Clinical Services for Women with Bleeding Disorders

KALINDA WOODS, MD, FACOG

ASSISTANT PROFESSOR
DEPARTMENT OF GYNECOLOGY AND OBSTETRICS
EMORY UNIVERSITY SCHOOL OF MEDICINE

HEMOPHILIA STATE COMPREHENSIVE CARE MEETING
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I have no financial disclosures to report.
Knock it off stupid, we're tampons.
Objectives

- Discuss prevalence and pathophysiology of common bleeding disorders
- Define abnormal uterine bleeding
- Discuss treatment goals
- Review therapeutic options
- Discuss pregnancy and postpartum implications
- Discuss case vignettes
- Review emerging evidence
Clinical Disorders

- Von Willebrand disease
- Hemophilia A
- Platelet function disorders
- Thrombocytopenia
- Aplastic anemia
Von Willebrand Disease

- Identified in 19th century by Finnish internist Erik von Willebrand

- Most common inherited bleeding disorder among American women (0.6-1.3%)

- More prevalent in Caucasians than AA (15.9% to 1.3%)

- Types 1-3 described
  - Deficiency
  - Ineffectiveness
  - Absence
Pathophysiology

**AGGREGATION**
- Platelet
  - GpIIb/IIIa
  - vWF

**ADHESION**
- Platelet
  - GpIb
  - vWF

**Subendothelial Collagen Receptors Exposed at Injury Site**
- Endothelium

**GpIb Binding Induces GpIIb/IIIa Expression**
VWD- Signs and Symptoms

- AUB- 74-92%
- Epistaxis (38-63%)
- Gingival bleeding (26-35%)
- Bleeding after dental extraction (29-52%)
- Bleeding from minor cuts/ abrasions (36%)
- Post surgical bleeding (20-28%)
- GI bleeding (14%)
- Joint bleeding (6-8%)
Hemophilia A

- X-linked recessive
- Affected women are carriers
- Counseling regarding male offspring
- Phenotypic variability/ Factor VIII levels
Hemophilia A

- 1 in 5000 live births
- 1/3 of cases caused by spontaneous gene mutation
- Severity depends on percentage of Factor VIII in the blood
  - Mild: prolonged bleeding after trauma, birth, menses
  - Moderate: bleeding after minor injuries
  - Severe: bleeding after injury AND spontaneous bleeding
Clinical Screening

- Heavy bleeding since menarche **PLUS**
- **ONE** of the following:
  - PPH
  - Surgical bleeding
  - Dental bleeding
- **TWO** of the following:
  - Epistaxis
  - Gum bleeding
  - Family history of bleeding symptoms
Abnormal Uterine Bleeding

- Complete history/physical
  - Interferes with QOL
  - Interferes with social/ emotional well being
  - Exceeds 8 days duration
- Pelvic exam with or without Pap/STI screening
- Lab testing
  - CBC
  - Pregnancy testing
  - PT, PTT, fibrinogen
  - VWF antigen, ristocetin cofactor, factor VIII
Approach

- Multidisciplinary team
- Ensuring access to care
- Awareness of resources
Hormonal Therapies

- Limited data
- Levonorgestrel-releasing intrauterine system
- Progestin only contraceptives
  - Depo provera
  - Implant
  - Pills
- Combined oral contraceptives
Mirena IUD

- Concurrent contraception

- Induces permanent secretory endometrium, no withdrawal

- 80% amenorrhea rate after 1 year

- Contraceptive failure rate less than sterilization
Mirena IUD

- Thin lining of the uterus
- Inhibition of sperm movement
- Thickening of cervical mucus
<table>
<thead>
<tr>
<th>Myth</th>
<th>Fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not appropriate for nulliparous women</td>
<td>Indicated for all women</td>
</tr>
<tr>
<td>Increased PID risk</td>
<td>No increased risk infection</td>
</tr>
<tr>
<td>Only for monogamous women</td>
<td>Very few medical contraindications</td>
</tr>
<tr>
<td>Can “migrate” and cause infertility</td>
<td>Does not “migrate”</td>
</tr>
</tbody>
</table>
Synthetic Progestins

- Progestin only pills
- Depo medroxyprogesterone acetate
- Etonorgestrel implant
- Norethindrone, high dose
Combined Oral Contraceptives

- Pill
- Patch (not very well studied in BD, limited data)
- Ring
Combined hormonal contraceptives

- Ovulation inhibition
- Thinning of endometrium
- Synthetic withdrawal
- Consider cardiovascular risk factors
Tranexamic Acid

- Non hormonal, antifibrinolytic action
- Inhibit conversion of plasmin to plasminogen-stabilize clot
- Can exacerbate thrombotic risk (theoretical)
- GI effects
Obstetric Considerations

- **Von Willebrand**
  - Higher risk for spinal/ epidural hematoma
  - Can be transmitted as autosomal dominant OR recessive: avoidance of fetal scalp electrode/ circumcision
  - Avoid operative vaginal delivery
  - Assess VWF levels in 3rd trimester for planning in event of PPH
  - Risk for PPH 50% higher
Obstetric Considerations

- **Hemophilia A**
  - Transmission rate 50% for male fetuses
  - Prenatal genetic testing available
  - Risk fetal intracranial hemorrhage intrapartum low, but significant
  - Cesarean decreases risk ICH by estimated 85%
Obstetric Considerations

- Prepare for PPH
  - Personnel
  - Inform pediatric team, anesthesiology
  - Crossmatch blood products
  - IV access
- Uterotonics
  - Oxytocin
  - Methergine
  - Hemabate
  - Misoprostol
- Tamponade balloon
Case Study: JT

- **CC:** passed out at school
- **HPI:** 22 yo G0, daily bleeding for 5 weeks
  - On OCP since age 13, typically 3-4 days light bleeding in placebo week
  - Lightheaded and dizzy
  - Sexually active w male partner
  - No pelvic pain/ cramping
  - Taking pills daily
• ObHx: Go
• GynHx: 12/reg. No STIs. 1 lifetime male partner
• MedHx: VWD Type I, since age 2
• SHx: tonsillectomy 2011, uncomplicated
• SocHx: senior in college, marketing. Lives w roommate
  non smoker, alcohol 2-3 servings/week
• FHx: Father w VWD
• ROS- nothing pertinent
• Physical Exam
  ○ 98/60, 126, 14, 37.4
  ○ Normal chest and abd exam
  ○ Pelvic: mucoid blood in vault, active slow bleeding from os
• Labs: Hemoglobin 6.6, normal platelets, hCG neg
• US: suggestive of submucosal myoma (fibroid) 1.5cm
Admitted for transfusion of RBCs
Stimate (desmopressin)
Lysteda (tranexamic acid)
OCP taper
Bleeding resolved, home on hosp day 3 with Hb 10.1
• AUB persisted despite OCP

• Office visit 4 weeks after admission
  ○ Hb stable at 10.0
  ○ hCG neg
  ○ Poor QOL
  ○ Ongoing unscheduled VB

• Scheduled for hysteroscopic myomectomy
• Uncomplicated same day procedure

• OCP maintained

• Returned to typical bleeding pattern
Case Study: AM

- CC: I want a hysterectomy
- HPI: 33 yo G4 P4004 with menorrhagia,
  - Normal labs, hCG neg.
  - Tubal ligation for BC, sexually active w male partner
- ObHx: SVD x 4, PPH x 1, treated medically w uterotonics, Lysteda, transfusion
- GynHx: 10/reg. No STIs, normal Paps, long hx heavy menses lasting 7-10 days, uses Stimate w periods. Cannot tolerate OCPs, expelled Mirena IUD 2013
- PMHx: VWD diagnosed in childhood
- PSHx: tubal ligation, uncomplicated
- SocHx: Married, at home mother, no smoking, 4-5 wine/week
- FHx: Aunt w VWD, Sister w VWD
- PE: Normal
- US: Normal
- Endometrial biopsy: Normal
- Labs: Hb: 11.7, normal platelets, hCG neg
Options counseling:

- Medical therapy
- Conservative surgery
- Definitive surgery
Conservative surgery: Endometrial ablation

- Radiofrequency
- Hydrothermal
- Resectoscopic
- Symptoms resolved
- No menses post procedure
Case Study: BI

- CC: in labor

- HPI: 30 yo G1P0 at 38.6 weeks presents in active labor, cervix 6cm dilated, reassuring fetal testing.

- PMHx: Hemophilia A carrier, diagnosed at birth. Easy bruising, but no bleeding problems

- PSHx: none
• SocHx: teacher, married, no tob, EtOH or drugs

• Prenatal course uncomplicated, declined invasive prenatal testing

• Exam is only remarkable for painful contractions and cervical dilation
Case Study: BI

- Undergoes uncomplicated primary Cesarean delivery
- Delivers healthy unaffected male
- Lysteda TID x 2 weeks post partum
- Uncomplicated post partum course
CASE REPORT

Levonorgestrel intrauterine system as a treatment option for severe menorrhagia in adolescent with type III von Willebrand disease

Carla Donato Silva, Fernanda Geraldes, Isabel Santos Silva

SUMMARY
The authors describe a case of an adolescent with type III von Willebrand disease and severe menorrhagia since menarche. Antifibrinolytic, hormonal (estroprogestative pill in high doses, etonogestrel implant and gonadotropin-releasing hormone agonist goserelin) and Von Willebrand Factor/Factor VIII replacement therapies were prescribed to the patient, but symptomatic control was only obtained with high doses of VWF/FVIII twice a week. In March 2012, a levonorgestrel intrauterine system was inserted in a 14-year-old. At present, the patient is asymptomatic without regular replacement hormone over time. The initial release rate of approximately 20 μg per day occurs after insertion, and gradually decreases to approximately 10 μg per day after 5 years of use.

CASE PRESENTATION
A 14-year-old girl attended our consult for severe menometrorrhagia since menarche, associated with iron deficiency anaemia and physical activity restriction; this condition had a great impact on the patient’s quality of life.
REVIEW ARTICLE

Improving care and treatment options for women and girls with bleeding disorders

Roshni Kulkarni

Department of Pediatrics and Human Development, Center for Bleeding and Clotting Disorders, Michigan State University, East Lansing, MI, USA

Abstract

Women and girls may experience increased bleeding symptoms as carriers of haemophilia. They can also be affected by other hereditary bleeding diatheses such as von Willebrand disease, platelet dysfunction defects or deficiencies of coagulation factors (F) such as F1, F11, FV, FVII, FX, FXI and FXIII. In addition to general bleeding symptoms, such disorders pose unique problems for women due to their impact on reproductive health. Women and adolescent girls with undiagnosed bleeding disorders frequently experience heavy menstrual bleeding (HMB; menorrhagia), leading to impairment of daily activities. Other gynaecological and obstetric manifestations, for example miscarriage, bleeding during pregnancy and postpartum haemorrhage (PPH), can occur. Treatment for HMB should consider patient wishes relating to preservation of fertility, and management options include hormonal measures, desmopressin, antifibrinolytics, platelet concentrate transfusions and clotting factor therapy. During pregnancy, monitoring clotting factor levels informs the need for prophylactic therapy; subsequent haemostatic cover can
Emerging Evidence

Would the patient like to preserve fertility?

- **YES**
  - Would the patient like to become pregnant now?
    - **YES**
      - Haemostatic measures:
        - Antifibrinolytic drugs (traxemesis acid and aminocaproic acid)
        - DAVP (intranasal or subcutaneous)
        - Clotting factor replacement
    - **NO**
      - Hormonal measures:
        - Levonorgestrel IUS
        - Combined oral contraceptives
        - Progestins
        - GnRH therapy

- **NO**
  - In women with pelvic pathology or for whom other measures have failed, can also consider surgical options:
    - Endometrial ablation
    - Hysterectomy
  - *Consider haemostatic evaluation prior to surgery*
Emerging Evidence

[Intervention Review]

Desmopressin acetate (DDAVP) for preventing and treating acute bleeds during pregnancy in women with congenital bleeding disorders

Laxminarayan Karanth¹, Ankur Barua², Sachchithanantham Kanagasabai¹, Sreekumar Nair³

¹Department of Obstetrics and Gynecology, Melaka Manipal Medical College, Melaka, Malaysia. ²Department of Community Medicine, International Medical University (IMU), Kuala Lumpur, Malaysia. ³Department of Statistics, Manipal University, Manipal, India

Contact address: Laxminarayan Karanth, Department of Obstetrics and Gynecology, Melaka Manipal Medical College, Bukit Baru, Jalan Batu, Hampar, Melaka, 75150, Malaysia. karanthkl@ymail.com.

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Questions/ Comments
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