Purpura fulminans as the presenting manifestation in a patient with juvenile SLE

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We present a 12-year-old girl with systemic lupus erythematosus and associated antiphospholipid syndrome who developed an unusual manifestation of purpura fulminans in an accelerated fashion. The patient improved after prompt treatment with anticoagulants, aggressive immunosuppressive drugs and plasmapheresis. This is the first pediatric case of purpura fulminans due to secondary antiphospholipid syndrome of systemic lupus erythematosus. We suggest that SLE patients with lupus anticoagulant should be followed closely for similar complications.

Key words: systemic lupus erythematosus, antiphospholipid syndrome, purpura fulminans, plasmapheresis.

Systemic lupus erythematosus (SLE) is a challenging autoimmune disease with multiorgan involvement. It has a significant morbidity and mortality. Although rare, antiphospholipid syndrome (APS) may be identified in the pediatric age group with arterial and venous thrombosis. It may be primary or secondary to an underlying disease such as SLE[1]. On the other hand, purpura fulminans (PF) is a very severe and rare acute thrombohemorrhagic presentation. This life-threatening disorder is characterized by progressive hemorrhagic infarction of the skin caused by disseminated intravascular coagulation and dermal vascular thrombosis. It may be secondary to an inherited or acquired abnormality of the protein C and S pathway, acute severe infections, autoimmune acquired protein C and S and antithrombin III deficiency, or rare conditions like coumadin-induced skin necrosis and APS[2]. Herein, we report a 12-year-old girl with SLE and secondary APS who was diagnosed to have PF. This is the first case report of such an association.

Case Report

A 12-year-old girl was admitted to our outpatient clinic with the complaints of recurrent painful swelling, erythema and tenderness of the small joints of her hands and feet. She also complained of fatigue and hair loss for the last three months and concomitant fever for the last two months. While in the waiting room of the rheumatology clinic, she abruptly developed large purpura on her legs. Her initial physical examination revealed hair loss, swelling and erythema of both ankles. Bilateral painful, purpuric lesions on the gluteal regions and the lateral sides of the thighs (increasing in size within hours) were noticed (Fig. 1). She was immediately admitted to the hospital.

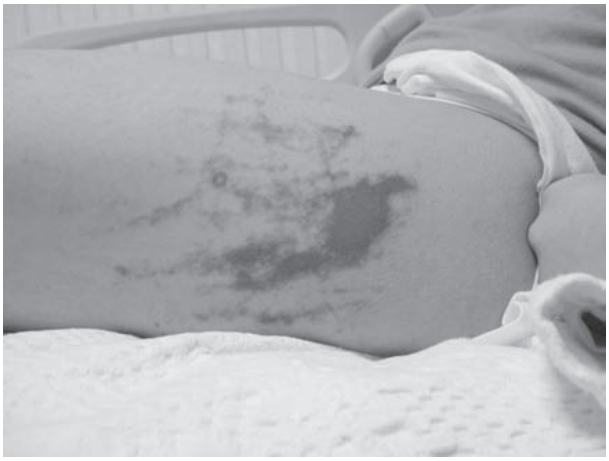

Fig. 1. Purpuric lesions on the lateral sides of the left thigh.

The laboratory assessments showed mild anemia (hemoglobin 11.1 g/dl), leukopenia ($4.2x10^3/\mu l$) and thrombocytopenia (141000/μl). The blood smear showed 60% neutrophils, 26% lymphocytes, 10% monocytes, and 4% eosinophils without any atypical cells. Erythrocyte sedimentation rate was 60 mm/hr and the C-reactive protein level was 1.36 mg/dl (N: 0-0.8). She had trace amounts of proteinuria, hematuria (13-15 rbc/high power field [hpf]) and pyuria (7-8 wbc/hpf). Blood biochemistry, prothrombin time and activated partial thromboplastin time were normal. Testings for disseminated intravascular coagulation were also unremarkable. The antinuclear antibody (ANA) titer was 1/160 and in homogeneous, nucleolar pattern, the anti-ds DNA antibody level was 752 IU/ml (N: 0-100), and C3 and C4 levels were decreased. The anticardiolipin antibodies (ACA IgM and IgG) were negative, antiphospholipid antibodies (aPL) Ig M and aPL Ig G and lupus anticoagulant (LA) were positive. Protein C, protein S and antithrombin III levels were normal, whereas the patient was found to heterozygous for factor V Leiden and methylene-tetrahydrofolate reductase (MTHFR) and negative for the prothrombin 20210 A mutations. The blood cultures were negative. Transthoracic echocardiography showed pericardial effusion and minimal aortic valve insufficiency. The patient was diagnosed as SLE with secondary APS and PF. Intravenous (IV) bolus methylprednisolone (500 mg/day) was commenced for three days, followed by oral prednisolone (1 mg/kg/day) and azathioprine (1 mg/kg/day) therapy. She was anticoagulated with IV heparin (10 U/kg/hr). During the first week of treatment, most of the purpuric lesions faded. However, on the 8th day of the therapy, new purpuric and painful lesions appeared, this time on both hands and the gluteal region. Skin biopsy from one of the new lesions in the gluteal region revealed both microthrombosis and small vessel vasculitis (Fig. 2). Since the patient also described a short-lasting diplopia attack on the same day, brain magnetic resonance imaging (MRI) was performed, which showed bilateral acute, subacute and chronic ischemic lesions of the centrum semiovale and in the watershed regions of the internal carotid arteries. MR angiography showed irregularities of the contours of the bilateral middle cerebral arteries and the right anterior cerebral artery.

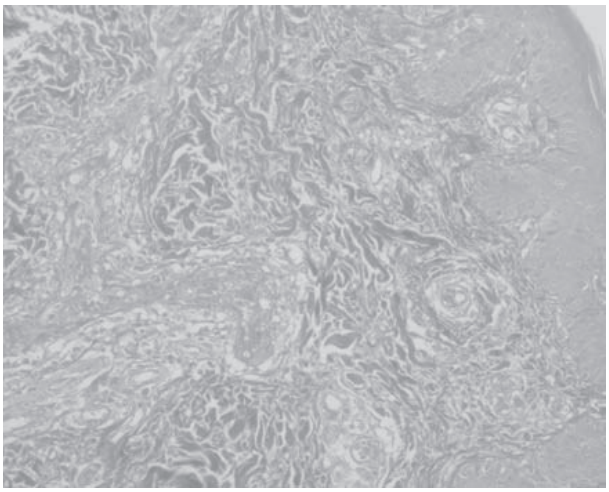

Fig. 2. Skin biopsy showed a dermal mixed-type inflammatory infiltrate including neutrophilic leukocytes, lymphocytes and histiocytes around the small arteries, endothelial swelling, karyorrhexis and erythrocyte extravasation. Some of the dermal vessels were obliterated with fibrin thrombi. A diagnosis of leukocytoclastic vasculitis and thrombosis associated with APS was made (trichrome × 200).

The central nervous system (CNS) involvement and recurrent PF prompted us to change her immunosuppressive to cyclophosphamide IV bolus (500 mg/day) and increase the heparin dose to 20 U/kg/hr. Plasmapheresis was also performed six times on alternate days with fresh frozen plasma. Subsequently, C3 and C4 returned to normal levels and the anti-ds DNA level decreased. As the skin lesions on the left gluteal region became necrotic, the patient was consulted to plastic surgery. After serial debridement, necrotic lesions healed with scar formation and the rest of the skin lesions vanished without scarring. No other lesions or neurological findings recurred.

After a one-month hospital stay, the patient was discharged with oral prednisolone (60 mg/day), acetylsalicylic acid (3 mg/kg/day) and subcutaneous enoxaparin (2 × 0.4 ml). Two months after discharge, her physical examination was normal and she returned to school.

Discussion

About 15-20% of all SLE cases are diagnosed during childhood. Secondary APS has been reported in approximately 50% of children with SLE; otherwise, it is rare in the pediatric population. APS onset before the age of 15 years occurred in only 2.8% of patients in the largest APS cohort[3]. APS describes the association of antiphospholipid antibodies with

particular clinical manifestations, including arterial thrombosis, venous thrombosis and a variety of neurological complications.

Neuropsychiatric involvement is an indicator of disease severity and activity and a very important determinant of quality of life in patients with SLE. The rates for the presence of neurological involvement in SLE vary within a wide range owing to various factors[4,5]. In a previous study of ours, while seven patients (35%) had neurological signs and symptoms at presentation, during follow-up, the frequency of neurological signs and symptoms increased to 55%[6]. The mechanism is thought to be due to vascular damage and immune-mediated injury to neuronal cells[7-9]. Among patients with SLE, the presence of antiphospholipid antibodies, notably the LA, and ACA may cause visual disturbances due to thrombosis from a hypercoagulable state[10]. Our patient -with a short-lasting diplopia attack and high anti-cardiolipins (aCLs)- showed multiple infarcts on CNS imaging. They were interpreted to be in association with these antibodies as well as microangiopathy. In fact, she developed widespread purpura over her skin simultaneously. The skin biopsy showed microangiopathic changes. Remission was achieved with immunosuppression and plasmapheresis. The overall neurological prognosis was good in our patient, and may be attributed to the intense immunosuppressive treatment she received.

The reported frequencies of aCL and LA in pediatric SLE patients have ranged from 19% to 87% and from 10% to 62%, respectively[1]. LA was found to be the strongest predictor of thrombosis risk in SLE patients, ranging between 11-100%[11,12].

Several non-classical aPL-related skin manifestations such as livedo reticularis, skin ulcers, and cutaneous necrosis have also been reported; however, this is the first description of PF due to APS in a SLE patient. One should be aware of this potential complication in SLE patients secondary to APS. We believe that the clinical presentation of our patient was quite interesting in that although she had certain SLE-related complaints for the last 2-3 months, the scenario of PF emerged during the time she was waiting to be seen in the outpatient clinic within an hour. On the other hand, we would like to draw the attention of physicians to two similar clinical scenarios: hemorrhagic LA syndrome[13] and catastrophic form of APS[14]. The former should be kept in mind especially in previously healthy children with new-onset bleeding and prolonged activated partial thromboplastin time. The latter has been and is mainly seen in SLE patients, easily mimicking SLE vasculitis, disseminated intravascular coagulation and thrombocytopenic purpura.

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