Weak correlation of bleeding scores to platelet electron microscopy: A retrospective chart review of pediatric patients with delta-storage pool disorder

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Background

Delta granule storage pool deficiency (δ-SPD) is a rare platelet disorder in which a deficiency of platelet granules leads to poor aggregation, resulting in varying clinical bleeding phenotypes. Children with δ-SPD have variable laboratory results between patients, making diagnosis often quite difficult. Platelet electron microscopy (PEM) is classically the diagnostic test of choice, but a lack of consensus exists in appropriate diagnostic threshold in children. Lumiaggregometry and PFA-100 are platelet function studies which are normal in a large portion of δ-SPD patients. The International Society on Thrombosis and Hemostasis (ISTH) developed a bleeding assessment tool (BAT) as a screening tool to aid in the diagnosis of mild bleeding disorders, which has been validated in the pediatric population. The BAT assesses 12 different bleeding categories, with a possible score range of 0 to 4 in each section. After summation of each section, a score ≥2 is considered abnormal. Demographic and laboratory trends in this patient population are poorly understood due to its rare prevalence.

Objectives

To describe the epidemiology and demographic characteristics of this population, describe symptom and laboratory trends surrounding diagnosis, and assess the value of PEM in diagnostic evaluation in this population.

Methods and Design

We performed a retrospective, observational study of 109 children younger than 18 years of age diagnosed with δ-SPD. After application of exclusion criteria, 96 children were included in the analytic sample. We collected demographic information and also pertinent laboratory results such as hemoglobin, PEM, PFA-100, lumiaggregometry, platelet count, and bleeding scores. The BAT was performed routinely in the hemostasis clinic for all patients with bleeding symptoms. Descriptive and exploratory analyses were performed using Chi squared and ANOVA techniques. Correlation coefficients were applied scoring PEM against age, BAT, and platelet aggregation studies.

Results

Delta granule storage pool deficiency (δ-SPD) has variable laboratory results between patients, making diagnosis often quite difficult. Platelet electron microscopy (PEM) is classically the diagnostic test of choice, but a lack of consensus exists in appropriate diagnostic threshold in children. Lumiaggregometry and PFA-100 are platelet function studies which are normal in a large portion of δ-SPD patients.

The correlation coefficient between PEM and bleeding scores is 0.30 (p= <0.001).

Table 1: Continuous variables stratified by sex

<table>
<thead>
<tr>
<th>PEM Score</th>
<th>Overall Score</th>
<th>Female Score (F=67, Mean=30)</th>
<th>Male Score (M=32, Mean=34)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>46 (27.2%)</td>
<td>34 (30.5%)</td>
<td>10 (38.5%)</td>
<td>0.016</td>
</tr>
<tr>
<td>Normal</td>
<td>99 (39.8%)</td>
<td>56 (35.6%)</td>
<td>43 (51.6%)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>19 (13.2%)</td>
<td>10 (12.2%)</td>
<td>9 (25.0%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Categorical variables stratified by sex

<table>
<thead>
<tr>
<th>Bloodtype</th>
<th>Overall Score</th>
<th>Female Score (F=67)</th>
<th>Male Score (M=32)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>20 (33.3%)</td>
<td>12 (34.6%)</td>
<td>8 (24.2%)</td>
<td>0.663</td>
</tr>
<tr>
<td>A</td>
<td>30 (48.4%)</td>
<td>15 (45.5%)</td>
<td>15 (46.9%)</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>5 (8.1%)</td>
<td>3 (8.8%)</td>
<td>2 (6.3%)</td>
<td></td>
</tr>
<tr>
<td>Notting</td>
<td>5 (8.1%)</td>
<td>3 (8.8%)</td>
<td>2 (6.3%)</td>
<td></td>
</tr>
</tbody>
</table>

Results Summary

- The majority of patients were female (67.7%, n=66) with an average age at diagnosis of 11.61 years.
- Females were diagnosed at a significantly older age (13.36 years vs 7.7 years, p< <0.001) presenting most often with menorrhagia, while males presented most commonly with epistaxis (p< <0.001).
- The average bleeding score for PEM between 3.69 dg/pl and 2 dg/pl was 7, while the average bleeding score for PEM below 2d/pl was 4.65.
- Using a cut-off of 2 dg/pl, only 31% of patients would have met diagnostic criteria for DSPD.
- The correlation coefficient of PEM and bleeding scores is 0.30 (p< <0.001).
- Quartile ranges for the bleeding scores are as follows: 1st quartile was 2-4, 2nd was 5-7, and 3rd was >8.

Conclusions

- We cannot recommend routine use of PEM in diagnostic evaluation of patient referred for mild bleeding disorders.
- Platelet EM cannot predict abnormal platelet function testing.
  - Dense granule deficiency alone does not cause poor aggregation.
  - Patients with more severe dense granule deficiency do not have more severe bleeding symptoms.
- ISTH-BAT would be a successful screening tool in SPD patients.
- Using BAT quartile ranges at time of diagnosis may aide in phenotype severity classification.