RESEARCH PAPER

Diagnosis And Management Of Von Willebrand Disease Type 3 In An Adolescent Girl Presenting With First-Episode Menorrhagia And Severe Anemia: Case Report

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Abstract

Von willebrand disease (vwd) is a common inherited bleeding disorder characterized by quantitative or qualitative deficiencies in von willebrand factor, which ultimately impairs platelet adhesion and reduces the stabilization of coagulation factor viii. This case report presents the clinical journey of a 13-year-old girl who experienced a life-threatening first-episode of menarche, manifesting as persistent per-vaginal bleeding for 11 days. At presentation, the patient exhibited severe pallor and profound anemia, with a hemoglobin level of 4.6 g/dl. Her clinical history was further notable for delayed wound healing and a prior requirement for blood transfusion at three years of age, suggesting an undiagnosed congenital coagulopathy. Laboratory evaluation demonstrated an activated partial thromboplastin time of 60.1 seconds, a bleeding time greater than 10 minutes, and a factor viii level of 2.8%. Further specialized assays revealed a ristocetin cofactor activity of 21% and a von willebrand antigen level of less than 2.2, confirming the diagnosis of type 3 von willebrand disease with severe secondary factor viii deficiency. Initial clinical stabilization was achieved through the administration of two blood transfusions, followed by the use of tranexamic acid and vitamin k. Hemostasis was definitively achieved after the targeted administration of purified freeze-dried human coagulation factor viii at a calculated dose of 750 iu/day for her 50 kg body weight. This case highlights the vital importance of early recognition and systematic screening for inherited bleeding disorders in adolescent girls presenting with heavy menstrual bleeding, particularly when accompanied by life-threatening anemia and a suggestive pediatric bleeding history.

Keywords: Adolescent Menorrhagia, Severe Anemia, Factor Viii Deficiency, Ristocetin Cofactor, Von Willebrand Antigen, Von Willebrand Disease Type 3.

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1. Introduction

Von Willebrand disease (vWD) is recognized as the most prevalent inherited bleeding disorder, yet it's most severe manifestation, Type 3 vWD, remains a rare and clinically daunting entity. Characterized by a near-complete absence of von Willebrand factor (vWF) in both plasma and cellular compartments, Type 3 vWD typically presents with a profound hemorrhagic phenotype that can mirror severe coagulation factor deficiencies [1], [2]. Because vWF serves as the essential carrier protein for Factor VIII, its absence results in a secondary, significant reduction in FVIII levels, leading to a hybrid clinical picture of both mucocutaneous bleeding and deep-tissue or joint hemorrhages [1], [3].

In the female population, the onset of menarche represents a critical physiological stress test for the hemostatic system. Heavy menstrual bleeding is a hallmark of vWD and is frequently the sole presenting symptom in post-menarchal females [4]. Despite its

prevalence, diagnostic delays are common, often misattributed to the hormonal immaturity of the adolescent hypothalamic-pituitary-ovarian axis [5]. In women, undiagnosed vWD often leads to a cycle of refractory menorrhagia and significant iron deficiency anemia, which profoundly impacts quality of life if not addressed through targeted hemostatic management [6], [7]. For adolescent girls, the first episode of menarche may be the index event that uncovers an underlying bleeding disorder, where a delay in recognition can rapidly escalate to hemodynamic instability and the need for urgent blood product transfusions [8].

The clinical presentation of Type 3 vWD is often more severe than milder forms, manifesting early in life through recurrent epistaxis, easy bruising, and prolonged bleeding from minor cutaneous injuries [3]. These symptoms, while suggestive, frequently overlap with other pediatric conditions, contributing to a general lack of awareness among healthcare providers. This diagnostic gap is particularly problematic given that sex-specific symptoms like menorrhagia can lead to recurrent complications during reproductive years, including peripartal hemorrhage and severe chronic anemia [6]. Studies have highlighted that while bleeding symptoms often begin in childhood, the definitive diagnosis of a bleeding disorder is frequently delayed until adulthood, increasing the risk of avoidable morbidity [5].

Effective management of Type 3 vWD necessitates a vigilant, multidisciplinary approach that combines rapid hemostatic correction with long-term prophylactic strategies. The primary therapeuti**2.** intervention involves the administration of plasma-derived vWF/FVIII concentrates to restore functional factor levels and prevent spontaneous hemorrhages [3], [9]. In cases of intractable or life-threatening menorrhagia at menarche, conventional hormonal therapies may prove insufficient, requiring advanced interventions such as recombinant factor VIIa or the placement of levonorgestrel-releasing intrauterine systems to achieve hemostasis [10], [11].

This case report details the presentation of a 13-year-old adolescent who presented with life-threatening menorrhagia and profound anemia shortly after her menarche. The patient's clinical history was marked by significant indicators of a bleeding diathesis, including delayed wound healing and a requirement for blood transfusion at age three. Upon admission, her laboratory profile revealed a critical hemoglobin level of 4.6 g/dL, a prolonged activated partial thromboplastin time (aPTT) of 60.1 seconds, and a Factor VIII level of 2.8%. Coupled with a vWF antigen level of less than 2.2 and a ristocetin cofactor activity of 21%, these findings definitively supported a diagnosis of Type 3 vWD. By reorganizing this clinical data into a structured case-report format, this manuscript aims to highlight the diagnostic and therapeutic challenges associated with severe vWD in the adolescent population and provides a framework for effective multidisciplinary management. The patient received a comprehensive treatment regimen, including two packed red blood cell transfusions and subsequent administration of tranexamic acid and vitamin K, ultimately achieving hemostatic stability through purified freeze-dried human coagulation factor VIII concentrate. Despite the efficacy of factor VIII/vWF concentrates, hypersensitivity reactions are a rare but significant management challenge due to limited alternative treatment options [9]. This necessitates careful monitoring and the availability of immediate interventions for potential allergic responses during concentrate administration, especially in patients with a history of atopy or previous adverse reactions. Moreover, the inherent variability in vWF levels, which can be influenced by factors such as anemia, inflammation, and hormonal fluctuations, often complicates the accurate diagnosis of VWD, especially when initial inpatient testing for VWF antigen and activity levels is performed during an acute bleeding episode [12]. Therefore, repeated testing after resolution of the acute phase is often crucial for confirmation and accurate subtyping of VWD [6].

Case Presentation

A 13-year-old female patient presented to the outpatient department of Prasutitantra evum Striroga with a chief complaint of persistent and excessive per-vaginal bleeding (menorrhagia) lasting for 11 days. The patient described a significant volume of blood loss, requiring the use of four to five saturated sanitary pads daily. Her menarche had occurred approximately six months prior, and this current episode was her third menstrual cycle. Upon detailed history taking, it was revealed that the patient had a history of delayed wound healing following minor injuries. Most notably, she had required a blood transfusion at the age of three due to a bleeding episode after a minor trauma, although no definitive hematological diagnosis was established at that time.

On clinical examination, the patient appeared ill and exhibited marked pallor, suggesting severe acute-on-chronic blood loss. Her vital signs indicated early hemodynamic compensation for hypovolemia, with a

pulse rate of 108 beats per minute and a blood pressure of 100/60 mmHg. A general systemic examination was performed; while the abdomen was soft with no palpable masses or organomegaly, a cutaneous examination revealed multiple ecchymoses and petechiae on the upper and lower limbs. These mucocutaneous findings are classic indicators of a primary hemostatic defect, typically involving platelet dysfunction or a deficiency in von Willebrand factor (vWF) [13].

Laboratory investigations were immediately prioritized to address the clinical suspicion of a severe inherited coagulopathy. The initial complete blood count confirmed life-threatening anemia, with a hemoglobin level of 4.6 g/dL. Her total leukocyte count was 11,200/mm³, and her platelet count was 310,000/mm³, which effectively ruled out thrombocytopenia or leukemia-associated bleeding as the primary cause. Coagulation screening revealed a prothrombin time within normal limits, but a significantly prolonged activated partial thromboplastin time (aPTT) of 60.1 seconds. This isolated prolongation of the aPTT, coupled with a bleeding time exceeding 10 minutes, pointed toward an intrinsic pathway defect,specifically a deficiency in Factor VIII or its essential carrier protein, vWF [8], [13].

To differentiate between various types of von Willebrand disease (vWD), specialized hemostasis assays were conducted. The results showed a Factor VIII coagulant activity (FVIII:C) of 2.8%, a ristocetin cofactor activity (vWF:RCo) of 21%, and a von Willebrand factor antigen (vWF:Ag) level of less than 2.2 IU/dL. These values,particularly the nearly undetectable vWF antigen and the severe secondary Factor VIII deficiency,are pathognomonic for Type 3 vWD, the most severe and rare form of the disease [3]. While Type 1 vWD is the most common cause of menorrhagia in adolescent females [7], Type 3 leads to much more profound clinical manifestations that mirror the severity of hemophilia [14].

The diagnosis of vWD in post-menarchal adolescents is often challenging due to the high prevalence of anovulatory cycles and hormonal imbalances in this demographic [4], [15]. However, the patient's history of transfusion in early childhood was a critical "red flag" that necessitated a comprehensive hematological workup [16]. In adolescent females experiencing refractory heavy menstrual bleeding, the lack of a formal diagnosis can lead to rapid hemodynamic instability and significant morbidity [8]. This case highlights that while mild bleeders often remain elusive to diagnosis [16], severe cases like Type 3 vWD require immediate recognition and specialized therapeutic interventions, including factor replacement, to stabilize the patient and prevent recurrent life-threatening episodes [14]. The combination of a suggestive pediatric history and severe adolescent menorrhagia should always trigger a thorough investigation into inherited bleeding disorders [4]. Prompt recognition and accurate characterization of VWD, especially Type 3, are crucial for instituting appropriate management protocols, which often involve desmopressin, VWF concentrates, or antifibrinolytics, tailored to the specific subtype and clinical presentation [14], [15]. For severe cases such as the adolescent described, recombinant factor VIIa may also be considered in intractable bleeding circumstances [11]. This approach is particularly critical given that menorrhagia is a frequent presentation of VWD in adolescent females and can be the sole presenting symptom, necessitating a high index of suspicion [4], [11]. The prevalence of von Willebrand disease in adolescent females experiencing menorrhagia is significantly higher than in the general population, ranging from 7% to 20%, compared to 1.3% [14]. Consequently, an expedited diagnostic pathway for VWD is warranted in adolescent patients presenting with heavy menstrual bleeding to mitigate delays in diagnosis and treatment, which can lead to increased morbidity [5]. Such delays are especially concerning given that, despite awareness efforts by organizations like the American College of Obstetricians and Gynecologists, bleeding disorders often remain underdiagnosed in women [17]. This underdiagnosis is particularly problematic as up to 20% of adolescents with menorrhagia may have an underlying bleeding disorder, with von Willebrand disease being the most common [18], [19].

3. Diagnostic Assessment

The diagnostic evaluation of an adolescent presenting with refractory menorrhagia requires a systematic approach to differentiate between common physiological anovulation and rare, life-threatening coagulopathies. In this case, the assessment began with a transabdominal ultrasonography, which revealed a uterus of normal dimensions and an endometrial thickness of 8 mm. These findings effectively ruled out significant structural abnormalities or intrauterine pathologies as the primary cause of the bleeding. Interestingly, imaging also noted mild splenomegaly, a finding that occasionally accompanies severe hematological disorders.

The patient’s laboratory profile at admission was dominated by severe, symptomatic anemia, with a

hemoglobin level of 4.6 g/dL. Such a profound drop in hemoglobin in a post-menarchal adolescent is rarely due to hormonal imbalance alone and strongly suggest an underlying systemic defect in hemostasis [7]. Initial screening for coagulation defects revealed a significantly prolonged activated partial thromboplastin time (aPTT) of 60.1 seconds (reference: 24–35 seconds), while the prothrombin time remained within normal limits. An isolated prolongation of the aPTT, when paired with a bleeding time exceeding 10 minutes, indicates a defect in the intrinsic pathway, often involving Factor VIII or its carrier protein, von Willebrand factor (vWF) [13], [20].

To confirm the specific nature of the coagulopathy, a comprehensive hemostatic panel was performed. The results showed a FVIII level of 2.8% (reference: 50–150%), which explains the observed aPTT prolongation [20]. Further specialized assays revealed a von Willebrand factor antigen (vWF:Ag) level reported as less than 2.2 IU/dL (reference: 50–200 IU/dL) and a ristocetin cofactor activity (vWF:RCo) of 21% (reference: 50–200 IU/dL). These laboratory markers,specifically the near-complete absence of vWF antigen and the secondary severe deficiency of FVIII,are the defining diagnostic criteria for Type 3 von Willebrand disease [3]. Unlike Type 1 or Type 2 vWD, which involve partial or qualitative defects, Type 3 represents a total quantitative deficiency that leads to a severe bleeding phenotype resembling moderate-to-severe hemophilia [1], [3].

The diagnostic process also considered the vWF:RCo/vWF:Ag ratio, which in this patient was calculated at approximately 0.09. Such a low ratio, coupled with absent platelet aggregation at a ristocetin concentration of 1.5 mg/mL, reinforces the diagnosis of severe vWD and necessitates a differential diagnosis that includes Bernard-Soulier syndrome due to the profound impact on platelet-vessel wall interaction [21]. Furthermore, clinicians must remain aware that adolescent menorrhagia can occasionally be the presenting sign of other systemic conditions, such as severe hypothyroidism, making a comprehensive history and pediatric bleeding assessment (e.g., Self-BAT scores) essential to avoid diagnostic pitfalls [22], [23].

In summary, the combination of nearly undetectable vWF:Ag, severely depressed FVIII, and a positive history of childhood bleeding provided definitive evidence for Type 3 vWD. This classification was critical for guiding the subsequent management strategy, as Type 3 patients typically require aggressive and specialized factor replacement therapy rather than standard hormonal or antifibrinolytic treatments alone to achieve hemostasis [3], [4].

4. Therapeutic Intervention

The therapeutic management of the patient was divided into two critical phases: immediate hemodynamic stabilization to address life-threatening anemia and targeted hemostatic correction to resolve the underlying coagulopathy. Upon admission, the patient's clinical status was critical, with a hemoglobin level of 4.6 g/dL. Emergency intervention began with the administration of two units of packed red blood cell transfusions, which provided the necessary oxygen-carrying capacity to stabilize her vital signs. Following the initial resuscitation, a multi-pronged pharmacological and factor-replacement strategy was implemented to achieve definitive hemostasis.

Pharmacological adjuncts included the administration of antifibrinolytic therapy and vitamin supplementation. Tranexamic acid was administered at a dose of 1 g intravenously in 100 mL of normal saline every 12 hours for a duration of three days. TXA serves as a pivotal agent in managing heavy menstrual bleeding by inhibiting plasminogen activation and stabilizing existing fibrin clots [24]. Complementing this, vitamin K (10 mg) was administered intravenously once daily for three days to support the synthesis of vitamin K-dependent clotting factors, providing a baseline for stable coagulation. Such multidisciplinary care, integrating both antifibrinolytic agents and specific factor replacement, is essential for managing the severe hemorrhagic complications associated with profound von Willebrand factor (vWF) deficiency [2], [25].

The definitive hemostatic intervention involved the administration of purified freeze-dried human coagulation Factor VIII/vWF complex. In Type 3 von Willebrand disease (vWD), the near-complete absence of vWF leads to a secondary, severe deficiency of FVIII, as vWF is required to protect FVIII from proteolytic degradation. The required dose was calculated based on the patient's body weight and the severity of the deficiency using the formula: $50 \text{ kg} \times 30 \text{ IU} \times 0.5 = 750 \text{ IU}$. Consequently, 750 IU/day of Factor VIII was transfused. Following this targeted replacement, the per-vaginal bleeding ceased promptly, underscoring the necessity of precise factor replacement in managing acute presentations of Type 3 vWD [11].

The rapid cessation of hemorrhage following Factor VIII/vWF administration supports the diagnosis of Type 3 vWD and differentiates it from other coagulopathies where response to factor replacement

may be less predictable. While desmopressin is often used in milder forms of vWD to induce the release of endogenous vWF stores [26], it is strictly contraindicated and ineffective in Type 3 vWD due to the total lack of synthesized protein [27], [28], [29]. In such severe cases, exogenous vWF-containing concentrates are the only reliable therapeutic option for both acute hemorrhage and long-term prophylaxis [30], [31].

In refractory clinical scenarios where standard factor replacement may fail,such as patients with alloantibodies or surgical complications,advanced hemostatic agents like recombinant Factor VIIa (rFVIIa) have been utilized to achieve bypass hemostasis [11], [32], [33]. Additionally, the use of vWF concentrates has been specifically validated for the reduction of menorrhagia in women with vWD, offering a safer and more targeted alternative to systemic hormonal therapy [34]. However, clinicians must also navigate the risks associated with various treatments; for instance, in cases of acquired von Willebrand disease (aVWD) or those requiring extracorporeal support, the risk of thromboembolism necessitates a nuanced benefit-risk assessment [35].

Long-term management for this patient will transition toward a personalized prophylactic regimen. This encompasses regular infusions of vWF-containing concentrates to prevent spontaneous hemorrhages, alongside iron replacement and potentially the use of levonorgestrel-releasing intrauterine systems or hormonal suppression to manage recurrent heavy menstrual bleeding [10], [28], [30]. This comprehensive, multidisciplinary approach is vital for minimizing the physical and psychological morbidity associated with the most severe form of von Willebrand disease.

5. Outcome and Follow-up

The immediate clinical outcome for the 13-year-old patient was the successful cessation of per-vaginal bleeding following the targeted administration of purified freeze-dried human coagulation Factor VIII/vWF complex at a dose of 750 IU/day. This rapid hemostatic response not only stabilized the patient's hemodynamic status but also provided definitive clinical confirmation of the laboratory diagnosis. This case strongly underscores the diagnostic value of early hematology consultation in adolescent girls presenting with first-episode menarche characterized by disproportionate blood loss, life-threatening anemia, or a pediatric history suggestive of hemostatic dysfunction,such as the patient's prior requirement for a blood transfusion at age three.

While the patient achieved acute stabilization, the long-term management of Type 3 von Willebrand disease (vWD) requires a chronic, multidisciplinary approach to prevent recurrent morbidity. Given the severe quantitative deficiency of vWF, these patients remain at high risk for future life-threatening menorrhagia and spontaneous mucocutaneous hemorrhages. Consequently, continued monitoring and individualized prophylactic factor replacement strategies are often warranted to maintain adequate hemostasis [11], [28]. For many adolescents, ongoing hormonal therapies, such as combined oral contraceptives or progestogen-only regimens, are integrated into the management plan to regulate the menstrual cycle and reduce the volume of menstrual blood loss [12]. In cases of persistent or refractory bleeding, further investigation is required to exclude concurrent gynecological pathologies, such as ovarian cysts or uterine abnormalities, which may exacerbate the bleeding phenotype [36].

For patients who prove refractory to conventional factor replacement or hormonal suppression, advanced hemostatic interventions may be necessary. Recombinant Factor VIIa (rFVIIa) has demonstrated efficacy as a "bypass" agent in adolescent patients with Type 3 vWD, particularly during surgical procedures or intractable bleeding episodes where standard therapies are insufficient [2], [11]. Additionally, in complex cases where patients develop allergic reactions or inhibitors to vWF/FVIII concentrates, successful desensitization protocols have been implemented to allow for continued use of essential replacement therapy [9]. In resource-limited settings where commercial factor concentrates may be unavailable, clinicians may rely on fresh frozen plasma, cryoprecipitate, and platelet transfusions as alternative measures to manage severe Type 3 vWD phenotypes [3].

It is critical to note that several common treatments for milder forms of vWD are inappropriate for Type 3. For instance, while desmopressin is an effective first-line treatment for Type 1 and some Type 2 vWD variants, its efficacy is non-existent in Type 3 due to the total absence of endogenous vWF stores [18], [29]. Furthermore, hormonal therapies alone often fail to control bleeding in patients with severely low vWF levels, as they do not address the underlying primary hemostatic defect [1]. Because post-menarchal adolescents often experience anovulatory cycles due to hormonal immaturity, the use of antifibrinolytics and factor replacement must be carefully balanced with hormonal regulation to ensure long-term stability and

prevent the cycle of recurrent severe anemia [6], [37]. This structured follow-up and prophylactic framework are essential for improving the long-term quality of life and reducing the healthcare burden for patients with this rare and severe coagulopathy.

6. Discussion

The clinical trajectory presented in this case serves as a paradigm for the diagnostic challenges associated with severe inherited coagulopathies in the adolescent population. Menarche represents a physiological "stress test" for the hemostatic system, where heavy menstrual bleeding often emerges as the index manifestation of an underlying bleeding disorder. In this patient, the constellation of severe anemia (hemoglobin 4.6 g/dL), a prolonged activated partial thromboplastin time (aPTT) of 60.1 seconds, and nearly undetectable levels of Factor VIII and von Willebrand factor (vWF) antigen is pathognomonic for Type 3 von Willebrand disease (vWD). The identification of such a rare and severe phenotype in the context of first-episode menorrhagia underscores the necessity of a high index of suspicion among primary care providers and gynecologists [12], [38].

The prevalence of bleeding disorders among adolescents presenting with HMB is significantly higher than previously recognized. Research indicates that between 17% and 50% of adolescent and adult women with increased or irregular menstrual bleeding may have an underlying coagulation defect, with vWD identified as the most frequent etiology [39]. Multicenter prospective studies have specifically found that approximately one-third of adolescents hospitalized for HMB possess a demonstrable bleeding disorder [38]. Despite this high prevalence, a profound "diagnostic gap" persists; the average age of diagnosis for women with bleeding disorders is often delayed until the fourth decade of life, frequently decades after the onset of their first symptoms [12]. In adolescents, this delay is largely attributed to the common clinical assumption that pubertal menorrhagia is a consequence of an immature hypothalamic-pituitary-ovarian axis and anovulatory cycles [37], [38].

The diagnostic barriers in this demographic are further exacerbated by laboratory and systemic challenges. For many adolescent females, heavy menstrual bleeding is normalized or misattributed to hormonal imbalances, which obscures the presence of underlying hemostatic defects [37], [38]. Furthermore, laboratory misdiagnosis remains a significant risk; specialized vWD assays are sensitive to various pre-analytical variables, and a single set of normal results may not definitively rule out the disorder, particularly in the post-menarchal period [4]. For patients with Type 3 vWD, however, the laboratory profile is usually unambiguous due to the near-total quantitative deficiency of vWF, which distinguishes it from the more common and often milder Type 1 vWD [3], [6].

A critical component of the diagnostic evaluation is the retrospective assessment of pediatric bleeding history. In this case, the patient's history of delayed wound healing and a prior requirement for blood transfusion in early childhood served as essential "red flags." When such clinical history is present alongside mucocutaneous findings such as ecchymoses or petechiae, it should immediately trigger a comprehensive hematological workup rather than a solely gynecological one [7]. Failure to recognize these signs can lead to inappropriate progression to definitive gynecological procedures, which can jeopardize future fertility and delay the administration of life-saving factor replacement [6], [12].

The clinical consequences of undiagnosed vWD extend beyond acute hemorrhagic episodes. Chronic, refractory HMB often leads to severe iron deficiency anemia, which profoundly impacts the physical and psychosocial quality of life for adolescent girls [6], [7]. Furthermore, Type 3 vWD represents the most severe phenotypic expression, where the total absence of vWF renders standard treatments like desmopressin ineffective, as there are no endogenous stores to be released [28], [29]. Consequently, cause-directed management using vWF/Factor VIII concentrates is the only reliable method for achieving hemostasis and preventing recurrent morbidity in this high-risk population [3], [30].

In conclusion, this case highlights the critical need for standardized screening protocols for all adolescents presenting with severe or refractory heavy menstrual bleeding. The integration of hematological evaluation early in the clinical pathway is essential to bridge the diagnostic gap, prevent life-threatening complications, and ensure that these patients receive targeted, multidisciplinary care that preserves their long-term health and fertility [12], [38].

7. Conclusion

The case of this 13-year-old patient demonstrates that first-episode adolescent menorrhagia can be the primary presenting symptom of Type 3 von Willebrand disease, the most severe and rare form of the disorder. By employing a targeted hematological workup, a life-threatening presentation characterized by profound anemia and persistent hemorrhage was successfully converted into a manageable clinical condition. The patient's rapid and positive response to purified Factor

VIII/von Willebrand factor complex, alongside essential supportive measures like blood transfusions and tranexamic acid, highlights the critical clinical necessity of cause-directed factor replacement therapy in managing severe bleeding phenotypes.

The high prevalence of von Willebrand disease among females presenting with heavy menstrual bleeding underscores the urgent need for the implementation of standardized diagnostic protocols. Persistent delays in diagnosis, which often exceed a decade, reflect a critical gap in clinician awareness and a historical gender bias that has skewed research and resources toward male-centric conditions such as hemophilia. Implementing robust screening tools and improving global access to specialized hemostasis testing are essential steps toward mitigating the disproportionate health and economic burden faced by women and girls with bleeding disorders.

Looking forward, the management of von Willebrand disease must transition toward a more personalized and proactive approach. While current treatment standards are effective, there remains a clear imperative for more targeted therapies and continued research into curative strategies, such as gene therapy. Addressing the historical underrepresentation of women in clinical research is pivotal in optimizing long-term outcomes and restoring the quality of life for those living with this debilitating condition.

TABLES:

Table 1. Patient profile and presenting clinical features

Parameter	Details
Age/Sex	13-year-old female
Presenting complaint	Per-vaginal excessive bleeding for 11 days
Estimated bleeding burden	4-5 pads/day
Menstrual history	Menarche 6 months earlier; LMP 03/12/2025
Relevant past history	Delayed wound healing and prior blood transfusion at age 3 years
General examination	Pallor +++
Vital signs	Pulse 108/min; blood pressure 100/60 mmHg
Abdominal examination	P/A soft
Ultrasonography	Uterus normal size; endometrial thickness 8 mm; mild splenomegaly

Table 2. Laboratory findings documented in the case

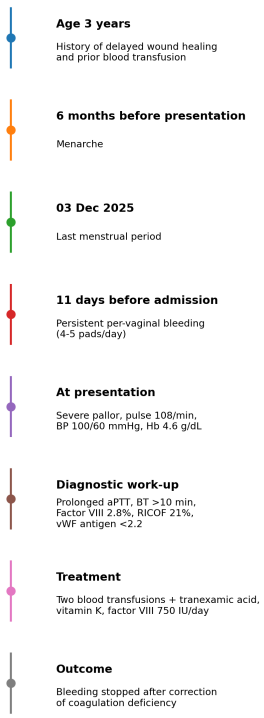
Investigation	Observed value	Reference range / note
Hemoglobin	4.6 g/dL	Severe anemia
Factor VIII	2.8%	50-150%
Ristocetin cofactor (RICOF)	21%	50-200%
Bleeding time	>10 min	Prolonged
aPTT / PTT	60.1 sec	24-35 sec
Von Willebrand antigen	<2.2	50-200

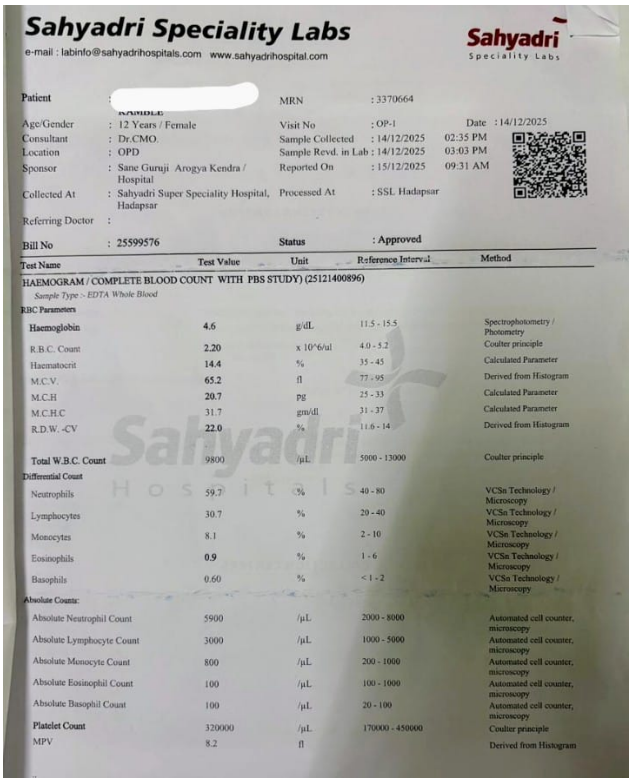
Table 3. Therapeutic interventions and in-hospital response

Intervention	Dose / schedule	Purpose / response
Blood transfusion	Two transfusions	Correction of severe anemia
Tranexamic acid	1 g IV in 100 mL NS every 12 hours for 3 days	Control of active bleeding
Vitamin K	10 mg IV once daily for 3 days	Supportive hemostatic measure
Purified freeze-dried human coagulation factor VIII	Calculated dose: 750 IU/day for 50 kg body weight	Targeted replacement therapy; bleeding stopped

FIGURES:

Figure 1. Clinical timeline from prior bleeding history to therapeutic response.

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Patient	:	MRN	: 3370664
Age/Gender	: 12 Years / Female	Visit No	: OP-1
Consultant	: Dr.CMO.	Sample Collected	: 14/12/2025 02:35 PM
Location	: OPD	Sample Revd. in Lab	: 14/12/2025 03:03 PM
Sponsor	: Sane Guruji Arogya Kendra / Hospital	Reported On	: 15/12/2025 09:31 AM
Collected At	: Sahyadri Super Speciality Hospital, Hadapsar	Processed At	: SSL Hadapsar
Referring Doctor	:		
Bill No	: 25599576	Status	: Approved

Test Name	Test Value	Unit	Reference Interval	Method
HAEMOGRAM / COMPLETE BLOOD COUNT WITH PBS STUDY) (25121400896)				
Sample Type :- EDTA Whole Blood				
RBC Parameters				
Haemoglobin	4.6	g/dL	11.5 - 15.5	Spectrophotometry / Photometry
R.B.C. Count	2.20	x 10^6/ul	4.0 - 5.2	Coulter principle
Haematocrit	14.4	%	35 - 45	Calculated Parameter
M.C.V.	65.2	fl	77 - 95	Derived from Histogram
M.C.H	20.7	pg	25 - 33	Calculated Parameter
M.C.H.C	31.7	gm/dl	31 - 37	Calculated Parameter
R.D.W. -CV	22.0	%	11.6 - 14	Derived from Histogram
Total W.B.C. Count	9800	/µL	5000 - 13000	Coulter principle
Differential Count				
Neutrophils	59.7	%	40 - 80	VCSn Technology / Microscopy
Lymphocytes	30.7	%	20 - 40	VCSn Technology / Microscopy
Monocytes	8.1	%	2 - 10	VCSn Technology / Microscopy
Eosinophils	0.9	%	1 - 6	VCSn Technology / Microscopy
Basophils	0.60	%	< 1 - 2	VCSn Technology / Microscopy
Absolute Counts:				
Absolute Neutrophil Count	5900	/µL	2000 - 8000	Automated cell counter, microscopy
Absolute Lymphocyte Count	3000	/µL	1000 - 5000	Automated cell counter, microscopy
Absolute Monocyte Count	800	/µL	200 - 1000	Automated cell counter, microscopy
Absolute Eosinophil Count	100	/µL	100 - 1000	Automated cell counter, microscopy
Absolute Basophil Count	100	/µL	20 - 100	Automated cell counter, microscopy
Platelet Count	320000	/µL	170000 - 450000	Coulter principle
MPV	8.2	fl		Derived from Histogram

Figure 2. Key laboratory values at presentation compared with reference limits.

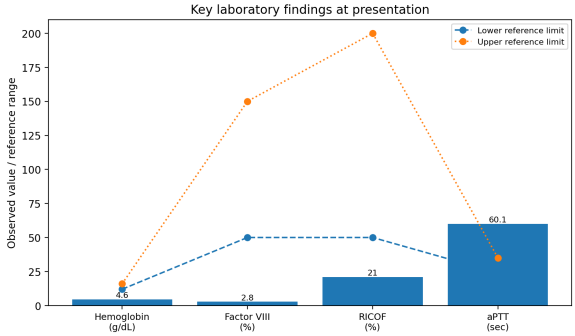
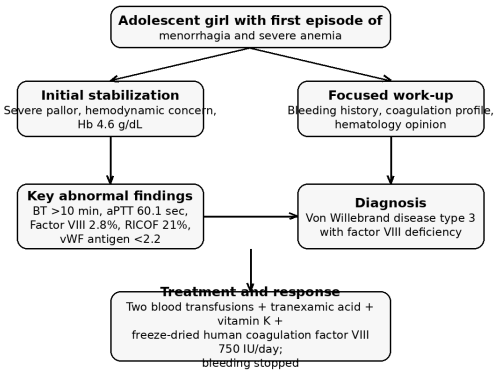
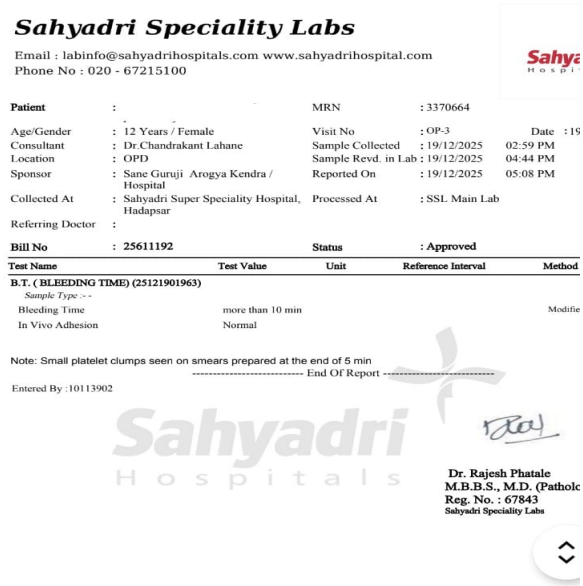


Figure 3. Diagnostic and management pathway reconstructed from the case details.

Clinical Image Documentation.




Sahyadri Speciality Labs
Email : labinfo@sahyadrihospitals.com www.sahyadrihospital.com
Phone No : 020 - 67215100

Patient	:	MRN	: 3370664
Age/Gender	: 12 Years / Female	Visit No	: OP-3 Date : 19
Consultant	: Dr.Chandrakant Lahane	Sample Collected	: 19/12/2025 02:59 PM
Location	: OPD	Sample Revd. in Lab	: 19/12/2025 04:44 PM
Sponsor	: Sane Guruji Arogya Kendra / Hospital	Reported On	: 19/12/2025 05:08 PM
Collected At	: Sahyadri Super Speciality Hospital, Hadapsar	Processed At	: SSL Main Lab
Referring Doctor	:		
Bill No	: 25611192	Status	: Approved

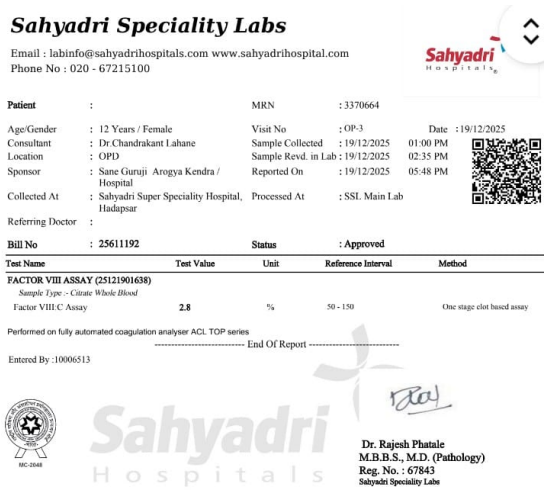
Test Name	Test Value	Unit	Reference Interval	Method
B.T. (BLEEDING TIME) (25121901963)				
Sample Type :- -				
Bleeding Time	more than 10 min			Modifie
In Vivo Adhesion	Normal			

Note: Small platelet clumps seen on smears prepared at the end of 5 min
End Of Report
Entered By :10113902
Dr. Rajesh Phatale
M.B.B.S., M.D. (Patholc
Reg. No. : 67843
Sahyadri Speciality Labs

Image 2. Laboratory image documenting coagulation-related investigation.

IMAGES:

Image 1. The initial detailed pathology report.



Sahyadri Speciality Labs

Email : labinfo@sahyadrihospitals.com www.sahyadrihospital.com
Phone No : 020 - 67215100

Patient	:		MRN	: 3370664	
Age/Gender	: 12 Years / Female		Visit No	: OP-3	Date : 19/12/2025
Consultant	: Dr.Chandrakant Lahane		Sample Collected	: 19/12/2025	01:00 PM
Location	: OPD		Sample Revd. in Lab	: 19/12/2025	02:35 PM
Sponsor	: Sane Guruji Arogya Kendra / Hospital		Reported On	: 19/12/2025	05:48 PM
Collected At	: Sahyadri Super Speciality Hospital, Hadapsar		Processed At	: SSL Main Lab	
Referring Doctor	:				
Bill No	: 25611192		Status	: Approved	

Test Name	Test Value	Unit	Reference Interval	Method
FACTOR VIII ASSAY (25121901638)				
Sample Type :- Citrate Whole Blood				
Factor VIII:C Assay	2.8	%	50 - 150	One stage clot based assay

Performed on fully automated coagulation analyser ACL TOP series

---------- End Of Report ----------

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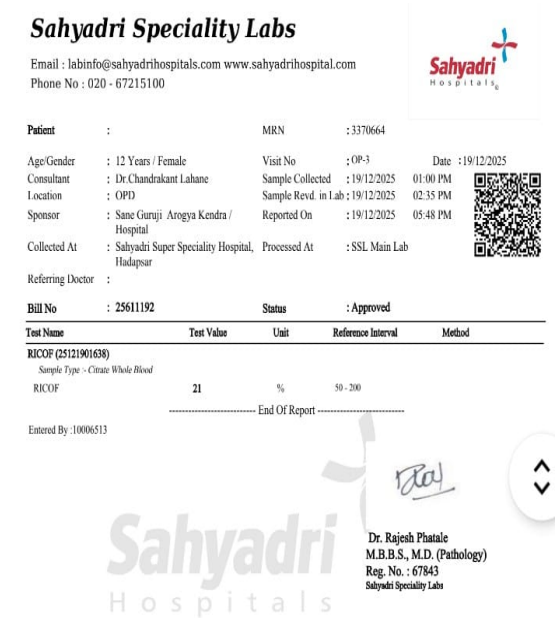
Image 3. Pathology image showing Factor VIII assay record as preserved.



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Email : labinfo@sahyadrihospitals.com www.sahyadrihospital.com
Phone No : 020 - 67215100

Patient	:		MRN	: 3370664	
Age/Gender	: 12 Years / Female		Visit No	: OP-3	Date : 19/12/2025
Consultant	: Dr.Chandrakant Lahane		Sample Collected	: 19/12/2025	01:00 PM
Location	: OPD		Sample Revd. in Lab	: 19/12/2025	02:35 PM
Sponsor	: Sane Guruji Arogya Kendra / Hospital		Reported On	: 19/12/2025	05:48 PM
Collected At	: Sahyadri Super Speciality Hospital, Hadapsar		Processed At	: SSL Main Lab	
Referring Doctor	:				
Bill No	: 25611192		Status	: Approved	

Test Name	Test Value	Unit	Reference Interval	Method
RICOF (25121901638)				
Sample Type :- Citrate Whole Blood				
RICOF	21	%	50 - 200	

---------- End Of Report ----------

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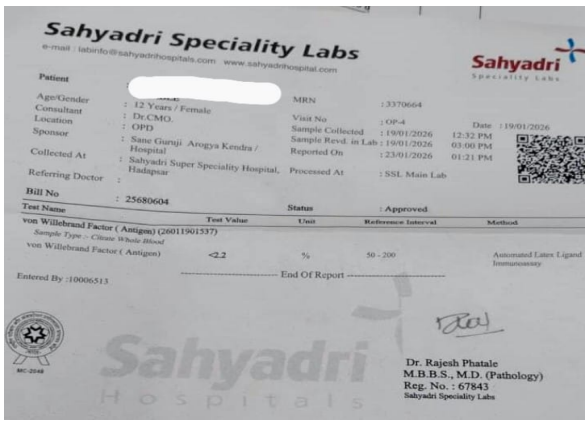
Image 5. Pathology image showing von Willebrand antigen report.



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Patient	[redacted]				
Age/Gender	: 12 Years / Female		MRN	: 3370664	
Consultant	: Dr.CMO.		Visit No	: OP-4	Date : 19/01/2026
Location	: OPD		Sample Collected	: 19/01/2026	12:32 PM
Sponsor	: Sane Guruji Arogya Kendra / Hospital		Sample Revd. in Lab	: 19/01/2026	03:00 PM
Collected At	: Sahyadri Super Speciality Hospital, Hadapsar		Reported On	: 23/01/2026	01:21 PM
Referring Doctor	:		Processed At	: SSL Main Lab	
Bill No	: 25680604		Status	: Approved	

Test Name	Test Value	Unit	Reference Interval	Method
von Willebrand Factor (Antigen) (26011901537)				
Sample Type :- Citrate Whole Blood				
von Willebrand Factor (Antigen)	<2.2	%	50 - 200	Automated Latex Ligand Immunoassay

---------- End Of Report ----------

Entered By :10006513

Dr. Rajesh Phatale
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Reg. No. : 67843
Sahyadri Speciality Labs

Image 6. Image of reference material included.

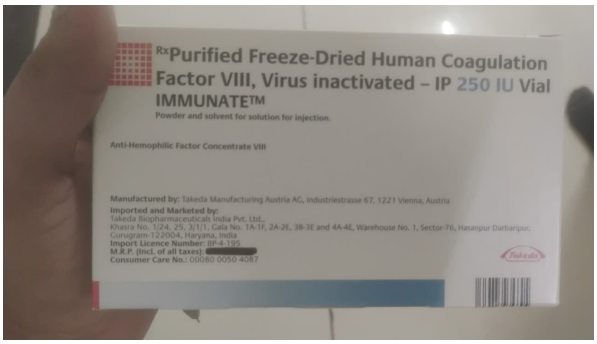
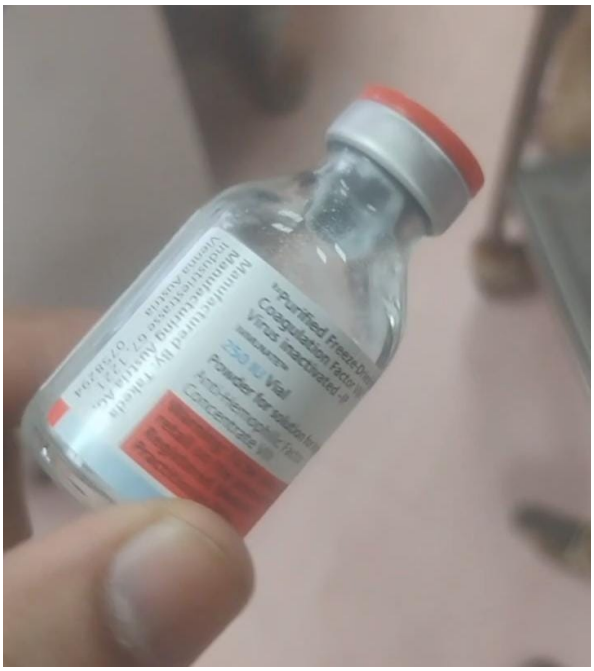


Image 7. Image of the administered coagulation-factor vial



Key Learning Points

• Severe adolescent menorrhagia should trigger evaluation for inherited bleeding disorders, especially when anemia is disproportionate or there is a prior bleeding history.

• Extremely low factor VIII, low ristocetin cofactor activity, prolonged a PTT, and markedly reduced von Willebrand antigen support the diagnosis documented in this case.

• Early hematology referral and targeted factor replacement can be decisive in stopping active bleeding and preventing further clinical deterioration.

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