Congenital homozygous protein S deficiency revealed by neonatal purpura fuminans

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To the Editor:

Neonatal purpura fulminans in congenital homozygous protein S deficiency is a rare autosomal recessive inherited condition characterized by rapid extensive skin necrosis occurring within hours after birth of a newborn initially in good general condition and without signs of sepsis. In the absence of early diagnosis and rapid and adequate management, the course is rapidly fatal with the risk of disseminated intravascular coagulation (DIC). We report a newborn with fatal disseminated intravascular coagulation in the context of a protein S deficiency.

A new-born male infant from a consanguineous marriage presented with large ecchymoses on the body a few hours after his birth (**Figure 1**). Our initial clinical impression included infectious purpura fulminans and antibiotic therapy with intravenous cephalosporins was started. However, the infant's general condition was atypical for sepsis. Laboratory assessments for infection were subsequently negative, including lumbar puncture and blood cultures. Hematologic assessment revealed thrombocytopenia at 55,000/mm^3, a spontaneously low prothrombin level at 36%, prolonged activated partial thromboplastin time (TCA), and hypofibrinogenemia. The tests for antiphospholipid antibodies were negative. Protein C activity and antithrombin III were normal and testing for resistance to protein C was negative. In contrast, protein S activity was 10%, favoring a congenital protein S deficiency associated with DIC. The newborn benefited from the infusion of fresh frozen plasma and the injection of vitamin K but unfortunately, improvement was not sustained and the evolution was quickly fatal.

Neonatal purpura fulminans is a clinico-pathological entity characterized by rapidly progressive hemorrhagic necrosis of the skin and disseminated intravascular coagulation [1]. It is a diagnostic and therapeutic emergency. The pathophysiological mechanisms include vasomotor disorder or occlusions of the arteriolar lumen by embolic or thrombotic mechanisms. The infectious origins common at this age, especially meningococcal infection, is often feared first and treated immediately. Exceptionally, there are cases of purpura fulminans related to congenital deficits in C and S coagulation proteins [2,3]. Protein S is a vitamin K dependent plasma protein with anticoagulant activity catalyzed by activated protein C. It is a physiological inhibitor of coagulation discovered in Seattle in 1977. It is involved as a cofactor of protein C in the inhibition of activated coagulation factors V and VIII, but also by other direct mechanisms. The frequency of congenital protein S

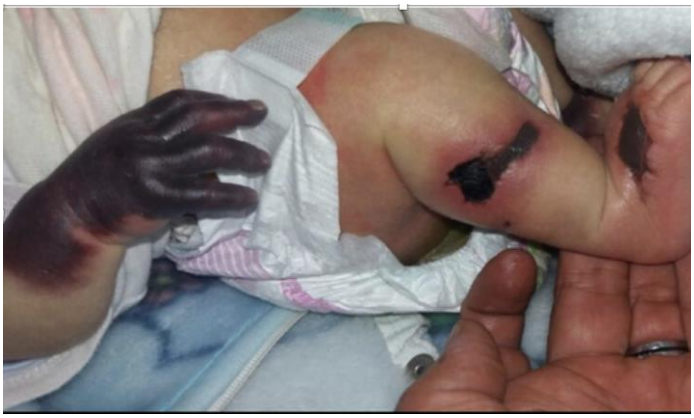

Figure 1. *Necrotic plaques of the body in a newborn.*

deficits range from 0.03% to 0.13% in the normal population and 1 to 5% in subjects with a history of venous thrombosis. These are usually heterozygous deficits with levels of protein S most often between 40 and 60% responsible for a picture of thrombophilia. A few cases of homozygous protein S deficits, as in our patient, have been reported with a picture of neonatal purpura fulminans [4].

Administration of fresh frozen plasma does not restore sufficient protein S levels, but it is often given for this purpose when there is a lack of protein S concentrate [5,6]. The protein C deficiency, which is more frequent, gives the same clinical picture with neonatal purpura fulminans, venous thrombo-embolism, and disseminated intravascular coagulation. Treatment is based on supplementation with intravenous purified plasma-derived protein C concentrate [7-9].

The diagnosis of homozygous protein C or S deficiency should be suspected in any newborn with skin necrosis, particularly if the newborn is otherwise in good general condition without signs of sepsis.

Potential conflicts of interest

The authors declare no conflicts of interest.

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