Bilateral periorbital swelling as the initial presentation of cutaneous lupus erythematosus

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INTRODUCTION

Cutaneous lupus erythematosus (CLE), defined as isolated cutaneous lesions without significant systemic involvement, has a reported incidence and prevalence of 4.3 and 73.2 per 100,000, respectively.[1] It occurs more commonly among women with a reported age of onset between the second and fourth decades of life.[1] The 3 more common subtypes of lupus are systemic lupus erythematosus (SLE), subacute cutaneous lupus, and discoid lupus erythematosus. A subset of patients shows atypical clinical manifestations of CLE, which are more rare subtypes and pose a diagnostic and therapeutic challenge. Antimalarial drugs are considered the mainstay of systemic therapy. Because it may take 2 to 3 months to note some improvement,[2] oral or topical steroids are used in conjunction to facilitate response. We report a patient with an atypical presentation of CLE who also responded to hydroxychloroquine and review similar cases in the literature.

Abbreviations used:

ANA:	antinuclear antibody
BID:	twice a day
CLE:	cutaneous lupus erythematosus
DIL:	drug-induced lupus
SLE:	systemic lupus erythematosus

CASE REPORT

A man in his 40s presented with persistent periorbital swelling for 7 months. The swelling first appeared 2 days after stripping floors during his work. He denied any associated pruritus, oral symptoms, facial pain, dyspnea, fever, weight changes, myalgias, arthralgias, weakness, or fatigue. He also denied coming into contact with any new products on his face or any new medications. He had a history of asthma but no history of allergies or photosensitivity. He also had eczema, hypertension, and depression well controlled with triamcinolone cream, amlodipine, and doxepin, respectively. He used ibuprofen about 4 times a week for tension headaches for several years without any adverse reactions, but he stopped using it within days of noticing the periorbital swelling. However, the swelling did not improve. A few months after, at an outside hospital, he was given a diagnosis of sinusitis and treated with amoxicillin/clavulanate and systemic steroids. Symptoms initially improved but relapsed when prednisone was tapered to less than 20 mg.

After 7 months of having the above symptoms and lack of improvement of the swelling, he presented to our service. Review of systems yielded normal results other than the indicated above. Physical examination found edema and erythema of the right lower and upper eyelids and on the left upper eyelid (Fig 1).

The following laboratory investigations were within normal limits: complete blood count, complete metabolic profile, C-reactive protein, creatine kinase, IgE levels, C4, C1-INH, C1q, and total hemolytic complement. Results for antinuclear antibody (ANA), anti-Sjögren's syndrome–related antigen A and antigen B, antineutrophil cytoplasmic antibody, antimicrosomal antibody, antihistone antibody, aldolase, anti-Jo1, and anti-Mi2 antibody were normal. Anti-dsDNA level was quantified at 45 IU/mL (nl < 4 IU/mL), and anti-Smith level was 1 AI (nl < 1 AI).

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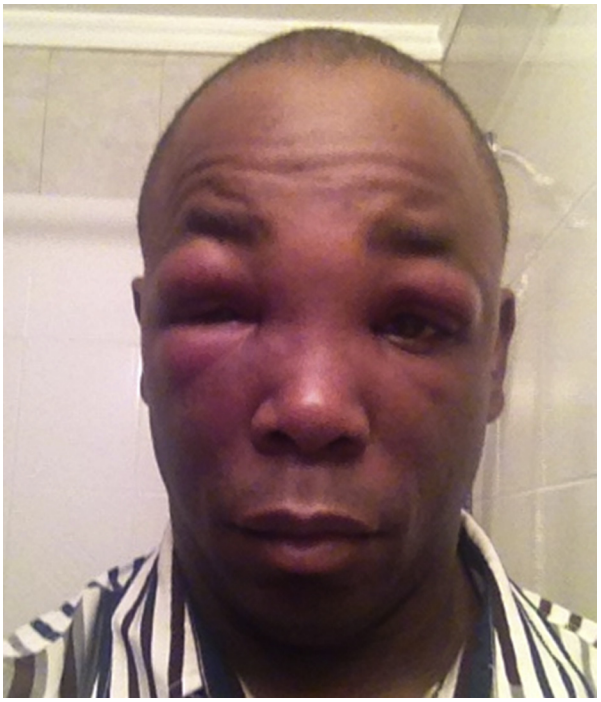

Fig 1. Clinical presentation. Marked edema and erythema of the right and left eyelids, with diminished palpebral aperture.

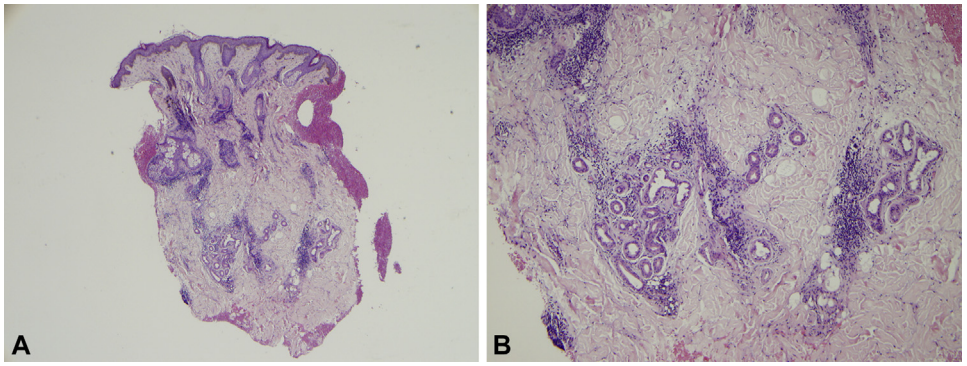

Fig 2. **A**, Superficial and deep lymphocytic infiltrate perivascular and periadnexal infiltrate. **B**, Deep periadnexal lymphocytic infiltrate with increased dermal mucin. (Original magnifications: A, ×40; B, ×100.)

Angiotensin-converting enzyme levels, chest radiograph, and urinalysis were normal. A maxillofacial computed tomography scan found soft tissue swelling in the right lacrimal fossa with no focal abscess. Biopsy results of the right lower eyelid are shown in Fig 2.

He was further evaluated by the rheumatology department, and no systemic findings were noted. Our patient's clinical presentation and histopathologic findings were consistent with a diagnosis of tumid lupus, a rare variant of CLE. Therefore, he was initially treated with oral prednisone (40 mg/d) and hydroxychloroquine (400 mg/d). The prednisone dose was tapered and discontinued over 2 months with complete resolution of the periorbital edema. Our patient remains under control and without a relapse of cutaneous disease or development of systemic symptoms on hydroxychloroquine 400 mg/d at his 1-year follow-up.

DISCUSSION

Periorbital edema is a rare and nonspecific presentation for several conditions including SLE, dermatomyositis, solid facial edema, drug reactions (including drug-induced lupus [DIL]), infections, angioedema, systemic contact dermatitis, superior vena cava syndrome, hypersensitivity reactions, sarcoidosis, and others.[3] Laboratory, histopathology, and imaging studies ruled out these diagnoses in our patient.

Table I. Demographics and clinical data in 6 patients with periorbital edema as the sole manifestation of CLE

Age	Gender/Race	Time to Diagnosis	Serology	Diagnostic Criteria	Histopathology	Treatment	Response
24	Female/Caucasian	3 y	ANA$^-$	Histopathologic findings	Hyperkeratosis, diffuse with hydropic degeneration, and superficial and deep perivascular, and periadnexal lymphocytic infiltrate	Hydroxychloroquine, 400 mg/d, with oral prednisone at 60 mg/d	Marked improvement after 1 month of therapy[7]
51	Female/Caucasian	2 y	ANA$^+$ at 1:140 Anti-Ro$^+$ Anti-La$^-$	ANA level above laboratory reference range Histopathologic findings Direct immunofluorescence with granular deposits of immunoreactants	Hyperkeratosis, diffuse epidermal atrophy with focal erosion and focal vacuolization of the basal cell layer, infundibular follicular epithelium with occasional civatte bodies, dermal edema, and a moderately dense, superficial and deep perivascular and focally perifollicular lymphohistiocytic infiltrate	Quinacrine, 100 mg/d	Marked improvement after 5 wk; however, therapy was discontinued because of generalized drug eruption. Edema and erythema remained in remission 10 months after therapy discontinued.[8]
45	Female/Caucasian	2 y	ANA$^-$ Anti-Ro$^-$ Anti-La$^-$	Histopathologic findings Direct immunofluorescence with globular deposits of immunoreactants	Epidermal atrophy with hydropic degeneration and multiple eosinophilic globules, dermal perivascular and periadnexal lymphohistiocytic infiltrate	Hydroxychloroquine, 200 mg/d, increased to 400 mg/d after 2 mo and added oral prednisone at 40 mg/d	Mild improvement with 200 mg/d hydroxychloroquine. Complete resolution 2 months after starting 400 mg/d hydroxychloroquine + 40 mg/d prednisone.[8]

42	Male/African-American	2 y	ANA^{-} Anti-Ro^{-}	Histopathologic findings Direct immunofluorescence with granular deposits of immunoreactants	Hyperkeratosis with focal areas of parakeratosis, dense lymphocytic infiltrate at the dermoepidermal interface and hair follicles, lymphohistiocytic infiltrate in the reticular dermis	Hydroxychloroquine, 200 mg/d	Complete resolution of edema and marked improvement in violaceous discoloration after 1 month of treatment. Only faint postinflammatory hyperpigmentation remained after 3 months.[9]
23	Male/Caucasian	1 y	ANA^{-} Anti-Ro^{-}	Histopathologic findings Direct immunofluorescence with granular deposits of immunoreactants	Hyperkeratosis, diffuse with hydropic degeneration, and superficial and deep perivascular, periadnexal lymphocytic infiltrate Second biopsy 1 year later: Normal epidermis with dermal fibrosis and presence of interstitial mucin	Chloroquine, 150 mg/BID after 2 months without improvement oral prednisolone was added at 60 mg/d.	Mild improvement after 2 months of chloroquine, 150 mg/BID + prednisolone 60 mg/d. Recurrent periorbital edema 1 year later treated with chloroquine, 150 mg/BID for 6 months failed to alleviate symptoms.[10]
36	Male/Caucasian	2 y	ANA^{-} Anti-Ro^{-} Anti-dsDNA^{+}	Photosensitive facial erythema Anti-dsDNA antibody level above laboratory reference range Histopathologic findings Direct immunofluorescence with granular deposits of immunoreactants	Epidermal atrophy and focal vacuolization of the basal layer with occasional Civatte bodies, dermal pigment incontinence, and superficial perivascular lymphocyte infiltration with a few plasma cells Strong staining with alcian blue indicated a marked dermal mucin deposition	Chloroquine, 150 mg/BID	Marked improvement after 3 months of therapy with regression of unilateral proptosis[10]

BID, Twice a day.

Our patient did not have any other local or systemic clinical features such as skin lesions (heliotrope rash, Gottron's sign, shawl sign) or musculoskeletal symptoms and signs of myopathy characteristic of dermatomyositis. Additionally, our patient failed to meet the criteria for SLE because of lack of systemic findings including fatigue, arthritis, or involvement of other systems (renal, pulmonary, cardiac, hematologic, neuropsychiatric). A drug-induced process including DIL was less likely, as the patient was taking ibuprofen for several years before the onset of the facial edema without any adverse reactions, and this did not resolve with the discontinuation of ibuprofen. DIL also is reported to be less likely to have a cutaneous presentation. There was also a notable absence of eosinophils on the biopsy findings. Results of serologic studies for dermatomyositis, SLE, and DIL were normal. A maxillofacial computed tomography scan also did not show any findings seen in chronic sinusitis.

Although eyelid edema is reported to have a 4.8% cumulative incidence in SLE,[4] and a few cases are reported in discoid lupus erythematosus and lupus erythematosus profundus,[5,6] periorbital edema as the sole presenting manifestation of CLE is extremely rare. Of note, our patient did not meet criteria for SLE or other systemic rheumatologic conditions. To our knowledge, only 6 similar cases have been reported.[7-10] A review of the data regarding these patients is presented in Table I. Both women and men were equally affected with ages at diagnosis ranging from 23 to 51 years. All cases required histopathologic analysis from periorbital areas to confirm the diagnosis with biopsies finding a combination of a variation of findings including superficial and deep perivascular and periadnexal lymphocytic infiltrate, marked interstitial mucin deposition, and vacuolar alteration of basal layers. The presence of the first 2 findings in our patient's biopsy along with a notable absence of other features including eosinophils were more consistent with a diagnosis of tumid lupus. All previously reported cases experienced a delay to diagnosis between 1 and 3 years. Five of the 6 patients had negative results for ANA, similar to our patient. The treatment of choice for the cases of CLE with periorbital edema was antimalarial drugs with or without systemic corticosteroids. All patients experienced some improvement with this therapy. Five patients reported marked improvement within 1 to 3 months of therapy, similar to our patient (Table I), suggesting that antimalarial drugs are an effective therapeutic option for these patients. We recommend CLE be considered in the differential diagnosis of patients with persistent periorbital edema.

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