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# Phlegmasia cerulea dolens in patient with systemic lupus erythematosus in the remote postpartum period

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## ABSTRACT

Vascular manifestations are not rare in systemic lupus erythematosus and, in most cases, are associated with antiphospholipid antibodies. Phlegmasia cerulea dolens is an unusual and severe complication of deep venous thrombosis of the lower limbs, which has a high mortality rate. In the literature, only two cases of phlegmasia cerulea dolens associated with primary antiphospholipid syndrome have been reported, but none associated with systemic lupus erythematosus. We report one case of phlegmasia cerulea dolens with rapid evolution to death in a patient with systemic lupus erythematosus in the remote postpartum period.

**Keywords:** systemic lupus erythematosus, postpartum period, thrombophlebitis.

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## INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease that can affect multiple systems and organs. Vascular impairment, both venous and arterial, is common and mostly associated with the presence of antiphospholipid antibodies.

In addition, pregnancy and postpartum period are known to increase the risk of thromboembolic events. Thus, pregnant patients with SLE are a group at high risk for thromboembolic phenomena. This risk is potentially increased in the presence of antiphospholipid antibodies.<sup>1</sup>

Patients with SLE should be carefully monitored during pregnancy and postpartum period because of the high likelihood of disease reactivation. In addition, it is during pregnancy, and mainly during the postpartum period, that the first symptoms of that complex disease often appear – a disease that still challenges researchers to elucidate its multiple manifestations.

The postpartum period, defined as the period from delivery of the placenta until the return of the female reproductive function, has a varied duration and is usually classified as immediate (up to 10 days), late (up to 45 days) and remote (after 45 days).<sup>2</sup>

We report a fulminant case of severe lower limb deep venous thrombosis (DVT) in a patient with SLE during the remote postpartum period.

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## CASE REPORT

The patient was a 31-year-old female of mixed heritage, undergoing treatment for SLE diagnosed four years prior to the current hospitalization, with joint, cutaneous, hematological, and renal manifestations, in addition to central nervous system impairment (lupus psychosis).

At the beginning, she had high titers for anti-DNA antibodies and negative titers on all occasions assessed for lupus

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anticoagulant and anticardiolipin antibodies. She had no history of thromboembolic events.

She was admitted at the emergency unit on the third postpartum month, complaining of fever and intense fatigue for 10 days. On physical examination, the patient was on poor general condition, pale, hemodynamically unstable, with pain and edema in the left lower limb.

The patient reported three pregnancies, the first two prior to the diagnosis of SLE, and all pregnancies ended in cesarean deliveries. Neither fetal loss nor episodes of venous or arterial thrombosis were reported. None of the three pregnancies had clinical intercurrent with either the patient or the newborn infants.

The last pregnancy was not planned and occurred during a period of SLE remission longer than one year, when the patient was on azathioprine (100 mg/day), which was withheld when pregnancy was diagnosed, hydroxychloroquine sulfate (400 mg/day), and low doses of prednisone. During pregnancy, only prednisone (10 mg/day) was maintained, and no complication was observed.

A cesarean delivery was performed, with complications to neither the patient nor the newborn infant. After discharge from the hospital, the patient missed all the scheduled postpartum visits.

Three months later, she had entered the emergency unit and was rapidly transferred to the Intensive Care Unit. The patient was pale, not cyanotic, on poor general condition, hemodynamically unstable, complaining of pain on the left calf accompanied by a significant volume increase and swelling. The pulses were present and symmetric.

The hypotheses of lupus activity and DVT in the left lower limb were raised. Blood analysis at hospital admission was as follows: hemoglobin, 7.0 g/dL; hematocrit, 21%; total leukocytes, 8,600/mm<sup>3</sup>; platelets, 2,000/mm<sup>3</sup>; creatinine, 2.2 mg/dL; positive ANA, 1:640, homogeneous pattern; positive anti-dsDNA, 1:80. Other autoantibodies, complement levels, and anti-B2GP1 were not assessed. Urinalysis evidenced proteinuria, hematuria and cylindruria, and her D-dimer test was positive. Changes were evidenced on neither the echocardiogram nor chest X-ray. The lupus anticoagulant and anticardiolipin antibody tests were negative.

The patient was treated with volume replacement, vasoactive drugs, antibiotics, heparinization, and pulse therapy with methylprednisolone. She evolved with persistent hemodynamic instability, worsening of her general state of health, significant increase in pain and edema in the entire left lower limb, cyanosis in left foot, appearance of phlyctenae with serosanguineous fluid, and progressive worsening of cardiovascular perfusion.

Phlegmasia cerulea dolens (PCD) was diagnosed, and venous thrombectomy with Fogart catheter indicated. However, it could not be performed, due to the fast worsening of her clinical findings.

The patient evolved with sudden dyspnea, respiratory arrest, and death 12 hours after hospital admission, probably due to pulmonary embolism. No postmortem examination was performed.

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## DISCUSSION

DVT is one of the most common vascular diseases. It is characterized by limb edema associated with capillary flow impairment, which increases pressure in the affected limb, leading to venous hypertension, and, more rarely, to ischemia of the limb.

The most common complications include chronic venous insufficiency and postphlebotic syndrome. Other more rare, but dramatic, complications are phlegmasia alba dolens (PAD) and PCD, and both can evolve to wet gangrene.<sup>3</sup>

PAD affects the lower limbs during pregnancy, evolving with intense paleness of the limb (“white as milk”). Its pathophysiology is complex, but the limb edema basically leads to increased pressure in the soft tissues, with consequent increase in capillary pressure. Ischemia occurs only in the presence of impaired capillary flow.<sup>4</sup>

PCD is a serious and rare complication of iliofemoral DVT. PCD has an equal incidence in both genders, is more common in the sixth decade of life, and more frequently affects the lower limbs, although in 5% of the cases the upper limbs can be affected.<sup>4</sup>

The affections most frequently associated with PCD are malignant neoplasias and severe heart failure.<sup>5</sup> However, the following affections have been more rarely reported: primary antiphospholipid syndrome;<sup>6-8</sup> femoral vein catheterization; abdominal aortic aneurysm and hypercoagulability situations;<sup>8</sup> and, even much rarer, heparin-induced thrombocytopenia thrombosis syndrome.<sup>9</sup>

The cases of PCD associated with lupus anticoagulant antibodies reported in the literature<sup>6-8</sup> are cases of primary antiphospholipid syndrome, which do not meet the diagnostic criteria for SLE, both with deep thrombosis of the lower limbs and good evolution with clinical treatment.

In PCD, the extensive iliofemoral venous thrombosis causes almost total venous occlusion. The limb becomes ischemic, extremely painful and cyanotic (a pathognomonic signal). Complete stasis of the venous flow leads to severe edema, which can interrupt arterial flow, resulting in gangrene.

PCD has high morbidity and mortality rates, requiring limb amputation in several cases. This condition falls under the concept described in the literature as “severe venous disease”,<sup>5</sup> which requires more aggressive interventions at the early phases of disease, aiming at avoiding major complications, such as gangrene and pulmonary embolism.

Despite the reports of PCD regression by use of heparin alone, it seems a consensus in the literature that a more aggressive therapy improves the prognosis of patients. Several modalities of intervention, such as surgical venous thrombectomy,

fasciotomies, placement of a filter in the inferior vena cava, and use of thrombolytic agents, have been reported.<sup>5</sup>

In the case reported, although the diagnosis of PCD has been established in an early phase, the severity of the SLE clinical findings might have contributed to the rapid unfavorable outcome. The association of the inflammatory activity of the underlying disease with the postpartum hormone alterations was a factor that certainly contributed to the occurrence of DVT, which evolved catastrophically to PCD and death.

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