Case Report

NEONATAL PURPURA FULMINANS IN A NEONATE WITH PROTEIN C DEFICIENCY

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ABSTRACT

We report a neonate who developed purpura fulminans shortly after birth. The patient was diagnosed to be homozygous for protein C deficiency (less than 1% activity). He was initially treated with fresh frozen plasma, then oral warfarin was administered. All necrotic skin lesions improved with treatment. He was the first offspring of his first cousin parents, who both were discovered to be asymptomatic heterozygous for protein C deficiency. None of the family members had history of thrombotic or bleeding episodes.


Key Words • Purpura fulminans • protein C deficiency, neonatal

Introduction

Purpura fulminans is a variant of disseminated intravascular coagulopathy (DIC) that occurs in children during or just after a bacterial (most often meningoccal or streptococcal) or viral (most often varicella) infection. It’s characterized by the sudden onset of tender ecchymosis. The acral portions of the body are most severely involved. Individual ecchymotic lesions may blister, but rapidly progress to necrosis and gangrene and shock. Coma and death may ensue. A neonatal form of purpura fulminans secondary to protein C (PC) deficiency is also recognized. 1

Protein C is a vitamin K dependent glycoprotein. When activated by the thrombin-thrombomodulin it becomes a protease that inhibits factor VIIIa and Va, which enhances fibrinolysis. 2 PC deficiency was first described in 1982. 3 To the best of our knowledge, no previous reports of homozygous PC deficiency from Iran exists in literature. However, there are at least 20 cases reported in the United States and Europe. 4,5

Case report

A neonate was transferred to our hospital due to an episode of GI bleeding and progressive skin necrosis with gangrene of left-hand fingers at the age of 6 days. The lesions appeared shortly after birth. The patient had an uneventful cesarean section birth, weighing 2700-gram. He was the first offspring of his symptom free parents, who were first cousins. There was no family history of any thrombotic or bleeding disorder.

Despite necrotic lesions, the baby appeared well and continued to feed well. Laboratory values were Hb: 9.4g/dL; WBC count: 14.9 \(10^9\)/L; platelet count: 79 \(10^9\) L; PT: 15 sec (80% activity); and PTT: 60 sec.
The patient was initially treated with vancomycin, ceftazidime, packed cell and FFP transfusion. At 7 days of age the patient had a generalized convulsion. Calcium was 5.6 mg/dl, therefore, intravenous calcium gluconate was added to his regimen. Blood glucose and urea, serum sodium and potassium were normal. CSF, brain CT scan and EEG were normal. In spite of treatment and the well appearance of the baby, skin lesions continued to progress (Figure 1). Testicular swelling with ecchymotic skin was also noted. In ultrasonographic examination it was suspected to be hemorrhage.

With a suspected diagnosis of PC deficiency, infusion of FFP 10 ml/kg every 12 hours was initiated. This rapidly led to regression of the cutaneous lesions. The baby was being treated with FFP and packed cell, therefore, the parents were checked for protein C and S levels. Both had normal protein S levels, however, the mother had 71% and the father 68% of PC (reference range 70-130%).

Ten days after antibiotic therapy was begun when there were no positive cultures, antibiotics were discontinued. To facilitate a gradual decrease in FFP transfusions, and also to carry outs test for PC, warfarin was administered orally. In order to check his PC level, prior to FFP infusion a blood sample was obtained to determine PC levels. His PC level was less than 1%. We gradually increased the intervals between FFP infusions. When FFP intervals became 4 day, ecchymotic lesions were seen along with eye leukocoria. Increasing FFP infusions seemed obligatory.

The patient was discharged from hospital at the age of 56 days. He is now 3 months old and taking warfarin and FFP infusion every 5-7 days. Unfortunately the fingers on his left-hand were amputated, and his left eye leukocoria has failed to improve due to his parents failure to continue treatment after discharge.

Discussion

Homozygous PC deficiency is a rare genetic defect that usually results in fatal thrombotic complications.4 It usually presents with neonatal purpura fulminans. These present as widely distributed areas of progressive skin necrosis and microvascular thrombosis over the body. The lesions appear mainly on the extremities but have been found on the buttocks, abdomen, scrotum, and scalp. Lesions may also develop at pressure points and also at sites of previous punctures. The areas become dark red, then purplish black with bullae. With time they become necrotic and gangrenous, sometimes resulting in loss of the extremities.6 In addition cerebrovascular occlusive accident,7 intraventricular hemorrhage,8 and ophthalmic manifestation such as vitreous hemorrhage and retinal artery thrombosis may present.6,9 Other (renal and GI) arterial or venous thromboses have been reported.6 There are also some reports of asymptomatic homozygous PC deficiency even in adults.10

The age at onset of the first symptoms ranges from 1 or 2 hours to 5 days after birth, with the majority of symptoms occurring about 2 to 12 hours after birth.6

For confirmation of homozygous PC deficiency in a neonate with purpura fulminans, the infant should have no detectable PC levels (less than 1%), and both parents should be heterozygous for PC deficiency.6 Since there are many consanguineous marriages in Iran, there should be greater awareness of this treatable autosomal recessive disorder.

At the onset of symptoms, the initial treatment should be plasma until all lesions have healed. Two modalities of long term treatment are accepted: oral anticoagulation, maintaining the PT 1.5-2 times control values or PC concentrate replacement. Liver transplantation has been performed successfully in one child.11 Today, administration of PC concentrate is the acute, as well as, long term therapy of
choice. Due to hazards related to prolonged venous access, PC concentrate is currently being used a subcutaneous infusion, for the long-term management of this condition, with satisfactory results.5,12,13

References