Postinfectious purpura fulminans: A case report

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ABSTRACT

Acquired postinfectious purpura fulminans is a rare, acute, and severe disease characterized by skin necrosis associated with disseminated intravascular coagulation (DIC) in the absence of active infection or previous coagulation disorders. It mainly affects the pediatric population and, in 90% of cases, it is preceded by an infectious process. The pathophysiological mechanism is a transient autoantibody-mediated protein S deficiency that favors a hypercoagulable state.

Here we describe the case of a previously healthy 8-year-old boy with purpuric skin lesions typical of purpura fulminans associated with DIC in the absence of sepsis. A transient plasma protein S deficiency was confirmed. He required replacement therapy with fresh frozen plasma and anticoagulation; he had a favorable course. Protein S activity remained decreased for 2 months.

Keywords: protein S deficiency; purpura fulminans; disseminated intravascular coagulation.

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INTRODUCTION

Purpura fulminans (PF) is a rapidly progressive disorder in which microvascular thrombosis and hemorrhagic infarction of the skin associated with disseminated intravascular coagulation (DIC) occur.¹

Postinfectious purpura fulminans mainly affects children, is associated with transient autoimmune depletion of protein S or protein C and, in most cases, develops during the convalescent phase of an infection; the most frequent include varicella (30%) and streptococcal infection (20%).²⁻⁵

It is characterized by the sudden development of erythematous-violaceous macules that progress rapidly with the development of blood blisters and areas of central, symmetrical skin necrosis, predominantly on the lower limbs, in the absence of clinical signs of sepsis. The diagnosis is made based on clinical findings and confirmed with a hemostasis test with DIC parameters and detection of a transient decrease in plasma protein S levels.¹,² The prognosis is variable, depending on the extent and course of the skin lesions and the development of systemic thromboembolic phenomena.²,³

CASE REPORT

An 8-year-old male patient, with no relevant personal or family medical history, consulted due to purpuric lesions on the lower limbs for the past week, with progression in the past 72 hours, associated with edema and severe pain. The only relevant history was odynophagia 10 days prior to symptom onset.

On admission, he did not have fever and was in good general condition. He had purpuric macules and plaques with diffuse boundaries on the anterior and posterior side of both lower limbs (Figure 1) and multiple tense blood blisters, whose content had a stellate appearance, on the left leg plate (Figure 2). The presumptive diagnosis was purpura fulminans versus Henoch-Schönlein bullous purpura, so the patient was hospitalized for study and management.

Lab tests, cultures and skin biopsy (light microscopy, direct immunofluorescence –DIF– and cultures) were performed.

The initial hemostasis test showed parameters compatible with DIC: thrombocytopenia (130 × 10⁹/L), prolonged prothrombin time (PT < 10%) and partial thromboplastin time (aPTT > 240 s), severe hypofibrinogenemia (FI 25 mg/dL), decreased factor V (23%), and increased D-dimer (25.6 μ/L). The white blood cell count and differential count were normal, as were the liver and kidney function tests.

On the second day of hospitalization, the baseline sample result showed severe protein S deficiency (5% activity; median of reference value for age: 78% [range: 41% to 114%]) with positive IgG and IgM anti-protein S antibodies and determination of protein C and antithrombin (AT) within reference values for age.

**Figure 1. Skin lesions in lower limbs**

A and B: Erythematous-violaceous macules and plaques, symmetrically located on both lower limbs, with involvement of extensive areas, leaving areas of healthy skin.
HIV serology and cultures performed on admission (blood, urine, and nasopharyngeal) were negative, and the skin culture was negative for common germs and fungi. A Doppler ultrasound of the lower limbs helped to rule out the presence of arterial or venous thrombosis. Due to the history of odynophagia prior to the onset of his clinical condition, antistreptolysin O (ASTO) antibody levels were measured and found to be elevated (493 IU/mL).

The histopathological examination of the skin biopsy showed leukocytoclastic vasculitis with numerous fibrinoid thrombi (Figure 3); negative DIF for IgA, IgM, IgG, and complement and positive for fibrinogen.

During the first week, the lesions showed progression of blood blisters and skin necrosis (Figure 4), so an escharotomy with debridement of necrotic lesions and vacuum-assisted closure (VAC) therapy, followed by skin grafting
in that area, were performed.

New samples were sent for histopathological examination, which showed the absence of epidermis, thrombi inside the small vessels in the papillary dermis, perivascular inflammatory infiltrate, fibrinoid necrosis, and red blood cell extravasation. All these were typical findings of PF.

Thus, given the clinical manifestations and course of the patient, together with the histopathological findings and the ancillary studies, the diagnosis was PF associated with an autoimmune protein S deficiency with positive anti-protein S antibodies, secondary to a previous streptococcal infection.

During hospitalization, the patient received empiric antibiotic treatment with intravenous ceftriaxone (for 6 days), clindamycin and vancomycin (for 14 days), transfusion of platelets and fresh frozen plasma; his laboratory parameters improved, so that, on the second day of hospitalization, he started anticoagulant therapy with sodium heparin for 72 hours; he was then switched to enoxaparin. The total length of his stay was 24 days. His parents were studied and hereditary protein S deficiency was ruled out. During his outpatient follow-up, he continued receiving anticoagulant therapy with acenocoumarol for 4 months, with protein S levels within normal values for his age at 2 months after the onset of the clinical condition.

DISCUSSION

PF is a hematologic emergency characterized by rapidly progressive purpura and necrosis of extensive areas of the skin, associated with DIC. The prevalence of PF in children ranges from 0.05% to 0.16%. It manifests in 3 clinical situations: in newborns with congenital (homozygous or double heterozygous) protein C or S deficiency (neonatal PF); in the context of severe acute infection, typically meningococcemia, although it has also been described in sepsis due to S. aureus, S. pyogenes, S. pneumoniae, H. influenzae, and gram-negative bacteria (acquired infectious PF); and, in the absence of acute infection, in association with a transient autoimmune protein S deficiency (acquired postinfectious PF). In most cases, the postinfectious type appears during the convalescent phase, usually 7 to 10 days after an infection, as observed in our patient. It has been proposed that it may be caused by cross-reactivity between the infectious agent and protein S through molecular mimicry.

This condition manifests clinically as well-defined erythematous-violaceous macules that rapidly progress with the development of areas of central skin necrosis, with stellate borders and surrounded by an erythematous halo. During its course, tense blood blisters may appear, which may involve extensive areas of the skin. It usually affects the buttocks, thighs, and calves symmetrically.

Skin lesions appear suddenly and progress rapidly, but in the absence of clinical signs of sepsis, unlike infectious purpura. It is accompanied by a hypercoagulable state secondary to a transient protein S or C deficiency.

The rapid clinical progression correlates to

**Figure 4. Blood blisters and skin necrosis**

*Tense blood blisters with central necrotic area, surrounded by macules and some purpuric plaques.*
histological findings; extensive venous thrombosis of the dermis with hemorrhagic infarction of adjacent tissues, presence of microthrombi causing capillary dilatation, and red blood cell congestion are observed in the early stages of PF. In more advanced stages, fibrinoid necrosis with red blood cell extravasation in the dermis and leukocytoclastic vasculitis phenomena are observed.

The diagnosis is made based on compatible clinical manifestations associated with DIC and the detection of low plasma protein S levels. The decrease in protein S is transient and the time to recover normal levels for age will depend on the gradual decrease in autoantibodies; usually 1 to 3 months.

In the case of our patient, due to the skin lesions he presented, Henoch-Schönlein bullous purpura was considered as the initial differential diagnosis because of the presence of palpable purpura and blisters; however, it does not cause skin necrosis and the progression of the clinical condition is usually slower.

The prognosis is variable, depending on the extent and course of the skin lesions and the development of systemic thromboembolic phenomena.

Treatment during the acute phase is targeted at controlling DIC and preventing the progression of thrombosis. For this purpose, transfusion support is suggested based on lab tests and the patient’s bleeding manifestations. When clinical and laboratory conditions allow it, anticoagulant therapy with unfractionated or low molecular weight heparin should be initiated. Antithrombotic therapy reduces the risk of progression of existing lesions or the development of new manifestations.

In case of progression while receiving anticoagulant therapy, plasma exchange may be considered.

Extensive skin necrosis may compromise deep tissue requiring surgical debridement, fasciotomy, or amputation. For this reason, a multidisciplinary patient follow-up, including plastic surgery and orthopedics healthcare teams, is critical for an early treatment and rapid rehabilitation.

The risk of the onset of new thrombotic complications is associated with the persistence of decreased protein S levels, so the recommendation is to maintain anticoagulant therapy until normalization.

To conclude, we highlight the importance of suspecting postinfectious purpura fulminans as a diagnosis in a patient in good general condition, with no signs of sepsis, who presents with rapidly progressive purpuric skin lesions, with DIC and protein S deficiency, and the presence of anti-protein S antibodies. Although it is a rare condition, without an early recognition and an adequate treatment, its morbidity and mortality are high.

REFERENCES