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CASE REPORT

Neonatal Onset Type 2B von Willebrand Disease due to p.Arg1306Trp Variant: a Case Report and a Literature Review

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SUMMARY

Background: **Type 2B von Willebrand disease (VWD) is a less common subtype and is difficult to diagnose. This case report and literature review highlights a rare neonatal onset of type 2B VWD initially misdiagnosed as neonatal alloimmune thrombocytopenia (NAIT).**
Methods: **The neonate presented with severe thrombocytopenia and was unresponsive to NAIT treatments. Genetic testing was conducted because of the unclear family history of thrombocytopenia.**
Results: **Next-generation sequencing revealed a p.Arg1306Trp von Willebrand factor variant, confirming type 2B VWD.**
Conclusions: **This study underscores the critical role of genetic testing in diagnosing challenging cases of neonatal thrombocytopenia, irrespective of family history, and aims to elucidate the clinical manifestations and course of neonatal onset type 2B VWD.**
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Supplementary Data

Table S1. Published cases of neonates diagnosed with type 2B von Willebrand disease by Next-Generation Sequencing.

Case [a]	Age/ gender [a]	Clinical manifes-tations [a]	Family history	Platelet counts (× 10^3/μL)	VWF: Rco (UI/dL)/ VWF: Ag (UI/dL) (ratio)	FVIII: C (UI/dL, %)	HMW multimers assay	RIPA (%, 0.6 mg/mL)	Genetic analyses	Treat-ment	Clinical course	Ref.
1	25 days/M	petechiae	no	20	8/40 (0.3)	50	reduced	ND	Het. p.V1316M (c.3946G>A)	anti-fibrino-lytic therapy, FVIII/ VWF & platelet trans-fusion	persistent thrombocyto-penia with some episodic mucosal bleeding until 5 years old	[9]
2	1 day/M	petechiae	yes (type 2B VWD)	4	25/106 (0.24)	100	ND	ND	p.V1316M (c.3946G>A) [c]	FVIII/ VWF & platelet trans-fusion	normal platelet count with no further bleeding, required intervention until 5 years old	[10]
3	1 day/F	petechiae small hematoma at an IV puncture site	yes (ITP)	9	normal	normal	absent	ND	Het. p.V1316M (c.3946G>A)	IVIG & platelet trans-fusion	anemia & thrombocyto-penia with 2 episodes of epistaxis until 12 months old	[11]
4	1 day/F	petechiae	no	10	8/105 (< 0.1)	94	decreased	ND	Het. p.L1460P (c.4379T>C)	IVIG & platelet trans-fusion	severe thrombocyto-penia with no spontaneous bleeding until 6 months old	[12]
5	1 day/M	petechiae	no	5 - 20	13/47 (0.3)	22	ND	ND	Hom. p.P1337L Hom. p.R854Q	IVIG & platelet trans-fusion	persistent thrombocyto-penia until 14 months old	[12]
6	6 days/F	petechiae, ecchy-moses, jaundice, subep-endymal hemor-rhage, bilateral intraven-tricular hemor-rhage	no	19	ND	ND	ND	ND	Het. p. V1316M (c.3946G>A)	IVIG, steroid & platelet trans-fusion	persistent thrombocyte-penia despite with no further treatment in need until 6 months old	[13]
7	4 days/F	jaundice, hemato-chezia, bruises, petechiae, hepato-spleno-megaly	yes [b]	10	5.1/50.3 (0.1)	58	ND	increased	Het. p.V1316M (c.3946G>A)	platelet trans-fusion	no further complaint of severe bleeding until 9 month-old age	[14]
8	3 days/F	multiple hema-tomas	yes (type 2B VWD)	10 - 11	40/146 (0.27)	110 - 147	absent	increased	Het. p.V1316M (c.3946G>A)	FVIII/ VWF & platelet trans-fusion	normal development with normalized platelet count without bleeding episodes at 8 month-old age	[15]
9	2 days/M	petechiae, ecchy-moses	yes [b]	8	32/83.2 (0.38)	84	ND	ND	Het. p.R1306W (c.3916C>T)	IVIG, steroid & platelet trans-fusion	almost normalized platelet count with intermittent ecchymoses due to trauma	pres-ent case

NGS - Next-generation sequencing, VWF - von Willebrand factor, Rco - ristocetin cofactor, Ag - antigen, FVIII - factor VIII, HMW - high molecular weight, RIPA - ristocetin-induced platelet aggregation, ND - not done, VWD - von Willebrand disease, ITP - immune thrombocytopenia, IVIG - intravenous immunoglobulin, Het - heterogeneous, Hom - homogeneous, Ref - references. [a] - Age/gender, clinical manifestations, and platelet counts were documented at the time of admission. [b] - The patient has a family history of bleeding, although its underlying etiology remains undetermined. [c] - It is not mentioned whether it is heterozygous or homozygous.