The PT-VWD Registry

Maha Othman MD MSc PhD
Professor Laurentian University – St Lawrence College
Collaborative BScN program
Adjunct Assistant Professor
Department of Pathology and Molecular Medicine
Platelet-Type Von Willebrand Disease (PT-VWD)

Rare bleeding disorder
Platelet not VWF defect
Mild bleeding
Low plasma VWF + Low platelet count
PT-VWD
A Diagnostic Challenge
PT-VWD & Type 2B VWD
“The non identical twins”

- Phenotypic discrimination:
  - RIPA mixing studies
  - Cryoprecipitate challenge
  - Simplified RIPA-mix

- Genotypic discrimination
  - DNA sequence analysis:
    - Exon 28 VWF gene
    - Platelet GP1BA gene

Fresh blood sample
Issues: application/interpretation

DNA sample
Conclusive evidence
PT-VWD Canadian Project

- Questions to be Addressed:
  - Is PT-VWD truly rare or under diagnosed?
  - How many cases are being misdiagnosed among type 2B VWD cases?

- Sample source:
  - Canadian
  - International
PT-VWD Canadian Project

Phenotypic diagnosis of type 2B VWD

DNA samples to Canada

VWF gene (Exon 28) sequencing

Mutation positive

Type 2B VWD

Mutation negative

Platelet GP1BA sequencing

Mutation positive

PT-VWD
Registry/Database

Reported Cases

Click here to view table of confirmed cases
Last updated August 22, 2008

About the Registry

Dears

The overall aim of the PT-VWD database/registry project is to determine the frequency of this rare bleeding disorder in the world and to collect data about the molecular pathology, phenotype/genotype correlations as well as treatment. Therefore, we invite you to complete a form that includes the main information in order to allow us to learn about your experience with PT-VWD patients and if you would like to participate in the Canadian PT-VWD project.

The objectives of the PT-VWD Registry are:

- To document patients with Platelet-type VWD worldwide.
- To characterize genetic abnormalities responsible for this phenotype.

pt-vwd.org
PT-VWD Registry

- 18 families
- 44 cases: 31 F, 13 M
- 10 families: G 233 V
- 4 families: G 233 S
- 3 families: M 239 V
- 1 family: 27 bp deletion
Data from the PT-VWD Project

Total cases : 86

Cases analysed in Canada (49):
  - 37 cases from across Canada
  - 8 cases from Brazil
  - 3 cases from Switzerland
  - 1 case from Boston, USA

Cases analysed outside Canada (37):
  - 16 cases from Australia
  - 15 cases from UK
  - 6 cases from Argentina
Data from the PT-VWD Project

Genetic mutation frequency (all regions) in 86 cases with phenotypic diagnosis as 2B VWD

- 2B VWD Mutations: 39 cases (45%)
- Unpublished VWF (A1 domain) mutations: 5 cases (5%)
- GP1BA (G233S and G233V): 17 cases (20%)
- Negative for VWF and GP1BA: 22 cases (26%)
- Other VWD subtypes: 3 cases (3%)
Genetic mutations in Canadian cases with phenotypic diagnosis as 2B VWD: N = 37

- 2B VWD Mutations: 18
- Unpublished VWF (A1 domain) Mutations: 5
- GP1BA (G233V): 2
- Other VWD subtypes: 2
- Negative for VWF and GP1BA: 10
## Canadian Hemophilia Registry

### Von Willebrand Disease, All Ages, April 13, 2009

#### Stats Canada - Age Groups

<table>
<thead>
<tr>
<th>Category</th>
<th>Gender</th>
<th>Count</th>
<th>(0-4)</th>
<th>(5-9)</th>
<th>(10-14)</th>
<th>(15-24)</th>
<th>(25-34)</th>
<th>(35-44)</th>
<th>(45-54)</th>
<th>(55-64)</th>
<th>(65-74)</th>
<th>(75-84)</th>
<th>(85+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Von Willebrand Disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VWD 2B</td>
<td>F</td>
<td>39</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>8</td>
<td>8</td>
<td>4</td>
<td>7</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>41</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>6</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>U</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>subtotal</td>
<td>81</td>
<td>1</td>
<td>3</td>
<td>6</td>
<td>15</td>
<td>15</td>
<td>12</td>
<td>13</td>
<td>8</td>
<td>5</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>VWD 2M</td>
<td>F</td>
<td>15</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>16</td>
<td>1</td>
<td>5</td>
<td>2</td>
<td>6</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>subtotal</td>
<td>31</td>
<td>1</td>
<td>7</td>
<td>4</td>
<td>7</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>VWD 2N</td>
<td>F</td>
<td>14</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>13</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>subtotal</td>
<td>27</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>5</td>
<td>5</td>
<td>1</td>
<td>4</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>VWD 3</td>
<td>F</td>
<td>44</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>8</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>33</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>9</td>
<td>2</td>
<td>4</td>
<td>5</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>U</td>
<td>12</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>subtotal</td>
<td>89</td>
<td>5</td>
<td>8</td>
<td>2</td>
<td>17</td>
<td>9</td>
<td>13</td>
<td>15</td>
<td>7</td>
<td>6</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>VWD unk</td>
<td>F</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Date: [Unknown Zone | Protected Mode: On]
PT-VWD World Wide Survey

Witnessed or Diagnosed Cases of PT-VWD: N = 35

- 0% (0 cases)
- 9% (3 cases)
- 40% (14 cases)
- 51% (18 cases)

Response: 35/60

Importance of discriminating between 2b VWD and PT-VWD: N=35

- 1 2 3 4 5 6 7 8 9 10
- Blue: Response Options
- Red: Frequency
Conclusion

- PT-VWD is misdiagnosed among 2B VWD
- PT-VWD should be included among RBD-Platelet function defects
- Genotyping is available and relatively easy
- Challenge remains to estimate the true incidence of PT-VWD:
  - Rarity of the disease
  - Insufficient collaboration with samples/data
Acknowledgments

David Lillicrap

Jayne Leggo
Colleen Notley
Hannah Brown

International Collaborators

Brazil
Margareth Ozelo
Erich V de Paula
Joyce Bizzacchi
University of Campinas

EQATH
John Olson &
Members

Australia
Emmanuel Favaloro
ICPMR.Westmead hospital

UK
Said Enayat
Birmingham children's
Hospital

Argentina
Juan Pablo Frontroth
Hospital de pediatría Buenos Aires

USA
Hedy Smith
Tuft Medical Center
Boston, MA

Switzerland
Anne Angelillo
Service and Central Laboratory of Hematology, Centre Hospitalier Universitaire Vaudois

Ahmed Hasswa
Web designer

Canadian Hemophilia Society
Help Stop the Bleeding

Alexander Hamilton
Year 3 Nursing Student
Southampton University 2003
PhD defence
Our Research Group
Pathology & Molecular medicine, Queen’s
Farwell 2005
My Canadian start and one of the achievements along the road
FAMILY
Canada Or World Wide Participation
DNA Samples or Data

Dr. Maha Othman MD MSc PhD
St Lawrence College
Health Science- Research
Kingston, Ontario, Canada
Phone: 1 613 544 5400 ext 1529
Email: MOrthman@sl.on.ca