Section: Pathology

Original Research Article

SPECTRUM OF UNUSUAL SKIN DISEASES: OUR EXPERIENCE

Divya Pathak[1], Rani Bansal[2], Dishant Kumar Malik[3]

[1] Junior Resident, Department of Pathology, Subharti Medical College and Hospital, Meerut, Uttar Pradhesh, India.
Professor, Department of Pathology, Subharti Medical College and Hospital, Meerut, Uttar Pradesh, India.
Assistant Professor, Department of Pathology, Subharti Medical College and Hospital, Meerut, Uttar Pradesh, India.

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Corresponding Author:
Dr. Divya Pathak,
Junior Resident, Department of Pathology, Subharti Medical College and Hospital, Meerut, Uttar Pradhesh, India.
Email: pathakdev29@gmail.com

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ABSTRACT

Background: The global burden of cutaneous disease continues to rise, yet the epidemiology of rare or histologically unusual dermatoses remains poorly characterised, particularly in South-Asian referral centres. Precise histopathological categorisation is indispensable for optimal patient management, but overlap with common mimics and limited tissue in small biopsies frequently hamper diagnosis.

Materials and Methods: We undertook a descriptive, cross-sectional study of all skin biopsies accessioned between January 2022 and August 2024 (n = 117). Formalin-fixed paraffin-embedded tissue was processed routinely; haematoxylin–eosin (H&E) sections were examined by two senior Pathologists. Special stains (Alcian blue, Perl's Prussian blue, Ziehl–Neelsen, Fite–Faraco) and immunohistochemistry (CD3, CD4, CD8, CD20) were applied when indicated. Lesions were categorised as "usual" (commonly encountered inflammatory, infectious, autoimmune or tumour-like processes) or "unusual" (rare entities, atypical variants or diagnostically challenging lesions). Clinicopathological concordance was assessed for all uncommon cases.

Results: Of 117 biopsies, 102 (87.2 %) were usual and 15 (12.8 %) were unusual. Leprosy (22/117, 18.8 %) was the single most frequent diagnosis. The uncommon cohort comprised: pseudopelade of Brocq (2), scleroderma of Buschke (1), Majocchi pigmented purpura (1), inverse psoriasis (1), Stevens–Johnson syndrome (1), PLEVA (1), Hailey–Hailey disease (1), Darier's disease with basal-cell downgrowth (1), poikiloderma of Civatte (1), nevus comedonicus (1), pigmented eccrine poroma (1), mycosis fungoides (1) and lupus miliaris disseminatus faciei (LMDF; 1). Clinicopathological concordance was complete in 8/15 (53 %) cases; two required clinico-histological re-review to reach the final diagnosis. Ancillary tests were decisive in 5/15 (33 %): Alcian blue confirmed dermal mucin in Buschke scleroderma, Perl's stain disclosed dermal haemosiderosis in pigmented purpura, and negative acid-fast stains together with perifollicular granulomas supported LMDF. Mycosis fungoides expressed CD3/CD4 and lacked CD8 or B-cell markers.

Conclusion: Unusual dermatoses constituted 12.8 % of cutaneous biopsies in our centre. Their accurate recognition requires meticulous correlation of history, morphology, special stains and, when necessary, immunohistochemistry. Early multidisciplinary dialogue remains pivotal to avoid missed or delayed diagnoses.

Keywords: Unusual skin disease; dermatopathology; clinicopathological correlation; histopathology; special stains; India.

INTRODUCTION

Skin and subcutaneous disorders collectively account for a major share of non fatal disease worldwide and rank among the leading causes of years lived with disability.[1] Recent iterations of the Global Burden of Disease study demonstrate a sustained rise in incident cutaneous conditions, with the highest absolute

numbers recorded in South Asia and male predominance across most diagnostic groups.[2] While common dermatoses such as eczema, psoriasis and superficial infections dominate outpatient visits, a substantial subset of patients present with uncommon entities or histological variants that confound clinicians and pathologists alike.[3,4]

Rarity in dermatology is a fluid concept. At one end of the spectrum lie bona fide orphan diseases such as Hailey–Hailey or Darier's disease, whose prevalence is estimated at <1 : 50 000.[5] At the other end, "unusual" may simply denote an atypical anatomical site (inverse psoriasis), an infrequent clinicopathological pattern (pseudopelade of Brocq), or a masquerading neoplastic process (mycosis fungoides mimicking chronic dermatitis).[6,7] Regardless of definition, such cases often traverse multiple specialties, incur diagnostic delay and carry significant psychosocial burden.

Histopathological examination remains the cornerstone for definitive diagnosis, yet even high quality biopsies may yield equivocal findings. Sampling error, partial lesional regression and overlapping reaction patterns blur classical criteria. Consequently, supplementary techniques—including alcian blue for mucinoses, Perl's for pigment disorders, and targeted immunohistochemistry—assume critical importance.[8] Correlation with detailed clinical information and iterative clinicopathological dialogue is essential to synthesise disparate clues into a final answer.

Although several single entity case series exist, systematic data addressing the spectrum and frequency of unusual skin diseases within a single centre are scarce, particularly from resource constrained settings. Such information is indispensable for laboratory planning, resident education and formulation of diagnostic algorithms tailored to local epidemiology.

Against this backdrop we conducted a two and a half year review of all skin biopsies received in a tertiary care teaching hospital in northern India. We quantified the proportion of diagnoses falling into an "unusual" category, delineated their clinicopathological characteristics, scrutinised the value of ancillary tests, and evaluated concordance with pre biopsy clinical impressions. By sharing our experience we aim to enrich the collective understanding of these diagnostic outliers and to highlight pragmatic strategies that enhance their recognition in routine practice.

MATERIALS AND METHODS

Study design and setting. This was a retrospective, descriptive study carried out in a 1200-bed tertiary referral centre covering both urban and rural populations.

Study period and sample. All skin biopsy specimens processed between 1 January 2022 and 31 August 2024 were eligible. Exclusion criteria comprised (i) transected or severely crushed tissue precluding interpretation and (ii) biopsies lacking clinical details.

Histopathological work-up

- Routine processing of 4-µm FFPE sections stained with H&E.
- Dual independent light-microscopic evaluation by two senior Pathologists.
- Special stains applied when dictated by morphology: Alcian-blue pH 2.5 for dermal mucin, Perl's Prussian blue for iron deposition, Ziehl–Neelsen and Fite–Faraco for acid-fast bacilli, Masson-Fontana for melanin.
- Immunohistochemistry (Ventana Benchmark®) for lymphoid markers (CD3, CD4, CD8, CD20) in suspected cutaneous lymphoma.

Data extraction. Demographics, anatomic site, clinical differential diagnosis, histological diagnosis, ancillary test results and final clinicopathological correlation were recorded in a pre-formatted spreadsheet.

Diagnostic categorisation. "Usual" = common inflammatory dermatoses, infectious lesions, autoimmune bullous diseases and benign adnexal tumours. "Unusual" = rare entities, atypical variants of common diseases, neoplasms masquerading as inflammatory lesions, or cases posing significant diagnostic challenge.

Statistical analysis. Descriptive statistics were generated using SPSS v25.0 (IBM Corp.). Categorical variables are expressed as frequencies and percentages; continuous data as mean ± SD. The study was exploratory; no inferential statistics were applied.

Ethical considerations. The project was approved by the Institutional Ethics Committee (IEC/SMC/2021/417). All procedures conformed to the principles of the Declaration of Helsinki. As anonymised archival tissue was used, informed consent was waived.

RESULTS

Table 1: Overall Distribution of Skin Biopsy Diagnoses (N = 117)

Category	Cases (n)	%
Infectious (Leprosy, Lupus vulgaris, viral)	28	23.9
Inflammatory/hypersensitivity	24	20.5
Autoimmune / genetic (psoriasis, pemphigus, morphea)	21	17.9
Tumour / tumour-like	29	24.8
Others (pigmentary, vascular, mixed)	49	41.9 †
Unusual lesions	15	12.8

†Overlaps exist; totals >100 % as multiple patterns occasionally co-existed.

Table 2: Spectrum and Frequency of Unusual Skin Diseases

Unusual diagnosis	Cases (n)	Ancillary test(s)
Pseudopelade of Brocq	2	–
Scleroderma of Buschke	1	Alcian blue +
Majocchi pigmented purpura	1	Perl's +
Inverse psoriasis	1	–
Stevens–Johnson syndrome	1	–
PLEVA	1	–
Hailey–Hailey disease	1	–
Darier's disease (basal-cell downgrowth)	1	–
Poikiloderma of Civatte	1	–
Nevus comedonicus	1	–
Pigmented eccrine poroma	1	PAS +
Mycosis fungoides	1	CD3/CD4 +
Lupus miliaris disseminatus faciei	1	ZN– / Fite–

Table 3: Clinicopathological Correlation in Unusual Cases (N = 15)

Outcome	Cases (n)	Examples
Complete concordance	8	Pseudopelade, LMDF, Darier's
Partial concordance (1 of ≥2 differentials)	5	Buschke scleroderma, MF
Discordant – diagnosis revised after review	2	SJS, Hailey–Hailey

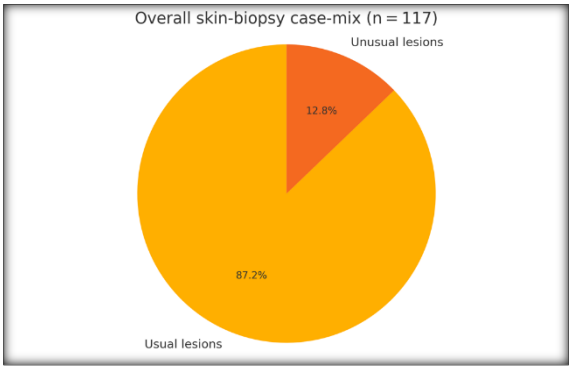

Figure 1: Pie chart of overall case mix

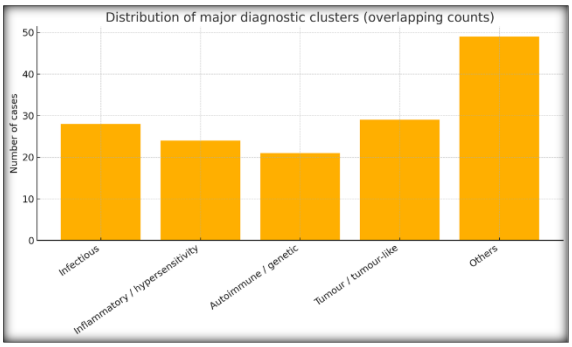

Figure 2: Bar chart of the five major diagnostic clusters

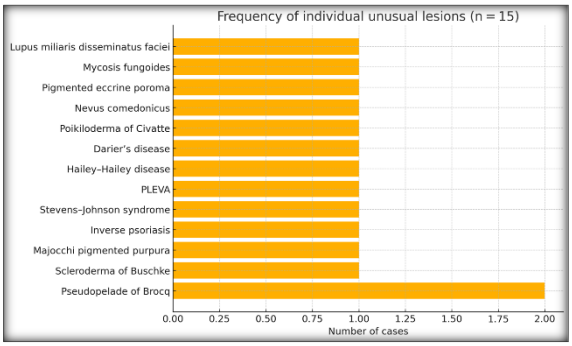

Figure 3: Horizontal bar chart of every unusual entity

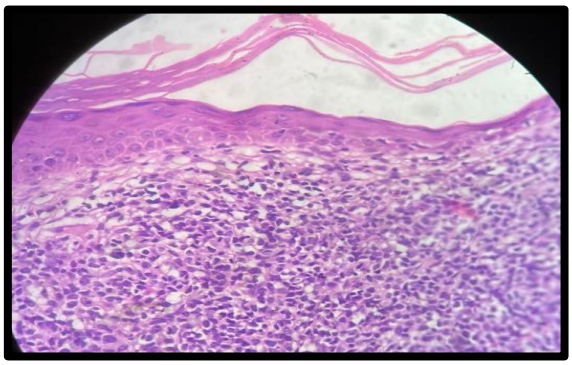

Figure 4A: H&E section Mycosis Fungoides (10x) view

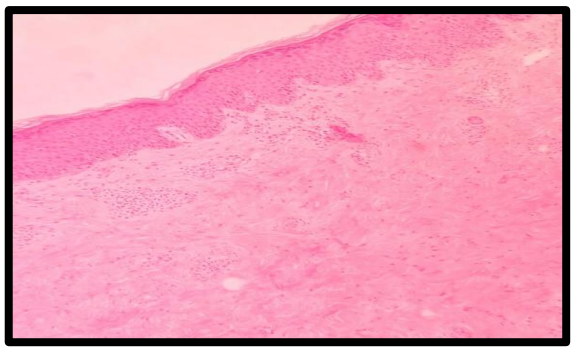

Figure 4B: &E section Scleroderma of Buschke (10x) view

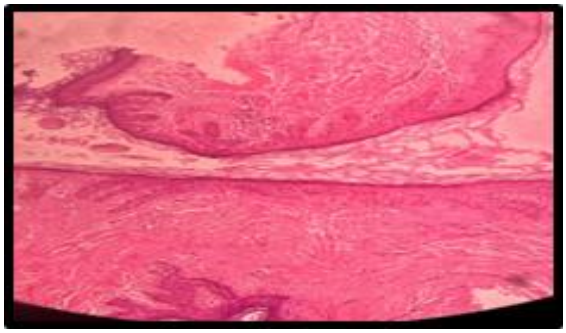

Figure 4C: H&E section Nevus Comedonicus (10x) view

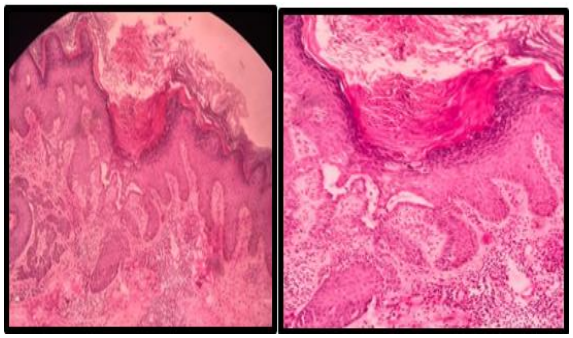

Figure 5: A&B-H&E sections of DARRIER'S DISEASE (10x) view

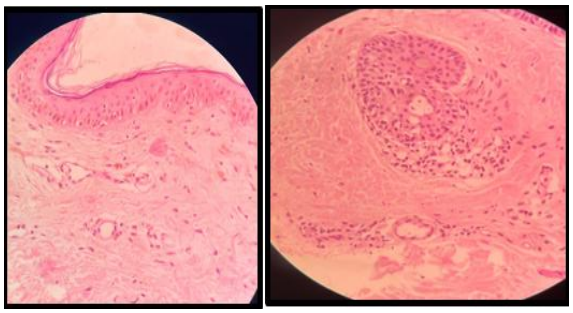

Figure 5: C&D- H&E section of POIKILODERMA OF CIVATTE (10 x) view

DISCUSSION

In the present series unusual dermatoses accounted for 12.8 % of cutaneous biopsies, a proportion comparable to 10–15 % reported from other Asian referral centres.[9,10] The heterogeneity of these entities underscores dermatopathology's dependence on meticulous pattern recognition augmented by clinicopathological dialogue.[11]

Diagnostic yield of ancillary techniques. One third of unusual cases required special stains or IHC for definitive diagnosis, mirroring observations by Weedon et al., who documented ancillary utility in 28 % of atypical biopsies.[12] Alcian blue positivity in Buschke scleroderma, although not pathognomonic, directed attention to mucinosis and away from morphea like processes. Likewise, demonstration of hemosiderin in pigmented purpura steered interpretation toward a vascular pathogenesis. The negative acid fast stains in LMDF, coupled with perifollicular location, permitted confident exclusion of paucibacillary cutaneous tuberculosis, concurring with recent consensus criteria.[13]

Clinicopathological discordance. Two lesions (Stevens–Johnson syndrome and Hailey–Hailey disease) were initially mis labelled clinically, emphasising that gross morphology may be misleading once partial treatment modifies lesions.[14] Prompt re evaluation in a multidisciplinary team averted potential therapeutic error. Similar scenarios have been highlighted in Western cohorts, where up to 20 % of inflammatory dermatoses are reclassified after histology.[15]

Epidemiological insights. The male predominance and scalp/flexural predilection observed among unusual cases parallel regional demography and clothing habits that encourage late presentation.[2] Our single case of mycosis fungoides adds to the limited Indian data on cutaneous T cell lymphomas, whose reported incidence is <0.1 / 100 000.[17-16] CD4 predominant phenotype aligned with global patterns and prognostic algorithms such as the revised ISCL/EORTC staging.[17-18]

Limitations. The retrospective design precluded uniform application of molecular studies (e.g., TCR γ clonality assays). Second, the modest sample size restricts extrapolation of prevalence estimates. Finally, follow up data to validate clinical outcome were unavailable in several cases referred from distant districts.[18-19]

Implications for practice. Despite limitations, our findings reinforce three pragmatic points: (i) bread and butter diagnoses dominate workload, but a not insignificant minority of unusual lesions necessitate heightened vigilance; (ii) judicious use of a limited ancillary test repertoire markedly enhances diagnostic certainty; and (iii) structured clinicopathological conferences remain invaluable, reducing discordance and facilitating evidence based management.[20]

Future prospective studies incorporating dermoscopy, direct immunofluorescence and molecular profiling are warranted to refine diagnostic algorithms for rare cutaneous disorders in resource limited environments.

CONCLUSION

Unusual dermatoses constituted nearly one eighth of cutaneous biopsies in our tertiary centre. Although numerically small, their diagnostic complexity demands a systematic approach integrating detailed clinical data, meticulous histomorphology and targeted ancillary techniques. Over half matched the clinician's initial impression, yet multidisciplinary discussion and special stains proved decisive in one third, underscoring the collaborative nature of dermatological diagnosis. Strengthening clinicopathological interfaces and ensuring access to basic ancillary tests can substantially improve accuracy, expedite therapy, and ultimately reduce the morbidity associated with these enigmatic skin diseases.

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