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*Case report*

# Constitutional Factor XIII Deficiency in a Young Adult: A Case Report

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## Abstract

Constitutional factor XIII deficiency is a rare inherited coagulation disorder, with an estimated worldwide prevalence of approximately 1 case per 2 million individuals. It is transmitted in an autosomal recessive pattern, and homozygous or compound heterozygous forms are associated with a characteristic bleeding phenotype, often marked by delayed hemorrhage after trauma and specific bleeding sites. We report a case diagnosed at the Central Hematology Laboratory of Ibn Sina University Hospital in Rabat. A 21-year-old patient was admitted to the medical emergency department with a dark bluish thigh hematoma associated with painful muscle contraction, swelling sensation, and limited knee flexion. The patient had previously been managed as having hemophilia A; however, administration of factor VIII, even at high doses, resulted in no clinical improvement. Repeated hemostasis testing showed normal coagulation screening results, with a prothrombin time of 71% and a normal activated partial thromboplastin time ratio of 1. Coagulation factor assays, including anti-hemophilic factors VIII and IX, were within normal ranges, except for factor XIII activity, which was markedly reduced at 2.5% compared with a normal range of 70–140%. Family history revealed factor XIII deficiency in the patient's younger brother, who had presented with bleeding after umbilical cord separation during the neonatal period. Based on these findings, a diagnosis of isolated factor XIII deficiency was established.Congenital factor XIII deficiency should be considered in patients presenting with unexplained hematomas, hemarthroses, or bleeding manifestations despite normal routine coagulation tests, particularly when there is no response to factor replacement therapy.

**Keywords:** *Factor XIII deficiency; congenital bleeding disorder; congenital bleeding disorder; normal coagulation tests.*

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**Abbreviations:**

FXIII: Factor XIII

PT: Prothrombin time

aPTT: Activated partial thromboplastin time

INR: International normalized ratio

FVIII: Factor VIII

FIX: Factor IX

FFP: Fresh frozen plasma

GCS: Glasgow Coma Scale

IU: International unit

## 1. Introduction

Factor XIII (FXIII) deficiency is a rare inherited coagulation disorder and is considered the rarest of the coagulation factor deficiencies, with a worldwide prevalence of about 1 in 2 million individuals. It is transmitted in an autosomal recessive pattern, and homozygous or compound heterozygous forms are associated with a hemorrhagic syndrome characterized by its specific sites of bleeding (such as umbilical stump bleeding and extensive subcutaneous hematomas) and by the delayed onset of bleeding several hours after trauma (Katona et al., 2000).

The hemorrhagic syndrome of factor XIII deficiency usually occurs in the homozygous or compound heterozygous state, with factor XIII levels below 1 IU/dL, whereas heterozygous individuals are asymptomatic (Kobayashi et al., 1990). It is more frequent in populations with a high rate of consanguinity (Naderi et al., 2015). Patients with factor XIII levels ≥ 30 IU/dL are asymptomatic, while those with levels between 5 and 30 IU/dL may present mild spontaneous or post-traumatic bleeding manifestations (Menegatti et al., 2017).

Umbilical cord bleeding, observed in 87–100% of cases, is the most frequent and most characteristic bleeding manifestation of the disease (Anwar & Miloszewski, 1999). Intracranial hemorrhages are less common, reported in 20–30% of cases, but are associated with high mortality and morbidity (Maaloul et al.,2017).

Other bleeding manifestations may occur in 30–90% of cases, such as subcutaneous hematomas, intramuscular hematomas, and menorrhagia in women of childbearing age (Anwar & Miloszewski, 1999). Mucosal bleeding, including epistaxis, gingival bleeding, hematuria, or gastrointestinal hemorrhage, is less common (Medhaffar et al., 2006).

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In addition to bleeding manifestations, congenital factor XIII deficiency is also characterized by impaired healing of traumatic or surgical wounds, often resulting in keloid-like scarring (Dupoirieux et al.,1976).

In this work, we report a case of constitutional factor XIII deficiency in a young patient, diagnosed at the Central Hematology Laboratory of Ibn Sina University Hospital in Rabat.

**2. Case presentation:**

A A 21-year-old male patient was admitted to the medical emergency department of Ibn Sina University Hospital in Rabat for a dark bluish hematoma of the right thigh, associated with painful muscle contracture, a sensation of swelling, and limitation of knee flexion. His medical history included post-traumatic blindness of the right eye and an initial diagnosis of hemophilia A, followed at the Orthopedic and Physiotherapy Hospital Center and then at the emergency department, treated with fresh frozen plasma (FFP) with no history of inhibitors, with a last hospitalization 18 months earlier for a right thigh hematoma. The current illness began one month prior with a post-traumatic swelling of the right thigh (minor trauma with ecchymosis), which initially evolved favorably and spontaneously, but worsened two days before admission with marked swelling and functional impairment of the right lower limb. On admission, the patient was hemodynamically stable and apyretic (temperature 36.9 °C). Cardiovascular, respiratory, and neurological examinations (GCS 15/15) were unremarkable. Examination of the right lower limb showed an antalgic flexion deformity, a tense swelling extending from the groin to the popliteal fossa with local inflammatory signs (redness, warmth, and tenderness on palpation), pain on knee extension, and palpable, symmetrical tibial and femoral pulses, while the popliteal pulse was difficult to palpate.

The complete blood count showed stable hemoglobin at 10.7 g/dL, an initial leukocytosis of 11,700/mm³ that decreased to 8,000/mm³ on the second assessment (71% neutrophils, 23% lymphocytes), and a platelet count ranging from 270,000 to 316,000/mm³. The biochemical workup revealed a normal electrolyte panel, urea at 0.25 g/L, creatinine at 6.3 mg/L, and an initial C-reactive protein level of 126 mg/L that decreased to 70.9 mg/L. Coagulation studies showed a prothrombin time of 65%, a normal INR, and an activated partial thromboplastin time (aPTT) ratio of 1, while fibrinogen and D-dimer levels were not initially specified. Soft tissue ultrasound demonstrated a heterogeneous oval fluid collection within the muscles of the posteromedial compartment of the right thigh, suggestive of an intramuscular hematoma. A diagnosis of simple hematoma with possible abscess or compartment syndrome was made, and the patient was treated with transfusion of 5 units of fresh frozen plasma, followed by human coagulation factor VIII at a dose of 2,000 IU three times daily.

One month later, the patient was readmitted for a painful circumferential swelling of the posteromedial aspect of the right thigh, the knee, and the popliteal fossa, this time without any clear history of trauma, associated with complete functional impairment of the limb. On examination, the patient was hemodynamically stable and afebrile. There was a tense swelling extending from the mid-thigh to the popliteal fossa with local inflammatory signs, and distal pulses were present. The complete blood count was unremarkable, and C-reactive protein was 38 mg/L. Ultrasound revealed well-defined oval hematomas in the posteromedial region of the thigh (24 × 15 mm), in the popliteal fossa (13 × 17 mm), and in the upper medial compartment of the leg (27 × 16 mm). Treatment consisted of administration of 2,000 IU of factor VIII every 8 hours, then every 12 hours, followed by tranexamic acid at a dose of 1 g three times daily and paracetamol one ampoule three times daily.

A third admission occurred for swelling of the right leg. Laboratory tests showed hemoglobin at 10.4 g/dL, leukocytosis of 8,500/mm³, a platelet count of 333,000/mm³, C-reactive protein at 117.9 mg/L, factor XIII activity at 2.5% confirming a severe deficiency, and factor VIII at 240%, thereby ruling out the initial diagnosis of hemophilia A. On examination, the patient was hemodynamically stable and afebrile, with tense swelling involving the thigh and knee, associated with local inflammatory signs and preserved distal pulses.

The coagulation workup showed a prothrombin time of 71% (reference range: 70–100%), an INR of 1, and an activated partial thromboplastin time (aPTT) ratio of 1 (normal < 1.2), with factor XIII activity reduced to 2.5% and normal levels of the other coagulation factors, thereby excluding the previously suspected diagnosis of hemophilia A.

Family screening revealed factor XIII deficiency in the patient's younger brother, who had been diagnosed in the neonatal period following umbilical stump bleeding, thereby confirming autosomal recessive inheritance.

The absence of mucosal or umbilical bleeding, together with the late onset in adulthood, was consistent with a constitutional homozygous or compound heterozygous form.

The patient showed no clinical response to factor VIII alone but improved with a combination of fresh frozen plasma and factor VIII at a dose of 2,000 IU every 8 to 12 hours, together with antifibrinolytic therapy (tranexamic acid, Exacyl®). After several discharges with analgesic and anti-inflammatory treatment, long-term prophylaxis with weekly factor XIII replacement was recommended.

This case illustrates a delayed diagnosis of constitutional factor XIII deficiency, a diagnostic pitfall characterized by normal routine coagulation tests and delayed post-traumatic bleeding, initially misinterpreted as hemophilia A, in a young patient originating from a region with probable consanguinity.

**3. discussion**

In this case, a 21-year-old male was admitted to the medical emergency department of Ibn Sina University Hospital in Rabat for a spontaneous hematoma of the right thigh, presenting as a dark bluish lesion with painful muscle contracture, a sensation of swelling, and limited knee

flexion. Initially followed for hemophilia A after an ocular trauma (treated with fresh frozen plasma without inhibitors), he had recent post-traumatic bleeding recurrences (thigh and leg hematomas) despite elevated factor VIII levels at 240%. The hemostasis workup showed normal routine coagulation parameters (prothrombin time 71%, activated partial thromboplastin time ratio 1) but a severely reduced factor XIII activity at 2.5% (reference range 70–140%), confirming the diagnosis of constitutional FXIII deficiency after 16 years of diagnostic delay. Family screening revealed a similar deficiency in his younger brother, who had presented with neonatal umbilical bleeding, suggesting autosomal recessive inheritance in a context of probable consanguinity.

Factor XIII (FXIII), also known as fibrin-stabilizing factor, is an intra-cellular and circulating protein that contributes to increased clot resistance at the terminal stage of the coagulation cascade by cross-linking fibrin and strengthening the fibrin network. Beyond its hemostatic role, FXIII also participates in angiogenesis, by supporting endothelial cell proliferation and new vessel formation, and plays an important role in maintaining pregnancy and normal implantation (Schroeder & Kohler, 2013).

In the absence of factor XIII, fibrin strands are not adequately cross-linked, remain mechanically weak, and break down rapidly, preventing the formation of a stable clot and leading to continuous bleeding (Karimi et al., 2024).

Unlike other coagulation disorders, factor XIII deficiency does not prolong the time required for clot formation, and routine clotting times remain normal, but the resulting clot is unstable. This means that biological diagnosis is only possible through a specific factor XIII assay, which should be requested when the patient's history and/or clinical signs are suggestive of this condition (Acharya et al., 2004).

Factor XIII deficiency is an extremely rare disease, with a worldwide prevalence estimated at approximately 1 case per 2 million individuals (Acharya et al., 2004).

The underlying genetic defect is transmitted in an autosomal recessive manner, and the disease therefore affects males and females equally. However, it is most often diagnosed at birth or during childhood, and in about 80% of cases factor XIII deficiency is revealed in the neonatal period by umbilical stump bleeding (Acharya et al., 2004).

Our case is noteworthy for the particularly delayed diagnosis of severe constitutional factor XIII deficiency in a young adult who had been initially labeled and treated for many years as having hemophilia A, despite consistently normal coagulation times and no documented inhibitors. Clinically, the presentation was not dominated by the classic neonatal manifestations (umbilical stump bleeding, intracranial hemorrhage), but rather by recurrent intramuscular hematomas of the thigh, knee, and calf, sometimes following minor trauma, with a striking discrepancy between the severity of bleeding and a reassuring standard coagulation profile (PT, aPTT, FVIII, FIX), illustrating a true diagnostic pitfall.

The key element that prompted diagnostic re-evaluation was the finding of a profoundly decreased factor XIII level at 2.5%, together with a supranormal factor VIII level, which challenged the initial diagnosis of hemophilia A and instead placed the patient within the spectrum of rare constitutional coagulation factor deficiencies. In addition, family investigation identified a history of neonatal umbilical bleeding in his younger brother, in a context of probable regional consanguinity, reinforcing the autosomal recessive nature of the disorder and underscoring the importance of targeted family screening in such settings.

Finally, this case illustratively highlights the limitations of an approach focused only on aPTT and factor VIII/IX assays, and shows the need to systematically include factor XIII measurement in any presentation of recurrent deep bleeding with a normal conventional coagulation workup, particularly in regions with a high rate of endogamy (Tahlan & Ahluwalia, 2014; Lakrami et al., 2024).

A Moroccan retrospective series of 8 cases of FXIII deficiency diagnosed over 5 years (2020–2024) shows a predominance of severe forms (<10%) with classic manifestations: neonatal umbilical hemorrhages and spontaneous intracranial hemorrhages (3/8 cases), whereas moderate forms (2.6–37%) present with minor bleeding (ecchymoses, gingival bleeding, menometrorrhagia) or post-traumatic bleeding (intramuscular hematomas, hemarthroses), occurring when FXIII levels are below 10% (Lakrami et al., 2024).

Our observation falls within this spectrum of moderate/severe forms, with an FXIII level of 2.5% associated with recurrent muscular hematomas of the thigh and leg, without personal history of intracranial hemorrhage or umbilical bleeding, but confirmed by the brother's family history of umbilical cord hemorrhage (3/8 similar cases in the series).

Unlike the predominant neonatal cases in the series (early manifestations), our patient has a late diagnosis at 21 years of age after a therapeutic wandering under ineffective FVIII, illustrating the delayed post-traumatic bleeding characteristic of residual levels of 1–10% and highlighting the clinical heterogeneity reported in consanguineous Moroccan populations (Biswas et al. 2014; Pelcovits et al., 2021).

**4. Conclusion**

Congenital factor XIII deficiency is a very rare genetic condition and is the rarest of the coagulation factor deficiencies. Classically, factor XIII deficiencies are revealed by umbilical cord stump hemorrhage in the neonatal period in 80% of cases or by spontaneous intracranial hemorrhage in 30% of cases; other types of bleeding have also been reported, including postoperative hemorrhages in 40% of cases, subcutaneous bleeding in 57% of cases, and muscular hematomas in 49% of cases. The occurrence of the different hemorrhagic manifestations depends on the plasma level of factor XIII, and bleeding such as intramuscular hematomas, hemarthroses, and gastrointestinal hemorrhages

has been described when plasma factor XIII activity is below 10%.

The diagnosis of factor XIII deficiency should be considered in any hemorrhagic syndrome presenting with hematomas and/or hemarthroses, especially if the patient does not respond to substitution treatment with coagulation factors. The family history interview made it possible to establish the diagnosis of factor XIII deficiency.

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**Conflicts of Interest**

The authors declare no conflicts of interest.

**Data availability statement**

Data will be available upon request from the corresponding author.

**Author Contributions**

Kholoud Krimi contributed to the conception of the case report, data collection, literature review, and drafting of the manuscript. Hassane Mamad contributed to clinical interpretation, manuscript revision, and supervision. Jalila Zirar contributed to data interpretation and critical revision of the manuscript. Mohamed Ifleh contributed to clinical interpretation, manuscript revision, and supervision. Marwa Nabil contributed to data collection, organization of clinical and laboratory information, and manuscript drafting. Souad Benkirane contributed to clinical interpretation, manuscript revision, and supervision. Azlarab Masrar contributed to clinical interpretation, manuscript revision, and supervision.

All authors read and approved the final version of the manuscript.

**Ethics approval statement**

This case report was prepared in accordance with the principles of the Declaration of Helsinki. All patient information was anonymized to protect confidentiality. No identifying personal information or images are included in this manuscript. According to local institutional requirements, formal ethics committee approval was not required for this single anonymized case report.

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**References**

Katona, É., Haramura, G., Kárpáti, L., Fachet, J., & Muszbek, L. (2000). A simple, quick one-step ELISA assay for the determination of complex plasma factor XIII ($A_2B_2$). Thrombosis and Haemostasis, 83(2), 268–273. https://doi.org/10.1055/s-0037-1613798.

Acharya, S. S., Coughlin, A., DiMichele, D. M., & the North American Rare Bleeding Disorder Study Group. (2004). Rare Bleeding Disorder Registry: Deficiencies of factors II, V, VII, X, XIII, fibrinogen and dysfibrinogenemias. Journal of Thrombosis and Haemostasis, 2(2), 248–256. https://doi.org/10.1111/j.1538-7836.2003.t01-1-00553.x

Anwar, R., & Miloszewski, K. J. (1999). Factor XIII deficiency. British Journal of Haematology, 107(3), 468–484.

Biswas, A., Ivaskevicius, V., Thomas, A., & Oldenburg, J. (2014). Coagulation factor XIII deficiency: Diagnosis, prevalence and management of inherited and acquired forms. Hamostaseologie, 34(2), 160–166. https://doi.org/10.5482/HAMO-13-08-0046.

Dupoirieux, J., Fitoussi, P. S., & Renard, X. (1976). Le déficit congénital en facteur stabilisant de la fibrine : Facteur XIII. La Presse Médicale, 5, 2941–2943.

Karimi, M., Bereczky, Z., Cohan, N., & Muszbek, L. (2009, June). Factor XIII deficiency. In Seminars in thrombosis and hemostasis (Vol. 35, No. 04, pp. 426-438). © Thieme Medical Publishers.

Kobayashi, T., Terao, T., Kojima, T., Takamatsu, J., Kamiya, T., & Saito, H. (1990). Congenital factor XIII deficiency with treatment of factor XIII concentrate and normal vaginal delivery. Gynecologic and Obstetric Investigation, 29, 235–238. https://doi.org/10.1159/000293395.

Lakrami, S., Mamad, H., Lfaquir, F. Z., Zkik, A., Lazreq, F., Benkirane, S., & Masrar, A. (2024). Coagulation factor XIII deficiency: A report of 8 cases over a 5-year period [Poster presentation]. Journées de l'Innovation Biologique (JIB).

Maaloul, I., Medhaffar, M., Louhichi, N., Krichen, I., Alibi, S., Kmiha, S., et al. (2017). Déficit congénital en facteur XIII de la coagulation dans le sud tunisien. Blood Coagulation & Fibrinolysis, 28(6), 485–489.

Medhaffar, M., Elloumi, M., Guermazi, S., Kallel, C., Mseddi, S., Bellaaj, H., et al. (2006). Congenital factor XIII deficiency in the south of Tunisia. Pathologie Biologie, 54(6), 349–352.

Menegatti, M., Palla, R., Boscarino, M., Bucciarelli, P., Muszbek, L., Katona, É., Makris, M., & Peyvandi, F., for the PRO-RBDD Study Group. (2017). Minimal factor XIII activity level to prevent major spontaneous bleeds. Journal of Thrombosis and Haemostasis, 15(9), 1728–1736. https://doi.org/10.1111/jth.13772.

Naderi, M., Alizadeh, S., Kazemi, A., Tabibian, S., Zaker, F., Bamedi, T., Kashani Khatib, Z., & Dorgalaleh, A. (2015). Central nervous system bleeding in pediatric patients with factor XIII deficiency: A study on 23 new cases. Hematology, 20(2), 112–118. https://doi.org/10.1179/1607845414Y.0000000175.

Pelcovits, A., Schiffman, F., & Niroula, R. (2021). Factor XIII deficiency: A review of clinical presentation and management. Hematology/Oncology Clinics of North America, 35(6), 1171–1180. https://doi.org/10.1016/j.hoc.2021.07.009.

Schroeder, V., & Kohler, H. P. (2013). Factor XIII deficiency: An update. Seminars in Thrombosis and Hemostasis, 39(6), 632–641. https://doi.org/10.1055/s-0033-1353392.

Tahlan, A., & Ahluwalia, J. (2014). Factor XIII: Congenital deficiency factor XIII, acquired deficiency, factor XIII A-subunit, and factor XIII B-subunit. Archives of Pathology & Laboratory Medicine, 138(2), 278–281. https://doi.org/10.5858/arpa.2012-0639-RS