

Spontaneous soft tissue haemorrhage in systemic lupus erythematosus

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SUMMARY

Diversity in clinical presentations and complications of systemic lupus erythematosus (SLE) make the diagnosis and management challenging. The mechanisms of haemorrhagic manifestations in SLE have not been well elucidated. A 47-year-old woman with no comorbidities was admitted after suffering fatigue and low grade fever for six months. She had bilateral soft tissue haemorrhage over the forearm and intra retinal haemorrhages. She was assessed and diagnosed as having SLE based on positive antinuclear antibody, strongly positive anti double stranded DNA, thrombocytopenia and low C3 and C4 levels. We describe a case of spontaneous bilateral soft tissue haemorrhage in SLE and discuss the various mechanisms causing bleeding in lupus.

Key words: Systemic lupus erythematosus; haemorrhagic manifestations; soft tissue haemorrhage.

Reumatismo, 2016; 68 (4): 199-202

INTRODUCTION

SLE is a frequently disabling autoimmune disease characterized by production of a vast array of autoantibodies and a variable clinical presentation. Early diagnosis can be difficult and often delayed because of the diversity in clinical manifestations. Haemorrhagic complications involving various systems can occur in SLE, but the actual mechanisms responsible are not well elucidated.

CASE REPORT

A 47-year-old woman was admitted after suffering fatigue and low grade fever for six months. She had no history of systemic hypertension and diabetes mellitus in the past. She had severe pallor, alopecia and bilateral symmetrical swellings over the anterior aspect of the forearms measuring 2x3 cms each which were firm in consistency, with no tenderness nor local rise in temperature. She gave no history of trauma or any vascular access on the forearm before hematoma. Fundoscopic examination showed multiple cotton wool spots and intra retinal haemorrhages (Figure 1). Haemoglobin was 7.7 g/

dL, MCV 74 fL, MCH 23 pg, MCHC 29 g/dL, total leukocyte count 5400/mL, platelet count $0.96 \times 10^9/L$, erythrocyte sedimentation rate 89 mm in 1 h and C-reactive protein was high. The haematocrit-corrected ESR level was 46 mm/h. In the peripheral smear, red blood corpuscles were microcytic, hypochromic, white blood corpuscles were normal and the platelet count was reduced. Serum iron was 30 $\mu\text{g/dL}$. The corrected reticulocyte count was 2.5%, direct and indirect Coombs tests were negative. Urinalysis showed no albumin with 2-4 leucocytes/high power fields. Biochemical parameters showed random blood sugar 101 mg%, urea 23 mg/dL, creatinine 0.7mg/dL, sodium 136 mmol/L, potassium 3.7 mmol/L, aspartate transaminase 36 IU/L, alanine transaminase 32 IU/L, alkaline phosphatase 47 IU/L, total bilirubin 1.1 mg/dL, direct bilirubin 0.1 mg/dL, total protein 8.3 g/dL, albumin 2.2 g/dL, globulin 6.1 g/dL. Chest X-ray and electrocardiogram were normal. HIV, hepatitis B and hepatitis C serologies were negative. Ultrasonography of abdomen was normal. Morning serum cortisol was 13.1 mg/dL. Bone marrow study showed normal myeloid series and megakaryocytes were increased in number

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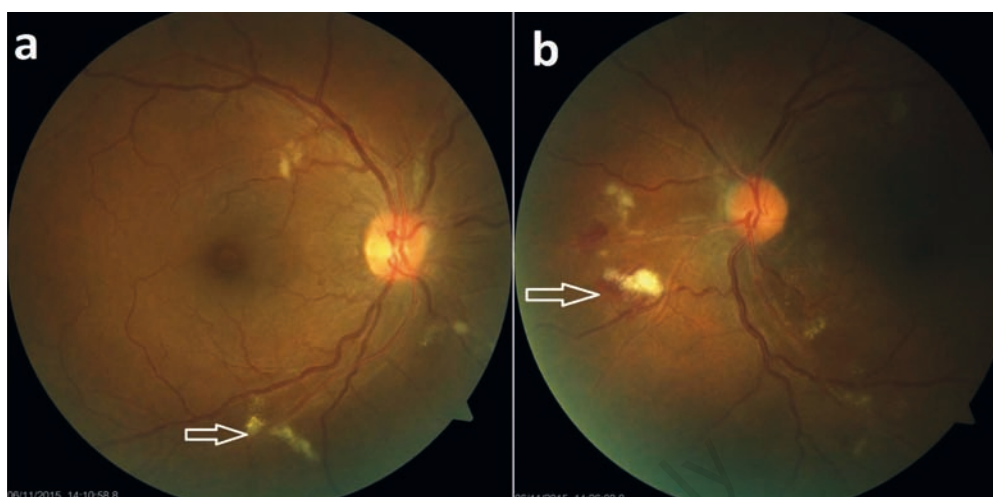


Figure 1 - Fundus photographs showing multiple cotton-wool spots (1a) and intraretinal haemorrhages (1b).

with normal maturation. Longitudinal ultrasonogram of forearms showed heteroechoic lesions bilaterally around elbow (2.1x1.5 cms on right and 1.6x1.0 cms on left) with vascularity outside the hematoma. Coronal T1 weighted magnetic resonance imaging of the forearm showed two well-defined iso-hyperintense lobulated hematomas on the right and one on the left in the intermuscular plane (Figure 2a and b). Axial gradient images showed a hypointense signal around the hematoma (blooming), suggestive of hemosiderin ring due to degradation of heme and a few hyper intense signals within suggesting liquefied components (Figure 2c and d). Prothrombin time and partial thromboplastin time were normal. The clotting factor assays including fibrinogen, factors VII, VIII and IX were also normal. Antinuclear antibody was positive (immunofluorescence method; titre 1:360) and anti double stranded DNA (semi-quantitative indirect fluorescent antibody method) was strongly positive. C3 and C4 levels were low (25 mg/dL and 6 mg/dL, respectively). IgG, IgM anticardiolipin antibodies, IgG and IgM anti-beta 2 glycoprotein and lupus anticoagulant tests were negative. A diagnosis of systemic lupus erythematosus with moderate lupus retinopathy and spontaneous bilateral soft tissue haemorrhage was made. She was started on methyl prednisolone 500 mg daily for 3 days fol-

lowed by oral prednisolone 40 mg daily; she became well and was sent home on oral steroids. Steroids were continued at a dosage of 40 mg/day for one month and then tapered over one month to a maintenance dosage 10 mg/day. When she returned for review after three months the size of the swellings was reduced and her steroid was tapered.

■ DISCUSSION AND CONCLUSIONS

Haemorrhagic complications involving various systems can occur in SLE, but the actual mechanisms responsible are not well elucidated. Haemorrhagic complications of SLE may be subdivided into two major groups: those related to aPL/APS and those unrelated. Major aPL/APS unrelated mechanisms may include the following.

Pulmonary alveolar haemorrhage is a rare complication (1), characterized by bland alveolar wall changes and is similar to the lupus microangiopathy of the kidney. Deposits of IgG, C3, or immune complexes have been found in up to 50% of patients with alveolar haemorrhage complicating SLE. Active nephritis with hypoalbuminemia after treatment with high dose steroids was found to be a major risk factor for severe pulmonary haemorrhage in a series of 13 cases of SLE (2). Various types of

intracranial and intraspinal haemorrhage; intracerebral, subarachnoid, subdural and epidural haemorrhages were reported in SLE (3). The proposed mechanisms causing nervous system haemorrhage include: hypertension, hypercholesterolaemia, prolonged corticosteroid medication, thrombocytopenia and changes induced by SLE (4). A patient with sequence of rare haemorrhagic complications in SLE at different sites including bilateral adrenal, subdural, soft tissue (scalp and orbit) haemorrhages was described previously (5). The patient had negative aPL antibodies but had thrombocytopenia. Autoantibodies may develop against coagulation factors altering their

function or promoting their rapid clearance in patients having autoimmune diseases, malignancies, pregnancy or advanced age (6). Acquired haemophilia or factor VIII deficiency, caused by factor VIII inhibitor antibodies is a rare condition which can cause haemorrhagic complications in SLE (7). SLE can cause bilateral adrenal haemorrhage secondary to antiphospholipid syndrome (APS) (8). Adrenal veins thrombosis in APS results in haemorrhagic infarction. The peculiar pattern of vascular anatomy of the adrenals with a rich arterial supply, but a limited venous drainage by a single vein, may favour the development of adrenal haemorrhage. Antiphospholipid antibody-

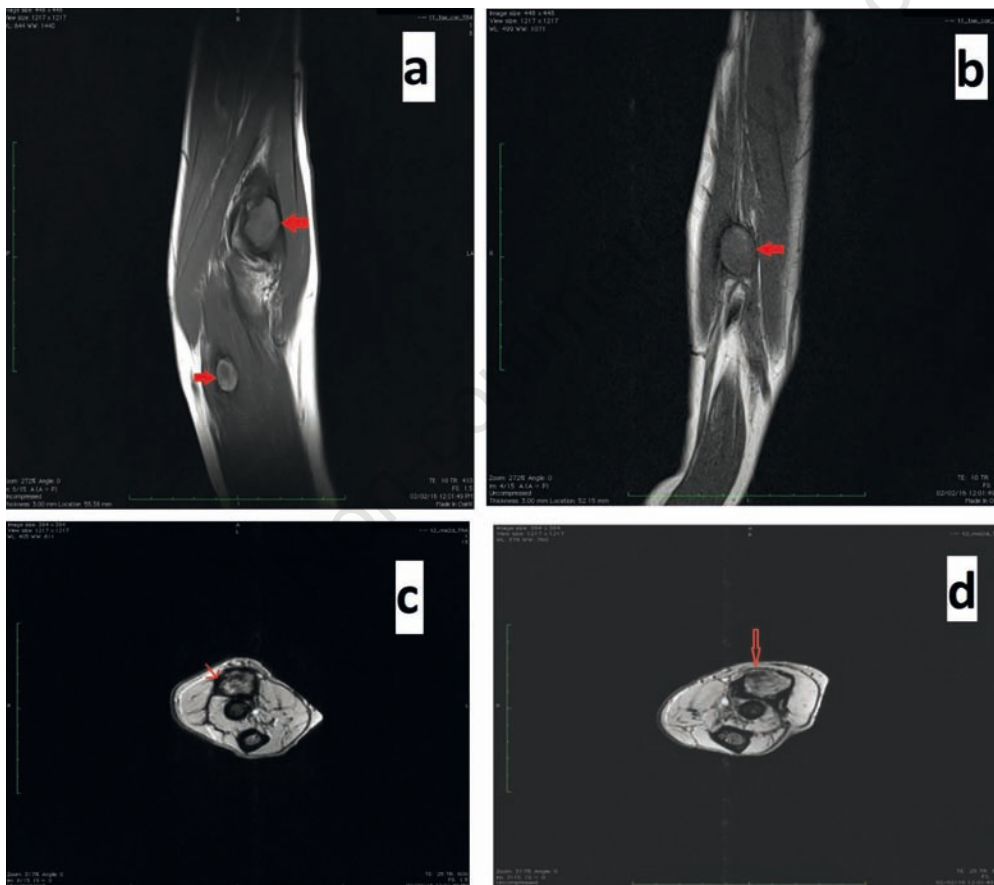


Figure 2 - Coronal T1W image of right elbow region showing two well-defined hematomas around elbow in intermuscular plane (2a). Coronal T1W image of left elbow region showing a hematoma around elbow in intermuscular plane (2b). Axial gradient image of right elbow showing hematoma. Hypointense signal around the hematoma 'blooming' (marked in solid red arrow) - suggestive of hemosiderin ring due to degradation of heme. A few hyperintense signals within signifying liquefied component (2c). Axial gradient image of left elbow shows 'hematoma' with blooming surrounding it (2d).

positive patients can develop bleeding due to capillaritis, microthrombosis, antiprothrombin antibodies, thrombocytopenia, and/or excessive antithrombotic therapy (9). Lupus anticoagulant-hypoprothrombinemia syndrome is the association of acquired factor II deficiency and lupus anticoagulant predisposing to severe bleeding in SLE (10). A 34-year-old woman having SLE with APS complicated simultaneously by thrombotic and haemorrhagic events presented with menorrhagia, gingival bleeding and hematoma in the psoas muscle was reported. Blood tests revealed a strongly positive lupus anticoagulant, factor XI deficiency and decrease of free protein S (11). Our patient had SLE with mild thrombocytopenia, negative aPL antibodies, normal prothrombin time, partial thromboplastin time and clotting factor assays, and had bilateral soft tissue and intraretinal haemorrhages. In both lungs and kidneys, the pathogenesis of the microvascular injury appears to be related to immune complex deposition and the induction of apoptosis. Since SLE patients are prone to develop haemorrhagic complications, the soft tissue haemorrhage in this case may be due to similar mechanisms compounded by thrombocytopenia.

Ocular manifestations of lupus are fairly common and may be the symptomatic feature of the disease. In the absence of presenting hypertension and diabetes cotton-wool spots representing microinfarcts of the retina due to precapillary retinal arteriolar occlusion are most often associated with systemic vasculitides such as lupus (12).

Haemorrhagic manifestations are extremely rare in SLE and can be either the presenting feature or occur after initiating treatment. We describe a case of SLE with bilateral soft tissue and intraretinal haemorrhages which responded well to treatment with steroids.

Compliance with Ethical Standards

Funding - nil

Conflict of Interest-nil

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical stan-

dards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors. Informed consent was obtained from the participants included in this study.

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