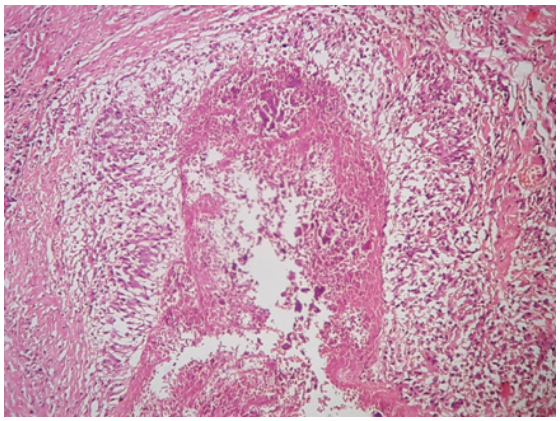

Fig. 11: Photomicrograph of Rheumatoid skin noduleshowing necrobiotic granuloma erevealing palisading and fibrosis. (H/E, 400X)

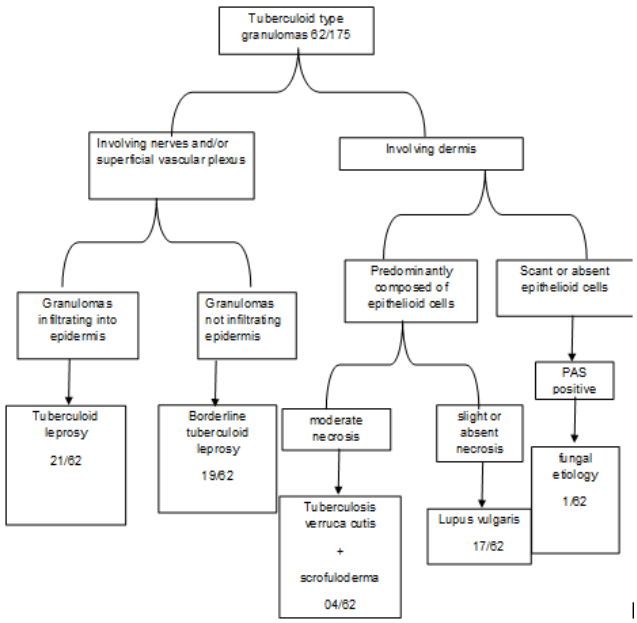

Fig. 12:

R.singh et al[7] where maximum biopsies received were in the age range of 41-60 years.

In the present study, largest group of lesions were of tuberculoid granuloma (62/175 cases, 35.43%). Similar findings were seen in the study of Srabanichakrabarti et al[1].Second most common group of lesions in our study were of foreign body type granuloma (51/175 cases, 29.14%) which is in contrast to study of Srabanichakrabati et al[1]where second most common lesions were of necrobiotic type granulomas.

In our study, 68.57% cases (120/175) were due to infectious etiology and leprosy was the commonest specific cause (68.33%, 82/120 cases) which is similar to the findings of Jayawardhana et al (39.8%)[8] and AmanjitBal et al (72.4%)[2] second commonest infectious etiology was tuberculosis (21/120 cases, 17.50%). In series of R Singh et al[7], Amanjitbal et al[2] and Jayawardhana et al[8] similar findings were seen with incidence of tuberculosis being 42.31%, 23.1%, and 13.3% of cases respectively.

5. Conclusion

Histopathological approach along with special staining is gold standard for diagnosis and categorization of granulomatous skin lesions. The classical clinical features may be absent and identifying the agent may not be always possible hence adequate work up in combination with histopathology and special staining help in making correct specific diagnosis.

6. Source of funding

None.

7. Conflict of interest

None.

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