Diagnosis and Management of Early Pregnancy Failure Through Case Studies

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Objectives

- Review diagnosis of early pregnancy failure
- Discuss options for management of early pregnancy failure
- Address workup, prevention, subsequent conception, and contraception
National Context

Texas Will Require Burial of Aborted Fetuses

By LIAM STACK  NOV. 30, 2016

- Texas Health and Human Services rule proposed immediately after the State’s loss of Whole Woman’s Health vs. Hellerstedt
- Original rule would have forced home miscarriages to bring in fetal tissue for burial services → final rule removed this portion
- Louisiana and Indiana (Mike Pence) have passed similar laws that have been legally challenged
- Texas will be first state to implement → December 19th

The New York Times
Ok, let’s start with an easy one......
Q1: 31 yo G3P2002 at 8w0d by LMP presents for first ultrasound and no cardiac activity is appreciated

What is the diagnosis?

A) Early pregnancy loss  
B) Miscarriage  
C) Missed abortion  
D) All of the above
Early Pregnancy Loss

• **Definition:** nonviable, intrauterine pregnancy with either an empty gestational sac or a gestational sac containing an embryo or fetus without fetal heart activity within the first 12 6/7 weeks of gestation

• Other terms are used interchangeably
  - Miscarriage
  - Spontaneous abortion

NICE Clinical Guidelines (2012)
Incidence

- 10% of all clinically recognized pregnancies

- Timing: 80% of all pregnancy losses happen in first trimester
Etiology and Risk Factors

• 50% due to fetal chromosomal abnormalities

• Most common risk factors:
  Advanced maternal age
  Prior early pregnancy loss

• Frequency of early pregnancy loss increases with increasing maternal age:
  20-30  9-17%
  35     20%
  40     40%
  45     80%
Q2: What is the most common aneuploidy found in early pregnancy loss?

a. Euploidy
b. Monosomy
c. Trisomy
d. Polysomy
e. Unbalanced translocations
Cytogenetic analysis of miscarriages from couples with recurrent miscarriage: a case–control study

M.D. Stephenson¹,³,⁴,⁵, K.A. Awartani¹ and W.P. Robinson²,³

- Cytogenetic analysis of 420 losses from 258 couples with recurrent pregnancy loss
- Median number of miscarriages was four, mean age was 34
- 54% euploid, 46% aneuploid
  - 67% trisomic
  - 19% polyploid
  - 9% monosomic X
  - 4% unbalanced translocations
- Women less than 36 years old with recurrent pregnancy loss have a higher rate of euploid losses compared to population controls
Q3: 22 yo G1P0 @ 5w4d by LMP presents for first ultrasound with the following findings
If she is asymptomatic, what should you do?

A) Refer to family planning
B) Repeat scan in 6 days for definitive diagnosis
C) Repeat scan in 14 days for definitive diagnosis
D) Refer her to Texas Health and Human Services for the appropriate burial services
Transvaginal Ultrasound Findings Diagnostic of Early Pregnancy Loss

- CRL (crown-rump length) 7mm or greater and no cardiac activity
- Mean sac diameter of 25mm or greater and no embryo
- Absence of embryo with cardiac activity 2 weeks or more after a scan that showed a gestational sac without a yolk sac
- Absence of embryo with cardiac activity 11 days or more after a scan that showed a gestational sac with a yolk sac
Study aimed to set definitive cutoff values to for CRL and MSD so early pregnancy loss could be diagnosed with a single measurement

1060 women with pregnancies of uncertain viability were followed until their screening ultrasound between 11 -14 weeks → 587 diagnosed as non-viable

Exams carried out by various trained doctors and nurses in four London hospitals

Results

- When yolk sac and embryo were not visualized
  - MSD of 16 mm resulted in 4.4% false positive result (continued viability)
  - MSD of 21 mm resulted in no misdiagnosed cases
- When yolk sac visualized without embryo
  - MSD of 16 resulted in 2.6% false positive result
  - MSD of 21 mm resulted in no misdiagnosed cases
- When an embryo is present without cardiac activity
  - CRL of 4 mm & 5mm resulted in 8.3% false positive result
  - CRL greater than or equal to 5.3 mm resulted in no misdiagnosed cases
Criticism of Diagnostic Criteria

- Cutoff values are too high
- Limited patients with measurements near decisional boundaries
- Conservative limits made on assumption that diagnostic values should be 100% specific, however, this might not be a important for patients → shared decision making
19 yo G1P0 @ 7w1d by LMP presents for first ultrasound with the following findings
Transvaginal Ultrasound Findings Suggestive of Early Pregnancy Loss

- CRL less than 7 mm and no cardiac activity
- MSD of 16 - 24 mm and no embryo
- Absence of embryo with cardiac activity 7 - 13 days after sono that showed gestational sac without yolk sac
- Absence of embryo with cardiac activity 7 - 10 days after sono that showed gestational sac with a yolk sac
- Empty amnion (amnion seen adjacent to yolk sac without embryo)
- Large yolk sac (greater than 7 mm)
- Small gestational sac in relation to embryo (less than 5 mm difference between MSD and CRL)
Empty Amnion @ 8w4d
Enlarged Yolk Sac
Small gestational sac in relation to embryo
Q4: Based on the AMAZING lecture you received from those two AWESOME UH Family Planning fellows, you diagnose your first patient with early pregnancy loss. She is asymptomatic. What management option would you choose?

A. Expectant management
B. Medical management
C. Surgical management
D. Referral to Texas Department of Health and Human Services for arranging the appropriate burial services
Expectant Management

- Expectant management should be reserved for 1st trimester losses
- With enough time (up to 8 weeks), up to 80% effective
- Counsel patients on bleeding, pain, and possibility of surgery
- Give prescription for pain medications
- Follow up sonography for completion should be strictly focused on absence of gestational sac
Medical Management

- Misoprostol reliably reduces the need for uterine curettage by up to 60%.
- Vaginal and sublingual dosing are more effective than oral, however, sublingual route is associated with more diarrhea.
- Best evidence recommends 800 mcg misoprostol vaginally with a repeat dose as necessary – repeat dose no earlier than 3 hours after first dose and up to 7 days if no response to first dose.
- Give Rh(D)- immune globulin within 72 hours of initial misoprostol administration for women who are Rh(D) negative and unsensitized.
Addition of Mifepristone to Medical Management

- Mifepristone, in combination with misoprostol, is used for first trimester abortion
- Conflicting evidence about utility in early pregnancy failure
  - 5 randomized controlled trials
  - 11 non-randomized trials
- Success rates of 67-93% (wide range due to variable dosing regimens and outcomes measured)

Q5: Your patient opted for expectant management, she reports 1 week of bleeding that has since stopped. Her follow-up sono is below, with an endometrial thickness of 35 mm what should you do?

A) Schedule D&C  
B) Prescribe vaginal misoprostol  
C) Nothing  
D) Report her to Texas Health and Human Services for unlawful home burial of fetal remains
Assess relationship between endometrial thickness and final treatment outcome in women treated with misoprostol for early pregnancy failure

Patients received up to two doses of 800 mcg misoprostol for EPL and were followed with vaginal sonography for gestational sac expulsion

4/35 women with endometrial thickness less than 15 mm and expelled gestational sacs required D&C for ongoing bleeding

0/20 women with endometrial thickness greater than 15 mm and expelled gestational sacs required D&C for ongoing bleeding

Absence of gestational sac along with clinical symptoms should guide management, not endometrial thickness
Surgical Management

- Immediate completion with less follow-up
- Should be first line in women who present with hemorrhage, hemodynamic instability, signs of infection, or medical comorbidities
- Setting: office or operating room
- Equipment: electric or manual evacuation device
- Anesthesia: local anesthetic or sedation
- Antibiotics: 200mg doxycycline 1 hour prior to procedure
Comparison of Management Options

- Surgical management is faster and more predictable (99%)
- Medical management with misoprostol
  - Anembryonic gestation: 81%
  - Embryonic or fetal death: 88%
  - Incomplete or inevitable abortion: 93%
- Expectant management
  - Lower success rate (25-76%) for anembryonic gestation or embryonic or fetal death
  - Unpredictable time course (up to 30 days)

Factors Related to Successful Misoprostol Treatment for Early Pregnancy Failure

Creinin, Mitchell D. MD; Huang, Xiangke; Westhoff, Carolyn MD, MS; Barnhart, Kurt MD, MSCE; Gilles, Jerry M. MD; Zhang, Jun PhD, MD; for the National Institute of Child Health and Human Development Management of Early Pregnancy Failure Trial

- Secondary analysis of Management of Early Pregnancy Failure Trial
- 485 women who underwent treatment with misoprostol
- Predictive of first-dose success
  - Bleeding within last 24 hours
  - Parity of 0 or 1
- Predictive of overall success (92%)
  - Bleeding within last 24 hours
  - Abdominal pain within last 24 hours
  - Nulliparity
  - Rh(D) negative blood type
- Gestational age and pregnancy failure subtype were not predictive of treatment success

Obstet Gynecol (2006)
Complications

- **Bleeding**
  - Drop in hemoglobin of 3g/dL or greater is more likely with medical compared to surgical management
  - 0.5-1% rate of hemorrhage-related hospitalizations with or without transfusion

- **Infection**: similar to induced abortion (1-2%)

Cost Comparison

- Surgical management in operating room is the most costly option
- In-office surgical management can be less costly and more effective than medical management if multiple visits are likely
- US cost analysis of all three management options: medical management LEAST costly option
  - Expectant management: $1172
  - Medical management: $1000
  - Surgical management: $2007
- Limitation of cost analyses: unable to account for nuances of individual patient presentation or patient preferences, which may impact adherence to treatment regimen

Counseling and Subsequent Conception

- Abstaining from vaginal intercourse for 1-2 weeks after complete passage of pregnancy is routinely recommended (not an evidence-based recommendation)
- No difference in early pregnancy loss or neonatal outcomes with immediate vs. delayed conception

Contraception

- Hormonal contraception may be initiated immediately after completion of pregnancy loss
- IUDs may be placed immediately following surgical management (with the exception of septic abortion)
Immediate versus Delayed IUD Insertion after Uterine Aspiration

Paula H. Bednarek, M.D., M.P.H., Mitchell D. Creinin, M.D., Matthew F. Reeves, M.D., M.P.H., Carrie Cwiak, M.D., M.P.H., Eve Espey, M.D., M.P.H., and Jeffrey T. Jensen, M.D., M.P.H., for the Post-Aspiration IUD Randomization (PAIR) Study Trial Group

- 575 women undergoing uterine aspiration for spontaneous or induced abortion between 5-12 weeks gestation
- Randomized to immediate vs. delayed insertion (2-6 weeks later)
- 6-month expulsion risk: 5% in immediate group vs. 2.7% in delayed group (not clinically significant)
Rhogam

- Women who are Rh(D) negative and unsensitized should receive 50mcg Rh(D) immune globulin
  - Immediately after surgical management
  - Within 72 hours of diagnosis of early pregnancy failure with planned medical or surgical management
- 300mcg dose may be used if 50mcg dose is not available
Workup

- Workup not recommended until after second consecutive clinical early pregnancy failure
- Antiphospholipid antibody syndrome is significantly associated with early pregnancy loss
Q6: You have a patient with one prior early pregnancy loss. What intervention has been proven to prevent recurrence?

a. Aspirin 81 mg daily
b. MTHFR gene testing
c. Vaginal progesterone
d. Hydroxyprogesterone injections
e. None of the above
Prevention

- No known effective interventions
- Bed rest should NOT be recommended
- Prophylactic progesterone (oral, IM, or vaginal) has not been shown to prevent early pregnancy loss except in women with three prior losses
- Use of anticoagulants, aspirin, or both does not reduce the risk of early pregnancy loss in women with thrombophilias with the exception of antiphospholipid antibody syndrome
Questions?

Early voting on November 1st…
….we were so full of hope