

# Protein C deficiency in a neonate with purpura fulminans

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## Abstract

We report a case of a neonate who developed bilateral intracerebral haemorrhage and purpura fulminans shortly after birth. The baby was diagnosed to have Protein C deficiency. He was initially treated with fresh frozen plasma. All necrotic skin lesions improved with treatment. He was the second baby of his first cousin parents who were discovered to be asymptomatic heterozygotes for protein C deficiency. The first offspring died with a history of gastroenteritis at one year of age.

## INTRODUCTION

Protein C deficiency is usually inherited as an autosomal dominant trait associated with an increased risk of venous thrombosis and caused by mutations in the Protein C gene<sub>1</sub>. 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, its deficiency was first described in 1982<sub>2</sub>. Deficiency of protein C is extremely rare although the genotype and phenotype have not been described in detail in all of them<sub>3</sub>.

## CASE REPORT

We describe here a term newborn that has homozygous protein C deficiency which led to a neonatal purpura fulminans like syndrome. The patient was delivered by an emergency caesarean section due to fetal distress. She was born flat with meconium stained liquor and was immediately intubated and meconium was suctioned from below the cord. Her apgar score was 4 at one minute and 8 at five minutes. She was admitted to the neonatal unit and started on intravenous antibiotics and discontinued after 48 hours following negative blood cultures. Her complete blood count was normal except for a platelet count of 75. On day 2 she developed abnormal movements of the upper and lower limbs which were diagnosed as neonatal seizures for which the baby was started on phenobarbitone. Repeat complete blood count on day 2 was normal apart from platelet count of 39 and coagulation screen with INR of 1.98 and normal PT and PTT. Platelet transfusions were given every 12 hours for 48 hours. Brain ultrasound on day 3 of life showed bilateral intracerebral haemorrhage with no

intraventricular haemorrhage, follow up head ultrasound showed significant hydrocephalus with bilateral encephalomalacia. Platelet count increased gradually to 279. On day 9 the baby developed bluish discoloration of the dorsum and palmar aspect of the left hand in a glove like distribution with a gangrenous area about 5cm in diameter on the dorsum of the right hand. There were two purpuric patches on the extensor aspect of the right arm. All peripheral pulses were normal. Neonatal purpura fulminans was suspected and replacement therapy with fresh frozen plasma was initiated at a dose of 20 ml/kg body weight every 12 hours. On day 10 a new purpuric lesion appeared on the abdomen. A diagnosis of protein C deficiency was suspected and thrombophilia workup was done for the baby and her parents. Doppler ultrasound of the head and abdomen was normal. There was no family history of venous thrombotic disease. The patient protein C level came back as 13% and the mother and the father protein levels came back as 43% and 52% respectively (reference range 70-90 %). A diagnosis of protein C deficiency was made and the baby was maintained on regular doses of fresh frozen plasma. No new ecchymotic or purpura lesions appeared and the old lesions started to resolve. Follow up CT Scan of the brain showed bilateral significant hydrocephalus with white matter atrophy. Ophthalmology examination on day 34 showed bilateral vitreous haemorrhage.

## DISCUSSION

With up to 320 mutations reported to the PROC data base, the homozygous or compound heterozygous deficiency of protein C deficiency is rare and severe condition which usually leads to neonatal purpura fulminans, while heterozygous deficiency predisposes to venous thrombosis in

adulthood<sup>4</sup>. Homozygous protein C deficiency is a potentially lethal disorder presenting in the neonatal period and can lead to ophthalmologic complications<sup>5</sup>. Purpura fulminans presents as widely distributed areas of progressive skin necrosis and microvascular thrombosis over the body.

This study reports a case of severe protein C deficiency with neonatal purpura fulminans. The thrombophilia study indicated the patient was most likely homozygous for protein C deficiency. Diagnosing homozygote infants with protein C deficiency depends upon the appropriate clinical picture, a protein C level that is essentially unmeasurable and confirmation of heterozygote state in the parents<sup>6</sup>. The level of protein C in this patient was 13% but this was measured on day 9 of life when the patient was already on 20ml/kg of FFP transfusions every 8 hours for the previous 7 days. Protein C deficiency is associated with massive thrombosis often in utero<sup>7</sup>. Intraparenchymal brain infarction and intrauterine hydrocephalus are often diagnosed<sup>7</sup>. In this case, abnormal findings in postnatal head ultrasound examination and the presence of purpura fulminans suggested a possible thrombophilia cause. Early diagnosis of this rare disorder is imperative as it is inevitably fatal without therapy. Therefore it is important to determine protein C levels in families who are at risk. The international committee on thrombosis and haemostasis published recommendations for initial and long term treatment of patients with severe protein C deficiency<sup>8</sup>. The standard initial treatment is FFP in a dose of 20 ml/kg every 12h until clinical symptoms disappear. Purified protein C has now become available<sup>9</sup> and it is the treatment of choice in patients with severe deficiency. The most widely used long term treatment is oral anticoagulation (warfarin) to maintain an INR range between 2.5 and 4.4. Other options such as low molecular weight heparin<sup>10</sup> and protein C Concentrate administration<sup>8,9</sup> have been tried with excellent results. Our

patient was treated with FFP for four weeks followed by oral anticoagulant.

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