PATTERN OF BLEEDING AND RESPONSE TO THERAPY IN GLANZMANN THROMBASTHENIA

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Introduction

- Glanzmann Thrombasthenia (GT) is a rare autosomal recessive bleeding syndrome affecting the megakaryocyte lineage characterized by quantitative and/or qualitative abnormalities of the αIIbβ3 integrin.

- This receptor mediates the binding of adhesive proteins that attach aggregating platelets and ensure thrombus formation at sites of injury in blood vessels.

- Bleeding symptoms in GT has clinical variability; ranging from minimal bruising to severe and potentially fatal hemorrhages.

Cristine et al Blood;1998 91: 1562-1571
Coppola et al Haemophilia 2008; 14 (Suppl. 1): 31–39

Introduction

- Diagnosis associates mucocutaneous bleeding with absent platelet aggregation in response to all physiologic stimuli and normal platelet count and morphology.
- Standard of care in GT is DDAVP, platelet transfusion and rFVIIa in patients with platelet alloimmunisaton.

Coppola et al Haemophilia 2008; 14 (Suppl. 1): 31–39
Hedner et al Thromb Haemost 2008; 100: 557–562

Objectives

- Primary objective:
  - to observe the pattern of bleeding in GT patients.
- Secondary objective:
  - to asses the response of symptoms to different treatment modalities
  - and duration between two bleeding episodes.

Materials and Methods

- Diagnosed GT patients.
- Duration from October 2008 – August 2009.
- Conducted at National Institute of blood diseases and bone marrow transplantation.
- Observational cross sectional study.
- Consecutive episodes were included in the study.
- The data of each episode of bleeding/ treatment was recorded in the GT Registry database.
- IRB approved.

Materials and Methods

- The following data has been obtained: age, sex, type of bleeding i.e. epistaxis, bruising, gum bleeding, bleeding at circumcision (in males), bleeding at dental extraction, muscle bleed, haematoma, subcutaneous bleed, haematuria, haematemesis, gastrointestinal bleeding, ear bleeding and mennorhagia (in females).

- Frequency of number of episodes, duration of bleeding between two episodes was recorded and response of the symptoms to different treatment modalities was observed.

- The treatment modalities offered were tranexamic acid, DDAVP, platelet transfusion and rFVIIa.

Materials and Methods

- The response to treatment was measured from the initiation of treatment to subsequent complete cessation of bleeding in <6hours duration, in >6 hours <24 hrs and >24 hrs and labelled as responders.

- Patients were considered non-responders to the episode of bleeding when they continues on bleed for >36 hrs from the start of the initial treatment.

Glanzmann Thromasthenia Registry

Statistical Analysis

- Percentage was used to measure different type of bleeding episodes.
- Mean and standard deviation of age was measured for overall patients and in male and female patients.

Results

- Total patients were 11
- 4 were males and 7 were females.
- Over all mean age was 10.56±9.78, range 0.7-23 yrs
- Mean age in male patients was 12.1±8.67 yrs, range 1.5-23 yrs.
- In females mean was 6.97 yrs±4.91, range 0.7-14 yrs.

Table 1: This shows the bleeding type per number of episodes recorded and the number of patients who has presented with that episode of the bleed.

Type of bleeding	Bleeding type per total number of episodes	% episodes	Number of pts with type of bleeding	% of patients
Epistaxis	32/41	78.04%	10/11	90.9%
Easy bruising	27/41	63.41%	11/11	100%
Gum bleeding	23/41	56.09%	9/11	81.81%
Bleeding on dental extraction	08/41	19.51%	8/11	72.72%
Mennorhagia	05/41	12.1%	*2/2	100%
Circumcision	04/41	9.75	**4/4	100%
GI bleeding	02/41	4.87%	1/11	9.09%
Muscle bleeding	01/41	2.43%	1/11	9.09%
Subcutaneous bleeding	01/41	2.43%	1/11	9.09%
Haematuria	01/41	2.43%	1/11	9.09%
Haematoma	01/41	2.43%	1/11	9.09%
Haematemesis	01/41	2.43%	1/11	9.09%

*out of 7 female patients 2 had attained the age of Menarche

* *total male patients were 04 in the study

Note: The total number is greater than 11 because several patients had more than one bleeding symptom.

Table2: This table shows the different treatment modalities that had been offered to the patients and their response.

Treatment Modality	Treatment offered	Responders	% Response	Response <6 hrs	Response >6<24hrs	Response >24hrs	Non-responders
Platelets Tx + Tranexamic acid	36	25	74.28%	05	09	11	11
Tranexamic acid+ Platelets transfusion+ DDAVP	11	10	90.9%	02	04	04	01
Tranexamic acid+ Platelets Tx+ DDAVP+rFVIIa	01	01	100%	0	01	0	0
*Tranexamic acid+Oral Contracepttives	05	05	100%	0	01	04	0

Only offered to females presenting with Menorrhagia.
Note: A single patient had presented with 17 episodes of bleeding out of 41. rFVIIa was given during one episode due to uncontrolled haemetemesis.

Results

- The mean duration between the two episodes in these patients was 64.5 days range 399 (3-400 days).

Conclusion

- Epistaxis, easy bruising and gum bleeding are the most frequent bleeding presentation in both genders.
- Most of the bleeding episodes can easily be controlled by use of platelet transfusions and DDAVP supplemented by anti-fibrinolytic agents.
- Mennorrhagia can be effectively treated with tranexamic acid and oral contraceptive (5/5- 100% response).
- Management with rFVIIa should be considered in patients presenting with life threatening haemorrhages where other measures fail to control the bleeding.
- There is a need to develop national registry for congenital platelet disorders.

Thank You