Case Report

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Epidermodysplasia verruciformis arising in a female with systemic lupus erythematosus: a rare case from Syria

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Introduction and importance: Epidermodysplasia verruciformis is a rare autosomal recessive genodermatosis. Clinical manifestations might be helpful in the diagnosis of this disease. However, the final diagnosis is made after a genetic and histological study. Acquired epidermodysplasia verruciformis is a form of epidermodysplasia verruciformis described in patients with compromised cell-mediated immunity.

Case presentation: A 42-year-old female with a history of a pain and itch on the soles and palms started a year ago. There were multiple flat papules on the dorsal hands, scarring alopecia, malar rash, oral ulcers, Raynaud phenomenon, and palpable purpura. A histological examination confirmed the diagnosis of epidermodysplasia verruciformis.

Clinical discussion: Epidermodysplasia verruciformis is an uncommon disease that affects the immune system. The coexistence of systemic lupus erythematosus and epidermodysplasia verruciformis is rarely reported in the medical literature. This paper reports a rare case in which these two diseases have coexisted.

Conclusion: This publication aims to document this rare case and highlight the ideal criteria in diagnosing and treating epidermodysplasia verruciformis.

Keywords: antinuclear antibody, case report, epidermodysplasia verruciformis, human papillomavirus, systemic lupus erythematosus

Introduction

Epidermodysplasia verruciformis (EV) is a rare, lifelong, genodermatosis condition that impairs the immune system. It is associated with an increased susceptibility to human papillomavirus (HPV) infection[1–6], and immunocompromised people may experience similar cutaneous changes[1]. HPV 5 and 8, referred to as "EV-associated" HPV types, are the most common types that lead to EV[4].

The type of inheritance in EV is autosomal recessive[1–4]. In ~75% of cases, EV involves two inactivating mutations in the EVER1 and EVER2 genes[1,2,4,6]. It is characterized by childhood-onset flat achromic, red or brownish skin lesions, pityriasis versicolor-like macules, and seborrhoeic keratosis-like plaques that mostly appear on areas that are exposed to the sun, like the face, neck, trunk, and limbs[2,3,5]. These lesions progress to cutaneous malignancies in 30–60% of patients[2–5]. EV-like syndrome has been recently described in patients who have compromised cell-mediated immunity, and the term "acquired EV" (AEV) has been established. AEV has been described secondarily in immunocompromised states, including patients who have immunodeficiency virus (HIV), organ transplantation[1,2,6], lepromatous leprosy, systemic lupus erythematosus (SLE), Hodgkin's disease, warts, immunoglobulin M deficiency, adult T cell leukaemia, lymphedema, and in the context of graft-versus-host disease[2]. The association of SLE and EV is a very rare condition[5]. We report a new case of SLE followed by EV in a 42-year-old patient and provide its brief documentation. This case has been reported in line with the SCARE criteria[7].

HIGHLIGHTS

- The coexistence of systemic lupus erythematosus and epidermodysplasia verruciformis is a rare condition.
- The diagnosis of epidermodysplasia verruciformis is made after a histological study.
- Further research is needed to figure out the ideal treatment regimen for epidermodysplasia verruciformis.

Case presentation

A 42-year-old female was admitted to the Department of Dermatology complaining of a severe pain and itch on the soles and palms. The pain started a year ago and gradually increased. A medical history of eczema treatment for 1 year without improvement and a history of smoking were reported. Familial

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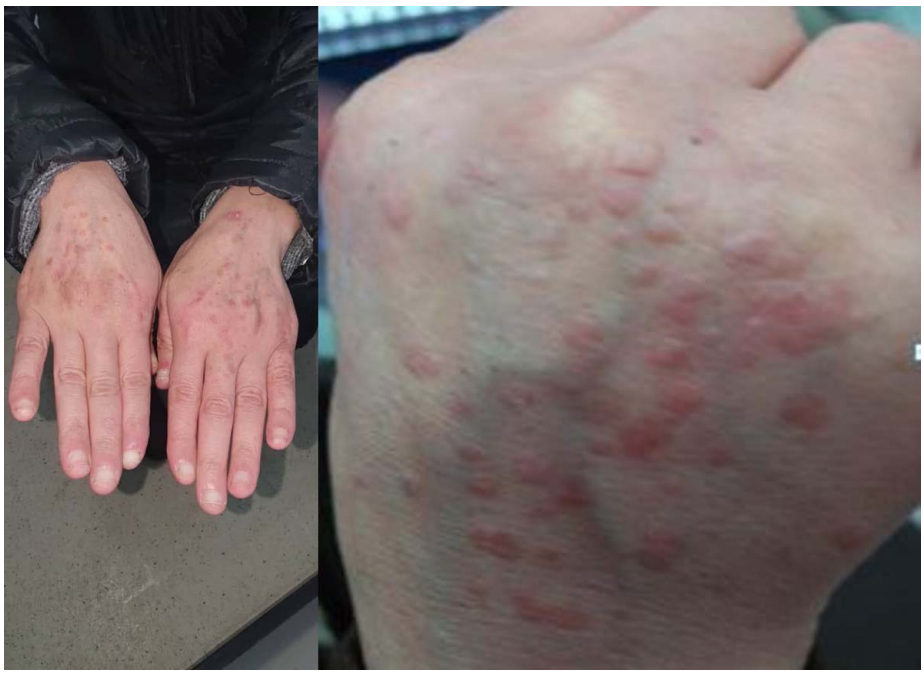

Figure 1. Multiple flat papules about 8–15 mm on the dorsal hands.

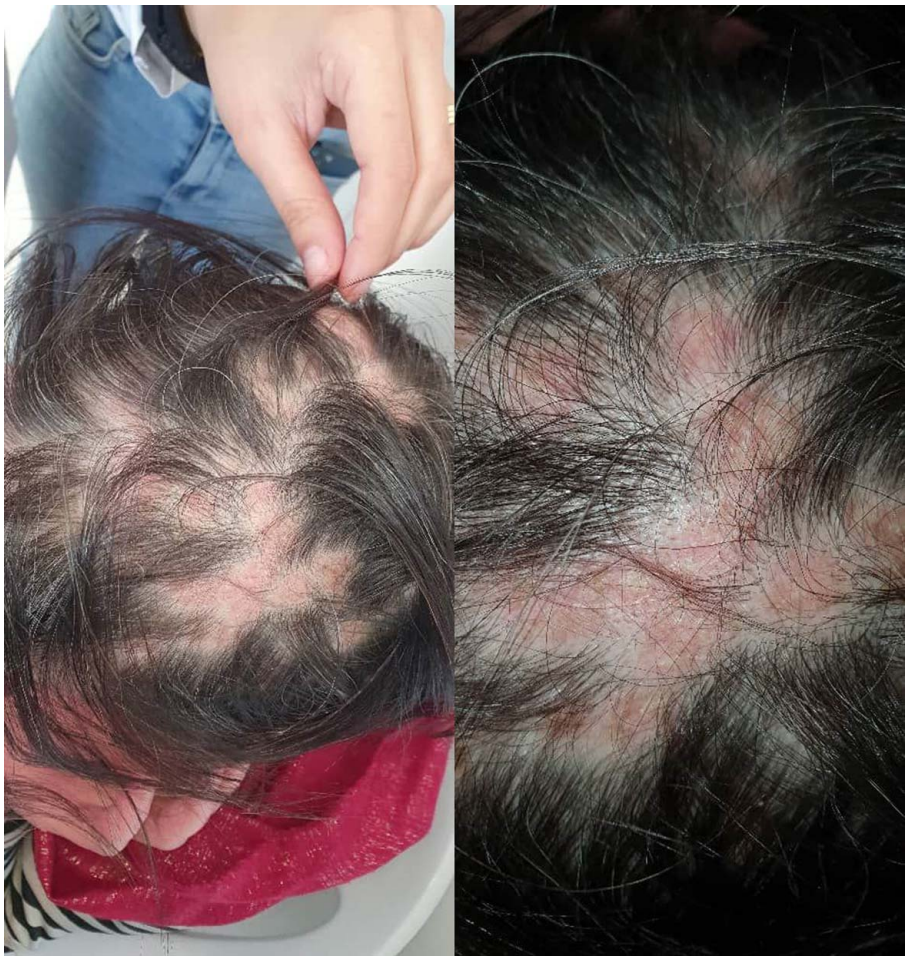

Figure 2. Discoid rash, disc-shaped erythematous lesions, depressed scarring.

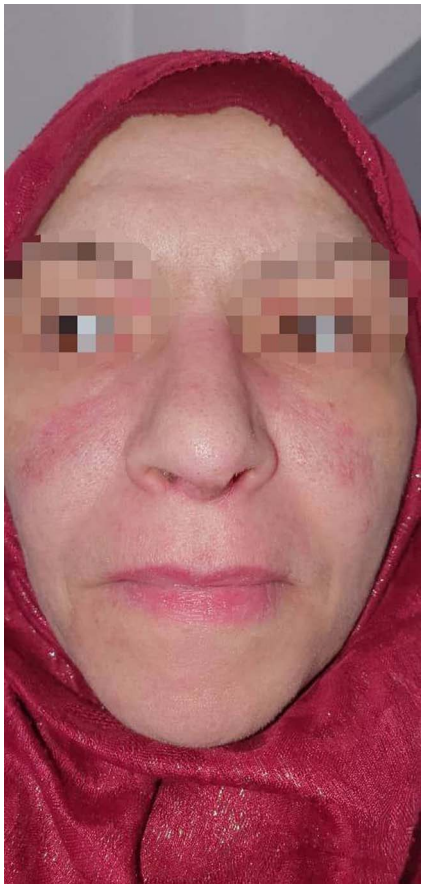

Figure 3. Malar rash, erythematous rash over the cheeks and nasal bridge spares the nasolabial folds.

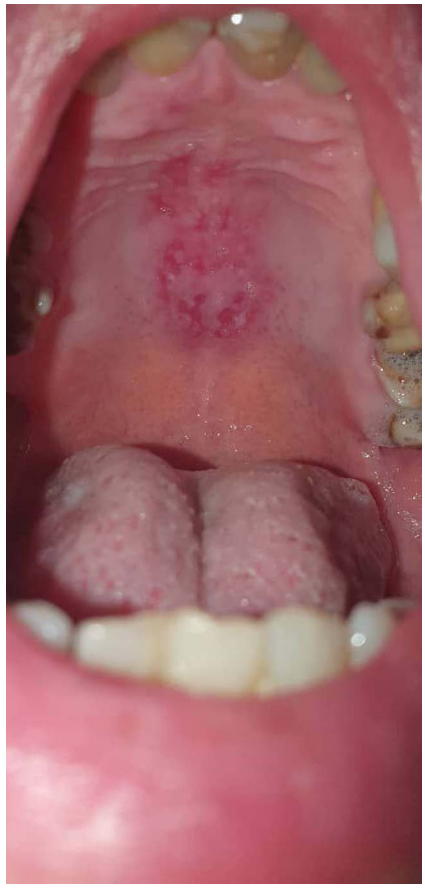

Figure 4. Palatal ulcers, erythematous discoid lesions.

history was unremarkable. Clinical examination showed multiple flat papules measuring about 8–15 mm on the dorsal hands (Fig. 1), and scarring alopecia on the scalp started 9 years ago (Fig. 2). Other clinical findings include malar rash (Fig. 3), painless oral ulcers (Fig. 4), Raynaud phenomenon (Fig. 5), and palpable purpura measures 2–3 mm (Fig. 6) for 1 year. Laboratory findings were within normal limits except leukopenia ($1690/mm^3$ and $2000/mm^3$ on two occasions), rheumatoid factor (RF) was 32 IU/ml, and erythrocyte sedimentation rate (ESR) was 60 mm/h. Antinuclear antibody (ANA) was positive (Table 1). These clinical and laboratory findings led us to the diagnosis of SLE later. A chest X-ray and electrocardiogram (ECG) showed no serositis. A biopsy from a papule on the dorsal hand reported that the epidermis showed focal hyperkeratosis, hypergranulosis, acanthosis, no papillomatosis, and the dermis was normal (Fig. 7). Keratinocytes were swollen and irregularly shaped. They showed abundant, slightly basophilic cytoplasm and contained round, basophilic keratohyalin granules. Some nuclei appeared pyknotic; others appeared large and round. Vacuolated cells were present in the upper stratum malpighi and granular layer (Fig. 8). As a conclusion of the pathologic findings, the morphological changes are consistent with EV. The treatment was with medications as follows: prednisolone 20 mg q12d decreased gradually; azathioprine 50 mg q12h; nifedipine qd; mupirocin q12d; antisolar cream; urea 40%. After a month's follow-up, the findings have markedly improved. The patient had no special concerns about the medical treatment.

Discussion

EV is a rare disorder first described by Lewandowsky and Lutz in 1922[2,8]. EV has no predilection toward a certain sex, ethnicity, or geographic region[3,6]. Although EV is considered an autosomal recessive genodermatosis, the autosomal dominant form of inheritance has been described in two cases[3]. EV can be sporadic or familial with more prevalence of the familial type[3]. In our case, due to the absence of a family history of EV and the age at which the disease was discovered, as the hereditary form of EV usually develops in childhood or early adolescence[4], we assume that the patient had acquired EV (AEV). AEV was first described in the 1970s and has now been identified in all ages, skin types, and races in patients with immunodeficiencies[6]. As mentioned earlier, the association between SLE and EV is a very rare condition. Until 2006, 3 cases of this association have been reported[5], and 3 other cases have been reported in 2009[1], 2013[2], and 2020[4]. Therefore, according to the best of our knowledge, our case is the seventh report of the association between SLE and EV. Clinical manifestations in our patient were malar rash, discoid rash, and oral ulcers. Abnormal laboratory findings were leukopenia, increased RF, and high ESR, and positive ANA. According to the American College of

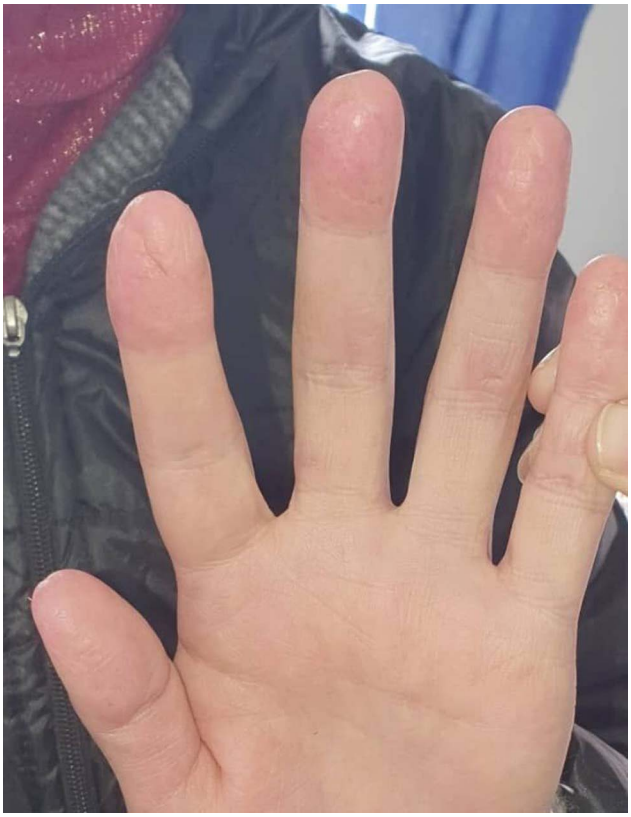

Figure 5. Raynaud phenomenon.

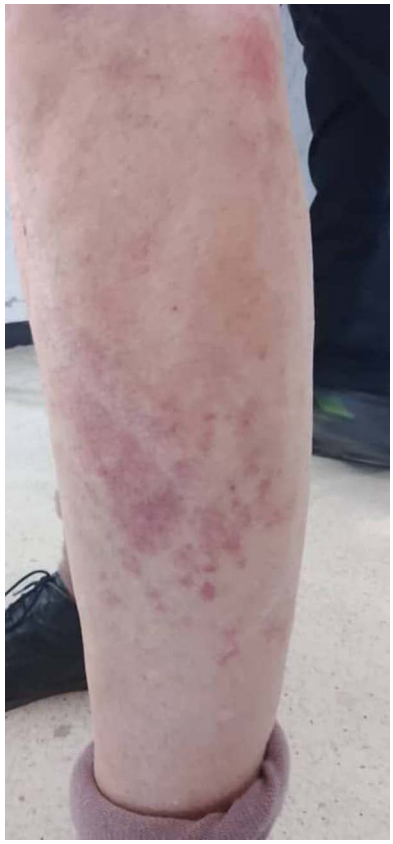

Figure 6. Palpable purpura.

Rheumatology (ACR), the co-occurrence of these clinical and laboratory findings confirms the diagnosis of SLE[9]. The confirmation of AEV diagnosis depends on DNA hybridization models and histological examination[6]. In our patient, a histopathological examination confirmed the diagnosis of EV. The effective topical treatment regimens for AEV include cidofovir, retinoids, imiquimod, and topical glycolic acid lotion, but no specific therapy has been approved yet[6]. In our case, the treatment regimen included prednisolone and azathioprine for SLE, nifedipine for Raynaud phenomenon, mupirocin for the secondary infection on palms and soles, and urea 40% for verrucous-like lesions. A follow-up after 1 month showed improved EV lesions and minimal SLE manifestations.

Conclusions

EV is a rare disease. Even though the association between SLE and EV is a rare condition, EV should not be excluded in patients with SLE. Since no treatment has been approved for AEV or EV lesions, larger, randomized, prospective studies are needed to determine whether the common AEV treatments are truly beneficial.

Ethical approval

Ethics approval is not required for case reports at our institution. Institution name: Department of Dermatology, National Hospital of Latakia, Latakia, Syrian Arab Republic.

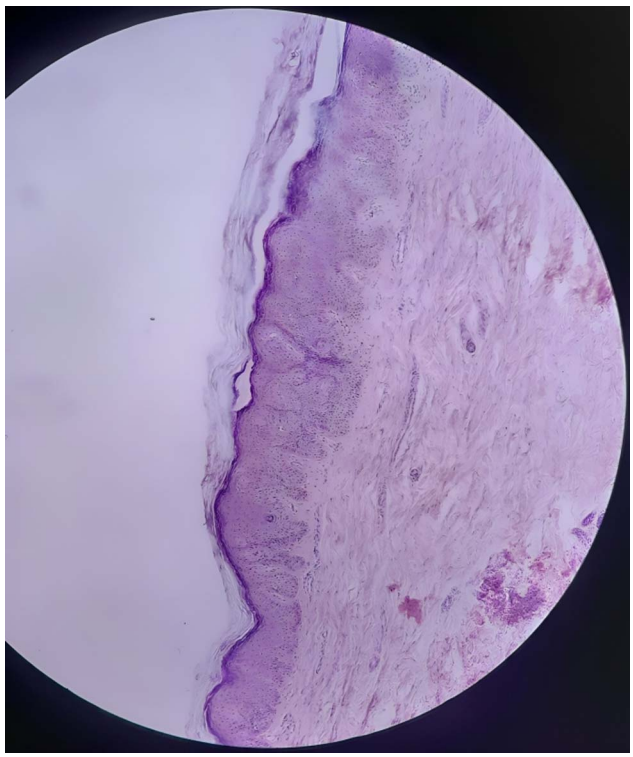

Figure 7. Mild to moderate acanthosis and hyperkeratosis (hematoxylin and eosin, 40×).

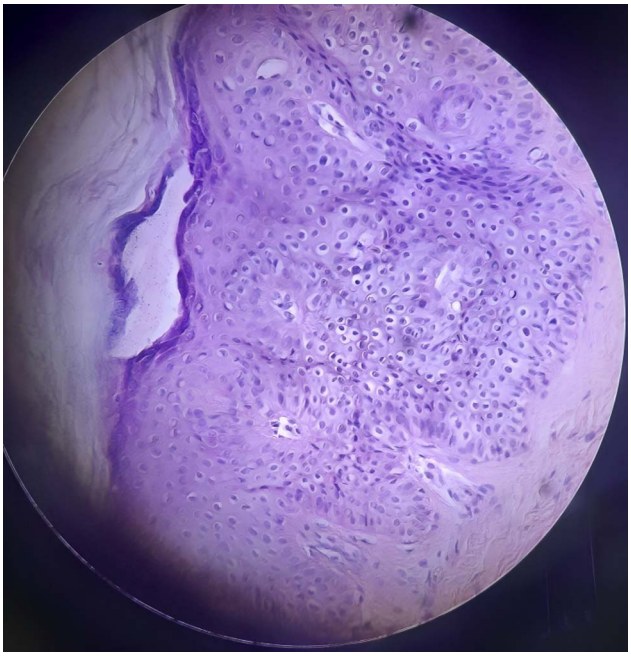

Figure 8. Large cells with blue-grey cytoplasm, perinuclear halos, often dysplastic changes, Irregular granular layer with rare perinuclear halos (hematoxylin and eosin, 200×).

Consent

A consent was obtained from the patient for the publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Sources of funding

No funding was required.

Table 1

Describes the laboratory findings

Leucocytes	2000 cells/mm^3
Erythrocytes	4 070 000 cells/mm3
Haemoglobin	11 g/dl
HCT	33.2%
MCV	82 fl
MCH	26.7 g/dl
MCHC	32.7 pg
Thrombocytes	180 000 cells/mm^3
Lymphocytes	44.5%
Eosinophils	12.2%
Neutrophils	43.3%
RDW	15%
ALT	21 U/l
AST	38 U/l
CRP	0 mg/dl
ESR	60 mm/h
Creatinine	0.97 mg/dl
Urea	14 mg/dl
Glucose	92 mg/dl
RF	32 IU/ml
ANA	2.1 U/ml

ALT, alanine aminotransferase; ANA, antinuclear antibody; AST, aspartate aminotransferase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HCT, haematocrit; MCHC, mean corpuscular haemoglobin concentration; MCV, mean corpuscular volume; RDW, red cell distribution width; RF, rheumatoid factor.

Author contribution

All authors read and approved the final manuscript. A.M.D.: design of the study, data collection, data interpretation and analysis, drafting, critical revision, preparing correspondence files, preparing the final manuscript, approval of the final manuscript. E.M.D.: data collection, data interpretation, and analysis, critical revision, drafting, approval of the final manuscript. L.A.: The Supervisor, patient care, drafting, critical revision, approval of the final manuscript.

Conflicts of interest disclosure

The authors declare that they have no conflicts of interest.

Research registration unique identifying number (UIN)

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Guarantor

Dr. Lina Al-Soufi.

Data availability statement

Not applicable. All patient data generated during this study is included in this published article and its supplementary information files.

Provenance and peer review

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References

[1] Holmes C, Chong AH, Tabrizi SN, *et al*. Epidermodysplasia verruciformis-like syndrome in association with systemic lupus erythematosus. Australasian J Dermatol 2009;50:44–7.

[2] Zampetti A, Giurdanella F, Manco S, *et al*. Acquired epidermodysplasia verruciformis: a comprehensive review and a proposal for treatment. Dermatol Surg 2013;39:974–80.

[3] Rasha A, Al-Issa A, Ghobara YA. Epidermodysplasia verruciformis: a rare case report. Cureus 2020;12.

[4] Ferronika P, Sijmons RH, Febiyanto N, *et al*. Acquired human papilloma virus type 6–associated epidermodysplasia verruciformis in a patient with systemic lupus erythematosus. The Am J Dermatopathol 2020;42:e156–8.

[5] Aghaei S, Aslani FS. Systemic lupus erythematosus arising in a patient with epidermodysplasia verruciformis. Lupus 2006;15:47–50.

[6] Moore S, Rady P, Tyring S. Acquired epidermodysplasia verruciformis: clinical presentation and treatment update. Int J Dermatol 2022;61:1325–35.

[7] Sohrabi C, Mathew G, Maria N, *et al*. Collaborators. The SCARE 2023 guideline: updating consensus Surgical CAse REport (SCARE) guidelines. Int J Surg (London, England) 2023;109:1136–40.

[8] Gül Ü, Kılıç A, Gönül M, *et al*. Clinical aspects of epidermodysplasia verruciformis and review of the literature. Int j Dermatol 2007;46:1069–72.

[9] Ameer MA, Chaudhry H, Mushtaq J, *et al*. An overview of systemic lupus erythematosus (SLE) pathogenesis, classification, and management. Cureus 2022;14.