Iloprost treatment in large-vessel vasculitis during systemic lupus erythematosus

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During the clinical course of systemic lupus erythematosus (SLE) the onset of a vasculitic syndrome is possible, whose clinical expression can vary from minor signs and symptoms to severe, potentially life-threatening, ischemic manifestations. Lupus vasculitic lesions usually affect small-size vessels, whereas the involvement of medium and large size ones is rather uncommon (1). It can, however, lead to ischemic lesions of the extremities, particularly in the legs, and is often associated with thrombotic lesions and the presence of anti-phospholipid antibodies.

A 34-year-old woman, non-smoker and with no other risk factors for peripheral vascular diseases, suffering from SLE diag-nosed 16 years previously (the disease was characterised by arthritis, malar erythema, Raynaud's phenomenon, relapsing pericarditis, leucopenia and thrombocytopenia and the presence of ANA and double stranded (ds)DNA autoantibodies and was treated with different doses of prednisone and immunosuppressive therapies based on clinical features and laboratory findings observed over the years) was admitted to our clinic due to the sudden onset of pain and cyanosis in the left leg and foot. At that time, the patient was on hydroxychloroquine (400 mg/day) and low dose prednisone (5 mg/day). On clinical examination, some small necrotizing periungual lesions on the foot were noted, associated to hypothermia distal to the left knee and the bilateral absence of a peripheral pulse in the anterior tibial, posterior tibial and popliteal arteries. Malar erythema and arthritis of metacarpo-phalangeal and inter-phalangeal joints of the hands were observed. Laboratory blood tests revealed an increase in inflammation markers (ESR 52 mm 1 h, CRP 78.2 mg/L), a polyclonal hypergammaglobulinaemia, a reduction of the C3 and C4 (55 mg/dl and 8 mg/dl respectively) complement fractions, an increase of dsDNA (140 U/ml) and high ANA titre (1:360, homogeneous pattern) which suggested an active disease. Renal function tests, full blood cell count, total serum proteins, electrolytes, cholesterol, triglycerides and urine analysis and D-dimers were normal. The Lupus Anti Coagulant Test was negative, anti-phospholipid antibodies and ANCA were absent. Angiography-MRI showed areas of segmental stenosis of the popliteal arteries alternating with areas with a normal or dilated aspect, associated to a significant stenosis of the left anterior and posterior tibial arteries (Fig. 1). An ultrasound scan of the legs excluded venous thrombosis. Treatment with oral prednisone 25 mg/day, pulse cyclophosphamide (700 mg/m^2 monthly for 6 months) was started associated to 10 days of continuous intravenous infusion of iloprost (1.5/ng/kg/min), followed by monthly intravenous administration (1.5/ng/kg/min per 6 h/day for five consecutive days). One month after the beginning of treatment, the biological parameters had normalized and a significant clinical improvement in ischemic signs was observed. It is likely that iloprost played a critical role in determining this favourable outcome, as a single dose of cyclophosphamide, although given together with high doses of prednisone, is not enough to determine this rapid and dramatic resolution of occlusive vascular lesions.

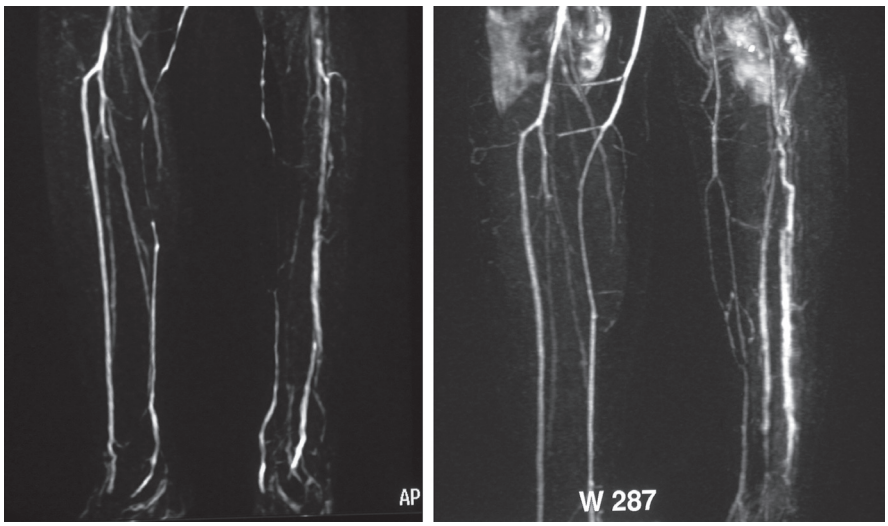

Fig. 1. Angiography-MRI before treatrment (**left panel**) showing areas of segmental stenosis of the popliteal arteries alternating with areas with a normal or dilated aspect, associated to a significant stenosis of the left anterior and posterior tibial ateries before treatment. Angiography-MRI performed after 6 months of treatment (**right panel**) showing a significant improvement in stenotic lesions in the vessels involved.

Clinical improvement was supported by anatomic findings evidenced by an angiography-MRI, performed 3 months later, in which a significant improvement in stenotic lesions in the vessels involved was observed (Fig. 1).

Occlusion of large vessels can occur during SLE because of anti-phospholipid antibodies or, very rarely, vasculitis. In cases with no thrombotic lesions and/or anti-phospholipid antibodies (which require anti-coagulant treatment as first choice therapy), early treatment with immunosuppressive drugs and high dose corticosteroids associated with vasodilators is able to control both vascular inflammation and the ischemic process. Iloprost is an analogue of natural prostacyclin (PGI_2) which is successfully used in the treatment of critical leg ischemia (2) and ischemic ulcers due to Raynaund's phenomena in connective tissue disease (3). As well as having a potent vasodilatory effect, the pharmacological activities of iloprost include anti-inflammatory properties such as leukocyte inhibition and reduction of TNF production (4) which further contribute to reducing the ischemic injury caused by vascular inflammation.

Although large vessel occlusion due to vasculitis has been described as an uncommon complication of SLE, its occurrence represents a life-threatening event which requires a rapid and correct diagnosis and appropriate therapy. Although very few reports on the efficacy of iloprost during vascular involvement in SLE have been published to date, the favourable outcome in the patient we have described suggests that early treatment with this drug, associated with conventional immunosuppresive and corticosteroid treatment, is useful to prevent irreversible complications such as gangrene and leg amputation.

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