Profile of Skin Biopsies and Patterns of Granulomatous Skin Diseases in a Tertiary Care Center of Western Nepal

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Article received: 30th Jan 2020

Article accepted: 7th June 2020

ABSTRACT

Background: Granulomatous skin diseases are one of the leading causes of morbidity in tropical countries like Nepal. These granulomatous skin lesions often pose diagnostic challenge to clinicians as well as to dermatopathologists. Histopathologic examination of a biopsy specimen represents one of the most informative and cost-effective procedure and may help to avoid other, costlier and invasive diagnostic workup. **Materials and Methods:** This cross-sectional observational study from October 2018 to October 2019, at department of dermatology, enrolled 142 cases of skin biopsies. Correlation between clinical impression and histopathological findings was evaluated. **Results:** Out of 13940 dermatology visits/ consultations, 142 (1.01%) skin biopsies were performed. Head, neck and face were the commonest sites of biopsies (29.6%). The most common biopsy technique was incisional type in 70 (50.4%). Histopathology showed granulomatous features in 49 (34.8%) cases, out of which tuberculoid type was the commonest, in 29 (58.0%). Positive clinicopathological correlation was seen in 117/142 (82.4%) for all biopsies and 41/49 (85%) for granulomaous skin lesions. **Conclusion:** Tuberculoid type was the most common cutaneous granuloma. High clinicopathological correlation in our study supports histopathology as an important tool for diagnosis of granulomatous as well overall skin disorders.
Keywords: Granuloma, histopathology, leprosy, skin biopsy.

INTRODUCTION

Skin biopsy is a crucial investigation in dermatology and histopathological findings help clinicians in reaching proper diagnosis, which further helps in holistic patient care.[1] Spectrum of dermatologic disorders varies globally, among them, granulomatous skin diseases are one of the leading causes of morbidity in tropical countries like Nepal. Clinically, granulomatous skin lesions appear as painless, non-itchy, tumid, space occupying lesion particularly in the dermis. Histologically, they are discrete collections of histiocytes or epithelioid histiocytes with variable numbers of admixed inflammatory and multinucleated giant cells due to persistence of non-degradable agents and cell mediated hypersensitivity. There is a complex interplay among inciting agents, prolonged antigenaemia, macrophage activity, The cell response, B cell overactivity and

myriad of biological inflammatory mediators. [2,3] Mycobacterial agents, non mycobacterial agents, leishmaniasis and fungal infections are common infectious etiologies. These granulomatous skin lesions often pose diagnostic challenge to clinicians as well to dermatopathologists because identical histological pattern may be produced by several causes, and conversely, a single cause may produce several histological patterns.[2]

Based on the constituent cells and other changes within the granulomas they are classified into six groups. 1. Tuberculoid granuloma, 2.Sarcoidal granuloma, 3. Suppurative granuloma, 4. Necrobiotic granuloma, 5. Foreign body granuloma and 6. Miscellaneous granuloma. The characteristic features of each one are as follows; tuberculoid has characteristic central "caseation" necrosis, sarcoidal has classic "naked" appearance, necrobiotic shows more loose arrangement and necrobiosis (collagenolysis), suppurative features central collections of neutrophils and foreign body-type by foreign body giant cells along with presence of exogenous or endogenous foreign materials. Histopathology remains a gold standard method for diagnosis of various granulomatous dermatoses.[3]

Among infectious disorders with granuloma formation, microorganisms are easily identified and treated while non-infectious diseases with granuloma are often challenging. There are overlaps in histopathological findings of different granulomatous reactions.[3] Therefore, a keen understanding of both infectious and non-infectious granulomatous disorders of skin is essential for patient care.

Skin biopsy is a simple out-patient department (OPD) procedure which can be performed irrespective of age and underlying clinical condition and are essential assets in the armamentarium of dermatologists. Properly performed, it is almost a confirmatory diagnostic tool, it treats cosmetically unacceptable lesions, and guide for definitive treatment for a variety of disorders. Skin biopsy is a unique procedure as the lesion is visible, allowing for proper selection of biopsy site and technique. Histopathologic examination of a biopsy specimen may represent one of the most informative and cost-effective procedure and may help to avoid other, more invasive diagnostic workups. [5] It is a maxim among dermatologists that more errors are made from failing to biopsy at correct time than from doing unnecessary biopsies. [6]Although literatures show that skin biopsy may exhibit diagnostic inefficiency, it remains an important aid for the dermatology clinical practice. [7]There is known under-recording of cutaneous granuloma incidence, partly because in country like Nepal qualified dermatologist and histopathology/dermatopathology facilities are scarce and the dermatoses are managed mainly on clinical judgements.

The objectives of this study were to determine the morphological and histopathological profile of dermatological lesions, to study relative frequency of granulomatous lesions of the skin and the level of clinicopathologic correlation.

MATERIALS AND METHODS

After institutional review board approval, we conducted this cross-sectional observational study from October 2018 to October 2019, at department of dermatology Manipal college of Medical sciences, Pokhara. The study population included all consenting out-patient department visits as well referred patients from different departments and institutes, needing skin biopsy. A total of 142 biopsies, out of 13940 (1.01%) dermatology consultations were performed. Biopsies were taken from one or more site at one session, as per indications. Predesigned performa were completed for each patient which included demographic information, duration of symptoms at presentation, clinical characteristics, modality of treatment if any, types and sites of biopsy performed, various aspects of health behavior and social factors. After getting histopathological report, correlation was measured among clinical and histopathological diagnosis and statistical significance were evaluated.

Statistical analysis: SPSS statistical package version 16 was used. The data were analyzed with descriptive statistics. Frequencies and percentage were used for numerical and categorical variables. Mean and SD were used for normal distribution , otherwise median and range were used.

RESULTS

The present study has documented the morphological and histopathological profile of skin lesions at

a tertiary care centre in Western Nepal. The age range of the study population was 43.0±2.0. A total of 142 biopsies, out of 13940 visits (1.01%) were performed. Duration of skin manifestations for which biopsies were done ranged from one month to ninety months with median of twelve months. Different clinical lesion for which biopsies were performed is summarised in table 1, where plaque was the most common clinical presentation 74 (53.6%) followed by nodule (18.1%). Head, neck and face were the commonest sites of biopsies (29.6%) followed by trunks and limbs as shown in table 2. Out of total biopsies, 51.2% of the patients were from dermatology OPD and rest were referred from other departments and institutes. Different types of techniques used for biopsies are summarised in table 3, which shows incisional biopsy, the most common type 70 (50.4%), followed by excisional in 36 (25.9%). Out of total biopsies, histopathology showed granulomatous features in 49 (34.8%) cases, out of which, tuberculoid type was the commonest in 29 (58.0%), followed by suppurative granuloma in 10 (20.0%) as shown in table 4. Overall pattern of skin diseases diagnosed by biopsy are shown in table 5, having leprosy (9.9%) followed by subcutaneous fungal infections and skin tuberculosis as common granulomatous skin disorders. Cutaneous malignancies of different types constituted 10.6 % of total biopsies performed.

Positive clinicopathological correlation was seen in 117/142 (82.4%) for all biopsies and 41/49 (85%) for granulomatous skin lesions.

Table 1: Different types of clinical lesions subjected to biopsy (N=138)

Plaque	74 (53.6%)
Nodule	25 (18.1%)
Ulcer	17 (12.3%)
Bullae	8 (5.8%)
Papules	10 (7.2%)
Macules	2 (1.4%)
Pustule/swelling	2 (1.4%)

Table 2: Sites of biopsy

Head, neck and face	42 (29.6%)
Upper limb	31 (21.8%)
Trunk	36 (25.4%)
Lower limb	32 (22.5%)
Multiple sites	1 (0.7%)

Table 3: Types of biopsy performed (N=136)

Excisional	36 (25.9%)
Incisional	70 (50.4%)
Punch	27 (19.4%)
Shave	6 (4.3%)

Table 4: Types of granulomas reported in histopathology.

Tuberculoid	29 (58.0%)
Foreign body	2 (4.0%)
Sarcoidal	1 (2.0%)
Necrobiotic	4 (8.0%)
Suppurative	10 (20.0%)
Miscellaneous	4 (8.0%)

Table 5: Overall pattern of skin diseases diagnosed by skin biopsies.

Leprosy	14 (9.9%)
Skin tuberculosis	7 (4.9%)
Subcutaneous fungal infection	8 (5.6%)
Bullous disorders	10 (7.0%)
Cutaneous malignancy	15 (10.6%)
Connective tissue disorders	12 (8.5%)
Disorders of keratinization	5 (3.5%)
Lichen planopilaris/lichen planus	7 (4.9%)
Benign skin tumor	13 (9.2%)
Erythema induratum/erythema nodusum	4 (2.8%)
Granuloma annulare	5 (3.5%)
Papulosquamous disorders	7 (4.9%)
Melanocytic nevus	7 (4.9%)
Xanthoma	3 (2.1%)
Others	25 (17.2%)

Discrepancies in total number (N) in tables are due to missing data.

DISCUSSION

Nepal, a landlocked country in South Asia lies between latitudes 26° and 31°N, and longitudes 80°and 89°E. The differences in elevation found in Nepal result in a variety of biomes, like tropical, subtropical, temperate, grasslands, shrub lands and rock and ice at the highest elevations. Majority of population is in tropical and subtropical climate, with high prevalence of tropical diseases. [8]

Out of 13940 OPD visits in the Dermatology department, a total of 142 biopsies (1.01%) were performed. Biopsy rate in same institution has gone down from 1.37% of all OPD visits/consultations in 2011-14[1] to 1.01 % in 2011-14, probably due to increasing dependency upon dermoscopy, which was Supported by Carli et al.[9] We found slight female preponderance (78/142), our findings agreed with previous studies by Zafar et al.[10] but not with others like Gautam et al, [2] Chakrabarty et al,[4] Dhar et al,[11] Rajbhandari et al,[12] and Adhikari et al, [13] where male outnumbered the females. The commonest site of skin biopsy in our study was head, neck and face like in study by Zafar et al, [10]whereas in study by Gautam et al [2] and Rajbhandari et al [12]it was upper limb.

In present study, granulomatous lesions constituted 34.8% of total skin biopsies, whereas in study by Gautam et al, [2] it was only 6.67% ,by Chakrabarty et al, [4] it was 14.53% , and by Rajbhandari et al[12] it was 16.7% of total skin biopsies, reason could be increased dependence on dermoscopy to diagnose non granulomatous skin diseases.

In present study, granulomatous lesions with highest prevalence were tuberculoid granuloma, constituting 29/141 (58%)), similar to other studies where tuberculoid granuloma has the highest prevalence but in different magnitude, by Rajbhandari et al [13] it was 43%, by Chakrabarty et al,[4] it was 73%, by Gautam et al, [2] it was 77.3% and by Dhar et al[11] it was 87.7%.

In our study, infectious etiology was the most common cause of granulomatous dermatoses, among them, leprosy was the most common(9.9%) of all skin biopsies. Our findings were consistent with Pawale et al,[14] with leprosy being the most common cause of granuloma but in much higher proportion (56.6%). Similar findings were observed in study by Bal et al,[15] Gautam et al,[2] Rajbhandari et al[12] and by Bansal et al,[16] which may be due to the endemicity of these condition in Southeast Asian countries whereas in study by Adhikari et al,[13] tuberculosis was the most common cause of granuloma followed by fungal infection. In a study by El-Khalawany et al,[17] 40.8% cases were cutaneous tuberculosis followed by 31.7% leprosy. Qureshi et al [18] reported cutaneous leishmaniasis in 56.7% being the leading cause of granulomatous dermatoses followed remotely by lupus vulgaris in 13.5% cases.

Overall, positive clinico-pathological correlation was seen in 117/142 (82.4%) for all biopsies, it was 76% in a study in same institute in 2011-2014 [1]. Similar Clinicopathological concordance of 88.98% was reported by Gupta et al, [19] and 78.38% by Kafle et al. [20]Clinico-pathological correlation for granulomatous skin lesion was found to be 41/49 (85%) in present study. The high clinico-pathological correlation might be due to open discussion among treating physicians and consultant pathologist whereas concordance between initial clinical impression and histological diagnosis was found in only 63% by Rajbhandari et al, [12] and 61.3% by Gautam et al.[2] study by Makwana et al [21] also reported positive concordance rate in 65.7% of cases and they encouraged the use of other advanced diagnostic methods like Polymerase chain reaction (PCR), rapid antigen detection, etc.

LIMITATIONS

Single institute and smaller sample size were major limitations.

CONCLUSION

Our study revealed infectious etiology mainly leprosy, subcutaneous mycosis and tuberculosis as common cause of granulomatous dermatoses, which supports the earlier study in similar geographical location. Our study gives prevalence of important granulomatous skin diseases in this region, which will help in implicating health programmes and management of individual cases. It also supports

histopathology as one of the important diagnostic modalities to diagnose granulomatous as well as overall skin disorders.

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