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Original Research Article

Skin stories unveiled: A histopathological journey through tertiary care dermatology

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ABSTRACT

Background: A variety of clinical phenotypes are observed in dermatological illnesses, which can occasionally make diagnosis challenging. Our study aimed to conduct a retrospective analysis of dermatopathological correlation and highlight its significance in establishing an accurate diagnosis.
Materials and Methods: Retrospective analysis was done on histopathological data gathered from a tertiary health care centre over a period of 18 months. To facilitate analysis, the results were categorised into various groups.
Results: Of the 336 cases that were examined in total, microbial infections accounted for the majority (33.93%, n = 114/336). Non-infectious erythematous papular and squamous disease (18.75% n = 63/336) and non-infectious vesiculobullous and vesicopustular disease (11.31% n = 38/336) were the other two prevalent groups. The least common categories were inflammatory disease of subcutis (0.3% n = 1/336) and disorder associated with physical agent (0.3% n = 1/336). The histological results were generally in agreement with the clinical observations (75.60 percent, n = 253/336). Partial concordance and discordance was seen in 10.12% (34/336) and 6.25% (21/336) cases respectively. Early histopathological diagnosis and clinicopathological correlation helped in timely management of partially concordant and discordant cases.
Conclusion: This study highlights the value of skin biopsies as an easy, reasonably priced, and useful tool in a dermatologist's toolbox. Histopathological analysis distinguishes between illnesses with similar morphologies, hence preventing misdiagnosis. Histopathology was useful in diagnosing a number of neoplastic disorders and in determining the progression or resolution of diseases like leprosy. Discordant cases were timely managed with the help of histopathological and clinical correlation.

1. Introduction

Dermatological conditions can manifest with diverse clinical presentations, sometimes deviating significantly from the typical characteristics. Distinguishing between different diseases can be challenging, as they may share similar appearances, making clinical diagnosis difficult. Histopathology serves as a crucial tool in resolving diagnostic uncertainties, acting as a bridge towards accurate identification. In our tertiary healthcare center, where a significant portion of patients hail from low socioeconomic backgrounds, extensive investigations are often not feasible, and biopsies are typically reserved for cases presenting diagnostic challenges. Skin biopsy plays a pivotal role in such scenarios, helping to exclude other potential diagnoses. Our study involved analysis of histopathological data spanning the nineteen months, aimed at elucidating the disease patterns within our setting. Additionally, we sought to establish clinicopathological correlations for various dermatological conditions and systemic conditions with

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unusual presentation.

2. Materials and Methods

This retrospective observational study involved the acquisition of histopathological records from all patients who underwent skin biopsy between January 2022 and July 2023, following proper informed consent. Formalin-fixed skin biopsy samples were transferred from the dermatology department to the pathology department for processing, sectioning, and staining. Most samples were stained with hematoxylin and eosin, while additional stains such as Ziehl-Neelsen, Periodic Acid Schiff, and Fite-Faraco were used when necessary. The slides were reviewed by a pathologist. In cases of doubt, the slides were reviewed by the consulting dermatologist also. Clinical records were also reviewed to gather patient demographics, clinical features, and diagnostic differentials.

Patient data including age, sex, duration of disease, clinical diagnosis, histopathological findings, and final diagnosis were recorded in Microsoft Excel for subsequent statistical analysis. Diseases were categorized into various groups such as microbial, vascular, adnexal etc. Cases were further classified as concordant, partially concordant, or discordant based on agreement between clinical and histopathological findings. Concordant cases exhibited histopathological features consistent with the suspected diagnosis, while partial concordance involved partial alignment with clinical suspicions (e.g., different pole of leprosy, variant of eczema, cutaneous tuberculosis variants). Discordant cases indicated a completely different histopathological diagnosis. Cases with non-specific findings were labelled as inconclusive, prompting further investigations and timely referral was done. In instances of partial concordance or discordance, the final diagnosis relied on histopathological findings and further investigations when required.

2.1. Statistical analysis

Data was analysed using IBM SPSS version 20. Mean, range and percentages were calculated.

3. Results

Total of 336 biopsy reports were collected from January 2023 to July 2023.

Among the histopathological spectrum most diseases were microbial (33.93% n = 114/336), followed by non-infectious erythematous papular and squamous disease (18.75% n = 63/336), non-infectious vesiculobullous and vesicopustular disease (11.31% n = 38/336). The least common was inflammatory disease of subcutis (0.3% n = 1/336) and disorder associated with physical agent (0.3% n = 1/336) [Table 1].

Among microbial diseases, bacterial diseases (87.72% n = 100/114) were most prevalent out of which 94% cases were diagnosed with leprosy. The 7.02% (n=8/114) cases of viral infections comprised of verruca vulgaris (4.39% n = 5/114), verruca plana (1.75% n = 2/114) and epidermodysplasia verruciformis (0.88% n = 1/114). 2.63% cases (n=3/114) among microbial diseases had features suggestive of dermatophytosis and deep fungal infections each [Table 2].

Psoriasis (47.62% n = 30/63) was the most common diagnosis among non-infectious erythematous papular and squamous diseases. The next common diagnosis in this category was lichen planus and lichenoid dermatitis in (26.98% n = 17/63). Other conditions such as keloids, hypertrophic scar, prurigo, acne, porokeratosis only comprised few cases in this category.

Non-infectious vesicobullous and vesicopustular diseases comprised of 38 cases that included 20 cases of spongiotic dermatitis (52.63% n=20/38), 9 cases of pemphigus and subepidermal bullous diseases each (23.68% n = 9/26).

Morphea was the most common connective tissue disease (50% n=6/12), followed by 4 cases of lupus erythematosus (33.3%, n=4/12), 1 each of systemic sclerosis and dermatomyositis (8.3%).

Inflammatory diseases of cutaneous adnexae included lichen planopilaris (n=6/14, 42.85%), alopecia areata (28.7%, n=4/14) and one case each of hidradenitis suppurativa, sebaceous cyst, folliculitis and atrophoderma vermiculatum.

There was one case of erythema nodosum (0.3%, n = 1/336) classified as inflammatory disease of subcutaneous tissue.

Vascular diseases included small vessel vasculitis (47.8% ,n=11/23), neutrophilic dermatoses (34.7% , n=8/23), capillary hemangioma (8.69% , n=2/23) and lymph vessel disease (8.69%, n=2/23).

There were 23 cases diagnosed with neoplastic diseases out which there were 12 tumors of epidermis (52.1%, n=12/23), tumors of dermis (17.3%, n=4/23), pigmented benign lesions (2.1%, n= 5/23), 1 each of malignant melanoma and tumor of epidermal appendage (4.3%, n=1/23).

Depending on the clinicopathological agreement the cases were divided into concordant (75.59%, n=254/336) where findings were consistent with any of the differentials and partially concordant (10.12%, n=34/336) where only a few histologic features were characteristic of the disease or a different variant of the disease was suspected. [Figure 1] Diseases where pathologist's diagnosis was substantially different from the clinical differentials were labelled as discordant (6.25%, n=21/336). [Figure 2] There were 5.65% inconclusive (n=19/336) and 2.38% inadequate samples (n=8/336) [Table 3].

Table 1: Spectrum of skin diseases based on histopathology

Histopathological category	Number of cases (n)	Percentage (%)
Microbial	114	33.93%
Non-infectious erythematous papular and squamous disease	63	18.75%
Non-infectious vesicobullous and vesicopustular disease	38	11.31%
Vascular diseases	23	6.85%
Neoplastic	23	6.85%
Inconclusive	19	5.65%
Inflammatory diseases of cutaneous adnexae	14	4.17%
Connective tissue disorder	12	3.57%
Pigmentary diseases	7	2.08%
Metabolic disorders	6	1.79%
Genodermatoses	5	1.49%
Photosensitive disorders	4	1.19%
Neutrophillic dermatoses	3	0.89%
Non-infectious granuloma	3	0.89%
Inflammatory disease of the subcutis	1	0.30%
Disorder associated with physical agent	1	0.30%
Grand total	336	100.00%

Table 2: Microbial diseases of skin

Microbial diseases of skin		Number of cases (n)	Percentage (%)
	Leprosy	94	82.46%
Bacterial	Lupus vulgaris	4	3.51%
	Donovanosis	1	0.88%
	Ecthyma gangrenosum	1	0.88%
	Epidermodysplasia verruciformis	1	0.88%
Viral	Verruca vulgaris	5	4.39%
	Verruca plana	2	1.75%
Fungal	Dermatophytosis	3	2.63%
	Deep fungal infections	3	2.63%
Grand total		114	100.00%

Table 3: Clinicopathological agreement

Clinicopathological agreement	Number of cases (n)	Percentage (%)
Concordant	254	75.59%
Partial concordance	34	10.12%
Discordant	21	6.25%
Inconclusive	19	5.65%
Inadequate sample	8	2.38%
Grand total	336	100.00%

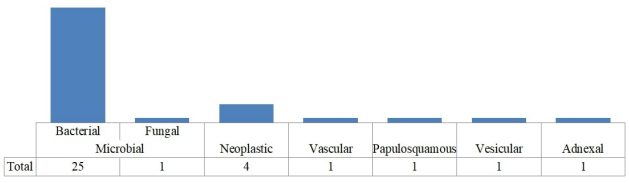

Figure 1: Distribution of partially concordant cases among various histopathological groups.

4. Discussion

Skin biopsy represents a critical tool in the arsenal of dermatologists, especially when confronted with atypical clinical presentations, altered clinical features due to treatment, or early-stage diseases lacking characteristic features. Our retrospective analysis, spanning nineteen months, aimed to delineate the spectrum of skin diseases encountered at our tertiary healthcare centre. However, it is important to note that our data may not fully reflect the epidemiological patterns, as biopsy was selectively performed, excluding cases with classical features, financial constraints, or patient reluctance towards invasive procedures.

The skin biopsies were divided into various categories and the most common category in our study was microbial. Microbial diseases with a predominance of Leprosy were

Table 4: Analysis of the spectrum of diseases encountered across different studies.

	Present study	Balasubramanian et al.[1]	Goswami et al.[2]	Adhikari et al.[3]	Chalise et al.[4]	Singh et al.[5]	Aslan et al.[6]	Albasri et al.[7]
Duration	19 months	3 years	3 years	3 years	6 months	1 year	9 years	11 years
Sample size	336	3006	610	1040	133	675	3949	1125
Microbial	114(33.93%)	Hansens – 454	151(28.4%)	NA	22(24.5%)	152(22.52%) Hansens – 110(16.29%)	206	NA
Papulosquamous	63(18.75%)	Lichenoid diseases – 286 Psoriasiform diseases – 274	89(16.8%)	269(25.9%)	21(23.4%)	Psoriasiform – 66(9.77%) Lichenoid – 61(9.03%)	NA	128(11.4%)
Vesiculobullous	38(11.31%)	204	177(33.3%)	297(28.6%)	42(46.6%)	56(8.29%)	157	28(2.5%)
Acquired vascular diseases	23(6.85%)	160	18(3.4%)	22(2.1%)	NA	33(4.88%)	202	19(1.6%)
Acquired connective tissue diseases	12(3.57%)	NA	19(3.6%)	25(2.4%)	5(5.5%)	28(4.14%)	370	32(2.8%)
Inflammatory diseases of adnexa	14(4.17%)	NA	NA	23(2.2%)	NA	31(4.59%)	73	334(29.6%)
Genodermatoses	6(1.79%)	NA	NA	11(1.1%)	NA	13(1.92%)	93	NA
Neoplastic	23(6.85%)	93	29(4.8%)	205(19.7%)	37(27.8%)	Benign – 43(6.37%) Malignant -38(5.62%)	Benign – 577 Malignant - 423	206(18.3%)
Clinicopathological concordance	254(75.59%)	1798 (59.8%)	NA	NA	NA	NA	76.8%	NA
Clinicopathological partial concordance	34(10.12%)	228 (7.6%)	NA	NA	NA	NA	NA	NA
Clinicopathological discordance	21(6.25%)	929 (30.9%)	NA	NA	NA	NA	23.2%	NA
Inconclusive	19(5.65%)	NA	50(8.1%)	NA	6(4.5%)	NA	NA	NA

Table 5: The clinicopathological correlation of various groups of disorders compared to other studies.

	Percentage of concordant histopathology	Other studies	Clinicopathological correlation
Hansens Disease	71.27%	Balasubramaninan et al.[1]	58.8%
		Bhatia et al.[8]	69%
		Moorthy et al.[9]	62.6%
		Rao et al.[10]	95%
Lichenoid disorders	94.11%	Balasubramanian et al.[1]	70.6%
		Aslan et al.[6]	94.6%
Psoriasiform disorders	93.33%	Balasubramanian et al.[1]	68.2%
		Aslan et al.[6]	94.6%
		Mehta et al.[11]	81%
Vesicobullous	91.30%	Balasubamanian et al.[1]	71.1%
		Aslan et al.[6]	94.6%
Vasculitic disorders	86.95%	Balasubramanian et al.[1]	56.3%
		Aslan et al.[6]	57.9%
		Khetan et al.[12]	77%
Neoplastic lesions	47.82%	Balasubramanian et al.[1]	52.7%
		Aslan et al.[6]	89.2%

Table 6: Few examples of cases exhibiting discordant clinicopathological correlation.

Patient details	History & Examination	Clinical Differentials	Histopathological diagnosis
24 yr/M	Solitary asymptomatic verrucous growth on lower lip of size 4*5 cm for 1 year. No history of smoking, tobacco chewing.	Tuberculosis verrucosa cutis	Squamous cell carcinoma
35yr/F	Asymptomatic hyperpigmented plaque over nose with areas of scarring for 1.5 year, gradually increasing.	Lupus Vulgaris	Basal cell Carcinoma
55 yr/M (Figure 4)	Solitary asymptomatic erythematous nodule over forehead for 7 months	Jessener's lymphocytic infiltrate	Lupus Vulgaris
6 yr/M (Figure 6)	Multiple dry hypopigmented macules with generalised xerosis over face.	Pityriasis alba	Borderline Tuberculoid leprosy
44 yr/M (Figure 7)	Multiple vesicles and pustules with few intervening papules over face on and off for 3 months, xerosis over body and no fever or sensory loss	Pemphigus foliaceous	Lepromatous leprosy
53 yr/M (Figure 5)	Solitary pedunculated nodular lesion over nape of neck for 10 months	Benign adnexal tumour/cyst	Leiomyoma
31 yr/M (Figure 8)	Multiple papules and few pustules over face not responding to anti-acne medicines with history of use of topical steroid containing creams.	Acne vulgaris	Tinea incognito

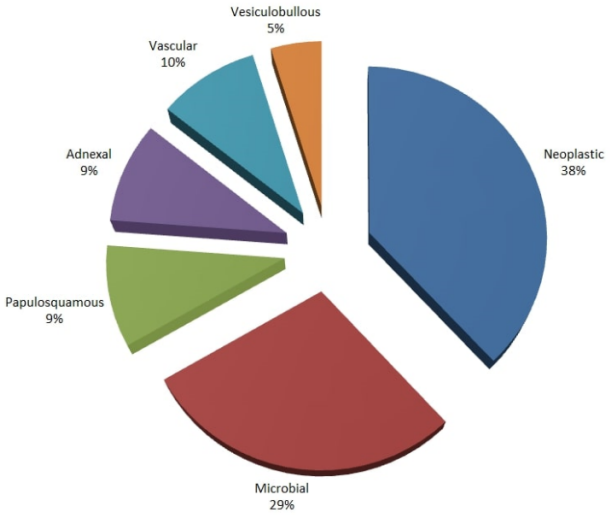

Figure 2: Distribution of discordant cases among various histopathological groups.

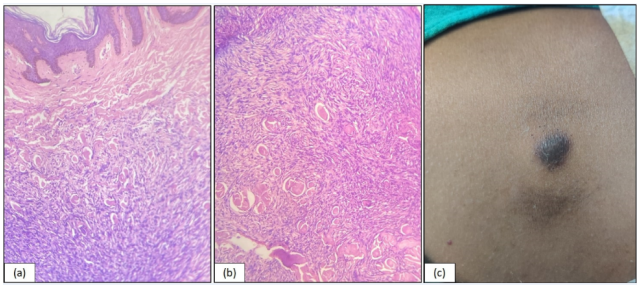

Figure 3: a: H&E: Clear subepidermal zone with spindle cells. (10X); **b:** H&E: Spindle cells with storiform to whorled pattern with abundant eosinophilic cytoplasm and variable mitotic activity suggestive of dermatofibrosarcoma. (40X); **c:** A solitary hyperpigmented nodule over upper back.

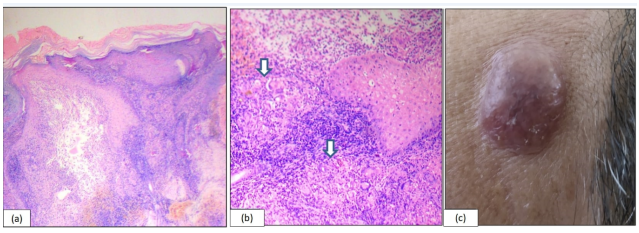

Figure 4: a: H&E: Focal hyperkeratosis and acanthosis. Dermis showing aggregates of chornic inflammatory infiltrate with numerous epithelioid cell granulomas. (4X); **b:** H&E: Epithelioid cell granuloma with Langhans type giant cells (black arrows) surrounded by chronic inflammatory infiltrate suggestive of lupus vulgaris. (10X); **c:** Solitary erythematous nodule present over forehead.

seen in other Indian studies by Singh A et al,[5] Goswami P et al[2] and Vishwanath et al[13] as well. The high number of leprosy cases in our study can also be attributed to the protocol of routine histopathology before administering multi drug therapy and at completion of treatment at our institute. Among non-infectious erythematous papular and squamous diseases, the second most common category, psoriasis and lichen planus were most prevalent. Similar findings were observed by Singh et al, Vishwanath et al and Adhikari et al.[3,5,13] Spongiotic dermatitis was the most common non infective vesiculo-bullous and vesicopustular disease seen in majority of studies including ours.[3–5,13]

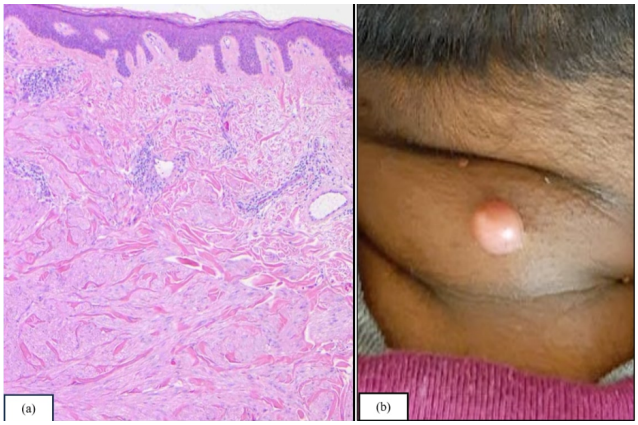

Figure 5: a: H&E: Proliferation of spindle cells arranged in interlacing and whorled pattern in the deep dermis showing blunt-ended cigar shaped nuclei with abundant eosinophilic cytoplasm without cytological atypia or mitotic activity suggestive of pilar leiomyoma. (4X); **b:** Solitary pedunculated pinkish nodule present over nape of neck.

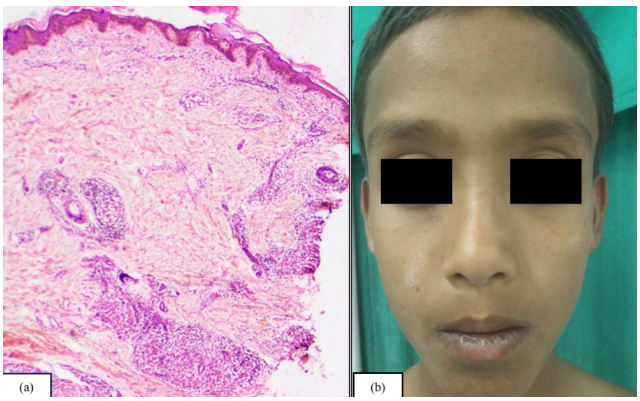

Figure 6: a: H&E: Epithelioid cell granuloma seen in deeper dermis with moderate lymphohistiocytic infiltration. Periappendageal and perivascular infiltrate suggestive of borderline tuberculoid leprosy. (4X); **b:** Hypopigmented dry plaques present over face.

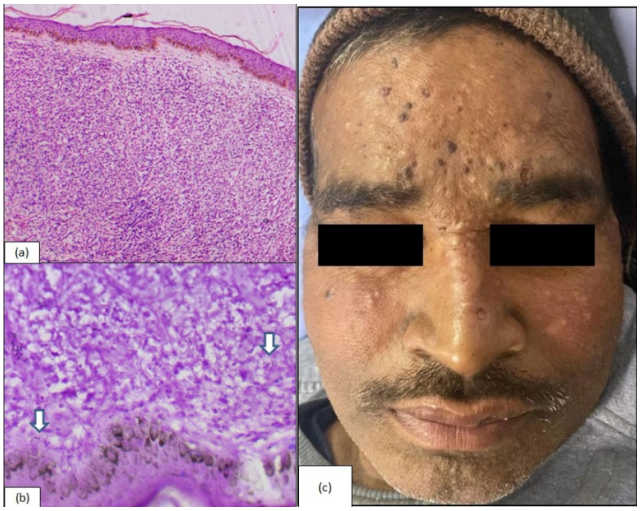

Figure 7: a: H&E: Subepidermal clear grenz zone seen with granulomas in dermis. (10X); **b:** Ziehl Neelsen staining: Acid fast bacilli seen in the dermis (black arrows) suggestive of lepromatous leprosy. (10X); **c:** Multiple crusted vesicles, papules and few nodules present over face.

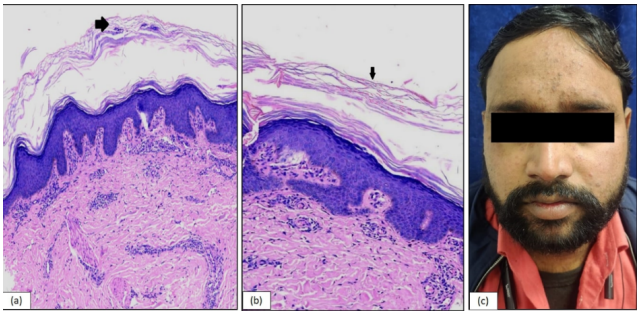

Figure 8: a: H&E: Parakeratosis, spongiosis and inflammatory infiltrate (black arrow) seen in the epidermis. (10X); **b:** PAS staining: Multiple fungal hyphae (black arrow) seen in stratum corneum suggestive of tinea infection. (10X); **c:** Multiple erythematous to hyperpigmented papules present discretely over face.

Neoplastic diseases constituted only 5.95% of all cases. Singh et al found 6.37% cases of benign skin tumors in their study.[14] This figure was lesser than other studies by Chalise et al (27.8%),[4] Adhikari et al (19.7%),[3] Achalkar et al (24%)[15] and Bansal et al (32.1%),[16] where non-neoplastic diseases were predominant similar to our study. Vishwanath et al[13] observed 6.3% of neoplastic conditions in their study but it was done on pediatric age group in contrast to other studies. On the other hand, neoplastic lesions were more common in studies by Bezbaurah et al,[17] Abubaker et al[18] Sushma et al[19] and Bhardwaj et al.[20] In our study, tumors of epidermis were most common similar to other studies. Some studies found basal cell carcinoma as the most common[2,3] while others found squamous cell carcinoma[21,22] the predominant neoplastic lesion. Melanoma was seen in only one case in our study similar to other studies from South Asian population due to lesser predisposition to develop cutaneous malignancies.[2,7] Table 4 summarizes the distribution of different disease categories and compares it with findings from other studies.

In our research, there was a clinicopathological correlation observed in 75.29% of cases, akin to the 76.8% reported in the study conducted by Aslan et al.[6] Balasubramanian et al[1], however, documented concordance in 59.8% of biopsies, a lower rate compared to our findings. It is worth noting that their study encompassed a notably larger sample size of 3006 cases, which may account for this variance. In our study, all cases suspected of connective

tissue disorders exhibited 100% concordance. Furthermore, high rates of concordance were evident in other common dermatoses like papulosquamous disorders (87.3%), vesiculobullous diseases (86.8%), vascular diseases (82.6%), and microbial diseases (71.05%). Table 5 presents the histopathological correlation among various disease categories, comparing them with findings from other studies. Partial concordance, defined as the presence of some features aligning with the suspected clinical diagnosis, was observed in 10.12% of cases in our study and in 7.6% in the study conducted by Balasubramanian et al.[1] Among partially concordant diseases, microbial diseases were predominant. Specifically, 22% (26 out of 114) of all microbial diseases exhibited partial concordance, with 25 cases attributed to bacterial infections. The majority of these cases involved variations in leprosy subtype diagnosis on histopathology or features consistent with reaction state. Three out of the total 23 neoplastic diseases demonstrated partial concordance. Two cases of acquired melanocytic nevi initially suspected as junctional and compound melanocytic nevi were later identified as compound and intradermal nevi, respectively. Furthermore, a middle aged male patient presenting with a solitary, asymptomatic nodule on their back was initially suspected to have dermatofibroma clinically. However, histopathological examination revealed neoplastic alterations, leading to the diagnosis of dermatofibrosarcoma. (Figure 3)

Among the cases analyzed, there were 6.54% (21 out of 336) cases where the histopathological diagnosis differed from clinical suspicion. Neoplastic conditions comprised the highest proportion with almost a third of cases lacked clinical suspicion initially. This observation could be attributed to the relatively low prevalence of cutaneous neoplasms in the Indian population, often resulting in a lack of suspicion by treating dermatologists.[23] We observed neoplastic changes in several immunocompetent young patients with no predisposing risk factors. In one instance, a young male presented at the outpatient department with a verrucous lesion on his lower lip, devoid of any predisposing risk factors. Initially, tuberculosis verrucosa cutis was suspected based on clinical history and examination. However, upon histopathological analysis, dysplastic changes were detected, prompting an immediate referral to the oncology department for radiotherapy. Another case involved a middle-aged female displaying a slowly growing hyperpigmented to erythematous plaque with areas of scarring. Although lupus vulgaris was initially suspected due to the lesion's prolonged duration and scarring, biopsy results revealed basaloid cells, indicating basal cell carcinoma.

A man presented with an erythematous nodular lesion on the forehead. Histopathology revealed epithelioid cell granuloma. On further investigation montoux was positive and a diagnosis of lupus vulgaris was made. The patient responded gradually to antitubercular medication (Figure 4). Additionally, another middle-aged man presented with solitary erythematous nodular pedunculated lesion on the nape of the neck, which was suspected to be a benign adxenal tumour. It was excised and on biopsy showed features suggestive of pilar leiomyoma (Figure 5). Biopsy helped in early diagnosis and prompt management of such cases, thereby preventing complications. All the discordant microbial cases were attributed to leprosy, where patients presenting with long-standing ulcers, nodules, and vesicobullous lesions lacking sensory or motor nerve involvement were diagnosed with leprosy upon histopathology, along with the presence of acid-fast bacilli. A 6-year-old boy exhibited dry, hypopigmented, poorly defined patches on his face. Despite extended treatment for pityriasis alba, the patient showed no improvement. Consequently, a biopsy was performed, revealing borderline tubercular leprosy. (Figure 6) In another instance, a middle-aged man with vesiculopustular lesions on his face was diagnosed with leprosy upon histopathological examination. Remarkably, the patient displayed no neurological symptoms or hypopigmented, hypoesthetic patches. (Figure 7) This underscores the endemic nature of leprosy in our region and highlights the necessity of considering it as a potential differential diagnosis even in cases lacking classical symptoms so that treatment can be begun as early as possible. Few examples of cases with clinicopathological discordance have been described in Table 6.

This atypical clinical presentation in many cases could be attributed to the low socioeconomic status of most patients at our institute, who typically seek medical attention only after lesions fail to resolve following prolonged self-medication or treatment from non-specialist doctors. The widespread use of over-the-counter multiple combination creams often contributes to drastic changes in the morphology of lesions, further complicating clinical diagnosis. A young male presented with acneiform lesions on face with a history of application of multiple steroid containing creams. There were no lesions elsewhere on the body and upon no response to anti-acne medication, the lesions were biopsied. On histopathology dermatophytes were seen establishing a diagnosis of tinea incognito. (Figure 8) Steroid-modified dermatophytosis differs significantly from its clinical presentation and can be mistaken for other conditions, potentially exacerbating without proper antifungal treatment.

In 5.65% of cases, the diagnosis remained inconclusive, primarily due to features such as non-specific inflammatory infiltrate observed upon histopathological examination. In 2.48% of cases, the biopsy samples were deemed inadequate for definitive diagnosis. These patients underwent further evaluation and were subsequently subjected to another biopsy. The slides from these cases were reviewed

once more in the presence of both the pathologist and the consulting dermatologist to ensure a comprehensive assessment and reach a conclusive diagnosis. In one such case an 8 year old boy presented with unilateral swelling of face and clinically mucormycosis was suspected. Histopathology was inconclusive revealing non-specific chronic infiltrate. Patient was subjected to further workup. On Fine Needle Aspiration Cytology small round cells with high nucleocytoplasmic ratio and nuclear polymorphism was observed. On MRI neoplastic etiology of mediastinum with metastasis to face was revealed. The child was referred to oncology department immediately for further management. Such cases are eye opening and further highlight the importance of a multimodal approach in difficult scenarios.

Skin biopsy serves as a valuable diagnostic tool, capable of uncovering information that may remain concealed during clinical examination alone. Previous studies conducted at our institute have demonstrated its utility in diagnosing complex cases, such as cutaneous metastasis presenting in a zosteriform pattern from a melanoma[24] and adenocarcinoma masquerading as eruptive xanthomas.[25] In our current study, skin biopsy significantly contributed to the diagnosis of neoplastic conditions. Without the aid of histopathological analysis, achieving an accurate diagnosis would have been considerably challenging.

5. Conclusion

Skin biopsy emerges as an indispensable tool in the diagnostic armamentarium of dermatology, facilitating the identification of underlying pathologies that may not be apparent through clinical assessment alone. This study underscores the synergy between dermatology and pathology in enabling precise diagnosis and treatment.

6. Source of Funding

None.

7. Conflict of Interest

None.

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