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Haematuria: A Rare Manifestation of Glanzmann Thrombasthenia

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Abstract **Case Report**

***Summary*:** Glanzmann Thrombasthenia (GT) is a congenital thrombopathy characterised by bleeding manifestations that are sometimes severe. Treatment is based on platelet transfusions during bleeding. We report a case of TG revealed by haematuria and which presented a severe bleeding syndrome refractory to transfusions. Treatment with injections of recombinant activated factor VII was necessary. This case illustrates the value of using recombinant activated factor VII in TG in case of antiplatelet alloimmunisation or in case of lack of response to platelet transfusions.

Keywords: Glanzmann Thrombasthenia; Haematuria, Platelets, factor VII.

INTRODUCTION

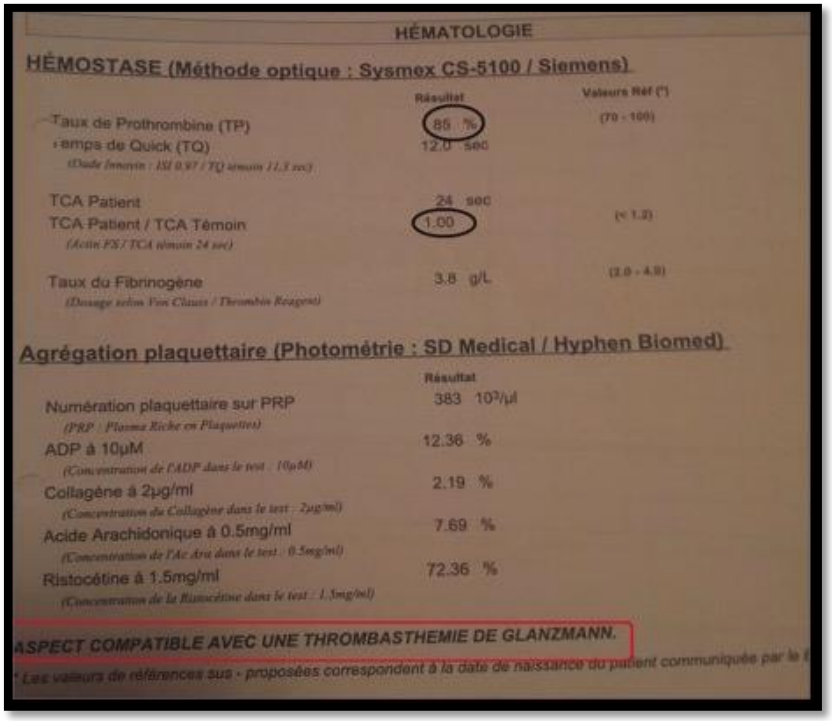
Glanzmann Thrombasthenia (TG) is a rare disorder caused by a deficiency of glycoprotein IIb/IIIa resulting in a defect in platelet aggregation [1]. The prevalence of this disease is estimated to be 1/1,000,000 [2]. This result in a disruption of primary haemostasis, the ultimate goal of which is to stop bleeding by forming a platelet plug [3]. The most common biological expression is prolonged bleeding time. It is an autosomal recessive inherited disease and appears to be more common in highly consanguineous ethnic groups such as Indians, Iranians, Iraqis, Palestinians and Jordanian Arabs, and even in populations of Roma origin [1]. Haematuria is a rare presentation of TG. Patients with TG usually respond well to platelet transfusions. On the other hand, the indiscriminate use of platelet concentrates could lead to alloimmunisation and thus to a refractory state [4]. We report the case of a young girl who presented with haematuria in the foreground of a clinical picture, which led to the diagnosis of Glanzmann thrombasthenia.

CLINICAL CASE

This was a 6-year-old girl, 1st of 2 siblings, attending school, from a second-degree consanguineous marriage. The history includes a well-monitored pregnancy, carried to term, vaccinated according to the national immunisation programme, with no notion of a stay in an endemic zone. Parents and siblings without any notable pathology, notably no notion of haematuria or deafness. In addition, we note the presence of bleeding after dental avulsions lasting several days. The patient consulted for a total macroscopic non-clotting haematuria evolving since 5 days, without notion of trauma, fever, mictional symptoms or physical effort. The clinical examination revealed a patient in good general condition, with discoloured conjunctiva, normal blood pressure, no purpura or oedema and abdominal palpation was unremarkable. A blood count was performed which showed haemoglobin of 6.7g/dl; platelets of 117,000 elements/mm3, and a normal prothrombin rate and activated partial thromboplastin time (PTT). The blood ionogram was normal with correct renal function. And the 24-hour proteinuria was negative. The cytobacteriological examination of the urine showed haematuria without leucocyturia, and the culture was sterile, which ruled out infection.

An abdominal ultrasound and an abdominal CT scan with injection of contrast medium were carried out, which came back normal, notably without any image of tumour or malformative uropathy. The patient continued to deglobulate, which prompted a blood transfusion and haemostatic treatments. In addition, the patient presented with profuse epistaxis requiring anterior and posterior packing to stop the bleeding. It should be noted that during the taking of a peripheral venous line, the patient presented a significant haemorrhage, which required a pressure dressing for

several hours. A haematological opinion was sought. An emergency haematological work-up was performed which showed a normal prothrombin level of 85% (N= 70-100), prothrombin time of 12 seconds, a patient/ control a PTT of 1.00 (N < 1.2), a fibrinogen level of 3.8 g/l (N= 2.0-4.0). Platelet function tests showed no aggregation with all agents tested. Platelet flow cytometry quantification revealed a complete absence of GPIIb/IIIa glycoprotein expression on the platelet surface, confirming the diagnosis of Glanzmann thrombasthenia [Fig1]. The patient received platelet transfusion without stopping the bleeding. She was put on Recombinant Activated Factor VII and a transfusion of packed red blood cells depending on the haemoglobin level. The evolution was marked by the disappearance of haematuria and epistaxis after several days of treatment and meching. A family survey was performed; the siblings were unaffected [Fig 2].


HÉMATOLOGIE

HÉMOSTASE (Méthode optique : Sysmex CS-5100 / Siemens)

	Résultat	Valeurs Réf (*)
Taux de Prothrombine (TP)	85 %	(70 - 100)
Temps de Quick (TQ)	12.0 sec	
TCA Patient	24 sec	
TCA Patient / TCA Témoin	1.00	(< 1.2)
Taux du Fibrinogène	3.8 g/L	(2.0 - 4.0)

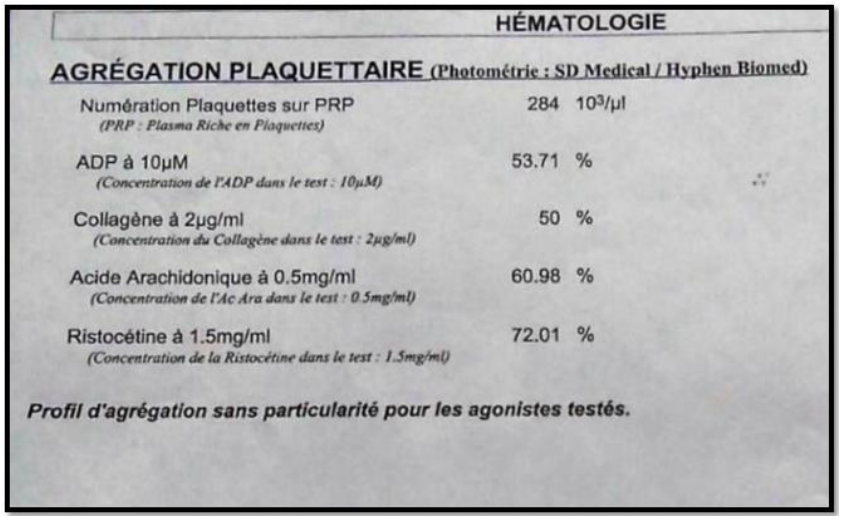
Agrégation plaquettaire (Photométrie : SD Medical / Hyphen Biomed)

	Résultat
Numération plaquettaire sur PRP (PRP : Plasma Riche en Plaquettes)	383 10^3/µl
ADP à 10µM (Concentration de l'ADP dans le test : 10µM)	12.36 %
Collagène à 2µg/ml (Concentration du Collagène dans le test : 2µg/ml)	2.19 %
Acide Arachidonique à 0.5mg/ml (Concentration de l'Ac Ara dans le test : 0.5mg/ml)	7.69 %
Ristocétine à 1.5mg/ml (Concentration de la Ristocétine dans le test : 1.5mg/ml)	72.36 %

ASPECT COMPATIBLE AVEC UNE THROMBASTHEMIE DE GLANZMANN.

(*) Les valeurs de références sus - proposées correspondent à la date de naissance du patient communiquée par le

Fig-1: **Absence of platelet aggregation in response to ADP, collagen, and Ristocetin confirm Glanzmann's Thrombathenia**


HÉMATOLOGIE

AGRÉGATION PLAQUETTAIRE (Photométrie : SD Medical / Hyphen Biomed)

Numération Plaquettes sur PRP (PRP : Plasma Riche en Plaquettes)	284	10^3/µl
ADP à 10µM (Concentration de l'ADP dans le test : 10µM)	53.71	%
Collagène à 2µg/ml (Concentration du Collagène dans le test : 2µg/ml)	50	%
Acide Arachidonique à 0.5mg/ml (Concentration de l'Ac Ara dans le test : 0.5mg/ml)	60.98	%
Ristocétine à 1.5mg/ml (Concentration de la Ristocétine dans le test : 1.5mg/ml)	72.01	%

Profil d'agrégation sans particularité pour les agonistes testés.

Fig-2: **Normal platelet aggregation study**

DISCUSSION

Glanzmann thrombasthenia is a rare autosomal recessive inherited disorder [5], first described in 1918 by a German paediatrician Glandzmann as <<Hereditary Haemorrhagic Thrombasthenia>> [6]. It is a thrombopathy related to a qualitative abnormality of platelets and inducing a disorder of primary haemostasis [7]. It is characterised by the inability of

platelets to aggregate despite a normal platelet count due to the absence of GPIIb/IIIa glycoproteins on the platelet membrane [1, 8]. Most often, the disease is diagnosed in early childhood before the age of 5 years, but it can also be diagnosed at an advanced age [9]. In our patient, the diagnosis was made at the age of 6 years. Its clinical manifestations are cutaneous-mucosal haemorrhages such as epistaxis, gingivorrhages, haematuria, petechiae, menometrorrhages and haemarthrosis [9, 10]. Bleeding is often abundant, leading to the development of martial deficiency anaemia requiring constant iron supplementation [5].

In the literature, haematuria during TG is not exceptional but rather rare [4]. In a study published by George *et al*. comprising a large cohort of 177 patients with the disease, only 10 patients had haematuria (6%) [5,11]. In another recently published retrospective study by Irem *et al*. involving 163 patients with TG, haematuria was present in only 13 patients (8%) [12]. Generally the treatment of haematuria in this condition is conservative [4] as in our patient, with only one case reported in the literature having undergone angio-embolisation to control the haematuria [13]. The severity of haematuria depends on the type of TG. Types I and II are characterised by quantitative abnormalities of the IIb/IIIa complex: in type I, the deficit is major and the complex is only present in trace amounts (<5%); in type II, the residual level is in the range of 5-20%. Type III, also known as the variants, is characterised by qualitative abnormalities of the complex, which may be present on the platelet surface at near-normal levels [14].

Although platelet concentrates are very effective, some patients become refractory to this treatment due to alloimmunisation and develop antibodies against the missing fraction (anti-GPIIb/IIIa), making subsequent platelet transfusions ineffective [15]. The efficacy of recombinant factor VII has been established in patients with anti-GPIIb/IIIa or anti-HLA alloimmunisation or lack of response to platelet transfusions [16]. An international study [17] of 59 patients with TG (including 29 alloimmunised and 23 platelet refractory patients) showed efficacy of recombinant activated factor VII in 64% of cases. In our patient, the use of recombinant activated factor VII helped to stop the bleeding. This therapy is given at a dose of 90 m/kg every 1.5 to 2 hours in an intravenous bolus of 2 to 5 minutes. Treatment is continued as long as the bleeding persists. The interval between doses can be gradually increased (from 4 to 12 hours) for as long as necessary. Treatment with recombinant activated factor VII does not require special biological monitoring [18]. It is expected to be the standard treatment for alloimmunised TG in the future [19-21]. TG is a serious disease; prevention of bleeding is important and should include healthy lifestyle avoiding sports activities with a high risk of trauma, the prohibition of drugs that interfere with platelet activity and the prohibition of intramuscular injections. Systematic screening for the disease in the patient's relatives using specific tests is essential for better management of the disease [7].

CONCLUSION

TG is a rare thrombopathy of infrequent neonatal onset. Its management requires above all preventive measures. Recombinant activated factor VII could be a therapeutic alternative in cases of refractory haemorrhagic syndrome or alloimmunisation.

REFERENCES

1. Saxena, R., Kannan, M. (2009). Glanzmann's thrombasthenia: An overview. Clin Appl Thromb Hemost, 15; 152-65.
2. Küçükkaya, R.D. (2013). Inherited platelet disorders including Glanzmann thrombasthenia and Bernard-Soulier syndrome. *ASH Educ Book, 1*; 268-75.
3. Nurden, A.T. (2006). Glanzmann thrombasthenia. *Orphanet J Rare Dis, 6*; 1-10.
4. Krishnamoorthy, S., Kumar, S., & Kekre, N. (2010). Hematuria: An uncommon presentation of Glanzmann's thrombasthenia—Lessons learnt. *Indian Journal of Urology: IJU: Journal of the Urological Society of India*, *26*(1), 115.
5. Franchini, M., Favaloro, E. J., & Lippi, G. (2010). Glanzmann thrombasthenia: an update. *Clinica Chimica Acta*, *411*(1-2), 1-6.
6. Glanzmann, E. (1981). Hereditare hamorrhagische Thrombasthenie, Ein Beitrag zur Pathologie der Blutplattchen. *Jb. Kinderheilkd*, *88*, 113-141.
7. Odoulami-Yehouessi, L., Sounouvou, I., Anani, L., Tachabi, S., Doutentien, C., & Latoundji, S. (2009). Rétinopathie drépanocytaire proliférante révélatrice d'une thrombasthénie de Glanzmann. *Journal Français d'Ophtalmologie*, *32*(10), 757-e1.
8. Saatchi, A. O., Kuvaki, B., Oner, F. H., Oren, H., Saatci, I., Durak, I., & Irken, G. (2002). Bilateral massive choroidal hemorrhage secondary to Glanzmann's syndrome. *Ophthalmic Surgery, Lasers and Imaging Retina*, *33*(2), 148-151.
9. Nurden, A. T. (2005). Qualitative disorders of platelets and megakaryocytes. *Journal of Thrombosis and Haemostasis*, *3*(8), 1773-1782.
10. Salles, I. I., Feys, H. B., Iserbyt, B. F., De Meyer, S. F., Vanhoorelbeke, K., & Deckmyn, H. (2008). Inherited traits affecting platelet function. *Blood reviews*, *22*(3), 155-172.
11. George, J. N. (1990). Caen JP, Nurden AT. Glanzmann's thrombasthenia: the spectrum of clinical disease. *Blood*, *75*, 1383-95.
12. Iqbal, I., Farhan, S., & Ahmed, N. (2016). Glanzmann thrombasthenia: a clinicopathological profile. *J Coll Physicians Surg Pak*, *26*(8), 647-50.
13. Briët, E., Vismans, F. J., & Van Voorthuisen, A. E. (1980). Renal embolisation in Glanzmann's

thrombasthenia. *British Medical Journal*, *281*(6247), 1039.

14. Bellucci, S., & Caen, J. (2002). Molecular basis of Glanzmann's thrombasthenia and current strategies in treatment. *Blood Reviews*, *16*(3), 193-202.
15. Poon, M. C., Zotz, R., Di Minno, G., Abrams, Z. S., Knudsen, J. B., & Laurian, Y. (2006, January). Glanzmann's thrombasthenia treatment: a prospective observational registry on the use of recombinant human activated factor VII and other hemostatic agents. In *Seminars in hematology* (Vol. 43, pp. S33-S36). WB Saunders.
16. Hedner, U. (2001, October). Recombinant factor VIIa (NovoSeven®) as a hemostatic agent. In *Seminars in hematology* (Vol. 38, pp. 43-47). WB Saunders.
17. Hedner, U. (2006). Mechanism of action, development and clinical experience of recombinant FVIIa. *Journal of biotechnology*, *124*(4), 747-757.
18. Boyer-Neumann, C., Mercier, F. J., & Veyradier, A. (2006). Facteur VII active recombinant (NovoSeven®): indications et limites. *Réanimation*, *15*(7-8), 576-583.
19. Poon, M. C. (2007). Clinical use of recombinant human activated factor VII (rFVIIa) in the prevention and treatment of bleeding episodes in patients with Glanzmann's thrombasthenia. *Vascular Health and Risk Management*, *3*(5), 655.
20. Poon, M. C., Zotz, R., Di Minno, G., Abrams, Z. S., Knudsen, J. B., & Laurian, Y. (2006, January). Glanzmann's thrombasthenia treatment: a prospective observational registry on the use of recombinant human activated factor VII and other hemostatic agents. In *Seminars in hematology* (Vol. 43, pp. S33-S36). WB Saunders.
21. Poon, M.C., D'Orion, R., Hann, I. (2001). Use of recombinant factor VII (Novoseven) in patients with Glanzmann thrombasthenia. *Semin Hematol*, *38*; 21–5.