MANAGEMENT OF PREGNANCY IN WOMEN WITH BLEEDING DISORDERS

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UNC-CH
Disclosures

- Advisory Boards: Bayer, NovoNordisk
Case 1

- A 25 y.o G1 who is an obligate carrier of Hemophilia A, baseline FVIII level of 47% is 14 weeks pregnant and is sent by OB for a birth plan.
Case 2

- A 32 y.o G1 who is known to be a Lyonized carrier of Hemophilia B, baseline FIX level of 4% presents at 15 weeks gestation for a birth plan
Case 3

- A 30 y.o. woman G1P0 with h/o type 1 VWD presents for a birth plan at 15 weeks gestation
- Baseline levels: FVIII 35%, VWF Ag 15%, VWF activity 12%
Case 4

- A 30 y.o. woman G1P0 with h/o type 2B VWD presents at 13 weeks gestation for a birth plan.
- Baseline levels
  - VWF Ag 38%
  - VWF Act 12%
  - FVIII 62%
  - Platelets 187
Overview

- Antenatal complications
  - First trimester bleeding
  - Antepartum hemorrhage
  - miscarriage
- Delivery
  - Mode of delivery
  - Management of labor
- Postpartum complications
- Hemostatic drugs in pregnancy and post-partum
Simpler Overview

- Treating/preventing bleeding in the Mom
- Preventing bleeding in the baby
- Treating anxiety in the delivery team
First trimester Bleeding

- Spontaneous miscarriage
- Bleeding from prenatal invasive procedures
- Termination of pregnancy
Antepartum Hemorrhage

- Occurs after week 24 of gestation
- Occurs in 3-5% of pregnancies
- Leading cause of perinatal and maternal morbidity

Causes:

- Bleeding at placental site
  - Placenta previa
  - Placental abruption
- Bleeding from lesions of cervix or vaginal
- Fetal bleeding
Miscarriage

- Increased in women with bleeding disorders
- Fibrinogen and FXIII deficiency
  - Placental abruption
- FX deficiency
  - Retroplacental hemorrhage
- ?VWD
Hemostatic Factors during Pregnancy

- FVIII and VWF levels rise
- Other factors?
  - FIX – no change
## Mode of Delivery and ICH

- Nulliparous women, non-breech deliveries between 1992 and 1994

<table>
<thead>
<tr>
<th>Mode of Delivery</th>
<th>SDH/ICH</th>
<th>Intraventricular</th>
<th>Subarachnoid</th>
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<tbody>
<tr>
<td>NSVD</td>
<td>2.9</td>
<td>1.1</td>
<td>11.3</td>
</tr>
<tr>
<td>Vacuum</td>
<td>8 (2.7)</td>
<td>1.5 (1.4)</td>
<td>2.2 (1.7)</td>
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<tr>
<td>forceps</td>
<td>9.8 (3.4)</td>
<td>2.6 (2.5)</td>
<td>3.3 (3.5)</td>
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<td>V+C</td>
<td>21.3 (7.3)</td>
<td>3.7 (3.5)</td>
<td>10.7 (8.2)</td>
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<tr>
<td>Caesarean</td>
<td>6.7 (2.3)</td>
<td>2.1 (2.0)</td>
<td>0.9 (0.7)</td>
</tr>
</tbody>
</table>

Towner, M. et al., NEJM 1999 341: 1709
Mode of Delivery and ICH in Hemophilia

- ICH in hemophilic boys

<table>
<thead>
<tr>
<th>Vaginal Delivery</th>
<th>Caesarean</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.8</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Kulkarni, R. et al., Haemophilia 2009 15: 1281
Postpartum Hemorrhage

- Causes: uterine atony, retained placenta, abnormal placentation (placenta accreta), surgical bleeding, and systemic (medical) bleeding

- Incidence increased in women with bleeding disorders
  - 6% in VWD and 4% in controls (James A, et al, JTH 2007 5: 1165)
  - Norwegian study: PPH 3fold increased with VWD (Hogan, et al, Lancet 2010 375: 1609)
  - Mild d/o s including low fbg, prolonged PFA-100, blood group increased PPH (Chauleur, JTH, 2008, 6:2067)
Hemostatic Drugs during Pregnancy

- Factor Concentrate
  - Throughout pregnancy in women deficient in FXIII aor fibrinogen
  - At the time of delivery
    - Hemophilic Carriers
    - Severe VWD
    - Platelet disorders

- DDAVP

- Antifibrinolytics
Generic Birth Plan for a woman with Bleeding Disorder

- Assess h/o bleeding to assess likelihood of bleeding
- Measure hemostatic parameters
- Administer hemostatic agents at appropriate times

Mode of Delivery:
- No forceps
- No vacuum
- No fetal scalp monitoring
- No circumcision until child is evaluated
- Plan for cord blood testing of child, if appropriate
How comfortable do you feel in managing pregnant women with bleeding disorders?

- A. Very
- B. Fairly
- C. Sort of
- D. Not at all
How comfortable do you think your OB department feels in managing pregnant women with bleeding disorders?

A. Very
B. Fairly
C. Sort of
D. Not at all
How comfortable do you think your anesthesia department feels in managing pregnant women with bleeding disorders?

A. Very
B. Fairly
C. Sort of
D. Not at all
Case 1

- A 25 y.o G1 who is an obligate carrier of Hemophilia A is 14 weeks pregnant and is sent by OB for a birth plan. Baseline FVIII level is 47%
Case 1

- Which mode of delivery would you/your center recommend?
  - A. Planned C-section
  - B. NSVD
  - C. Scheduled induction
  - D. Per obstetric indications
C Section vs NSVD

- Ljung, Haemophilia 2010 16:415
  - The optimal mode of delivery for the haemophilia carrier expecting an affected infant is vaginal delivery

- James and Hoots, Haemophilia 2010 16:420
  - The optimal mode of delivery for the haemophilia carrier expecting an affected infant is caesarean delivery

- WFH guidelines: “route of delivery in carriers with a normal fetus should be as per obstetric indications” (http://www1.wfh.org/publications/files/pdf-1495.pdf)
Case 1

- At what level of FVIII would you feel comfortable letting her have a NSVD?

- A. 50%
- B. 80%
- C. 100%
Case 1

- At what level of FVIII would you feel comfortable letting her have an **epidural**?
  - A. 50%
  - B. 80%
  - C. 100%
Case 1

- At what level of FVIII would you feel comfortable letting her have a caesarean?
  - A. 50%
  - B. 80%
  - C. 100%
Case 1

- A 25 y.o G1 who is an obligate carrier of Hemophilia A is 14 weeks pregnant and is sent by OB for a birth plan.

- Plan: Monitor FVIII during pregnancy until levels are above target, then use generic birth plan. Mode of delivery as per obstetric indications.
Case 2

- A 32 y.o G1 who is known to be a Lyonized carrier of Hemophilia B presents at 15 weeks gestation for a birth plan.

- Plan for FIX concentrate at the time of delivery, then Q12 hrs
Case 2

- For how long would you continue administering FIX concentrates after an NSVD—no epidural?

- A. 24 hours
- B. 48 hours
- C. 72 hours
- D. 1 week
Case 2

For how long would you continue administering FIX concentrates after a Caesarean section?

- A. 24 hours
- B. 48 hours
- C. 72 hours
- D. 1 week
Case 3

A 30 y.o. woman G1P0 with h/o type 1 VWD presents for a birth plan at 15 weeks gestation.

Baseline levels: FVIII 35%, VWF Ag 15%, VWF activity 12%

When do you recheck levels?
- A. at time of presentation
- B. late second trimester
- C. mid-third trimester
- D. late third trimester
- E. all of the above
Case 3

- A 30 y.o. woman G1P0 with h/o type 1 VWD presents for a birth plan at 15 weeks gestation.
- At what level of VWF Ag would you feel comfortable letting her have a NSVD?
  - A. 50%
  - B. 80%
  - C. 100%
Case 3

- A 30 y.o. woman G1P0 with h/o type 1 VWD presents for a birth plan at 15 weeks gestation.
- At what level of VWF Ag would you feel comfortable letting her have a Caesarean?

- A. 50%
- B. 80%
- C. 100%
Case 3

- A 30 y.o. woman G1P0 with h/o type 1 VWD presents for a birth plan at 15 weeks gestation.

- At what level of VWF Ag would you feel comfortable letting her have an epidural?

- A. 50%
- B. 80%
- C. 100%
Case 3

- G1P0 with h/o type 1 VWD
- Baseline levels: FVIII 35%, VWF Ag 15%, VWF activity 12%
- Levels at 24 weeks: FVIII 55%, VWF Ag 30%, VWF activity 28%
- Levels at 38 weeks: FVIII 65%, VWF Ag 38%, VWF activity 36%
- Product choice at delivery?
  - A. DDAVP
  - B. VWF concentrate
  - C. antifibrinolytics alone
Management of post-partum period

- Hemophilia A carrier

- What would you prescribe in case of post-partum bleeding at home?
  - A. Lysteda
  - B. Amicar
  - C. FVIII
  - D. Stimate
Management of post-partum period

- Type 1 VWD?

- What would you prescribe in case of post-partum bleeding at home?
  - A. Lysteda
  - B. Amicar
  - C. FVIII/VWF concentrates
  - D. Stimate
Management of post-partum period

- Hemophilia B carrier?

- What would you prescribe in case of post-partum bleeding at home?
  - A. Lysteda
  - B. Amicar
  - C. FIX concentrates
Tranexamic Acid

  - Reduced blood loss during elective C-section
  - Reduced blood loss in vaginal delivery
- Use of TA in emergency PPH (Ducloy-Vouthors et al, Crit Care 2011, 15:R117
  - Reduced total blood loss, RBC transfusion requirements
  - Fewer patients progressed to massive PPH
- In animal studies, no mutagenic activity. Low excretion in breast milk
DDAVP in pregnancy

- Systematic review of use (Trigg et al, Haemophilia 2012 18: 25-33)
  - Used in 51 pregnancies in 1st 2 trimesters for prevention of bleeding from invasive procedures—no related neonatal complications
  - Maternal side effects: flushing and headache
  - Most common indication was prevention of PPH
  - 172 pregnancies total
    - No bleeding in 167 deliveries
    - No premature births or neonatal complications

- Concerns about use in pregnancy
  - Seizures
  - Uterine contractures in 3rd trimester
  - Released in small amounts in breast milk
A 30 y.o. woman G1P0 with h/o type 2B VWD presents at 13 weeks gestation for a birth plan.
30yo w/vWD 2B, G1P0, 36 weeks pregnant

HPI:
Pregnancy has gone well. She has continued to work full-time. No bleeding. No contractions.

BLEEDING HISTORY:
- dx’d at birth d/t fam hx of 2B vWD
- TCP at birth to 20,000
- Two hematomas → responded to Humate-P
- Menorrhagia → improved with Nuva Ring
- Oozing with dental procedures

PMH:
Asthma
vWD 2B

MEDS:
Asthma inhalers prn
Prenatal MVI

SOCIAL:
Aesthesia resident.
Our Patient: Platelet Trend

Platelet Count vs. vWF levels

Platelet Count (x10^9/L)

1st Trimester
2nd Trimester
3rd Trimester

Platelets
vWF:Ag
vWF:act
f.VIII

Platelet Trend

- 1st Trimester: Platelet count decreases from 180 to 100
- 2nd Trimester: Platelet count remains low
- 3rd Trimester: Platelet count increases to 100

vWF and f.VIII levels:
- vWF:Ag levels remain stable
- vWF:act levels increase from 0 to 30
- f.VIII levels remain stable

Date Points:
- 7/3/2013: Platelet count 180
- 9/11/2013: Platelet count 100
- 11/1/2013: Platelet count 100
- 12/17/2013: Platelet count 100
- 1/10/2014: Platelet count 100
- 1/17/2014: Platelet count 100
Our Patient: Platelet Trend

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<th>Date</th>
<th>Platelet count (x10^9th/L)</th>
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<td>3/5/2014</td>
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</table>

**Induction**
- Wilate (RCOu/kg) 50
- Lysteda 1300 tiw

**C-sxn**
- 40 q12
- 30 q12
- 20 q12
- 20 q12
- 20 x1

**D/C home**

*Rxn
<table>
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<tr>
<th>Date</th>
<th>Platelets</th>
<th>Notes</th>
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<td>Baseline</td>
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<td>81</td>
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<td>Feb 2</td>
<td>TCTC</td>
<td>Admit for induction</td>
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Operative & Post-Op Course

- 1200ml blood loss during surgery (ULN)
  - 2U pRBCs
- POD 8: Dyspnea w/Wilate infusion -> cancelled.
- Excellent hemostasis to POD ~10
- Vaginal bleeding ➔ Lysteda
- 3/5/14: Incision healing well, still on Lysteda
2B Pregnancy Cases in the Literature

Haemophilia (2012), 18, 406–412
2B Pregnancy Cases in the Literature
2B Pregnancy Cases in the Literature

Fig. 1. VWF parameters and platelet counts during pregnancy for the three patients.
 Managed similarly to our case

 1 of 3 pts had intra-op oozing
  - Had R1308C mutation
  - Other 2 had R1306 mutation
The 4 multimeric patterns found in the entire cohort of VWD2B patients.

The 4 platelet morphology patterns identified in the VWD2B patients.

Distribution of platelet counts according to bleeding severity score in the 67 patients enrolled in the study.

Platelets (x 10^3/uL)

< 4 4-8 > 8

Bleeding severity score


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Summary

- Women with bleeding disorders are susceptible to bleeding complications during pregnancy, delivery and the post-partum period.
- Careful coordination between the OB service and the HTC is required.
- A written birth plan should be developed, including prohibition against use of vacuum and forceps, recommendation for factor replacement (dose and duration), factor levels at which safety for vaginal delivery, C-section, and regional anesthesia, and also prospective management of PPH, plan for diagnosis of fetus.
- Guidelines and registries should be developed.
"I'm telling you, Sylvia, labor was so much easier than I ever imagined. He was delivered in 30 minutes or less!"