

## Acquired Protein S Deficiency in a Patient with Lupus Nephritis

Sir,

Protein S deficiency is a hypercoagulable state predisposing to thromboembolic complications in systemic lupus erythematosus (SLE) patients. In addition, lupus nephritis can expose to thrombosis through nephritic syndrome, especially when associated with membranous glomerulonephritis (MGN).<sup>[1]</sup>

A 44-year-old female who was diagnosed with SLE based on the American College of Rheumatology criteria (malar rash, photosensitivity, oral ulcers, nonerosive arthritis, leucopenia, positive antinuclear antibodies, and the presence of anti-DNA)<sup>[2]</sup> developed Class V glomerulonephritis 5 years later. This was treated with prednisone, angiotensin-converting enzyme inhibitors and azathioprine. In the subsequent 5 years of evolution, she had two relapses of glomerulonephritis, which required two further renal biopsies, showing the same histological lesions.

Then, a year later, the patient developed cyanosis and hyperalgesic paralysis of the left lower limb. The femoral pulse was absent. Blood pressure and cardiopulmonary examinations were normal. A thromboembolectomy using a Fogarty catheter was performed and the patient was further treated with subcutaneously administered heparin, which was subsequently relayed by oral anticoagulants. Microscopic hematuria was detected by Labstix test. Laboratory tests confirmed nephrotic syndrome (NS) with proteinuria (4.8 g/24 h), albuminemia (23 g/L) and protidemia (43 g/l); the renal function tests were normal. Test for antinuclear antibodies was positive and low complement (C3, C4, and CH50) levels were observed. Estimation of antiphospholipid antibodies and circulating lupus anticoagulant were negative. Laboratory evaluation of hypercoagulability revealed a reduced level of free protein S (37%), but the level of protein C was normal. Based on these findings, the authors concluded that the patient had a relapse of lupus nephritis concomitant with acute ischemia of the lower left limb. A third renal biopsy was performed, showing proliferative active glomerulonephritis (Class IV + V) associated with MGN along with severe vascular lesions. The patient was started on corticosteroids with intravenous cyclophosphamide pulses (a cumulative dose of 37 mg/kg) every 2 weeks,

followed by oral corticosteroids and mycophenolate mofetil (2 g/day). Since then, the patient remained in partial remission with no further thromboembolic complications.

In the presented case, the patient was diagnosed with multiple hypercoagulable states predisposing to thrombotic risk such as NS, MGN and protein S deficiency. NS is common in patients with lupus nephritis, and they are at a high risk of developing venous and arterial thromboembolism. The primary glomerular defect of NS results in the leakage of high molecular mass proteins, antithrombin and protein S.<sup>[3]</sup> Subsequently, the liver produces a high density of prothrombotic proteins.<sup>[4]</sup> Moreover, MGN can lead to thromboembolic complications independently of NS by injury of the glomerular basal membrane, including glomerular basement degradation.<sup>[5]</sup> Protein S is a vitamin K-dependent plasma anticoagulant protein and its deficiency leads to hypercoagulability syndromes. Several reports have shown that free functional protein S is markedly depleted in lupus because of excessive binding to the C4 binding protein.<sup>[6]</sup> In addition, in SLE, free protein S is decreased in patients with a history of serositis, neurologic, hematologic or immunologic disorder, especially those with low C3 and C4 protein level.<sup>[7]</sup> Similarly, our patient also presented with a low C4 level.

Here, the authors present a rare case of arterial thrombosis occurring in lupus nephritis accompanied by protein S deficiency with renal relapse, but no association to antiphospholipid syndrome.

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### Conflicts of interest

There are no conflicts of interest.

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