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CASE REPORT

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Challenges in neonatal care: a case report of purpura fulminans in a 10-day-old infant

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Abstract

Background Purpura fulminans (PF) is a rare but severe thrombotic disorder affecting small cutaneous blood vessels. It may present as bruising and discoloration but can rapidly progress necrosis and life-threatening complications if not promptly diagnosed and treated. This paper presents a rare case of neonatal PF associated with protein C and S deficiency, highlighting the importance of prompt recognition and diagnosis.

Case presentation A 10-day-old male infant presented with extensive purpura fulminans, microcephaly, and craniofacial abnormalities. Laboratory investigations revealed severe deficiencies in protein C, protein S, and antithrombin III. Treatment involved a multidisciplinary approach including antibiotic therapy, blood transfusions, and anticoagulation.

Discussion Neonatal PF poses significant challenges due to its high mortality rate and potential neurological complications. Prompt diagnosis and management are crucial, although outcomes can vary. Long-term care and genetic counseling are essential for families affected by this rare disorder.

Conclusion This case underscores the importance of early recognition and intervention in neonatal PF, especially in resource-limited settings. Improved strategies for diagnosis, management, and patient education are necessary to enhance outcomes and support affected families.

Keywords Blood coagulation disorders; Fetal mortality; Hematologic diseases, Hematologic diseases, Morbidity, Protein C deficiency, Protein S deficiency, Purpura fulminans

Background

Purpura fulminans (PF) is a rare, potentially fatal disorder of cutaneous microvascular thrombosis connected to perivascular bleeding and disseminated intravascular coagulation (DIC) [1]. Purpura fulminans is classified into three types: neonatal, idiopathic, and acute infectious. Neonatal purpura fulminans is associated with a genetic deficit of the anticoagulants protein C, protein S, and antithrombin III. It appears extremely early in life, and treatment is targeted at correcting these inadequacies [2]. Congenital protein C deficiency manifesting as neonatal purpura fulminans is extremely rare with a 1 in 4 million incidences [3]. Patients with PF may also present with multi-organ failure or severe massive venous thrombosis, both of which have a high initial mortality and long-term morbidity. The mortality rate in PF patients has been reported to be up to 50%, with DIC and multi-organ failure being the most common causes; therefore, prompt identification and diagnosis of the underlying etiology of PF may help to avoid these negative outcomes [4].

We present a rare case of a 10-day-old male with extensive purpura fulminans, concurrent protein C and protein S deficiency, and cerebral complications, suggestive of potential neurological involvement, characterized by microcephaly and craniofacial malformations.

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Case

Case presentation

A 10-day-old male infant, delivered vaginally at full term following an uneventful pregnancy and uncomplicated delivery, was brought to the emergency room due to purplish patches on his right foot and buttocks that had been present for 1 day. Aside from these patches, the infant was in good health and was breastfeeding without any issues. There were no noteworthy details in the birth and prenatal history. He was the fifth child of parents in a consanguineous marriage (fourth-degree consanguinity). The mother had encountered three first-trimester miscarriages previously. However, obtaining the exact gestational age was not possible due to the mother's inability to recall and the absence of documented proof. There was no family history of similar skin lesions. Notably, the newborn did not receive vitamin K prophylaxis or vaccination at birth. Initially, the patches manifested on the right ankle but progressed distally to cover approximately two-thirds of the right foot and extended proximally to the mid-thigh. Subsequently, a similar patch emerged on his right buttock, eventually involving the genital area (Fig. 1). Over time, these patches evolved from purplish lesions to necrosis, forming black eschars.

On examination, the patient's vital signs indicated stability, with a heart rate of 140 beats per minute, a respiratory rate of 35 breaths per minute, and a temperature of 98.6 °F. Peripheral pulses in the left lower limb were detectable, while the right lower limb showed good blood flow in the femoral and popliteal arteries but weak flow in the tibialis anterior and posterior. Capillary refill time was less than 2 s in the upper limb and left lower limb, but it exceeded 2 s in the right lower limb. All extremities exhibited normal warmth.

The infant exhibited good tone, fair sucking, and an incomplete Moro's reflex. Microcephaly and craniofacial abnormalities likely contributed to the infant's presentation of an incomplete Moro reflex. The anterior fontanelle was open and flat, measuring approximately 0.5 cm, while the posterior fontanelle was closed. Fundus examination revealed normal findings: clear media, pink optic disc with sharp margins (cup-to-disc ratio ~ 0.35), normal vasculature, and a healthy retinal nerve fiber layer evidenced by a striated sheen. Additionally, clinical signs of microcephaly, a long philtrum, a small chin, and low-set ears were observed, possibly indicating craniofacial abnormalities. However, other systemic examinations yielded unremarkable findings.

With suspicions of a coagulopathy and an underlying syndrome, the neonate's care plan involved essential interventions. These encompassed maintaining a nil per os (NPO) status with the insertion of a nasogastric (NG) tube, providing oxygen support, and ensuring the maintenance of an intravenous (IV) line. Antibiotic therapy included cefotaxime and amikacin, and transfusions of red blood cells, platelets, and fresh-frozen plasma (FFP) were administered as needed. Continuous monitoring was in place to assess for complications, with vital signs and blood sugar levels checked every 6 h. Comprehensive laboratory tests, including a thrombotic workup, were initiated to diagnose the underlying condition.

Investigation

Laboratory assessments at presentation revealed the following results: hemoglobin at 15 g/dl, TLC (total leukocyte count) of 15,000 cells/mm^3, platelet count of 87,000 cells/mm^3, prothrombin time (PT) extending to 61 s, activated partial thromboplastin time (APTT) slightly prolonged at 34 s, and an INR of 3.9, all indicative of coagulation abnormalities. Following management, laboratory tests were repeated at different intervals (Table 1).

Specific coagulation factor levels unveiled severe deficiencies: protein C at 10% (normal range: 72–106%), protein S at 41% (normal range: 60–110%), and antithrombin III at 55% (normal range: 80–120%). Blood and urine cultures were initially conducted to investigate infection upon presentation, yielding negative results.

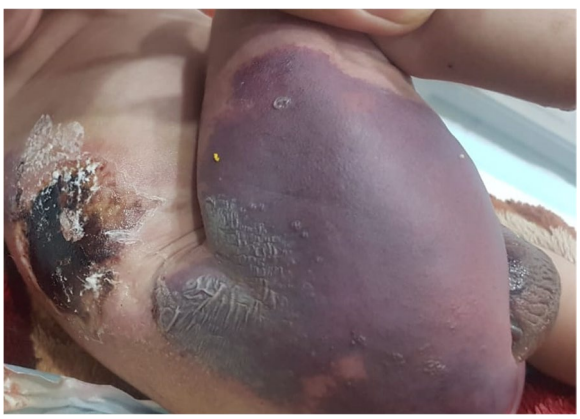

Fig. 1 Purpuric rash involving right hip and thigh

Table 1 Blood parameters at admission, 48 h, and 120 h

	0 h	48 h	120 h	Normal ranges
Hgb (g/dl)	15	12.5	4	Male: 13.5–17.5 Female: 12.0–16.0
TLC (cells/mm^3)	15	12.5	25.7	4500–11,000
PLT (cells/mm^3)	87	147	18	150,000–400,000
PT (s)	61	16	40	11–13.5
APTT (s)	34	41.5	45	35–45
INR	3.9	1.58	2.5	0.8–1.2

Subsequently, these cultures were repeated twice at different intervals of 1 week, and all results came back negative effectively eliminating the possibility of secondary protein C and S deficiency due to infection, and adequate hydration was ensured through the maintenance of IV lines in the infant, thereby ruling out the possibility of protein C and S deficiency caused by Z dehydration. A lumbar puncture was also conducted, yielding unremarkable findings. An ultrasound of the brain was conducted due to the neonate's comparatively small anterior fontanelle, which revealed bilateral dilated lateral ventricles, measuring 3.4 cm on the right, displacing the choroid plexus in the depending portion with internal echoes. These findings indicated non-communicating hydrocephalus. However, further brain imaging modalities such as MRI and CT scan could not be performed due to the unstable condition of the baby. Limitation of resources prevented the conduction of genetic testing, serological assays, and molecular techniques, including PCR, which are essential for ruling out TORCH infections and cause of craniofacial malformations.

Management

Recognizing the complexity of the case, a collaborative approach was adopted, with the involvement of a senior hematologist, vascular team, pediatric surgery team, and infectious diseases team for further evaluation.

Following the vascular team's assessment, a Doppler ultrasound of the limbs indicated a monophasic spectrum with a normal peak velocity in the right posterior tibial artery at the site of an ulcerated wound. In contrast, the rest of the arteries displayed a triphasic spectrum with normal peak systolic velocities. In response to this assessment, the vascular team recommended the initiation of local glyceryl trinitrate (GTN) application at 8-h intervals.

The treatment plan included subcutaneous injections of enoxaparin at a dose of 2 mg/kg/day, administered twice daily to maintain anticoagulation. IV antibiotics and elevation of the legs were continued as part of the management. An echocardiogram, as suggested by the vascular team, was performed to rule out any cardiac causes, revealing a patent foramen ovale (PFO) with a left-to-right shunt. Subsequent Doppler ultrasounds showed gradual improvement in arterial insufficiency, allowing for the continuation of enoxaparin treatment. As the INR began to normalize, no further FFP transfusions were required. By the 7th day of admission, there was an improvement in the purpura of the right foot.

However, by the 10th day of admission, the neonate started to develop multiple bruises and eschar involving various areas, including the bilateral flank, perianal region (Fig. 2), and bilateral hands and feet. The infectious disease team was consulted, and they recommended discontinuing vancomycin after establishing a central line and starting clindamycin while continuing meropenem and colistin. Despite these efforts, the purpura worsened and took on a darker appearance. Due to the risk of developing necrotizing fasciitis, the LRINEC (laboratory risk indicator for necrotizing fasciitis) scoring system was applied, and the calculated score was 11, indicating a high risk. Pediatric surgery was consulted and advised debridement. However, due to the neonate's hemodynamic instability and parental refusal to provide consent, the procedure was not performed.

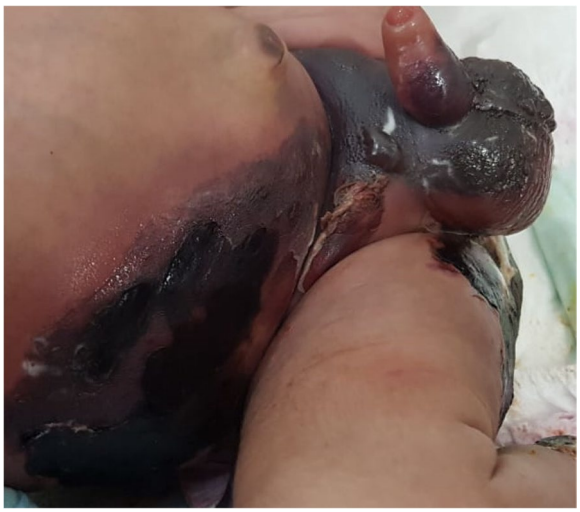

Fig. 2 Multiple eschars involving bilateral flanks, genitalia, and perianal region

On the 19th day of admission, the neonate experienced apneic episodes and intermittent desaturation, with oxygen support including epinephrine. The infant went into apnea and bradycardia, and despite medical intervention, the parents declined cardiopulmonary resuscitation (CPR), resulting in the declaration of the neonate's passing.

Discussion

Purpura fulminans (PF) is a rare and serious disorder characterized by cutaneous microvascular thrombosis, perivascular bleeding, and disseminated intravascular coagulation (DIC) [5]. Skin necrosis and DIC may quickly develop to multiorgan failure in this hematological emergency because of the thrombotic blockage of tiny and medium-sized blood vessels [6].

This case involves a 10-day-old baby boy with purpuric patches on the foot and buttock, which progressed to necrosis with black eschar formation over time. The patient's laboratory investigations revealed low levels of protein C (10%), protein S (41%), and antithrombin III

(55%), indicating a genetic deficit of anticoagulants and a potential underlying cause for neonatal purpura fulminans. A common driving cause is often a transient or hereditary decrease in protein C or protein S [7].

The clinical presentation in this case underscores the critical importance of promptly recognizing and diagnosing neonatal purpura fulminans (PF), particularly in infants lacking a history of vitamin K prophylaxis at birth. The absence of vitamin K administration may have contributed to the deficiency of anticoagulant proteins, potentially leading to PF in this patient [8]. Affected infants often experience significant neurological impairments, primarily resulting from prenatal or early postnatal cerebral venous thrombosis due to clotting factor deficiencies, which can lead to secondary periventricular hemorrhage and hydrocephalus. Blindness is a common manifestation of severe protein C deficiency and can arise from conditions such as vitreal hemorrhage, retinal vein or artery thrombosis, and retinal detachment, presenting as leukocoria or ischemic optic atrophy [9]. In our case, the mother's history of first-trimester miscarriages may have contributed to these abnormalities in the patient, as vascular irregularities within the uterine environment, although not necessarily causing miscarriages, can hinder fetal development and neurogenesis, potentially resulting in long-term complications in offspring of women with a history of recurrent miscarriages [10].

The treatment of neonatal purpura fulminans involves maintaining a platelet count > 50,000 109/L and fibrinogen levels > 1 g/L [1]. The cause determines the type of management to use. Intravenous antibiotics are essential if the condition is infection related [11]. Fresh-frozen plasma (FFP) or cryoprecipitate is used for replacement therapy. Protein C replacement can be initiated with FFP or a protein C concentrate, targeting a trough protein C activity > 10 IU/dL [12]. Liver transplant is considered in severe cases [13]. Surgical prophylaxis can be achieved with protein C concentrate [14]. The acute phase of replacement therapy for congenital protein C and S deficiency should be followed by maintenance therapy, warfarin anticoagulation, and regular monitoring of INR and D-dimer levels. These neonates and children require long-term antithrombotic medication. PC replacement treatment, either alone or in combination with coumarins or low-molecular-weight heparin, is frequently required. In certain cases, anticoagulant medications alone may be sufficient to avoid recurrent PF. Liver transplantation provides a long-term treatment for hereditary protein C (PC) deficiency [10, 15]. The management of PF in this case involved immediate treatment measures, including administration of fresh-frozen plasma (FFP), injection vitamin K, and antibiotics (cefotaxime and amikacin) to address the underlying septic etiology. The use of heparin infusion aims to prevent further thrombotic events. Despite treatment, the patient's condition worsened, leading to their passing on the 19th day of admission.

Neonatal purpura fulminans carries a reported mortality rate of 43%, with the most common causes of death being disseminated intravascular coagulation (DIC) and multi-organ failure, a risk that is heightened in immunocompromised individuals and children [16, 17]. The lower incidence of neonatal purpura fulminans makes it a challenging clinical scenario, while acute management can be lifesaving, is not always curable. After the acute phase, treatment typically continues to maintain adequate blood coagulation and prevent further complications, necessitating ongoing therapy and regular monitoring. However, knowledge regarding well established treatment guidelines and optimal therapeutic approaches is still not clear. The initiation of appropriate treatment is imperative for improved outcomes [18]. The prognosis significantly improves with early and effective treatment, but outcomes can vary, with some patients requiring long-term care [2]. For couples who have experienced multiple pregnancy losses due to this condition or other genetic factors, it is essential to undergo genetic counseling, considering genetic testing, and closely monitoring future pregnancies with the support of high-risk obstetricians and hematologists. Decisions about the next pregnancy will depend on individual circumstances and underlying causes, with options like prenatal diagnosis and postnatal interventions as needed.

Conclusion

Purpura fulminans is a rare disorder often associated with clotting factor deficiencies, notably protein C and S. While it can rarely lead to cerebral and optic complications, its lack of a cure contributes to a higher mortality rate. This article highlights a unique case of neonatal purpura fulminans with cerebral complications and its management in a developing country. Healthcare providers should prioritize patient education on genetic counseling, especially in cases of unexplained recurrent miscarriages. In developing countries, strategies should be developed for the diagnosis and management of such rare diseases.

Abbreviations

PF	Purpura fulminans
DIC	Disseminated intravascular coagulation
FFP	Fresh-frozen plasma
IV	Intravenous
PC	Protein C deficiency
INR	International normalized ratio
CPR	Cardiopulmonary resuscitation
NG	Nasogastric
NPO	Nil per os

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None to declare.

Authors' contributions
All authors attest that they meet the current ICMJE criteria for authorship. HS, YZ, and AJ conceptualized and designed the study, drafted the initial manuscript, reviewed and revised the manuscript, and did final editing of the manuscript. DIS and AL conceptualized and designed the study, drafted the initial manuscript, and critically reviewed the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Declarations

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Not applicable.

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Competing interests
The authors declare that they have no competing interests.

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