Case Report

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Congenital Multiple Antithrombotic Factors Deficiency in Neonate: A Rare Case Report

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Abstract

Background: Protein C, Protein S and Antithrombin III are negative regulators of coagulation. Homozygous protein C deficiency is a rare inherited disorder manifesting as neonatal purpura fulminans. A two week old female baby delivered at term, developed purpuric lesions over the left thigh and progressing to other areas. Investigations showed negligible protein C level, besides meagre protein S and antithrombin III levels. The diagnosis of inherited combined protein C, protein S and antithrombin III deficiency was made.

Conclusion: Genetic analysis will help in prenatal diagnosis in future pregnancies.

Keywords: Antithrombin III; Purpura fulminans; Thrombophilia.

Introduction

Neonatal purpura fulminans with onset during the first few days after birth is a fatal disorder. The newborn with homozygous protein C or protein S deficiency develops DIC and thrombosis of small cutaneous vessels followed by necrosis of dermis and subcutaneous tissue. Purpura fulminans its characterized by rapid spread hemorrhage into the skin, bullae formation and rapid death. Prevalance of severe protein C deficiency 1 in 200000. Prevalence of protein S and antithrombin III deficiency is much lower.

Case Report

A 2 week old neonate presented with acute onset of purple coloured bullous skin lesions that developed spontaneously. The lesions ruptured spontaneously to leave raw areas. The lesions were found on the trunk and limbs of the child. There was no associated fever, poor feeding or altered cry. Child did not look toxic. She was first born of non consanguineous parents. Child was born out of full term normal vaginal delivery appropriate for gestational age with no history of asphyxia or neonatal sepsis. Intramuscular vitamin K 1mg was given to the child soon after birth. Child was discharged on day three of life after zero dose oral polio vaccine (OPV), Hepatitis B and BCG vaccine. Child was exclusively breastfed. There was no history of similar illness in the family. Examination of the skin lesions was suggestive of cutaneous necrosis. On account of the ischemic skin lesions, causes of vascular thrombosis was considered. Her complete blood count was normal. Renal and liver function tests were appropriate to the age. C reactive protein (CRP) was normal. Blood and urine cultures were negative.

USG of the cranium and abdomen were normal. The system examination was found to be normal. Hence prothrombotic workup was done which showed abnormal values. Protein C–22 IU/dl (65–140), protein S– 49 IU/dl (70–130), Antithrombin III – 68 IU/dl (80–120). Diagnosis of purpura fulminans

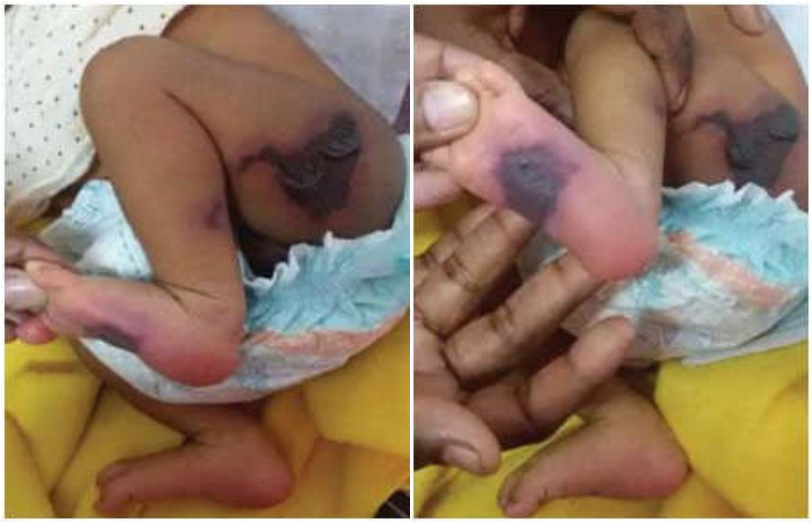

Fig. 1: Purpura fulminans on left thigh, leg and sole in two week old infant.

due to Congenital Multiple Antithrombotic Factors Deficiency was made.(Fig. 1). Nature of illness was explained to parents. Warfarin, oral anticoagulant was initiated. Need for lifelong follow up and treatment was insisted.

Discussion

Protein C prevents blood clotting in the body. Deficiency of protein C may be inherited or acquired. Inherited deficiency of protein C can lead to familial thrombophilia. It is caused by mutations in the PROC gene and transmitted mostly as autosomal dominant.[1] Acquired protein C deficiency may be caused by liver disease, disseminated intravascular coagulation (DIC), infection (sepsis), vitamin K deficiency, use of warfarin or certain types of chemotherapy. While most people with protein C deficiency do not have problems, some are at risk for deep vein thrombosis and pulmonary embolism. Also, abnormal bleeding can occur in various parts of the body causing purple patches on the skin. Treatment depends on the symptoms severity.[2] *Type I deficiency:* patients typically have levels that are about one half that of normal patient plasma. *Type II deficiency:* associated with decreased function of protein C.

Very severe protein C deficiency is classically associated with neonatal purpura fulminans (NPF); intracranial thromboembolism may also occur in babies. Some patients present with venous thromboembolism in childhood or adolescence. (3) A diagnosis of protein C deficiency might be suspected in someone with a deep venous thrombosis (DVT) or a pulmonary embolism, especially if it occurs in a relatively young person (less than 50 years old) Genetic testing is not necessary to make a diagnosis. Most people with mild protein C deficiency never develop abnormal blood clots and thus do not require treatment. However, people who have experienced a deep venous thrombosis or a pulmonary embolism are treated with heparin or warfarin, which help to prevent recurrence.[4] Preventative treatment with these drugs may also be considered in higher risk situations such as pregnancy. A protein C concentrate (Ceprotin) was approved by the Food and Drug Administration in 2007 for the treatment of protein C deficiency, prevention and treatment of venous thrombosis and purpura fulminans. Protein S is also an inhibitor of coagulation.[5]

Protein S deficiency is a rare disorder of coagulation which can be acquired or inherited. Inherited deficiency is due to variation in PROS1 gene inherited as autosomal dominant. Acquired protein S deficiency may be due to Nephrotic syndrome, pregnancy or use of oral contraceptives. Two most common findings associated with protein S deficiency are DVT and pulmonary embolism. Infants with severe forms of protein S deficiency develop symptoms within hours to a few days after birth. They develop potentially life threatening purpura Fulminans.[6,7] It is due to generalized thrombosis involving several vessels in the body leading to tissue necrosis. Without treatment, this condition can be fatal. Anti Thrombin III inhibits generation of thrombin by impeding factors Xa and IXa. Congenital deficiency of anti thrombin III is due to mutations in SERPINC1 gene. Acquired deficiency may be due to disorders of liver, kidney or drugs like L-Asparaginase.[8]

Conclusion

Milder forms of antithrombotic factors deficiency are asymptomatic or precipitated under specific conditions. Severe homozygous deficiency manifests in the neonatal period. Without treatment purpura fulminans is fatal. With management recurrences are common. Genetic testing is available but not mandatory for diagnosis.

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