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Case Report

Neonatal Cholestasis and Bleeding Tendency in a Consanguineous Family: A Novel Case of Homozygous *ABCB11* Variant Associated with CD36 Deficiency

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Abstract
Neonatal cholestasis accompanied by acute hemorrhage in consanguineous families serves as a primary clinical indicator of autosomal recessive disorders. Severe bile flow obstruction leads to conjugated hyperbilirubinemia and profound malabsorption of fat-soluble vitamins, particularly vitamin K, which can precipitate life-threatening bleeding crises. This report describes a 5-month-old male infant, born to consanguineous parents via normal vaginal delivery, who experienced recurrent and prolonged neonatal jaundice starting in the second week of life. At four and a half months of age, despite receiving vitamin K prophylaxis at birth, the patient presented with severe spontaneous ecchymoses across the face and trunk. Laboratory investigations revealed marked transaminitis with elevated aspartate aminotransferase (380 U/mL) and alanine aminotransferase (294 U/mL), alongside significant hypocalcemia (7.0 mg/dL) and hypomagnesemia (1.3 mg/dL). Echocardiography demonstrated dilated cardiomyopathy. Subsequent genetic analysis via whole exome sequencing identified a novel homozygous *ABCB11* variant associated with CD36 deficiency. The patient was managed with aggressive clinical stabilization, vitamin supplementation, and targeted metabolic support, which halted the bleeding diathesis and improved hepatic and cardiac parameters. This case highlights the critical necessity of screening infants from consanguineous lineages presenting with prolonged jaundice for hereditary cholestatic syndromes. Immediate clinical intervention combined with timely genetic testing is imperative to avert systemic metabolic failure, optimize therapeutic outcomes, and mitigate associated hereditary risks.

Keywords: ABCB11 variant; CD36 deficiency; Consanguinity**;** Neonatal cholestasis.

الركود الصفراوي الولادي وحدوث النزف في العائلة القريبة: حالة جديدة من متغير *ABCB11* المتماثل الزيجوت المرتبط بنقص CD36

الخلاصة
يعد داء الركود الصفراوي الولادي المصحوب بنزيف حاد في الأقارب مؤشرا سريريا رئيسيا للاضطرابات المتنحية الوراثية. يؤدي انسداد تدفق الصفراء الشديد إلى ارتفاع مستوى الصفراء المرافقين وسوء امتصاص عميق للفيتامينات القابلة للذوبان في الدهون، وخاصة فيتامين ك، مما قد يؤدي إلى أزمات نزيف تهدد الحياة. يصف هذا التقرير رضيعا ذكرا يبلغ من العمر 5 أشهر، ولد لوالدين قريبين عبر ولادة طبيعية، وقد عانى من اليرقان المتكرر والمطول لحديثي الولادة بدءا من الأسبوع الثاني من الحياة. في عمر أربعة أشهر ونصف، وعلى الرغم من تلقيه الوقاية من فيتامين ك عند الولادة، ظهرت بقع نزف جلدي تلقائي شديد عبر الوجه والجذع. كشفت الفحوصات المخبرية عن وجود التهاب واضح مع ارتفاع في إنزيم الأسبارتات أمينوترانسفيراز (380 U/mL) وإنزيم ألانين أمينوترانسفيراز (294 U/mL)، إلى جانب نقص كالسيوم ملحوظ (7.0 ملغ/ديسيلتر) ونقص المغنيسيوم (1.3 ملغ/ديسيلتر). أظهر تخطيط صدى القلب اعتلال عضلة القلب الموسع. حدد التحليل الجيني اللاحق عبر تسلسل الإكسوم الكامل متغيرا جديدا متماثل الزيجوت *ABCB11* مرتبط بنقص CD36. تمت معالجة المريض من خلال تثبيت الحالة سريريا، وأعطاء مكملات للفيتامينات، ودعم أيضي مستهدف، مما أوقف النزيف وحسن معايير الكبد والقلب. تسلط هذه الحالة الضوء على الضرورة الحرجة لفحص الرضع من سلالات أقارب يعانون من اليرقان المطول لمتلازمات الركود الصفراوي الوراثية. يعد التدخل السريري الفوري مع الفحوصات الجينية في الوقت المناسب أمرا ضروريا لتجنب الفشل الأيضي الجهازي، وتحسين النتائج العلاجية، والتخفيف من المخاطر الوراثية المرتبطة به.

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INTRODUCTION

Neonatal cholestasis is a challenging clinical entity characterized by prolonged conjugated hyperbilirubinemia, affecting approximately 1 in 2,500 live births. In regions with high rates of consanguinity, autosomal recessive genetic disorders represent a significant underlying etiology [1,2]. Impaired bile flow severely compromises the intraluminal absorption of fat-soluble vitamins (A, D, E, and K) [3]. Vitamin K is a crucial cofactor for the gamma-glutamyl carboxylase enzyme, which activates clotting factors II, VII, IX, and X [4]. Consequently, profound cholestasis-induced vitamin K malabsorption can precipitate late-onset vitamin K deficiency bleeding (VKDB), presenting as life-threatening hemorrhagic diathesis. This case report describes a 5-month-old infant from a consanguineous family presenting with persistent jaundice, severe spontaneous ecchymoses, dilated cardiomyopathy, and electrolyte derangements, ultimately diagnosed with a novel homozygous *ABCB11* variant and CD36 deficiency.

Case Presentation

A 5-month-old male was admitted to the department of pediatrics, Azadi Teaching Hospital, on December 18th, 2025. Initial laboratory evaluation revealed a

hemoglobin level of 12.3 g/dL, a white blood cell count of 10.1×10^9/L with mild eosinophilia, and a platelet count of 344×10^9/L. Liver function tests demonstrated marked transaminitis, with aspartate aminotransferase (AST/SGOT) elevated to 380 U/L and alanine aminotransferase (ALT/SGPT) to 294 U/L. Additionally, lactate dehydrogenase (LDH) and creatine kinase (CK) levels were significantly elevated at 831 IU/L and 987 IU/L, respectively. Coagulation studies showed markedly prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT), attributed to reduced activity of coagulation factors VII and IX. Serum ferritin was elevated at 436 ng/mL, while alpha-fetoprotein was significantly increased to 528 ng/mL. Infectious and metabolic evaluations, including the TORCH panel and expanded newborn metabolic screening, were unremarkable. During hospitalization, the infant developed recurrent and severe electrolyte disturbances, notably persistent hypocalcemia (7.0 mg/dL) and hypomagnesemia (1.3 mg/dL). Imaging studies revealed that abdomin-pelvic ultrasonography demonstrated diffusely increased echogenicity of both renal parenchyma. Neck color Doppler ultrasonography identified a severe localized inflammatory process involving the left buccal and maxillary regions, characterized by subcutaneous edema and thickening of the buccinator muscle and an overlying cheek ecchymosis **(**Figure 1**).**

Figure 1: Left infraorbital and cheek swelling with ecchymosis.

This was associated with a reactive lymph node measuring 10×8 mm and a small fluid collection measuring 11×6 mm anterior to the buccinator muscle, with preservation of the underlying bony cortex. Severe spontaneous ecchymoses were also clinically prominent across the right flank and lower back **(**Figures 2 and 3**)**. Echocardiography revealed findings consistent with dilated cardiomyopathy. To establish a definitive diagnosis, Whole Exome Sequencing (WES) was performed by the EXOGEN laboratory.

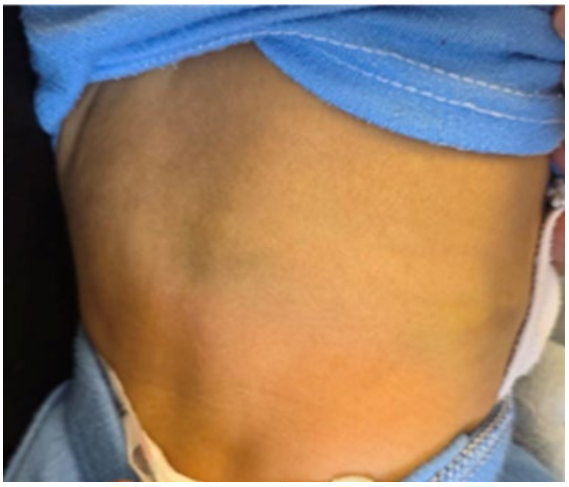

Figure 2: Right flank swelling with ecchymosis.

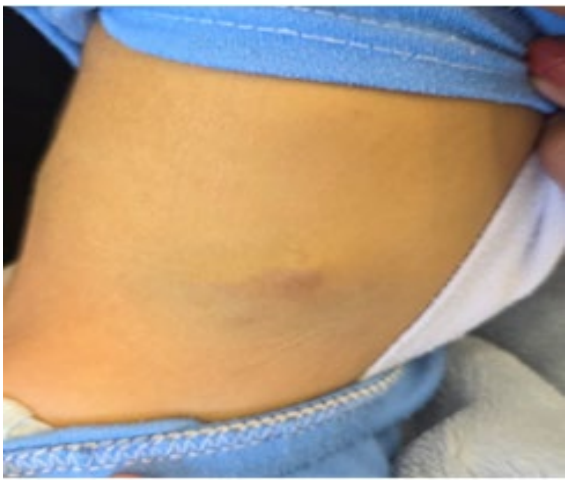

Figure 3: Lower back swelling with ecchymosis.

The molecular genetic analysis identified a novel homozygous variant of uncertain significance (VUS) in the *ABCB11* gene, which correlates clinically with progressive familial intrahepatic cholestasis type 2 (PFIC2) and benign recurrent intrahepatic cholestasis type 2. Concurrently, the analysis revealed a co-existing homozygous likely pathogenic nonsense variant in the *CD36* gene, confirming a state of platelet glycoprotein IV deficiency.

Treatment Protocol

The therapeutic strategy focused on immediate stabilization, correcting coagulopathy, managing heart failure, and providing nutritional support. The bleeding tendency was managed with immediate fat-soluble vitamin supplementation (Vitamins A, D, and E) and parenteral Vitamin K. Recurrent hypocalcemia and hypomagnesemia were treated with intravenous calcium gluconate and targeted electrolyte replacements. For the newly diagnosed dilated cardiomyopathy, anti-heart failure therapy was initiated, comprising low-dose digoxin and diuretic therapy with furosemide.

Aggressive hydration and optimized caloric intake were maintained to support hepatic and metabolic recovery.

DISCUSSION

This case highlights a complex clinical intersection where neonatal cholestasis, late-onset vitamin K deficiency bleeding, electrolyte disturbances, and dilated cardiomyopathy coexist due to underlying genetic mutations. While vitamin K deficiency is mitigated by standard prophylaxis at birth, exclusively breastfed infants with underlying hepatobiliary pathology remain at extreme risk [5,3]. Absent bile drainage leads to profound fat malabsorption, directly causing vitamin K depletion. Because vitamin K serves as an obligate cofactor for the gamma-glutamination of clotting factors, its deficiency causes a severe consumptive-like coagulopathy, explaining the spontaneous facial and trunk ecchymoses observed in this patient [4,6]. The systemic manifestations in this infant extend beyond typical cholestasis. Severe liver dysfunction and chronic intestinal malabsorption account for refractory hypocalcemia and hypomagnesemia, which required aggressive intravenous correction [6,2]. Furthermore, the identification of a novel homozygous *ABCB11* mutation—traditionally linked to progressive familial intrahepatic cholestasis type 2 (PFIC2)—alongside CD36 deficiency expands our understanding of these rare phenotypes [1,7]. *ABCB11* encodes the bile salt export pump (BSEP); its disruption causes severe intrahepatic cholestasis, transaminitis, and markedly elevated alpha-fetoprotein, as observed here. Interestingly, CD36 deficiency has been critically linked in literature to metabolic abnormalities and myocardial dysfunction, which likely contributed to the development of dilated cardiomyopathy in this infant [1,2]. This underscores the necessity of performing advanced genetic screening like WES in consanguineous families to unmask complex, overlapping autosomal recessive syndromes.

Conflict of interests

The authors declared no conflict of interest.

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The authors did not receive any source of funds.

Data sharing statement

The data that supports the findings of this study are available from the corresponding author upon a reasonable request.

Conclusion

Any infant presenting with jaundice persisting beyond 21 days requires urgent screening for neonatal cholestasis to prevent catastrophic bleeding secondary to vitamin K malabsorption. In regions where consanguinity is prevalent, clinicians must maintain a high index of suspicion for underlying genetic and metabolic etiologies. Early multidisciplinary intervention, immediate fat-soluble vitamin supplementation, and timely genetic sequencing are pivotal to optimizing clinical outcomes and preventing systemic metabolic and academic failure.

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