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Utility of skin biopsy in patients with systemic lupus erythematosus

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INTRODUCTION

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that can affect multiple organs, commonly the skin in 70%–85% of patients.[1] Cutaneous lupus is associated with the common typical histological finding of perivascular lymphocytic infiltration and interface dermatitis.[2] While suggestive, these findings are non-specific and require clinicopathological correlation, which may be challenging in clinically ambiguous cases. Patients with SLE who present with a rash are often diagnosed clinically without a biopsy in the context of classic appearance of clinical features together with systemic symptoms and suggestive serologies. Therefore, data on the importance of skin biopsy in confirming or refuting the clinical diagnosis in this population have been limited. There exists one small descriptive study of 20 patients showing that skin biopsies are useful for evaluation of cutaneous manifestations of rheumatological disease.[3]

The objective of this study is to determine how frequently skin biopsy results were concordant/discordant with clinical diagnosis in patients with SLE.

METHODS

This study was approved by the Institutional Review Board of the Ohio State University (#2023E0927). Connective tissue disease patients seen by rheumatology who had a skin biopsy between 2015 and 2022 were identified via a database search provided by research informatics at a single institution. Of these, 56 patients had a clinical diagnosis or prior history of SLE confirmed by rheumatology with an ICD 10 code of M32; these were selected for retrospective chart review. Of note, some patients had skin changes representative of SLE, whereas others simply had a previous medical history of SLE but were evaluated for skin changes that are not necessarily representative of lupus (eg, melanocytic nevi, urticarial vasculitis, etc). Medical records were reviewed individually, and descriptive statistics on demographics, clinical diagnosis and histopathologic findings of skin biopsy were recorded. Concordance was defined as the histopathologic result matching the diagnosis that was rendered clinically. Discordance was defined as the histopathologic result differing from the clinical diagnosis.

Patient and public involvement: patients or the public were not involved in the design, or conduct, or reporting or dissemination plans of our research.

RESULTS

Of 56 patients in this study, 72.9% showed concordance between clinical and histopathologic diagnosis, and 27.1% showed discordance between clinical and histopathological diagnosis (table 1). In five cases of discordance, histopathology showed findings consistent with psoriasis vulgaris. Similarly, four discordance cases showed spongiotic/nummular dermatitis. The most common clinical subtype of cutaneous lupus among concordance cases was subacute cutaneous lupus erythematosus, and this was found in 18 patients.

DISCUSSION

Skin biopsies are infrequently performed in the evaluation of a rash in patients with SLE. Our results show that in the cases where skin biopsy is performed, results were mostly consistent with clinical diagnosis, but 27.1% of cases were not. Subacute cutaneous lupus was the most frequently recorded subtype, possibly owing to the commonly recognised papulosquamous appearance that can appear similar to psoriasis. Biopsies performed with the clinical impression of subacute cutaneous lupus commonly showed psoriatic and lichenoid findings in addition to interface dermatitis. Non-specific skin manifestations are also seen in patients with SLE, including non-scarring alopecia, urticarial vasculitis,

Table 1 Clinicopathologic concordance and histopathologic diagnoses in 56 patients who were either clinically diagnosed with systemic lupus erythematosus or have a prior history of systemic lupus erythematosus who underwent skin biopsy for new skin changes

Concordance between clinical diagnosis and biopsy results	Number of patients (percentage of total)	Histopathologic diagnosis	Number of patients (percentage of subset)
Concordant	43 (76.7%)	Subacute cutaneous lupus erythematosus	18 (41.9%)
		Urticarial vasculitis	6 (14.0%)
		Discoid lupus	4 (9.3%)
		Melanocytic nevus	3 (7.0%)
		Contact dermatitis	2 (4.7%)
		Drug eruption	2 (4.7%)
		Calcinosis cutis	1 (2.3%)
		Haemangioma	1 (2.3%)
		Livedoid vasculopathy	1 (2.3%)
		Basal cell carcinoma	1 (2.3%)
		Dermatofibroma	1 (2.3%)
		Molluscum contagiosum	1 (2.3%)
		Pyoderma gangrenosum	1 (2.3%)
		Lichenoid keratosis	1 (2.3%)
Discordant	13 (27.1%)	Psoriasiform changes	5 (38.5%)
		Spongiotic/nummular dermatitis	4 (30.8%)
		Folliculitis	1 (7.7%)
		Fungal dermatitis	1 (7.7%)
		Verrucal keratosis	1 (7.7%)
		Hypertrophic lichen planus	1 (7.7%)

livedo reticularis and calcinosis.[1] These conditions are not frequently biopsied except for urticarial vasculitis as seen in our cohort.

Skin manifestations of SLE can vary widely and may mimic other conditions. For cases that had discordant clinical and histopathological impressions, clinicians were more likely to make a clinical diagnosis of lupus, and histopathology was more likely to support a different inflammatory skin condition such as psoriasis or spongiotic/nummular dermatitis. This could suggest a framing bias in which inflammatory rashes in patients with SLE are assumed to be cutaneous lupus and may explain why biopsies are infrequently performed in this population.

The major limitations of this study include the retrospective design and the small sample size from a single institution. The study is subjected to selection bias as the cases sent for biopsy are more likely to be clinically ambiguous cases. Another key limitation is the incomplete documentation both within each individual medical record and in the database provided by the institution's research informatics. It is unclear how frequently skin biopsies are used in the assessment of rashes in patients with SLE. Some of the biopsies done in this study were performed for the evaluation of melanocytic lesions and cutaneous carcinomas in patients that happened to have a history of SLE.

It is important to consider the logistics of performing skin biopsies in the context of rheumatological disease. Rheumatologists are not typically trained to perform skin biopsies, nor do they have the training to accurately assess the skin clinically or provide adequate differential diagnosis to inform evaluation by dermatopathology. Referrals to dermatologists are necessary but can lead to a delay as it may take several months to be seen due to the long wait time of dermatology clinics. It may take several weeks for histopathological results to be sent to a dermatologist and subsequently back to the rheumatologist. The extensive periods of time waiting for dermatology referrals and skin biopsy results could be deleterious. A potential solution involves partnering with dermatologists specialised in autoimmune connective tissue diseases with expedited referrals for these patients. The partnering of rheumatologists and dermatologists in combined clinics could be further increased to address the needs of patients with SLE with concerning skin changes.

CONCLUSION

Skin biopsy is a minimally invasive procedure that can add valuable data to help with accurate diagnosis in some patients with SLE who develop rashes. An important next step for individual clinicians is to determine what specific

clinical scenarios would warrant a biopsy; we suggest biopsies for cases in which the clinical appearance of a rash is ambiguous. It is worth performing a biopsy of clinically ambiguous rashes in patients with SLE as a significant percentage may show discordant results between clinical and histopathological diagnosis, which may impact subsequent treatment choices. This data further support the importance of the involvement of dermatologists in the care of patients with SLE with cutaneous abnormalities.

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