Factor II (Prothrombin) Deficiency in a Paediatric Patient: A Case Report

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ABSTRACT

Deficiency of Factor II, also known as prothrombin, is an exceedingly rare bleeding disorder. It has an estimated prevalence of 1 in 2 million individuals. While severe deficiency cases are well-documented, moderate deficiencies can present diagnostic challenges. A case of a one-year male patient presenting with subcutaneous nodules, rash, pruritus, gum bleeding, and joint swelling was reported. Laboratory investigations were initially performed soon after the transfusion appeared within or near normal ranges, but when repeated after an appropriate interval, they confirmed a moderate Factor II deficiency. The patient's clinical presentation underscores the potential for marked bleeding symptoms even in cases of moderate deficiencies. This case highlights the importance of Factor II deficiency in the differential diagnosis of unexplained bleeding in paediatric patients, even when standard coagulation tests are within normal limits.

Key Words: *Prothrombin deficiency, Bleeding disorder, Coagulation factors, Subcutaneous nodules*.

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INTRODUCTION

Factor II (prothrombin) is a vitamin K-dependent glycoprotein synthesised in the liver. It plays a pivotal role in the coagulation cascade after being converted to thrombin, which transforms fibrinogen into fibrin.[1] Congenital prothrombin deficiency is one of the rarest bleeding disorders. It has an autosomal recessive inheritance and an incidence of approximately 1 in 2 million people.[2] It is classified as either hypoprothrombinaemia if quantitative or dysprothrombinaemia if qualitative.[3] The severity of bleeding symptoms typically correlates with the degree of functional prothrombin activity.[4]

CASE REPORT

The authors report a case of one-year male patient presenting with subcutaneous nodules, rash, pruritus, gum bleeding, and joint swelling. The patient was born *via* spontaneous vaginal delivery, presented with a six-day history of multiple subcutaneous nodules, rash, pruritus, gum bleeding, and swelling of the left knee. His past history included an episode of meningitis at two months, confirmed *via* lumbar puncture. During this episode, he developed nodules, fever, and seizures. The nodules subsided but recurred at five months, with nasal bleeding and joint swelling.

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On examination, multiple firm, nontender, subcutaneous nodules with ecchymotic discolouration consistent with resolving haematomas ranging from 1-3 cm were noted on the patient's scalp, oral mucosa, and limbs. They were bluish to violaceous, did not blanch on pressure, and were non-fluctuant. Ultrasound showed hypoechoic lesions consistent with organising haematomas rather than true neoplastic nodules. No signs of neurofibromas (*e.g.*, *cafe-au-lait spots*, soft pedunculated masses) were present. Mild effusion of the left knee was noted with warmth and restricted range of motion without signs of infection. Ultrasound revealed an intra-articular hypoechoic fluid consistent with haemarthrosis rather than arthritis.

Laboratory evaluation revealed that the initial prothrombin time (PT) was 85.43 seconds and the activated partial thromboplastin time (APTT) was 62.14 seconds, both were markedly prolonged. Factor II activity was 43%. These tests were performed within 48 hours of receiving red cell and plasma transfusions. To avoid transfusion-related correction of clotting parameters, repeat testing was performed after a 14-day interval. At that time, the PT was mildly prolonged at 14.5 seconds compared to the reference range of 11 to 14 seconds. The APTT was also mildly prolonged at 38.2 seconds compared to the reference range of 25 to 35 seconds. The thrombin time (TT) was within normal limits at 18.5 seconds compared to the reference range of 14 to 20 seconds. Factor II activity was confirmed to be reduced at 39% which was consistent with moderate Factor II deficiency. The laboratory values before and after transfusion are summarised in Table I.

To differentiate between the Type I (hypoprothrombinaemia) and Type II (dysprothrombinaemia), both quantitative and qualitative (functional and antigenic) Factor II assays were planned.

Table I: Summary of all relevant laboratory values of the patient before and after transfusion.

Tests	Before transfusions	After transfusions (14 days later)	Reference ranges
PT (seconds)	85.43 (markedly prolonged)	14.5 (slightly prolonged)	11-14 seconds
aPTT (seconds)	62.14 (markedly prolonged)	38.2 (mildly prolonged)	25-35 seconds
Thrombin time	Not done	18.5 (normal)	14-20 seconds
Factor II activity (%)	43%	39%	70-146%
Factor XIII (%)	Normal	Normal	>70%

PT: Prothrombin time; aPTT: Activated partial thromboplastin time.

However, due to the unavailability of antigen testing at our centre, only a functional assay was performed, which showed an activity of 43%. Antigenic testing was planned on follow-up. Factor XIII assay was performed and was within normal limits. The levels of Factor V, VIII, and fibrinogen were elevated.

Vitamin D was severely deficient (10.3 ng/mL), and IgE levels were markedly elevated (698.1 IU/mL). TORCH screening in both the child and mother showed past exposure with positive IgG and negative IgM. Ultrasound revealed multiple superficial nodules, raising suspicion for neurocutaneous syndromes, such as neurofibromatosis or tuberous sclerosis.[5] Neurocutaneous syndromes, such as neurofibromatosis and tuberous sclerosis, were considered. However, the absence of *cafe-au-lait spots*, Lisch nodules, cortical tubers, and hypomelanotic macules on clinical examination and imaging made these unlikely. Other differential diagnoses of skin nodules, such as histiocytosis and panniculitis, were also ruled out based on the absence of systemic signs and imaging characteristics.

The patient was managed with vitamin D supplementation and transfusions, and follow-up was planned. Genetic testing of the Factor II gene for pathogenic variants was not performed in this case due to resource constraints, but remains an important next step for definitive diagnosis.

DISCUSSION

This case illustrates how bleeding can occur even with moderate prothrombin deficiency. In paediatric populations, bleeding severity does not always correlate with clotting factor levels.[6] Although moderate deficiency is defined as 10-30% activity, this patient had spontaneous mucosal bleeding despite Factor II levels ranging between 39-43% on repeat testing, indicating variable phenotypic expression.[7] This case highlights several important considerations in the evaluation of rare bleeding disorders. Firstly, it underscores the necessity of performing coagulation assays after the effects of transfused blood products have waned, as early testing can yield falsely reassuring results. Secondly, it demonstrates that the severity of bleeding symptoms can vary even at moderate levels of factor activity, likely influenced by modifying genetic and environmental factors, and therefore, cannot be predicted solely by laboratory values. The distinction between qualitative and quantitative prothrombin deficiencies remains clinically relevant, although in practice it may not always be feasible to perform the required antigenic testing due to resource limitations. This case also emphasises the importance of detailed clinical assessment of skin and soft tissue lesions to correctly distinguish subcutaneous nodules with ecchymotic discolouration (resolving haematomas) from other types of nodules, ensuring accurate diagnosis and appropriate management.

Routine coagulation screening tests, such as PT and aPTT, often fail to detect moderate deficiencies.[7] Thus, unexplained paediatric bleeding warrants targeted factor assays.[8] Genetic variants in the *Factor II* gene explain some variability. Prothrombin complex concentrate (PCC) and fresh frozen plasma (FFP) are treatments for acute bleeds or surgical coverage. Long-term prophylaxis remains controversial and is usually reserved for recurrent or life-threatening bleeds. PCCs carry thrombotic risks, especially with frequent use, requiring clinical judgement.

Mechanistic studies show that deficiencies in thrombin amplification can disrupt clot stability even when screening tests are normal.[9] Chronic symptoms and diagnostic delays must be considered. Children with nodules or recurrent bleeding often face stigma or misdiagnosis. Early diagnosis enables better counselling and quality-of-life planning.

This case underscores the need for repeat testing after transfusions, comprehensive assessment of lesions, and consideration of qualitative defects. Although genetic testing could not be performed, here it remains important to fully characterise the defect. Factor XIII was subsequently tested and found to be within normal limits, which helped exclude additional coagulopathies.

PATIENT'S CONSENT:

Informed consent was taken from the patient's parents to publish the data concerning this case.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

FH: Conceptualised the case report, supervised clinical care, and provided overall guidance on manuscript development.
MU: Literature review, drafted the initial manuscript, and contributed to data interpretation.
RR: Manuscript writing, critical revision of the manuscript, and finalised the submission of the draft**.**
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