

Neonatal Purpura Fulminans, a rare genetic disorder due to protein C deficiency: A case report

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Abstract

Neonatal Purpura Fulminans is a rare and fatal disorder associated with perivascular haemorrhage and disseminated intravascular coagulation. Early clinical recognition, timely investigation and treatment is utmost important. A 6 days old baby boy was brought to emergency with blackish ulcers all over the body. Initially these were over the feet and scalp but later appeared on the abdomen. On examination, child was vitally stable, mildly icteric and had multiple erythematous large bullous blackish lesions on scalp, lower abdomen, perineum, back and soles. Neonatal reflexes and systemic examination was normal. Laboratory investigations showed normal CBC, PT/APTT and Protein S level while Protein C and Antithrombin III levels were low.

Neonatal Purpura Fulminans is a life threatening condition and family screening is also mandatory for early recognition of disease in the siblings.

Keywords: Neonatal Purpura Fulminans, Protein C.

Introduction

Neonatal Purpura Fulminans (PF) is a clinical condition due to dermal micro vascular thrombosis; PF is a rare and often fatal disorder associated with perivascular haemorrhage and disseminated intravascular coagulation (DIC), initially present at neonatal age. Early clinical recognition, timely investigation and treatment is utmost important. PF, was first described in 1962 as a suspected inherited lesion found in three siblings with similar skin lesions.¹ Homozygous type protein C or proteins S deficiencies are rare genetic disorders with fatal PF like thrombotic complications mostly manifested during neonatal period.² The clinical presentation of typical rash of PF is of well-demarcated erythematous macules, which progress rapidly with irregular central areas of blue-black haemorrhagic necrotic areas.³ Patients with PF may also present with

multi-organ failure or with severe large venous thrombosis with high initial mortality and long-term morbidity, hence early recognition and diagnosis of the initiating cause of PF may avert these adverse outcomes.⁴

Case Report

A 6 days old baby boy, resident of Multan, was brought to the emergency department of our institute in November 2013 with the complaints of blackish ulcers all over the body started from second day of life. Initially these patches were over the feet and scalp but later they appeared on the abdomen as well (Figure-1). The child was otherwise healthy and was taking feeds normally. The antenatal and birth history were insignificant. He was a product of consanguineous marriage with one healthy male sibling alive. Family history was significant with the occurrence of same skin lesions in a baby girl developed on second day of life and then death of that girl in the neonatal period. On examination, child was vitally stable with heart rate of 140 beats/min, respiratory rate 38 breaths/min, and temperature of 37°C. Child was mildly icteric and had multiple erythematous and large bullous lesions of black colour on scalp, lower abdomen, perineum, back and soles of both feet (Figure-2,3). Neonatal reflexes were normal and systemic examination was also normal. Suspecting neonatal Purpura Fulminans, laboratory investigations including complete blood count (CBC), Prothrombin time (PT), Activated Partial



Figure-1: Large necrotic lesion on right sole.

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Figure-2: Large purpuric to blackish bullous lesion over lower abdomen extending up to the inguinal region.

Thromboplastin Time (APTT), Protein C, and Protein S were sent which showed following results:

Complete Blood Count (CBC): Hb 11.3 g/dl, HCT 36.3%, WBC 22.7/cu mm with neutrophils 46% and lymphocytes 27.7%, and platelets 146/cu mm. Prothrombin Time (PT): 11.7 seconds. Activated Partial Thromboplastin Time (APTT): 40.1seconds. Protein C level: 10% (72-106 %). Protein S level: 62.2% (60-110%). Antithrombin III: 59.7% (80-120%).

Paediatric haematology and neonatology was taken on board and admission was advised for Fresh Frozen Plasma (FFP) transfusion and further management but father refused to hospitalize the patient and took the baby back home. Later we contacted for follow up and got the information that the patient had expired on 23rd day of life as the elder sister.

Discussion and Conclusion

Neonatal Purpura Fulminans was assumed as an inherited disorder due to the presence of similar skin lesions in three siblings when it was first described in 1962.⁵ Relationship of PF and protein C deficiency was first described in 1983, and was effectively treated with protein C replacement therapy.⁶ Inherited causes of PF have been associated with homozygous deficiency of protein C or S, other than complex heterozygous and/or may be as co-inheritance with

other congenital thrombophilia.⁷ The occurrence of Protein C deficiency is 1 in 40000-25 0000 individuals and is vitamin K-dependent coagulation protein, synthesized in liver.

Neonatal Purpura Fulminans usually presents with a rapid onset of purpuric lesions within first 24 hours of life. The clinical presentation may vary depending on the severity of congenital protein C and S deficiencies. The skin lesions initially appear dark red and then become purple-black and indurated. They may be mistaken initially as bruising but later become necrotic and gangrenous which may results in extremities loss.⁸ Ophthalmologic complications including vitreous haemorrhage and retinal detachment that may result in partial or complete blindness are

often associated with severe protein C deficiency.⁹

Purpura Fulminans is a haematological emergency so early recognition and initiation of immediate treatment to prevent the complications is mandatory. Immediate treatment is the transfusion of FFP to replace pro-coagulants and anticoagulants that have been consumed. The main concern of transfusing FFP is to replace Protein C and Protein S which are severely deficient.³ Protein C concentrate is recommended in severe heritable deficiency of Protein C after confirming the diagnosis to minimize the use of FFP.

Neonates and children with severe protein C deficiency are at risk of recurrent PF and hence require long-term treatment with antithrombotic drugs are recommended. Replacement of protein C either alone, or in combination with coumarins or low molecular weight heparin is main stay of management.¹⁰

Neonatal Purpura Fulminans is a life threatening condition although it is very rare but early diagnosis and prompt management is crucial to prevent the complications and improve morbidity as well as mortality. Inherited causes require long term treatment with replacement of anticoagulant therapy and fresh frozen plasma. Family screening is also mandatory for early recognition of disease in the siblings.

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References

1. Van Der Horst RL. Purpura fulminans in a newborn baby. *Arch Dis Child.* 1962; 37: 436-41.
2. Marlar RA, Neumann A. Neonatal purpura fulminans due to homozygous protein C or protein S deficiencies. *Semin Thromb Hemost.* 1990; 16:299-309.
3. Chalmers E, Cooper P, Forman K, Grimley C, Khair K, Minford A, et al. Purpura fulminans: recognition, diagnosis and management. *Arch Dis Child.* 2011; 96:1066-71.
4. Francis RB, Jr. Acquired purpura fulminans. *Semin Thromb Hemost.* 1990; 16:310-25.
5. Price VE, Ledingham DL, Krumpel A, Chan AK. Diagnosis and management of neonatal purpura fulminans. *Semin Fetal Neonatal Med.* 2011; 16:318-22.
6. Branson HE, Katz J, Marble R, Griffin JH. Inherited protein C deficiency and coumarin-responsive chronic relapsing purpura fulminans in a newborn infant. *Lancet.* 1983; 2:1165-8.
7. Dogan Y, Aygun D, Yilmaz Y, Kanra G, Secmeer G, Besbas N, et al. Severe protein S deficiency associated with heterozygous factor V Leiden mutation in a child with purpura fulminans. *Pediatr Hematol Oncol.* 2003; 20:1-5.
8. Manco-Johnson MJ, Abshire TC, Jacobson LJ, Marlar RA. Severe neonatal protein C deficiency: prevalence and thrombotic risk. *J Pediatr.* 1991; 119:793-8.
9. Hattenbach LO, Beeg T, Kreuz W, Zubcov A. Ophthalmic manifestation of congenital protein C deficiency. *J AAPOS.* 1999; 3:188-90.
10. Goldenberg NA, Manco-Johnson MJ. Protein C deficiency. *Haemophilia.* 2008; 14:1214-21.