Diagnosis of platelet disorders despite normal platelet aggregations

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OBJECTIVES

Hereditary platelet delta granule storage pool deficiency (δ-SPD) is a platelet disorder that manifests as a mild to moderate bleeding diathesis, generally mucocutaneous in nature. The disorder may be considered if characteristic clinical symptoms are noted, if von Willebrand Disease can be ruled out, and by abnormal platelet aggregation tests. Electron microscopy testing can confirm the diagnosis. The purpose of this study is to ascertain whether electron microscopy testing in the absence of abnormal platelet aggregations may yield evidence of δ-SPD.

METHODS

A retrospective review of sixty-nine patients referred to the Children's Hospital of Richmond Hematology Clinic to rule out coagulopathy was conducted January, 2014-October,2015. A Red Cap database was constructed of all coagulation and hematology test results. Patients diagnosed with δ-SPD were then scored on the Pediatric Bleeding Questionnaire, based upon clinical history at intake.

RESULTS

Of the 69 patients, 12 (17%) had platelet EM testing done and 11/12 were found to have δ-SPD. Only 4 (36%) of the 11 patients had abnormal platelet aggregation studies. All 4 individuals had lowered response to epinephrine; two had decreased response to ristocetin and one individual also had abnormal response to collagen and arachidonic acid. The average bleeding score was 5.27 (range 2, 9; median 5). Almost all bleeding was mucocutaneous (i.e. epistaxis, oral bleeding, menorrhagia, gastrointestinal or easy bruising). The average deficiency of delta granules as determined by platelet electron microscopy at the University of Toledo was 2.53 DG/PL (range 1.43- 4.79; normal=4 - 6 DG/PL). All 10 δ-SPD patients had normal PT/ aPTT's, and thromboelastograms. Eight of the 11 tested had normal von Willebrand panels; 2 had a ristocetin cofactor activity of 43% and 48% (reference range 50-100 %) with normal Factor VIII and vW antigen. The average age was 10 years (range 3 - 16 years). There was no correlation between age, gender or bleeding score and severity of δ-PSPD.

Parameter	Mean (SD)	n
PT (sec)	14.2 (0.60)	9
PTT (sec)	32.3 (2.40)	9
Platelet Count ($10^3/mm^3$)	259 (86.29)	10
FVIII (%)	161.6 (64.80)	9
vWF Ag (%)	101 (25.45)	9
vWF Assay (%)	78.7 (31.70)	9
Collagen Aggregation (%)	63.7 (20.41)	9
ADP Aggregation (%)	76.5 (4.50)	10
Arachidonic Acid Aggregation (%)	68.3 (22.51)	10
Epinephrine Aggregation (%)	54.9 (26.32)	10
Ristocetin Aggregation (%)	68.8 (24.59)	10
R Kaolin (min)	4.6 (0.91)	8
K Kaolin (min)	1.2 (0.19)	8
ANG Kaolin (degrees)	72.0 (2.96)	8
MA Kaolin (mm)	63.8 (4.52)	8
EM (Dense granules/Platelet)	2.53 (0.54)	11

PT, Prothrombin Time; PTT, Partial Thromboplastin Time; FVIII, clotting factor VIII; vWF, von Willebrand Factor; R, Reaction time; K, Reaction kinetics; MA, Maximum Amplitude; EM, Electron Microscopy

Age	Gender	Bleeding Score	EM (DG/PL)
13	F	5	1.43
4	F	6	2.09
3	M	4	2.27
16	F	6	2.27
10	M	9	2.34
15	M	5	2.59
5	M	6	2.67
14	F	5	2.72
11	F	5	3.02
8	F	2	3.09
6	M	5	3.37
12	F	3	4.79

EM (DG/PL)	Age (Avg)	Bleeding Score (Avg)	n
<2	13	5	1
2.0-2.9	10	6	7
3.0-3.9	8	5	3
≥4.0	12	3	1

CONCLUSIONS

Delta granule storage pool deficiency cannot be ruled out in the presence of normal platelet aggregations in patients presenting for coagulation disorders evaluations with mild to moderate history of mucocutaneous bleeding. Study limitations include: sample size, the retrospective nature of the study including the conducting of the bleeding score from physician reporting, and the lack of standardization by age of platelet electron microscopy testing.

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Platelet disorders, inherited/acquired
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