

An unusually severe hemorrhagic phenotype leading to prolonged diagnostic delay in PTPN11 variant Noonan syndrome

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Abstract

Background: Noonan syndrome is a RASopathy which carries autosomal dominant inheritance and is characterized by variable phenotypic expression involving craniofacial, cardiovascular, skeletal, hematological, and neurodevelopmental abnormalities. Bleeding manifestations are common and may result from platelet dysfunction or coagulation factor defects, often posing significant diagnostic challenges.

Case summary: A 21-year-old female presented with recurrent per-rectal bleeding since childhood, severe transfusion-dependent iron deficiency anemia, short stature, developmental delay, intellectual disability, hearing impairment, and multiple dysmorphic features. Despite repeated evaluations, the severity of anemia was disproportionate to the identified second-degree hemorrhoids. Initial hematological investigations, including coagulation studies, were largely unremarkable. Clinical examination revealed characteristic features suggestive of Noonan syndrome, including hypertelorism, down-slanting palpebral fissures, ptosis, webbed neck, low-set ears, scoliosis, pectus deformity, and widely spaced nipples. Exome sequencing identified a pathogenic heterozygous PTPN11 variant, c.1510A>G (p. Met504Val), confirming the diagnosis. Further evaluation revealed severe factor XI deficiency, likely explaining her recurrent bleeding. Hemorrhagic disorders occur frequently in patients with Noonan syndrome and may arise from diverse abnormalities involving platelets, coagulation factors, or vascular structures. However, initial laboratory findings may not correlate with clinical severity, making diagnosis difficult. In this patient, recurrent severe bleeding with initial near-normal coagulation parameters contributed to a prolonged diagnostic course. Recognition of characteristic phenotypic features, molecular genetic testing, and later identification of severe factor XI deficiency were crucial in establishing the diagnosis and cause of bleeding.

Conclusion: This case highlights the importance of considering Noonan syndrome in patients with initial unexplained recurrent bleeding, severe anemia, short stature, developmental delay, and dysmorphic features. Early clinical suspicion combined with genetic confirmation may facilitate timely diagnosis, cause identification and appropriate multidisciplinary management. [*J Assoc Clin Endocrinol Diabetol Bangladesh*, 2026;5(Suppl 1): S60]

Keywords: Noonan syndrome, Autosomal dominant inheritance, Hemorrhagic disorders, Exome sequencing, PTPN11

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