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CASE REPORT

Systemic lupus erythematosus with toxic epidermal necrolysis-like presentation

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Abstract

Systemic lupus erythematosus (SLE) is a rare autoimmune disease with a wide spectrum of clinical manifestations, among which the skin involvement is one of the most common forms of presentation. Skin lesions specific to SLE are classified as either acute, subacute or chronic. Nevertheless, SLE patients can develop rare atypical skin lesions at onset which may pose diagnostic challenges. Toxic epidermal necrolysis (TEN)-like lupus is a rare and severe form of skin involvement which may develop in SLE patients, either in the course of the disease, during an acute flare, or at first presentation. Although TEN-like lupus can mimic true drug-induced TEN/Stevens–Johnson syndrome, presence of additional lupus-related clinical, immunology and histopathology features should be considered when making a differential diagnosis. Prompt diagnosis and screening for systemic involvement is essential for optimal management of SLE patients. We present a case report of a female patient diagnosed with SLE which developed diffuse TEN-like lesions at disease onset with good outcome after high-dose glucocorticoid combined with immunosuppressive therapy.

Keywords: systemic lupus erythematosus, toxic epidermal necrolysis, Stevens–Johnson syndrome.

Introduction

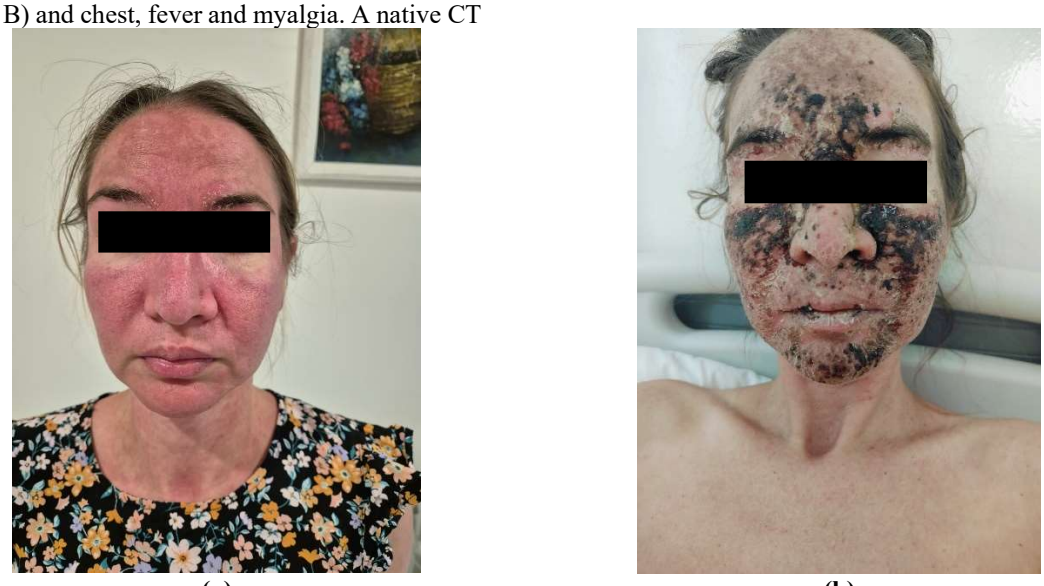
Systemic lupus erythematosus (SLE) is a rare autoimmune disease with a wide spectrum of clinical manifestations, among which the skin involvement is one of the most common forms of presentation. Skin lesions specific to SLE are classified as either acute, subacute or chronic. Nevertheless, SLE patients can develop rare atypical skin lesions at onset which may pose diagnostic challenges. Severe forms of acute cutaneous lupus erythematosus can manifest in the form of Stevens-Johnson syndrome (SJS)/ Toxic epidermal necrolysis (TEN)-like lupus. SJS and TEN are severe drug-induced mucocutaneous diseases with potentially fatal outcome characterized by large surface necrosis and exfoliation of the epidermis. These entities are part of a continuum of skin pathologies and can be divided based on percentage of body surface involvement, as such: SJS < 10%, SJS/TEN 10-30% and TEN >30% of the total body surface area [1]. To date, there are only limited number of cases of lupus patients presenting with TEN-like skin lesions [2]. TEN-like lupus erythematosus is a very rare disease that manifests as epidermal lesions and mucosal ulceration that occurs in patients with acute and severe exacerbations of systemic lupus erythematosus. The clinical picture is often similar to SJS/TEN, however, the absence of a potentially causative drug and the context of additional acute features of SLE help establish the appropriate diagnosis. TEN-like lupus manifests itself as an erythematous maculopapular form rash, most often occurring on skin areas after sun exposure, and can also affect the mucous membrane or become generalized. The diagnosis is confirmed histologically. Signs that help distinguish a TEN-like lupus diagnosis over SJS/TEN: recent diagnosis or exacerbation of SLE, skin lesions after exposure to the sun, subacute progression of epidermal necrosis (days to weeks), minimal involvement of mucous membranes [3]. We present a case report of a female patient diagnosed with SLE which developed diffuse TEN-like lesions at disease onset with good outcome after high-dose glucocorticoid combined with immunosuppressive therapy.

Case Report

We present the case of 35-year-old female patient, with no known past medical history, who was referred to the rheumatology outpatient service complaining of pain in the small joints of the hands and feet, mild myalgia and muscle weakness. Initially, treatment with nonsteroidal anti-inflammatory drugs was

recommended without significant symptom relief. After 2 weeks, the patient returns after developing diffuse erythema on the face (Figure 1A), dysphagia for solids and worsening muscle weakness, based on which suspicion of dermatomyositis was raised while screening also for other possible causes of myopathy and skin rash, including SLE. The patient confirms that she had contact with toxic substances at work (hydrochloric acid, silver nitrate, glass sand, hexane), although did not come into contact with these substances for the past month. Also, the patient claims to have taken antibiotic, amoxicillin and clavulanate, after to a dental procedure a month prior. Other medications administered before the second presentation at the rheumatologist include ibuprofen 400 mg per day and a single capsule of loperamide 2 mg for a persistent diarrhea. The laboratory tests carried out in the outpatient setting showed leukopenia (2.24x103/mm3) with lymphopenia and neutrophilia, low-grade anemia, increased liver enzymes (aspartate aminotransferase [AST]=145u/l, alanine transaminase [ALT]=142u/l), elevated muscle enzymes (creatinkinase [CK]=233u/l, lactate dehydrogenase [LDH]=431u/l), C reactive Protein and erythrocyte sedimentation rate within normal limits. Subsequently, glucocorticoid therapy with 32 mg methylprednisolone was initiated.

Because the patient's condition worsened, with the erythematous skin lesions on the face evolving into a bullous appearance, the patient was admitted to the Emergency Department. Upon admission, the patient presented psycho-motor agitation, disorientation, extensive bullous and hemorrhagic lesions on the face (Figure 1B) and chest, fever and myalgia. A native CT scan of the skull, abdomen and pelvis was performed without specific changes. She is hospitalized in the Internal Medicine department and a pulse-therapy is initiated with methylprednisolone 500mg per day, for 6 days (3g in total). After initiation of high-dose corticosteroids, the patient had a slight improvement of arthralgia, myalgia and dysphagia. Repeated testing for muscle enzymes showed a gradual decrease in AST, ALT, CK. Interestingly, the inflammatory makers remained normal during admission. The patient was transferred to the Rheumatology Clinic and continued oral administration of corticosteroids - prednisone 0.5mg/kg/day, with the continuous improvement in joint and muscle symptoms and also of the skin lesions. Additional investigations showed an immunologic panel positive for antinuclear antibodies, anti-nucleosome antibodies, hypocomplementemia, a positive Coombs test and a 24-hour proteinuria of 700mg. The heart ultrasound and CT scan did not detect serositis. Ten days after admission the patient showed marked improvement in movement, no difficulties in swallowing and the hemorrhagic crusting lesions on the face featured progressive desquamation with apparent healed epidermis underneath (Figure 2A). Upon discharge, the patient continued treatment with mycophenolate mofetil, with the progressive increase of the dose up to 2g/day, hydroxychloroquine 200 mg/day, and prednisone 0.5g/kg/day with the progressive dose tapering. At 2-week follow-up the patient reported a marked clinical improvement and a complete healing of the hemorrhagic crusting lesions on the face was observed (Figure 2B, 2C).



(a) **(b)**

Figure 1. *(A) Erythematous rash of the face at disease onset; (B) Rapid worsening of the skin lesions with bullous aspect that progressed to hemorrhagic lesions with crusting.*

(a) (b) (c)

Figure 2. *(A) Clinical aspect of skin lesions of the face after high-dose corticosteroid showing healed epidermis after desquamation; (B), (C) Complete resolution of skin crusts at 2-week follow-up examination.*

Discussions

The cutaneous manifestations observed in SLE patients are classified as SLE-specific (acute, subacute and chronic or discoid lupus) and SLE nonspecific. The latter include: palpable purpura, urticarial vasculitis, telangiectasias, livedo reticularis or Raynaud's phenomenon. These non-specific lesions can be observed in numerous other conditions. The most common SLE-specific cutaneous manifestations is the butterfly-shaped malar rash. It is located over the cheeks and nasal bridge; it spares the nasolabial folds and features photosensitivity. Subacute cutaneous lupus erythematosus manifests as non-scarring papulosquamous eruption, with typical erythematous borders and central clearing. It is localized on sun-exposed areas of the face, neck, trunk and outer arms. In discoid lupus, which is the most common form of chronic cutaneous lupus erythematosus, the patients develop scarring lesions which are disc-shaped and can progress to pigmentary changes, atrophy and alopecia [4].

Atypical and severe forms of cutaneous manifestations encountered in SLE patients include TEN-like lupus and Rowell syndrome, which are most frequently triggered by medications and some viruses such as herpesvirus and Mycoplasma [5]. Regarding ichthyosis acquis and plamoplantar livedoid hyperkeratosis, only a few cases have been described in the literature [6]. Multiple case reports and case series have described characteristic features of SLE patients with vesiculobullous manifestations which has led to the separate definition of TEN-like lupus erythematosus [7].

TEN is a rare disease associated with significant morbidity and mortality which is characterized by detachment of the skin (positive Nikolsky sign). In almost all cases it is drug induced and necessitates prompt diagnosis and treatment taking into account the potential life-threatening disease course [1]. Rowell Syndrome, known as erythema exudativum multiforme, is mostly seen in middle age women with all subtypes of cutaneous lupus erythematosus and is characterised by the presence of recurrent cutaneous lesion and typically positive immunology panel for speckled pattern ANA, positive anti-Ro/SSA or anti-La/SSB antibodies and rheumatoid factor [5].

TEN-like lupus erythematosus is a very rare subtype of cutaneous lupus with a limited number cases described in the literature. In a large single center study, Tankunakorn et al reported an incidence of SJS/TEN-like lupus cases of 0.07% among a cohort of 9074 patients diagnosed with cutaneous lupus erythematosus or systemic lupus erythematosus [7]. TEN-like lupus is characterized by apoptotic pan-epidermolysis with massive epidermal cleavage and necrosis. It manifests as extensive skin denudation and blistering similarly to a true SJS or NET. Lesion can appear on photo-exposed areas initially, but usually they become widespread [8]. Differentiation between TEN and TEN-like lupus is not always obvious and clinical context should be taken into consideration. In our case the diagnosis of SLE was suggested by the systemic involvement and positive immunology markers. A drug-induced reaction could not be clearly proven since the patient did not take other additional therapies prior to the severe and rapid worsening of the skin lesions, except the initiation of oral corticosteroid. There have been several reports describing clinical features that can discriminate between TEN and TEN-like lupus [1,3,7-9]. Patients with TEN-like lupus usually have a slower progression of skin lesions and significantly less involvement of mucous membranes. Also, there is a lack of ocular involvement, like conjunctivitis or corneal ulcerations, which is typically observed in SJS/TEN. Although the histopathology can be indistinguishable, TEN-like lupus patients may feature additional positive lupus band on direct immunofluorescence [9].

At present, there are no standard treatments for TEN-like lupus erythematosus. Treatments often includes high doses of intravenous corticosteroids, immunosuppressive agents (e.g., azathioprine, mycophenolate mofetil, cyclophosphamide, etc.), intravenous immunoglobulin (IVIG) and plasmapheresis [3,7]. As in most cases of autoimmune disease with acute and severe presentation, systemic

glucocorticoids are widely used as first-line treatment. In a review of 25 cases of TEN-like lupus erythematosus published by Baker et al, IVIG have proven effective with complete resolution of skin manifestations in 6 out of 8 patients with or without associatin of corticosteroid [3]. The potential benefit of IVIG stems from its effect on Fas (CD95), blocking the interaction with the Fas ligand which activates apoptosis of epidermal cells [10].

Conclusions

Toxic epidermal necrolysis-like lupus erythematosus is a rare and severe manifestation of cutaneous lupus erythematosus characterized by extensive epidermolysis and can mimic true Stevens-Johnson syndrome or toxic epidermal necrolysis. Several differentiating features have been defined based on the clinical context, immunology markers and histopathology features. Our case highlights a rare ocurrence of toxic epidermal necrolysis-like skin lesions in a patient with systemic lupus erythematosus.

Conflicts of Interest: The authors declare no conflicts of interest.

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