Glanzmann Thrombasthenia
A case report

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Glanzmann Thrombasthenia (GT)

- is a rare autosomal recessive bleeding syndrome
- characterized by the impaired function of platelets that are essential for proper blood clotting.
- The risk is the same for males and females.
- The symptoms of this disease are usually apparent at **birth (neonates) or during infancy**.

Rao, A.K., Coller, B.S. Hereditary qualitative platelet disorders. In Williams Hematology, eds. McGraw-Hill, Inc., 2015: 2039-2071.

GT Incidence

- estimated that one in one million individuals; but many cases have probably not been diagnosed.

Solh, T. Glanzmann's thrombasthenia: pathogenesis, diagnosis, and current and emerging treatment options. J.Blood Med,2015;6:219-227

- GT occurs with greater frequency in populations in which intermarriage within a group is more prevalent such as in some regions of the Middle East, India, and France.
- Recent evidence suggests that approximately 0.5% of healthy individuals in the general population are probably carrying one gene with an abnormal variant of GPIIb/IIIa.

Mutreja, D. Evaluation of platelet surface glycoproteins in patients with Glanzmann thrombasthenia: Association with bleeding symptoms. Indıan J Med Res.2017;215:629-634.

Symptoms

- The symptoms of GT usually begin **at birth or shortly later**
- include the tendency to bruise and bleed easily and especially postoperative bleeding
- GT is associated with clinical variability: some patients have only minimal bruising while others have frequent, severe and potentially fatal hemorrhages.
- to easy bruising, epistaxis, gingival bleeding, and/or purpura
- Women with GT often also have unusually heavy menstrual bleeding, irregular uterine bleeding, and excess bleeding in childbirth.

Glanzmann thrombasthenia: integrin alpha IIb beta 3 deficiency. Int J Hematol. 2000; 72(4):448-54.

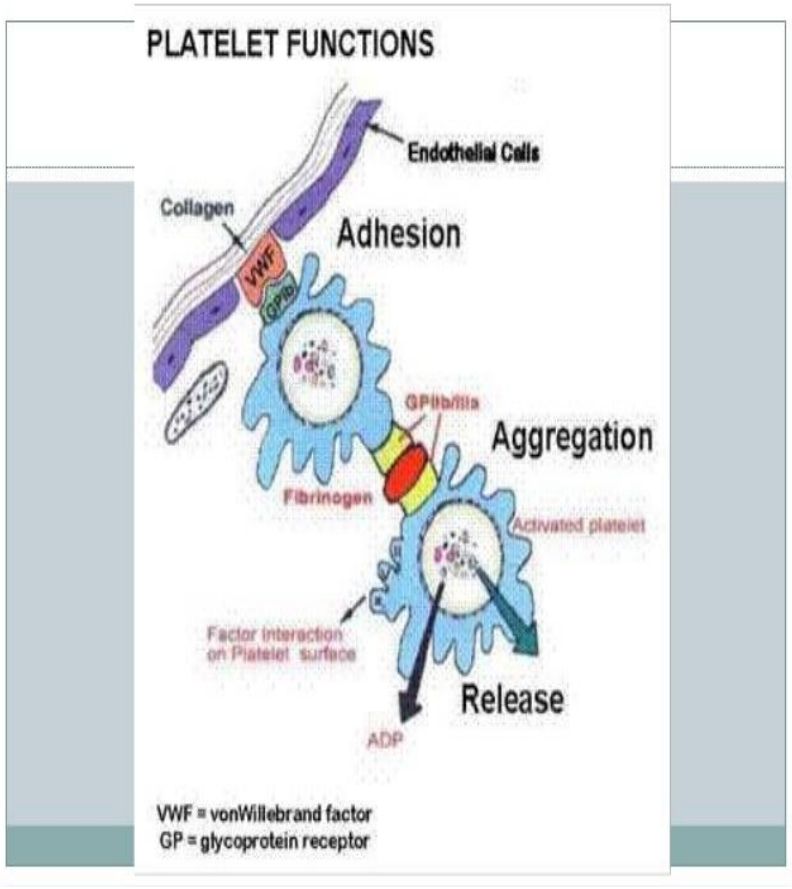
GT Diagnosis is made by;

- **CBC**- Most GT patients have a **normal number and morphology of platelets**
- **a prolonged bleeding time**
- **Platelet aggregation tests** are abnormal and show that platelets are not able to clump together when stimulated as they should to form platelet aggregates.
- GT is diagnosed by **flow cytometry CD41 /CD61 analysis-** tests that determine deficiency of the GPIIb/GPIIIa receptor.
- **Genetic tests mutations**

Aggregation of thrombocytes (platelets). Platelet rich human blood plasma (left vial) is a turbid liquid. Upon addition of ADP, platelets are activated and start to aggregate, forming white flakes (right vial)

Solh, T. Glanzmann's thrombasthenia: pathogenesis, diagnosis, and current and emerging treatment options. J.Blood Med,2015;6:219-227

Mechanism



Platelet glycoprotein IIb/IIIa (GP IIb/IIIa) complex is deficient or present but dysfunctional.

- The molecular basis is linked to quantitative and/or qualitative abnormalities of **GP IIb/IIIa** integrin.
- GPIIb/IIIa complex is heterodimer and acts fibrinogen receptor. This receptor mediates the binding of adhesive proteins that attach aggregating platelets and ensure thrombus formation at sites of injury in blood vessels.
- Defect in this complex leads to defective platelet aggregation and subsequent bleeding.
- Aggregation of platelets occurs in response to ristocetin, but not to other agonists such as ADP, thrombin, collagen, epinephrine or arachidonic acid.

Di Minno G. Glanzmann's thrombasthenia (defective platelet integrin alphaIIb-beta3): Proposals for management between evidence and open issues. Thromb Haemost 2009; 102 : 1157-64.

Classification of GT

- GT has three categories of severity, depending on the importance of the platelet deficiency in integrin complex GPIIb/IIIa.

- Type 1 : A level less than 5 % of normal
- Type 2 : A level between 5-20 % of normal
- Type 3 : with levels of more than 50 % of normal, but with major abnormalities in the way platelets aggregate

Glanzmann thrombasthenia: integrin alpha IIb beta 3 deficiency. Int J Hematol. 2000; 72(4):448-54.

Our Case

- 40 years old, male
- No family's story
- Posttraumatic bruises such as after playing football
- No severe compliants till two months ago the patient had epistaxis lasting one week
- After second epistaxis attack his physcian advices a nose operation for bleeding
- Hematology consultation is requested

Lab results

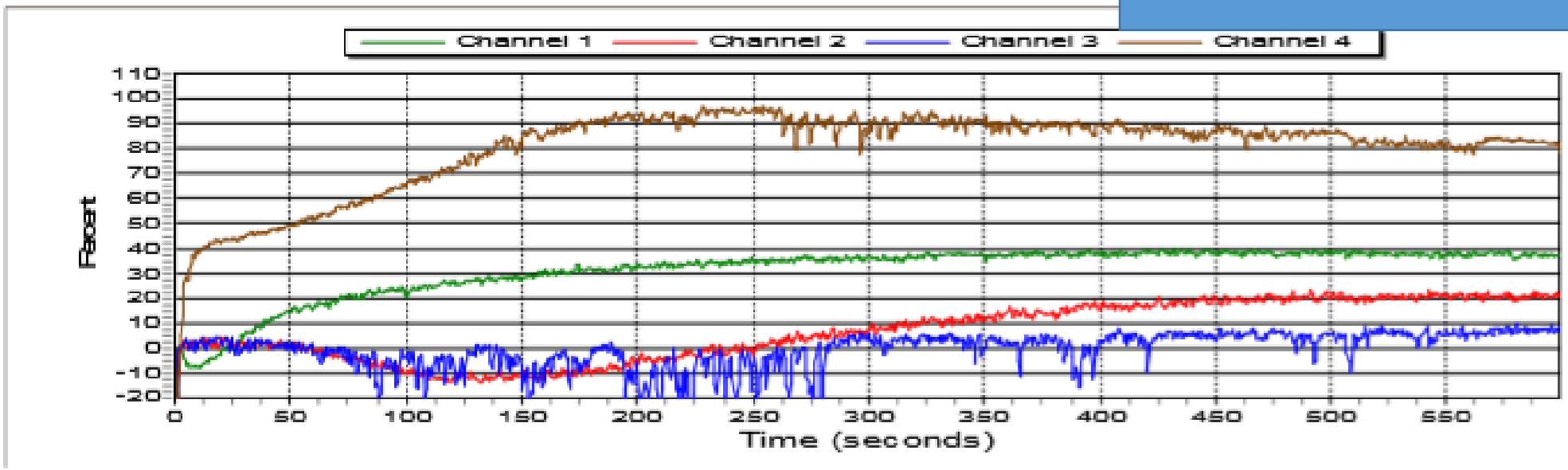
- CBC: normal,
- Platelet counts :normal $162*10^3/\mu L$
- PDW normal,
- INR 0.91, APPT 25 sec, fibrinogen 189 mg/dL,
- Peripheral smear normal,
- Bleeding time normal,
- Collagen-epinephrine closing time:>300 sec (PFA200-Siemens)
- Collagen-ADP closing time:>273 sec (PFA200-Siemens)

Platelet Aggregation Tests

We performed this analysis by AggRam (Helena Lab)

Aggregation of platelets occurs in response to ristocetin,

but not to ADP, collagen and epinephrine.



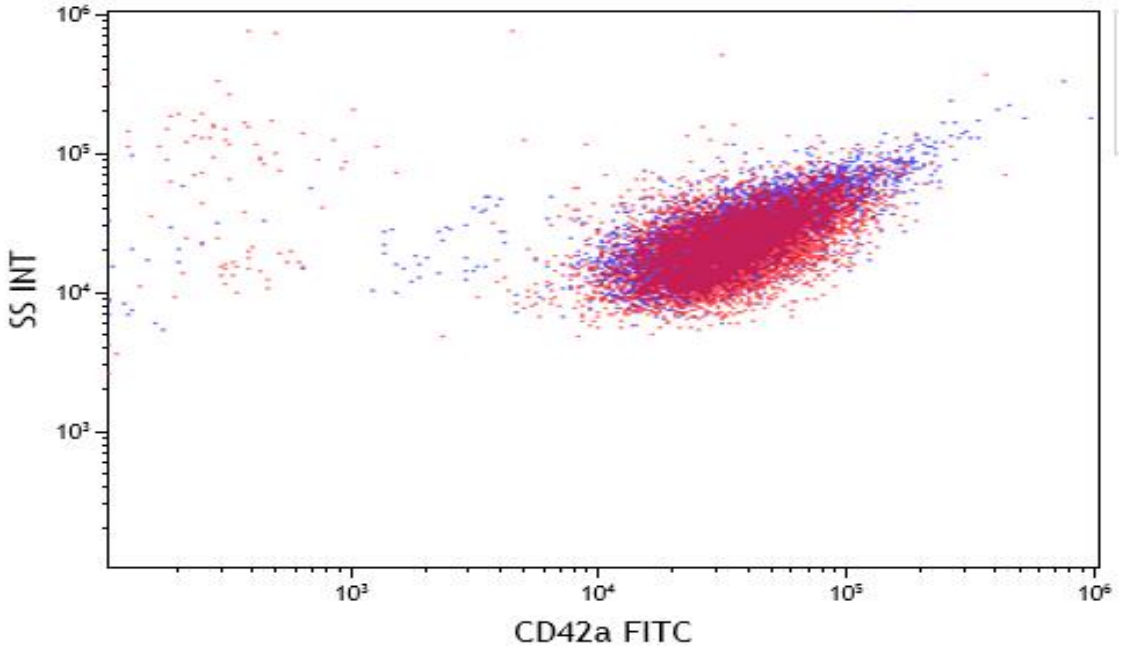
Chnl	Reag	Lot No.	Conc.	Units	PPP	PRP	Max %	TMax
1	Adenosine Diphosphate		10	µM	0,044	0,127	39,9	436
2	Collagen		10	ug	-0,004	0,039	23,8	543
3	Epinephrine		10	µM	0,043	0,087	9,6	580
4	Ristocetin		1,2	mg/mL	0,056	0,123	96,9	255

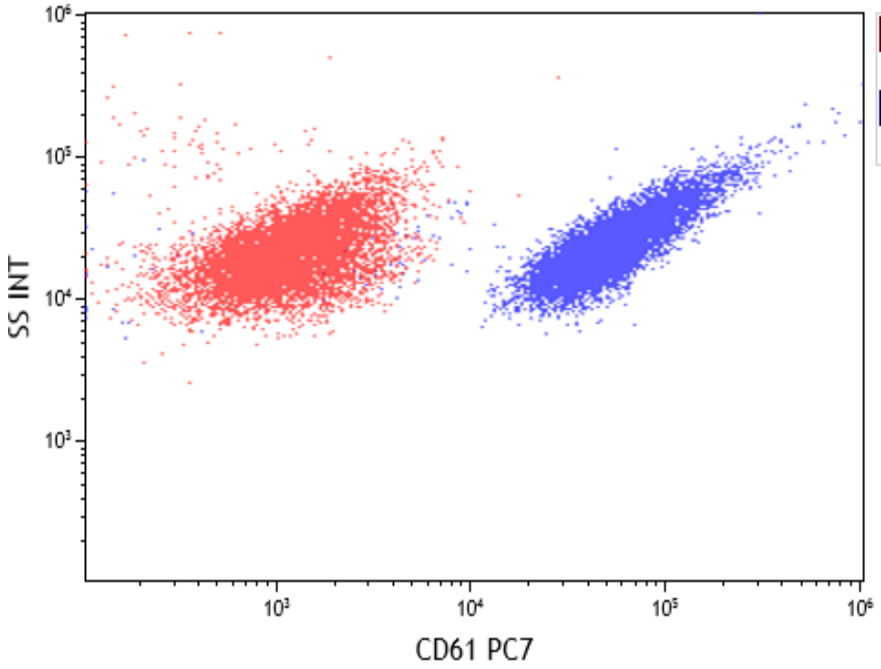
Flow cytometry analysis

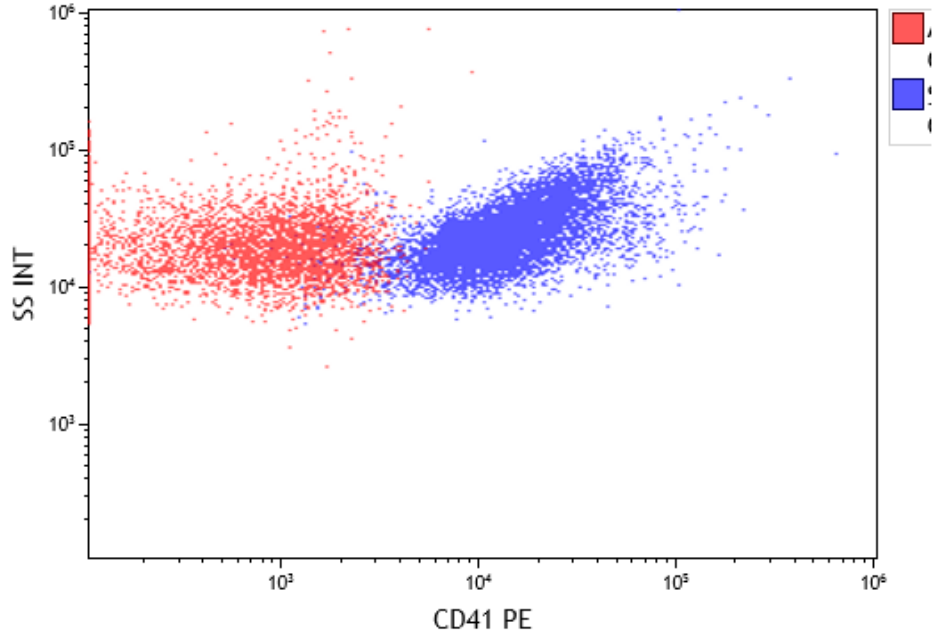
CD41 (GPIIb), CD61 (GPIIIa) agregation markers negative
CD42a adhesion marker
NaviosEX (Beckman Coulter) analyser

Red: Patient

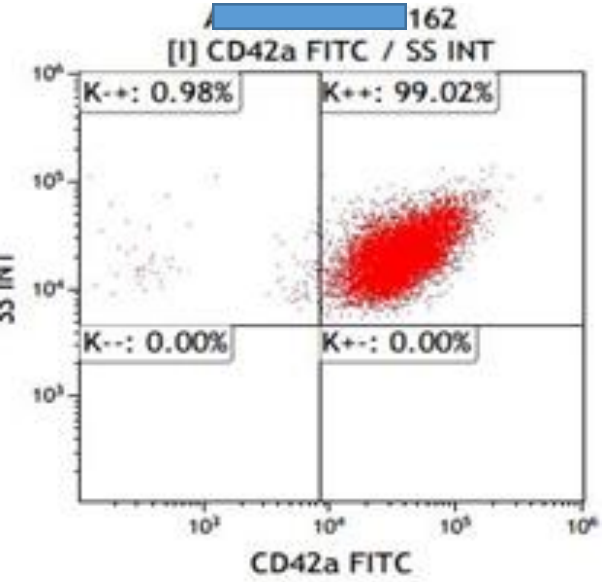
Blue: Healthy control

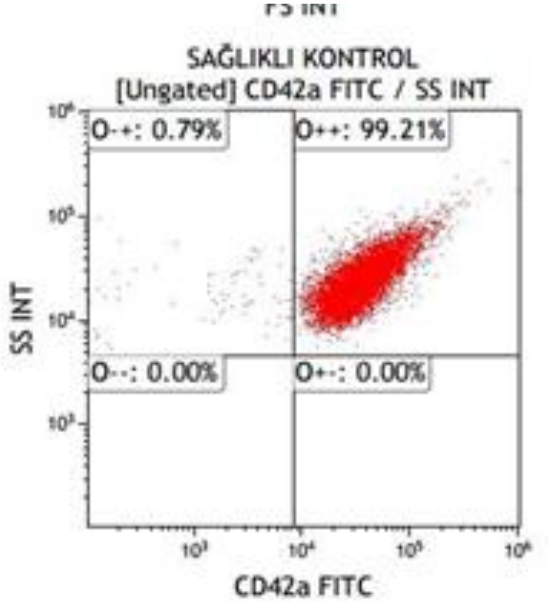


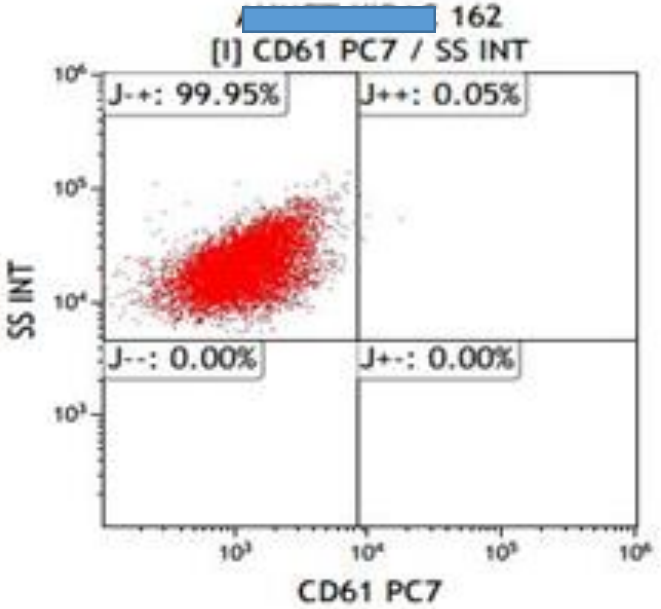


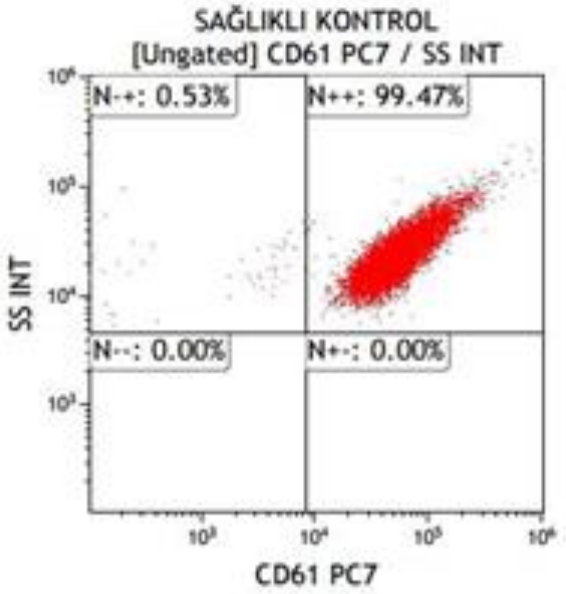


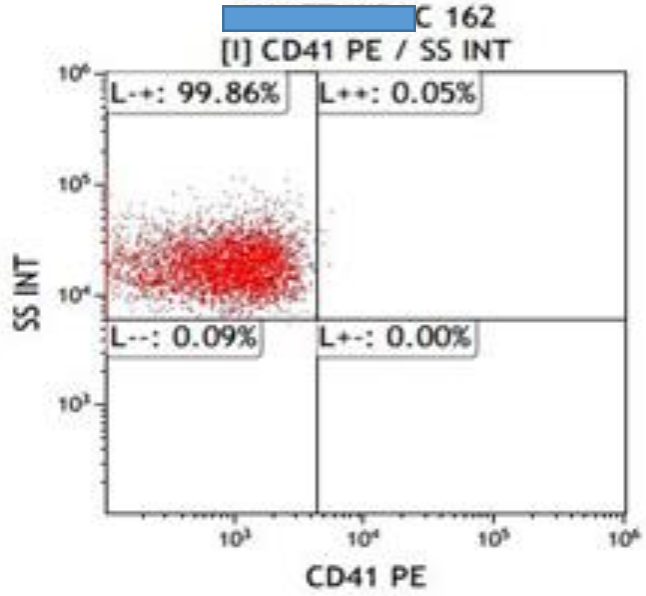
In our patient
CD42 expression is normal
and CD61&CD41 expression are deficient

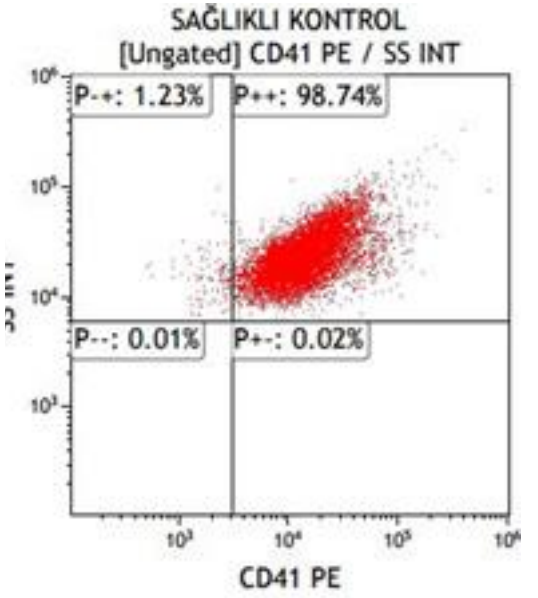




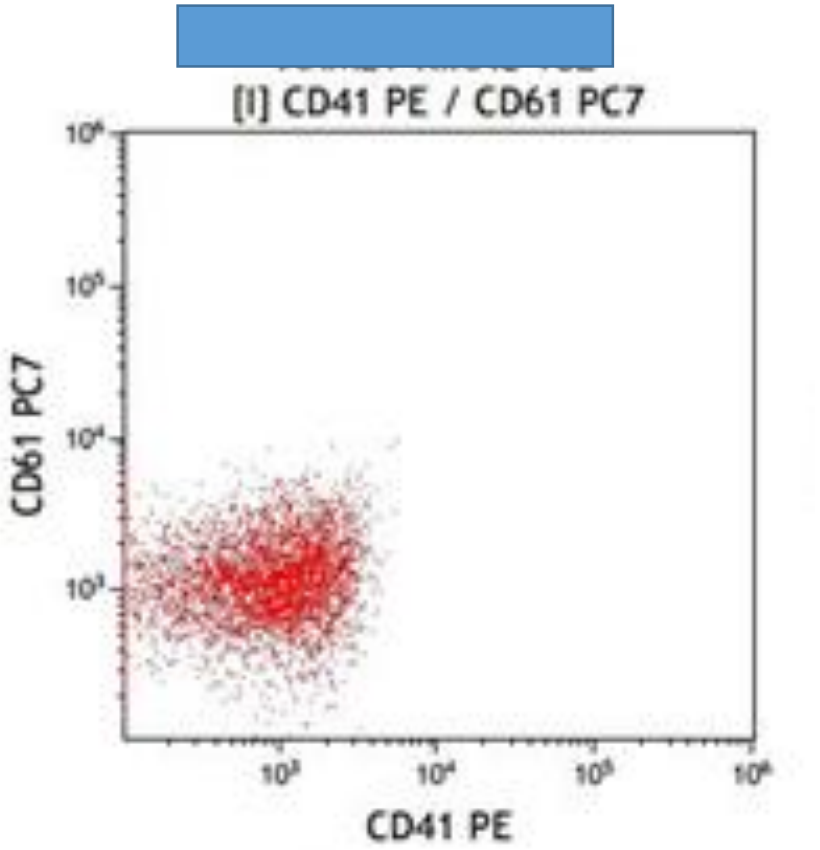


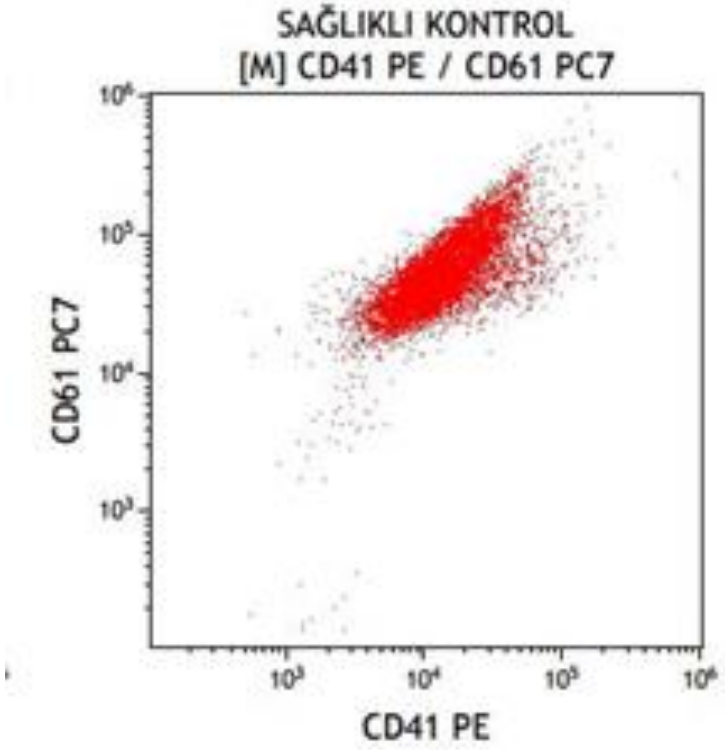






Diagnosis:
Moderate GT





Take to home message

- GT is associated with various clinical symptoms: some patients may have only minimal bruising while others may have frequent, severe and potentially fatal hemorrhages.
- We should keeping mind GT testing in these patients
- Our patient is an example of late diagnosed GT patient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