case report

Extensive ulcerations due to pyoderma gangrenosum in a child with juvenile systemic lupus erythematosus and C1q deficiency

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Systemic lupus erythematosus (SLE) is a multisystem chronic autoimmune inflammatory disease. SLE has been associated with numerous complement abnormalities including C1q deficiency.[1] Patients with SLE and C1q deficiency may have a severe multisystem disease, including cutaneous lesions.[2,3] Patients with antiphospholipid antibody syndrome often develop cutaneous ulcerations which mimic pyoderma gangrenosum (PG), particularly leg ulcers, and similar lesions have rarely been reported in patients with SLE.[4,5] We managed a young girl with familial SLE and C1q deficiency who developed progressive extensive ulcerations that were consistent with pyoderma gangrenosum.

CASE

A 14-month-old girl, a product of a full-term normal delivery with an uneventful pregnancy and normal post-natal period, presented initially with diffuse pustules on the face and extremities. These lesions had broken down and rapidly enlarged in size and had became ulcerative with discharge and crust formation. She had a history of intermittent fever and poor appetite, but no other systemic manifestations. All blood and surface swab cultures were negative. The patient was initially treated with various antibiotics without improvement. She had strong family history of SLE. The parents are first-degree relatives and healthy. The eldest sister, a 6-year-old also had SLE that was diagnosed and followed in our hospital.

The physical examination revealed an irritable, afebrile girl. Weight and height were at the 5th percentile. She had multiple ulcerative lesions involving the face, scalp, and both extremities (Figures 1, 2). There was oral mucosal ulceration, but no lymphadenopathy or hepatosplenomegly. She had bilateral knee arthritis. Other examinations were unremarkable. The initial laboratory findings showed a white cell count of 18.1×10^9/L, hemoglobin of 131 g/L, a platelet count of 267×10^9/L. The direct Coombs test was positive, C-reactive protein was high at 79.5 mg/L (normal, 0-5 mg/L). She had positive antinuclear antibody (ANA) to a dilution of 1:320 (speckled pattern) with positive anti-dsDNA at 156 U/mL (normal, 0-20 U/mL), but negative extractable nuclear antigens. However, her antiphospholipid antibody profile was positive: anticardiolipin IgM was 150 MPL (normal, 0-12.5 MPL), IgG 17.2 g/L (normal, 0-10 g/L) and anti-ß2 glycoprotein (IgG) was 48.4 SGU/mL (normal, 0-10 SGU/mL). She had low complement levels (C3 and C4) at 0.4 g/L and 0.06 g/L, respectively. Because of her extensive skin involvement, CH50 and C1q levels were done and were low at 5 U/mL (normal, 345-485 U/mL) and 55 mg/L (normal, 75-250 mg/L), respectively. Based on the oral ulceration, arthritis, the direct Coombs test positivity and high titers of ANA and anti-dsDNA, the diagnosis of SLE was made.

She was started on daily intravenous methylpred-

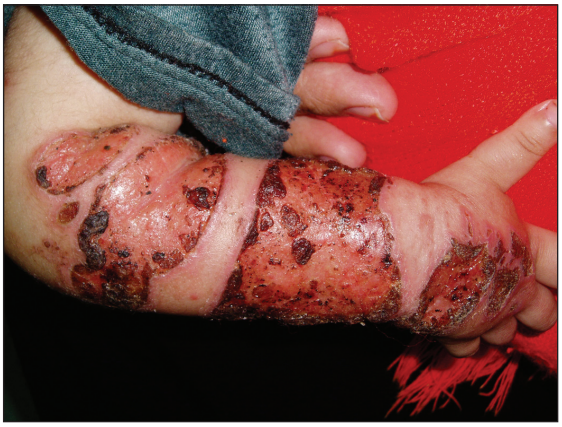

Figure 1. Multiple large necrotic ulcers on the forearm.

nisolone (30 mg/kg/day) for 3 consecutive days. A few days later she showed improvement and she was discharged home on oral prednisone 1 mg/kg/day in 2 divided doses and azathioprine 2 mg/kg/day.

A few weeks later she was seen in the clinic with active disease. She was extremely irritable and had extensive skin lesions. The dose of prednisone was increased and azathioprine was changed to cyclosporine 2 mg/kg/day. Afew months later she presented to the hospital with a high-grade fever and progressive skin lesions with pus collection. She was admitted to the hospital and underwent incision and drainage. The wound culture grew *Staphylococcus aureus* and group A streptococcus. However, the blood culture was negative. She was treated with antibiotics, intravenous methylprednisolone and intravenous immunoglobulin. The fever subsided and her condition improved, but the skin ulceration did not improve. Because of the disease progression, a skin biopsy was done, which showed dense pandermal inflammation, predominantly suppurative and extending to the superficial subcutaneous fat (Figure 3). The inflammation was associated with focally degenerated collagen. A naked hair shaft was observed entrapped within this inflammation (Figure 4), which indicates a ruptured suppurative folliculitis component and is consistent with PG. No basal cell vacuolization or thickening of the basement membrane was noted. There was no vasculitis. Special stains for fungus, acid fast bacilli and bacteria were negative. According to these findings, she was diagnosed with PG.

A skin biopsy for direct immunofluorescence taken from the nonaffected area revealed fine granular and discontinuous deposits of IgM and C3 along the basement membrane. Other immunoreacatants (IgG, IgA, C1q and fibrin) were negative, which was consistent with a background SLE. No deposits around dermal vessels were seen.

She was started on thalidomide for a few months without improvement. Apparently her disease was progressing. Ultimately we changed thalidomide to infliximab. She received four doses but unfortunately there was rapid deterioration in her skin lesions and she had a secondary bacterial infection. She was admitted to the local hospital with septic shock due to gram-negative sepsis and died.

DISCUSSION

PG usually begins as single or multiple pustules that rapidly progress to form ugly ulcerations. It is an idiopathic inflammatory ulcerative dermatosis that is commonly associated with inflammatory bowel disease. However, it has been reported in association with other

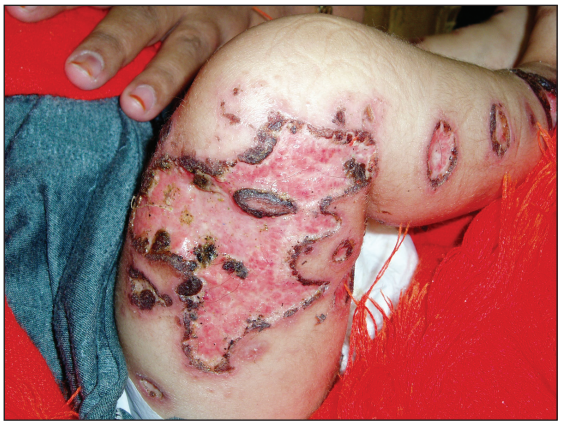

Figure 2. Large healed necrotic ulcer and multiple small ulcers on the thigh.

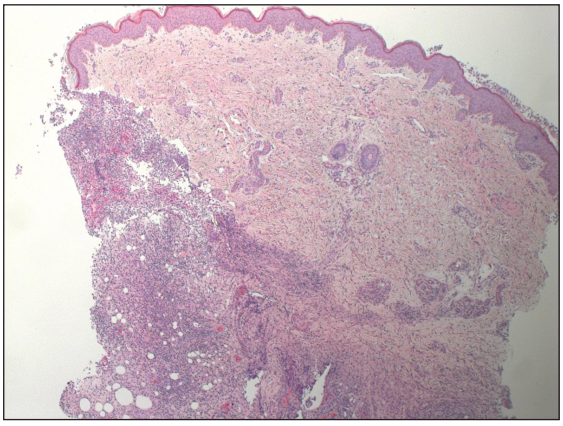

Figure 3. Low power photomicrograph (×5) of the lesion showing heavy pandermal inflammation focally extending to the superficial subcutaneous fat.

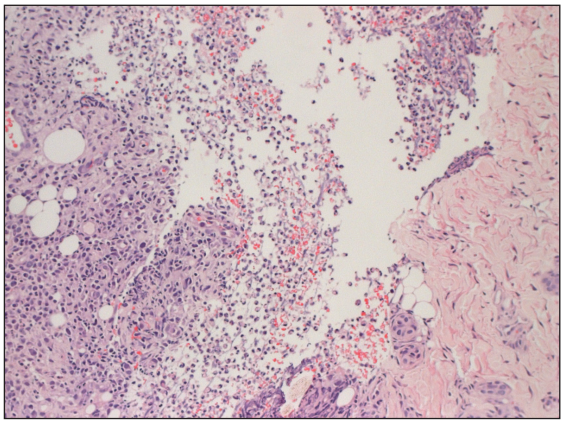

Figure 4. High power photomicrograph (×20) showing the mixed, predominantly suppurative inflammation, associated with collagen degeneration. Notice the naked hair shaft at the lower most central portion of the field, indicating a suppurative folliculitis component.

systemic diseases such as Behcet disease and in adult patients with SLE, particularly in those with antiphospholipid antibody syndrome.[4,5] C1q deficiency is one of the rare immune deficiency disorders. It may be associated with infection. Patients with C1q deficiency are at risk of developing autoimmune diseases, including SLE, and they may have unusual manifestations.[1,6]

We report a child with SLE and C1q deficiency manifesting with severe cutaneous ulceration that proved to be consistent with PG. To the best of our knowledge, there is no previous report of PG in children with SLE. In our patient, the diagnosis of SLE was based on the presence of constitutional symptoms, oral ulceration, arthritis, direct Coombs test positivity and a high titer of ANA and anti-dsDNA, low C3, C4 and C1q levels and a strong family history of SLE. The possibility of concomitant infection as a contributing factor was highly suspected; accordingly, she was given broad spectrum antibiotics. The rapidly progressive cutaneous ulcerations in the presence of antiphospholipid antibodies and poor response to conventional treatment raised the possibility of PG, which was confirmed by the histopathologic findings and exclusion of the infectious causes.

The pathogenesis of PG remains unclear, but abnormalities of the immune system have been described including defective neutrophil chemotaxis and phagocytosis.[7] In a large series of the patients with PG, half had immune complex deposition along the endothelial wall, which suggested a vasculitic etiology.[8]

We believe that SLE in patients with C1q deficiency has unusual manifestations.[2,9] The treatment of PG consists of corticosteroids, immunomodulating agents and recently, biologic agents. Although it is non-specific, the outcome is favorable.[10] Unfortunately, despite the intensive therapy our patient had a fatal outcome. In conclusion, PG is a rare complication of lupus in children. Therapeutic intervention may not be helpful in severe cases.

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