Case report
von Willebrand Disease

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Case

- A 15 years old adolescent female
- CC: hyper-menorrhagia for 16 days
- Vaginal blood loss gradually increased after 5\textsuperscript{th} day of menstruation
- Easy fatigability, decrease appetite, some degrees of depression
- Epistaxis, at the 10\textsuperscript{th} day
- Some ecchymosis
- No weight loss
Past Medical History

• Negative past history of:
  – bleeding diathesis
  – Surgery
  – bleeding during dental procedures
  – Abnormal previous menstruations (about 5-8 days)
  – bleeding diathesis and hyper-menorrhagia in her family members
Visited by physicians

• 1\textsuperscript{st} visit : a general practitioner; at 9\textsuperscript{th} day, recommended Ferrous sulfate (Daily) and Fluoxetine

• 2\textsuperscript{nd} visit : a Gynecologist; at 12\textsuperscript{th} day, normal external genitalia, performed Lab Test

• 3\textsuperscript{rd} visit : a hematologist; at 16\textsuperscript{th} day, referred from gynecologist with Lab results
Physical examination

• Pallor, Heart murmur (grade II/VI at LSB)
• Normal lung examination, No LAP and splenomegaly
• Some bruising on lower extremities
• Vital signs:
  – BP=105/70
  – PR=75
  – RR=16
  – T=36.9°C
Lab Test

- **CBC**
  - Hb = 6.5 g/dl, MCV = 95, MCH = 28.5, MCHC = 32
  - RBC count = 2,250,000, Retic = 8%
  - PBS: polychromasia, anisocytosis, macrocytosis
  - Platelet = 315,000

- **Direct Coomb’s test**: negative

- **PT** = 14 sec., **PTT** = 52 sec., **BT** = 8.5 min

- LH & FSH: within normal range for her age
More investigations after admission

- Chest X Ray: No cardiomegaly
- Consult with cardiologist: mild pericardial effusion
- TSH: 38 mU/L (HIGH)
- vWF Ag: 15 IU/dl (LOW)
- vWF-RCo 14 IU/L
- Factor VIII: 26 IU/dl (LOW)
- Mixing test: negative
- ANA, Anti DsDNA, APA: normal
Treatment

• Packed cell for anemia
• Tranexamic acid (IV)
• Consult with Endocrinologist:
  – Repeat :
    • TSH, T4, T3, T3RU and Thyroglobulin Ab, Anti Thyroid Ab
      ➢These tests confirmed her hypothyroidism with no anti-Thyroid Ab
• Work up her parents and sister for vWD: normal
Treatment

• Levothyroxine started: 50 μg/day
• Increase to 1.5 Tablet (75 μg/day)
  – TSH corrected, no more transfusion
  – At day 7: PT, PTT corrected
  – At day 10: menorrhagia ceased
  – At day 18: vWF tests was corrected
Patient’s laboratory findings

<table>
<thead>
<tr>
<th></th>
<th>1st (admission time)</th>
<th>2nd (4th day)</th>
<th>3rd (7th day)</th>
<th>4th (18th day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>6.5 g/dL</td>
<td>7.8 g/dL</td>
<td>11.9 g/dL</td>
<td>12.2 g/dL</td>
</tr>
<tr>
<td>TSH</td>
<td>38 mU/L</td>
<td>48 mU/L</td>
<td>29 mU/L</td>
<td>21 mU/L</td>
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<tr>
<td>vWF Ag</td>
<td>15 IU/dl</td>
<td>18 IU/dl</td>
<td>35 IU/dl</td>
<td>42 IU/dl</td>
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<tr>
<td>Factor VIII</td>
<td>26 IU/dl</td>
<td>33 IU/dl</td>
<td>49 IU/dl</td>
<td>59 IU/dl</td>
</tr>
<tr>
<td>vWF Act</td>
<td>14 IU/dl</td>
<td>20 IU/dl</td>
<td>41 IU/dl</td>
<td>53 IU/dl</td>
</tr>
</tbody>
</table>
Acquired vWD

– Described since 1968
– No personal & family history of bleeding
– Mucocutaneous bleeding
– Abnormal hemostasis screening tests
Acquired vWD

- Underlying disorders:
  1. Lymphoproliferative Disorder
  2. Myeloproliferative Disorders
  3. Solid tumors
  4. Immunologic disorders
  5. Cardiovascular problems
  6. Miscellaneous (Collagen Vascular Disease, Hypothyroidism, Valproate acid)
Acquired vWD

• Mechanism:
  1. Antibody, Immune Complex
  2. Absorption of vWF by malignant cells
  3. Loss of HMW vWF multimers, high shear stress
  4. High proteolytic degradations of vWF (circulating protease)
Acquired vWD

• Laboratory studies:
  – Prolonged BT
  – Low functional von Willebrand factor (Ristocetin cofactor activity, Collagen-binding assay)
  – Reduced HMW multimers
  – Search for evidence of an inhibitor (mixing with normal plasma, incubated in 37 °C)
Acquired vWD

• Treatment:
  – Control of active bleeding:
    • Desmopressin (choice in non-inhibitor)
    • Factor VIII/vWF concentrates (second choice)
    • IVIG ?
    • Immunosuppressive agents ?
    • Recombinant VIIa ?
  – Treatment of Choice:
    • Treat the underlying disease
Thank you for your attention!