

# Porphyria cutanea tarda and systemic lupus erythematosus

## Porfíria cutânea tarda e lúpus eritematoso sistêmico

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**Abstract:** The co-existence of systemic lupus erythematosus and porphyria although rare has been known for a long time. This association forces the physician to make a careful differential diagnosis of the bullous lesions that might appear in such patients and to be careful when prescribing certain drugs such as chloroquine. This drug, when used in the regular doses for treating lupus, may cause hepatotoxicity in patients suffering from porphyria. It is described here the case of a patient with lupus who developed bullous lesions compatible with porphyria cutanea tarda.

**Keywords:** Antibodies, antinuclear; Lupus erythematosus, systemic; Porphyrias; Porphyria cutanea tarda

**Resumo:** A associação de lúpus eritematoso sistêmico e porfíria, embora rara, é conhecida de longa data. Ela obriga o médico a realizar um cuidadoso diagnóstico diferencial das lesões bolhosas nesses pacientes e tomar cuidados com a prescrição de certas drogas, como a cloroquina. Esta, nas doses habituais para tratamento do lúpus, pode causar hepatotoxicidade em pacientes com porfíria. Descreve-se o caso de uma paciente com lúpus que desenvolveu lesões bolhosas compatíveis com porfíria cutânea tardia.

**Palavras-chave:** Anticorpos antinucleares; Lúpus eritematoso sistêmico; Porfíria cutânea tardia; Porfírias

Systemic lupus erythematosus (SLE) can present itself initially with cutaneous manifestations. This happens with around 23% of the cases.<sup>1</sup> In 3/4 of the patients with this collagenosis there will be some kind of cutaneous manifestation that can present proteiform features such as formation of bullae.<sup>1</sup> The bullous lesions of lupus are chronic and disseminated, they do not leave scars and they are located in the sub epidermal portio. However, they are rare affecting less than 5% of patients.<sup>1</sup> So, when a patient with SLE presents bullous lesions it is necessary for his/her doctor to make a careful differential diagnosis before ascribing such lesions to lupus.

It is reported here the case of a 45 year-old woman with SLE and disseminated bullous lesions that had the diagnosis of associated Porphyria Cutanea Tarda (PCT). This patient suffered from SLE

since she was 30 when she started to have arthritis, fever, photosensitive rash and feet vasculitis. At this time proteinuria was found but the patient declined renal biopsy being treated with prednisone, 60 mg/day with good response. The dosage of corticosteroids was decreased and it was lost track of the patient who kept using the medication irregularly. She returns complaining about the onset of bullae in areas that were exposed to sunlight. According to the patient, this had been happening for 18 months. She also reported general pain, and darkening of the skin and of the color of the urine described as "yellowish". She had used an infusion made of multiple herbs recommended by acquaintances.

In the physical examination pressure level was 120x80 mm Hg; and body temperature 37°C. The patient was icteric and pale but in general good con-

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dition. Facial hypertrichosis was present as though as a darkened skin and there were tense bullae on the region exposed to sunlight and multiple scars of previous lesions. Articular, lungs, heart and abdomen exams were normal. (Figure 1)

Laboratory tests showed the following results: SGOT: 531 U/L (RV: 5-34 U/L); SGPT: 413 U/L (RV: 0-55 U/L); TB (Total Bilirubins): 10 mg/dL (RV <1.2 mg/dL); DB (Direct Bilirubins): 9.3 mg/dL (RV <0.5 mg/dL); IB (Indirect Bilirubins): 0.7mg/dL (RV <0.8 mg/dL); alkaline phosphatase: 220 U/L (RV: 40-150 U/L); GGT: 92 U/L (RV: 9-36 U/L); albumin=3.7 g/dL (RV: 3.5-5.0 g/dL); Coagulation APT 90% (RV: 70-90%), HBsAg (Hepatitis B) negative, HIV (Human Immunodeficiency Virus) , HVA (hepatitis A) and HVC (hepatitis C) serology were negative. Serum iron: 98 ug/dL (RV: 25-156 ug/dL); transferrin saturation: 31.28%; creatinine: 0.62ng/dL (RV: 0.60-1.10 ng/dL); HSV (Hemo Sedimentation Velocity): 20 mm/hour (RV: 0-20 mm/hour), hematocrit =37% (RV: 36-47 %). Ferritin: 497.68 ng/mL (RV: 6-159 ng/mL); ANF (Anti-Nuclear Factor) level was 1:1280; homogeneous pattern. Antibodies anti-Ro were positive but anti-cardiolipin, LAC, anti-Sm, anti-DNA, anti-smooth muscle, anti-LKM and anti-mitochondria were negative. Dosage of Complements resulted in CH50: 43U CAE (RV: 60-144U CAE), C4: 9.3 mg/dL (RV: 10-40 mg/dL) e C3: 94 mg/dL (RV: 90-180 mg/dL) and proteinuria level in 0.13g/24hours; (RV: <0.15g/24hours).

Coproporphyrins and uroporphyrins were positive and the free protoporphyrins level was 468,2 g/dL (VR up to 60m g/dL). A tomography of the abdomen showed increase in splenic vein with slight splenomegaly. Biopsy showed epidermis with orthokeratosis and moderate regular acanthosis with infra basal cleft, a delicate basal membrane (PAS with digestion) and a superficial dermis with edema (Figure 2).

Jaundice disappeared gradually, without treat-

ment, and it was observed the normalization of the hepatic function

With the diagnosis of SLE and PCT the patient was treated with photo protection and sporadic bleedings every 2 weeks. The bullous lesions and musculoskeletal pain disappeared. After the normalization of the hepatic function checked by blood tests it was initiated treatment with chloroquine 150mg/twice a week.

The association of SLE and other bullous diseases such as pemphigus, bullous and cicatricial pemphigoid, dermatitis herpetiformis, child bullous dermatitis and acquired epidermolysis bullosa is recognized.<sup>2</sup> As for porphyria this association was found in 1952, when Wolfram and cols.<sup>3</sup> described the case of a patient with SLE that later developed acute intermittent porphyria. Since then it was recognized not only the association of systemic lupus with different types of porphyria but also of discoid lupus and sub acute lupus.<sup>3</sup> A study from the Mayo Clinic comprising 676 cases of porphyria followed for a period of 20 years showed that SLE was present in 2.2% of them.<sup>4</sup>

The reasons of the association between SLE and porphyria are unknown. Harris and cols.<sup>5</sup> proposed that porphyria can trigger an immune response favouring SLE. The accumulation of porphyrins causes activation of the complement system and increases neutrophil chemotaxis when there is exposure to ultraviolet rays.<sup>6</sup> Besides that, porphyrins are toxins that causing tissue damage release auto antigens that will serve as a source for antibody formation.<sup>6</sup> Allard and cols. carried out a study with 38 patients with porphyria and in 8 of them antinuclear antibodies were found. However, only one of them presented signs and symptoms of SLE.<sup>7</sup> Griso and cols. verified the presence of FAN in 12% of 158 patients with porphyria but they correlated this finding to aging or liver disease.<sup>8</sup> The explanation that cell destruction induced

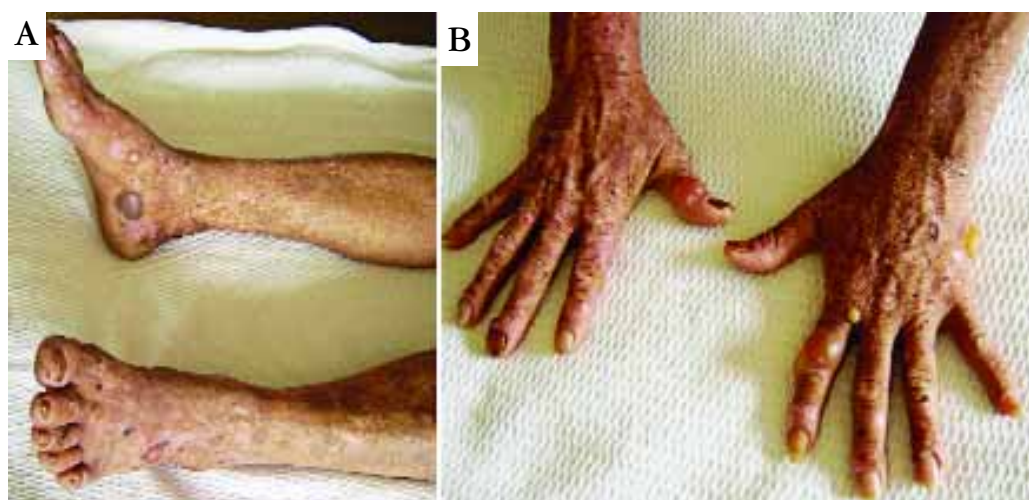


FIGURE 1 (A, B): Tense bullae on hands and feet of the patient

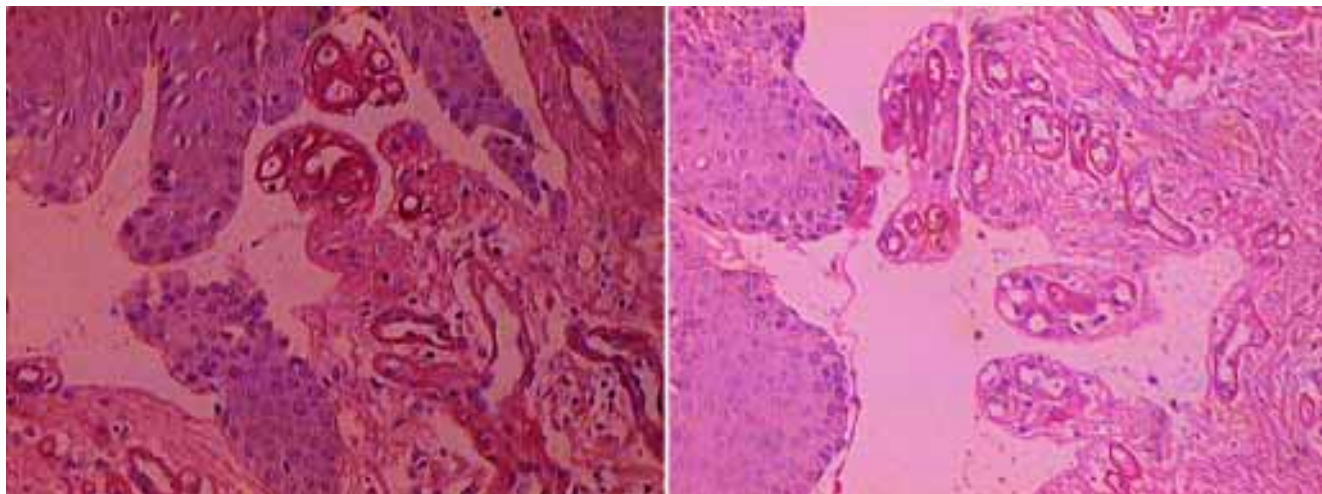


FIGURE 2: Histological section of skin biopsy sample showing bullae in the infra basal region

by porphyria stimulates the immune system causing SLE does not apply to the case described where the diagnosis of SLE preceded the diagnosis of porphyria for many years. Both SLE and porphyrias have a predisposing genetic component situated in the same chromosome. The gene for the decarboxylase of the uroporphyrinogen, the enzyme deficient in cases of PCT, is located in chromosome 1(1p34) and the region 1q41-1q42 has been associated with SLE.<sup>9</sup>

Although uncommon the association between porphyria and lupus deserves attention mainly because of the use of certain medications. Anti malaria, medication largely used for SLE, if prescribed in its full dose can lead to a massive porphyrinuria with fever, nausea and increase of the hepatic enzymes and some cases of hepatic necrosis.<sup>10</sup> □

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