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Case Report

Two case reports of Glanzmann thrombasthenia with intracranial hemorrhage and a review of the literature

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ABSTRACT

Background: Glanzmann's thrombasthenia (GT) is a rare autosomal recessive disorder characterized by impaired platelet function. Symptoms range from mild to life-threatening bleeding. However, it is extremely rare for a patient to have intracranial bleeding. This study presents two cases of GT: one with a spontaneous epidural hematoma (EDH) and the other with a subarachnoid hemorrhage due to traumatic causes. The discussion that follows then derives relevant supporting insights through a review of the literature.

Case Description: Case Report 1: A 9-year-old girl with a known case of GT presented to an emergency department with a severe headache but no other complaints or history of trauma. The physical examination was normal. Computed tomography (CT) head without contrast revealed multiple EDHs with no midline shift. She received factor VII, tranexamic acid, and platelets transfusion and was admitted to the intensive care unit to be managed conservatively. After a month, a CT head follow-up showed complete resolution of all hematomas. Case Report 2: A 20-year-old male with a known case of GT was brought to the hospital with a history of loss of consciousness for several minutes after a road traffic accident. He suffered from a headache on regaining consciousness and received analgesia. CT head showed diffuse subarachnoid hemorrhage. He was managed with factor VII, tranexamic acid, and platelets transfusion and was admitted to an intermediate care unit for close observation.

Conclusion: In a GT patient with intracranial hemorrhage, conservative management with close clinical observation and platelet transfusion in combination with recombinant activated factor VII and/or antifibrinolytics can be safely conducted.

Keywords: Case report, Epidural bleeding, Epidural hematoma, Glanzmann thrombasthenia, Subarachnoid hemorrhage

INTRODUCTION

In 1918, Dr. Eduard Glanzmann was the first to document a case of Glanzmann's thrombasthenia (GT). He described a platelet abnormality with defective clot retraction and an abnormal appearance on stained film.[15] GT is a rare autosomal recessive disorder characterized by impaired platelet function due to deficiency or abnormality of the membrane glycoprotein (GP) IIb-IIIa complex. Patients with GT present with a variety of hemorrhagic symptoms, ranging from mild to severe and life-threatening bleeds; however, intracranial bleeding represents just 2%

of overall hemorrhagic symptoms.[9,11] Despite how rare this kind of bleeding is and the extreme rarity of central nervous system (CNS) bleeding.[16]

CASE REPORT 1

A 9-year-old Saudi female presented to the Emergency Department (ED) of the Maternity and Children Hospital in our city, complaining of a severe headache and epigastric pain that had lasted for one week. The patient's history was mainly obtained from her mother. The headache was left unilateral, throbbing in nature, with intermittent attacks that responded partially to analgesia. It was preceded by photophobia, nausea, and vomiting. There was no history of head trauma, fever, neck pain, loss of consciousness, fits, neurological deficits, bruises, or bleeding from any body parts. This was a recurrent admission for the same complaint over the past six months. One month earlier, the patient was admitted to the Maternity and Children Hospital in Dammam City with the same complaint, which was diagnosed as a migraine. The patient has GT and shunted hydrocephalus since age one. Two of her younger siblings have GT, too. She also has helicobacter pylori gastritis on triple therapy. On examination, the patient was alert, conscious, oriented, and vitally stable. Her Glasgow coma scale (GCS) was 15/15. She looked ill and in pain. Pupils were round, regular, and reacting to light. There was no focal neurological defect. The ventriculoperitoneal shunt was working well with no signs of over-drainage**.** Other systems examination was unremarkable.

In the ED, she was given IV analgesics and proton pump inhibitors. Laboratory investigations were ordered. The results were as follows: hemoglobin 9.40 g/dL (N: 11.9–15), platelets count 442 × 10^16/mL (N:150–450), prothrombin time (PT) 7.50 (N:10.1–15), partial thromboplastin time (PTT) 25.40 (N: 26–40), and international-normalized ratio (INR) 0.58 (N: 0.8–1.2). Other findings were unremarkable. The patient underwent computed tomography (CT) of the brain, which revealed multiple biconvex hyperdense collections in the concavity of the skull bone, suggestive of acute epidural hematoma (EDH) [Figure 1]. She was admitted to the ward with a conservative management plan for neurosurgery consultation. Factor VII was given every two h for 12 h, then every 4–6 h for 24 h, based on the advice of a hematologist. The patient also received tranexamic acid and platelet transfusion. A follow-up CT was done after six hours. It showed the same results as the initial CT on admission. The patient was moved to the intensive care unit for close observation of her level of consciousness. No surgical intervention was done as the patient was fully conscious, and there was no change in the size of the hematoma.

On day 10 of her admission, the patient was doing well. She was conscious-oriented, with a GCS of 15/15 and stable vital signs. The headache had resolved, and there was no vomiting or neurological deficit. A fifth CT brain was done [Figure 2]. There was no change in hematoma size, and lysis of all the hematomas had started. The patient was discharged. A neurosurgery outpatient clinic follow-up for CT brain and further evaluation was arranged. The mother was instructed about what warning symptoms required an immediate ED visit. One month later, the patient was presented to the outpatient neurosurgery clinic in good health, where a follow-up CT showed complete resolution of all the hematomas [Figure 3].

CASE REPORT 2

A 20-year-old Saudi male came to the hospital via ambulance with a brief history of loss of consciousness after a road traffic accident that involved a traumatic brain injury. He was a backseat passenger whose head hit the window and experienced a severe headache after regaining consciousness. The patient did not complain of nausea, vomiting, convulsion, vision disturbances, slurred speech, or external bleeding. He is a non-smoker, a son of a consanguineous marriage, and a known case of GT. On physical examination, the patient was vitally stable, conscious, and oriented. His GCS was 15/15. His pupils were round, regular, and reacting to the light. There was no external bleeding, but there was purpuric eruption over his neck, upper and lower extremities, and a large hematoma over his right thigh.

There were no neurological deficits, and the other systems examination was unremarkable. Laboratory investigation revealed hemoglobin 14.60 q/dL, platelets 201 × 10^^{3}/micr, PT 12.50 s, PTT 32.70, and INR 1.10. Other findings were unremarkable. A CT brain revealed a bilateral subarachnoid hemorrhage that could be noted mainly at the basal cistern along the cerebellar tentorium and the high right occipital cortical sulci. It also showed a left high parietal extracranial subgaleal hematoma alongside a right occipital extracranial subgaleal hematoma. There was no midline structure shift, and the ventricular system was normal, with no signs or evidence of an underlying vascular pathology. The patient was given IV analgesia for the headache. The plan was to give 500 mg tranexamic acid; factor VII concentrate 90 mg/kg, and six units of platelets transfusion after a hematologist consultation [Figure 4].

The neurosurgery team has planned a conservative management approach. The patient was admitted to an intermediate care unit, with close monitoring of vitals, consciousness level, and pupil size, alongside further laboratory investigation, a follow-up CT brain after 24 h, and to continue with the hematologist's plan. In addition, the team was notified if there was any deterioration to require an urgent CT brain and to inform the on-call neurosurgeon. On the 2nd day, the patient was vitally stable, with no change

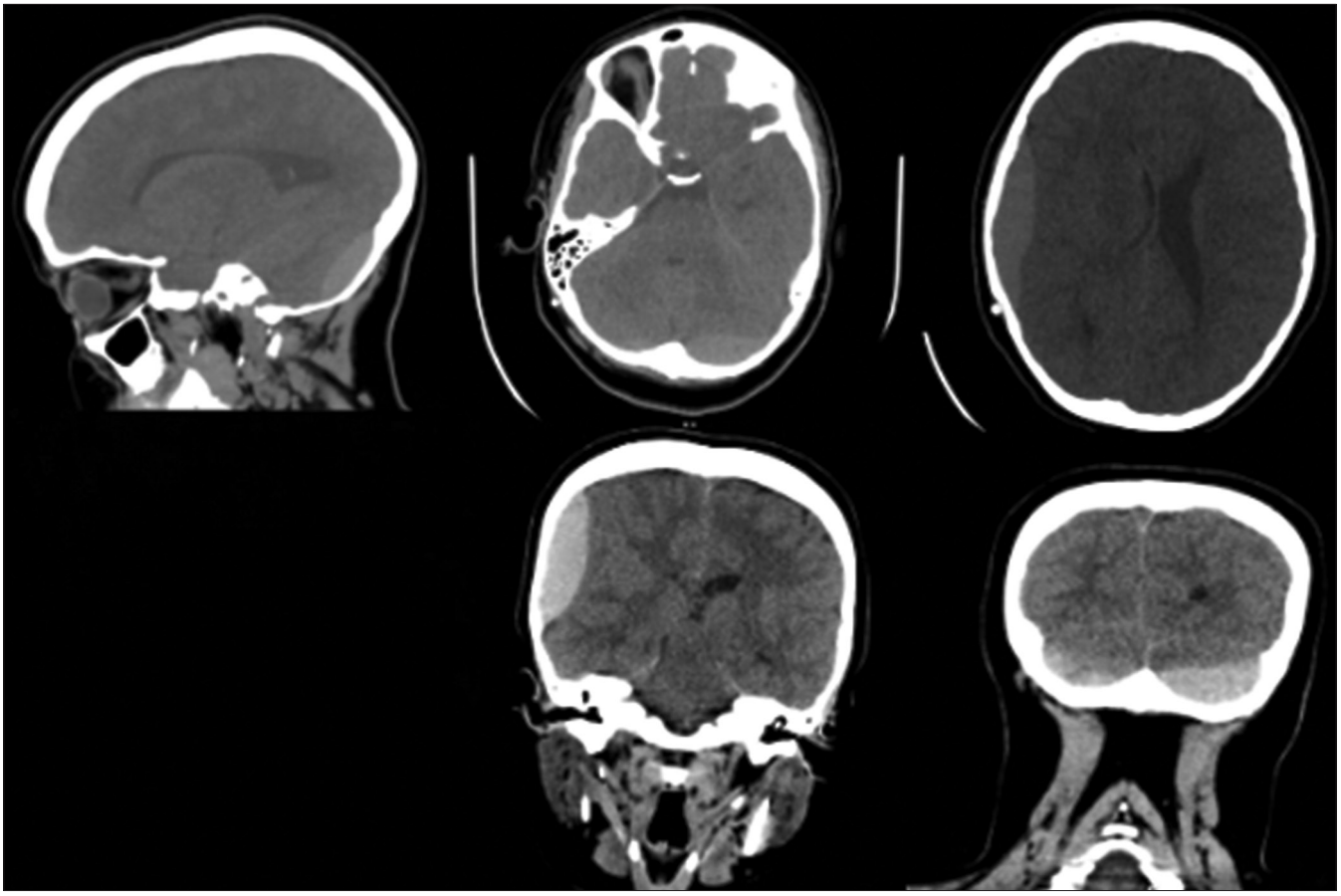

Figure 1: Initial computed tomography brain showing multiple biconvex hyperdense collection in the concavity of the skull bone, the largest in the right parietotemporal region measures 5.9 × 1.8 × 6.4m. Effacement of the right lateral ventricle with mild midline shift to the left with corresponding dilatation of the left lateral ventricle.

in consciousness level, no neurological deficits, nor changes in pupil size. There were no new complaints except for a headache, for which he received a 1 g perfalgan injection, to be given every six hours as necessary. A follow-up CT brain, when compared with the one done at admission, showed no appreciable time interval changes. Three days later, the patient was moved to a common room with continuity of the same management. After ten days of observation, the patient's condition was stable, and he was doing well, with no new complaints. A CT head was obtained [Figure 5]. It revealed a faint hyperdensity along the tentorium, though otherwise, no significant changes. He was discharged with a follow-up appointment after he was instructed about warning signs, which would require an ED visit.

DISCUSSION

GT is a rare autosomal recessive disorder characterized by impaired platelet function or a severe reduction in platelet aggregation due to deficiency or abnormality of platelet GP GPIlb and/or GPIlla receptors. Certain ethnic groups with higher rates of consanguinity, such as Indians, Iranians, Iraqi Jews, Palestinian and Jordanian Arabs, and French Gypsies, are more prone to GT.[10] In Saudi Arabia, too, consanguineous marriages are not uncommon.[3,13] Al-Fawaz *et al*. found that 18 of 168 patients with hereditary bleeding disorders had GT.[4] However, only 1–2% of GT patients experience intracranial hemorrhage. Clinical manifestations of GT include gastrointestinal bleeding, such as melena or hematochezia, gum bleeding, menorrhagia, and purpura. Epistaxis remains the most common cause of severe bleeding, especially in the pediatric population.[6] Similarly, a review of patients diagnosed with GT in Saudi Arabia found the most common clinical feature was epistaxis; no patient among the 16 included experienced CNS bleeding.[1] Like our cases, patients with GT tend to have normal platelet morphology and normal platelet count, prolonged bleeding time, and absent or decreased clot retraction. The management of GT consists mainly of avoiding the risk of hemorrhagic trauma. The treatment of bleeding in these patients is very difficult. However, recombinant factor VIIa has been used as a first line of therapy, which has yielded excellent clinical efficacy

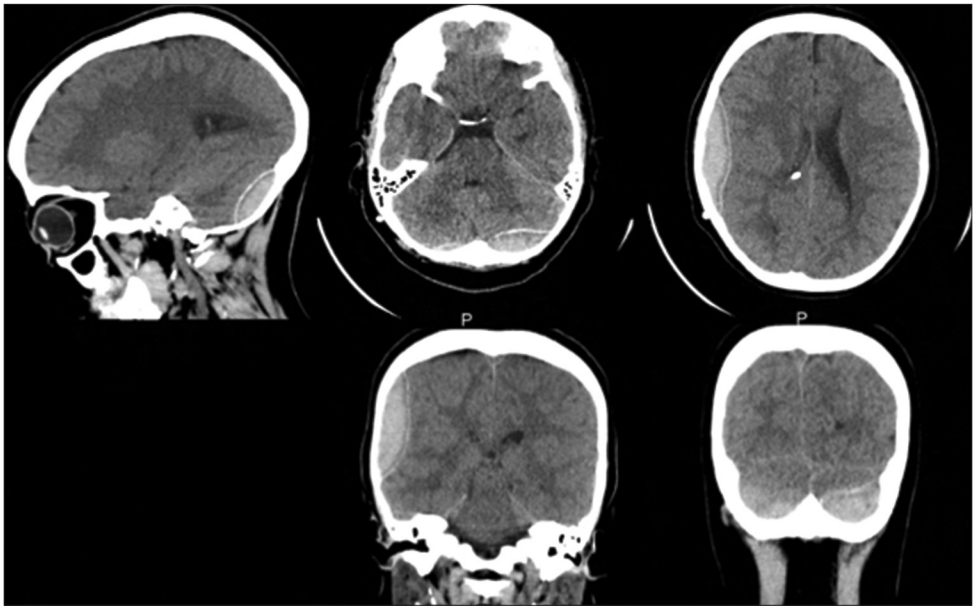

Figure 2: Computed tomography brain of day ten of admission showing multiple epidural hematomas. The new measure of right parietotemporal hematoma was 5.5 × 1.6 × 4.1 cm in its craniocaudal, transverse, and AP dimensions, and clot lysis probably taking place already.

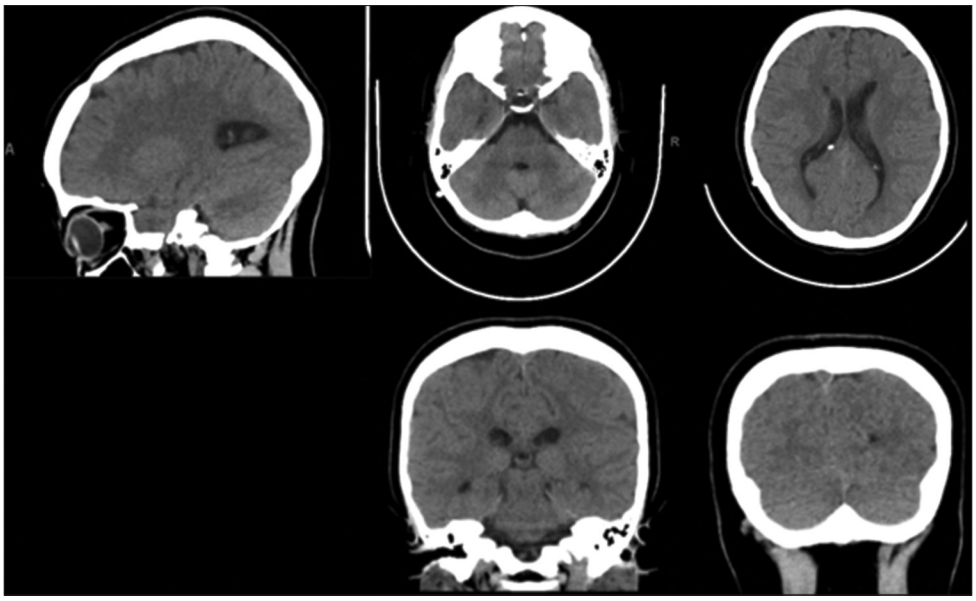

Figure 3: Follow-up computed tomography of the brain after a month revealing complete resolve of all hematomas.

in patients with GT. When the hemorrhagic symptoms are severe and resistant to platelet infusions, bone marrow transplantation is the sole curative option for GT patients.[14]

A literature search for cases of CNS bleeding in patients with GT yielded six studies, four of which included intracranial bleeding, and two were in the spinal cord.[2,5,7,8,12,17] Patients' ages ranged from 6 to 34. Three were pediatric cases, and three were adults.[2,5,7] Unlike our first case but like the second, the underlying cause of bleeding was due to traumatic injury (fall, surgical intervention, and motor vehicle accident) in five of the studies; only one involved spontaneous bleeding.[8] Bell and Savidge were the first to report a case of spinal dural hemorrhage in a patient with GT.[5] Al Barbarawi *et al*. reported a very complicated spinal EDH in a patient with undiagnosed GT, which was a complication of laminectomy, partial facetectomy,

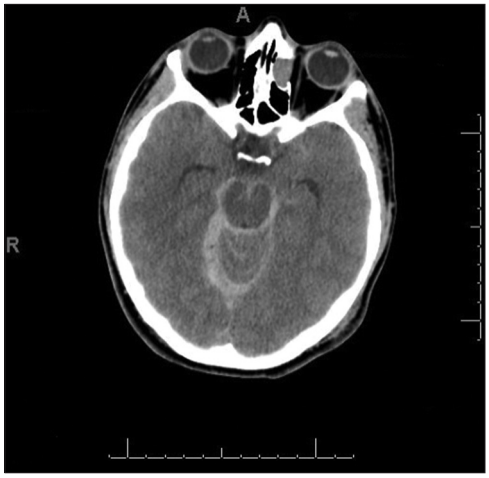

Figure 4: Computed tomography brain showing a bilateral subarachnoid hemorrhage that could be noted mainly at basal cistern along cerebellar tentorium and high right occipital cortical sulci and a left high parietal extracranial subgaleal hematoma in addition to a right occipital extracranial subgaleal hematoma.

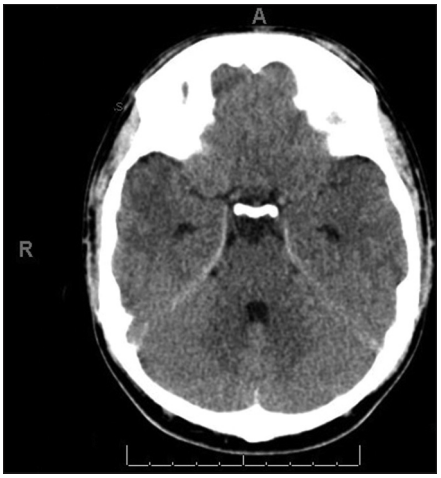

Figure 5: Computed tomography head on day 10 showing faint hyper density along the tentorium.

and discectomy with posterior interbody fusion and cage insertion. Furthermore, the patient underwent seven separate operations, four of which were for EDH evacuation, one for epidural collection evacuation, and one for laminectomy and larger cage replacement.[2] Similarly, Chakati *et al*. reported a complicated case of intracranial bleeding in a patient with undiagnosed GT, which required multiple surgical interventions to deal with the uncontrolled bleeding.[7] Like our first case, Fernández-Castellano *et al*. are the only ones to report spontaneous epidural bleeding in a known case of GT, but, in this case, the patient underwent two surgeries for two different EDHs during the same admission.[8] On the other hand, Yamahata *et al*. did not report any difficulties in dealing with EDH in a 7-year-old girl who presented after falling; the patient underwent craniotomy with hematoma evacuation.[17] Lee *et al*. reported a progressive EDH that also resulted from a fall; however, the patient did not undergo surgery until day four after admission, after a follow-up CT brain revealed that the volume of the hematoma was increasing slightly, along with edematous change.[12] Opposite to our cases, all cases in the literature necessitated surgical intervention; however, to control bleeding in patients, a systemic support system was also necessary.

CONCLUSION

GT is a rare inherited blood disorder, with spontaneous intracranial hemorrhage is an even rarer presentation of this condition, which can nonetheless be life-threatening. The reviewed cases showed that, provided the patient's level of consciousness is intact. Serial CT brain images do not reveal any change in the size of the hematoma; conservative management with close clinical observation and platelets transfusion in combination with recombinant activated factor VII and/or antifibrinolytics can be safely conducted in a GT patient with intracranial hemorrhage. The outcome was excellent and saved the patient from the risks of surgical intervention.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

Patients' consent not required as patients' identities were not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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