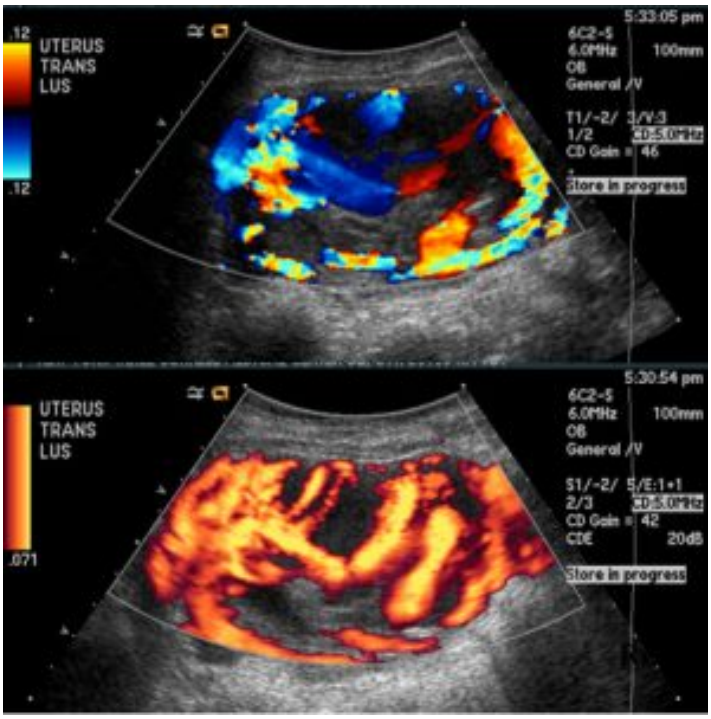
COURSE 15: OB/GYN MANAGEMENT OF VASCULAR ANOMALIES

Dr. Andrei Rebarber

Introduction: Ob/gyn management of vascular anomalies

Vascular anomalies are complex lesions which require the patient to be seen by numerous medical specialists for optimal care. When the patient is a pregnant woman, management can become problematic for the treating specialist, especially since these cases are rare.

Vascular anomalies of the uterus, especially when they accompany pregnancy, can result in profuse bleeding during delivery. Other complications can occur throughout the pregnancy, due to the already existing highly vascular condition. Thrombosis, rectal bleeding, and localized intralesional coagulopathy leading to system disseminated intravascular coagulation (DIC) may develop.



This module will focus on a generalized understanding of the potential issues faced by women with a vascular malformation as seen by the Ob/Gyn specialist.

Objectives

Upon successful completion of this activity, participants should be able to:

- Review important aspects of care of women with vascular anomalies
- Identify physiological changes in women during pregnancy
- Describe thromboembolism in depth
- Classify and describe malformations of the female pelvis
- Explain different aspects of Klippel-Trenaunay Syndrome (KTS)
- Summarize features of uterine arteriovenous malformations (AVM)

Physiologic changes of pregnancy

Cardiovascular

- Cardiac output increases by 30-50%
- Arterial pressure: initially falls (up to 24 weeks) then rises to surpass non-pregnant state by term
- Venous pressure: femoral venous pressure increases by 2-2.5x non-pregnant state
- Plasma volume increases by 50%
- Red blood cell mass increases by 18-30%

Breast size increase

- Estrogenic effect: ductal growth
- Progesterone effect
- Alveolar hypertrophy

Physiologic changes of pregnancy (2)

Leg edema

- Increased leg venous pressure
- Obstruction of lymphatic flow
- Reduced plasma colloid osmotic pressure

Physiologic changes of pregnancy (3)

Coagulation I

- Increased clotting factor levels (e.g. Fibrinogen, factors II, VII, VIII, X, XII, and XIII)
- Increased venous stasis
  - 1st trimester: increased vein distensibility
  - 3rd trimester: impaired flow due to gravid uterus
- Virchow triad
  - Injury to the vessel wall
  - Stasis *
  - Changes in local clotting factors *

*affected by pregnancy

Risk factors for thromboembolism

- Bedrest
- Varicosities
- Infection/trauma
- Obesity
- Dehydration
- Heart failure/shock
- Cancer

Hypercoagulable states:

- Antithrombin III, Protein S, Protein C deficiencies
- Antiphospholipid Antibody Syndrome
- Leiden Factor V mutation
- Prothrombin Gene Mutation
- Hyperhomocysteinemia

Impaired Fibrinolysis

- Plasminogen Activator Inhibitor 1 4G allele

Protein S Deficiency risk of thromboembolism

- 0-6% in pregnancy
- 7-22% during the postpartum period

Protein C Deficiency risk of thromboembolism

- 3-10% during pregnancy
- 7-19% during the postpartum period

Antithrombin III Deficiency risk of thromboembolism

- 12-60% during pregnancy
- 11-33% during the postpartum period

Risk factors for thromboembolism (2)

- Pregnancy-related phenomena
- Cesarean section
- Advanced maternal age (> 35)
- Operative vaginal delivery

Acquired thrombophilias

The Antiphospholipid Antibody Syndrome

- Defined by a history of arterial/venous thromboembolism, thrombocytopenia, or recurrent pregnancy loss in patients with either a lupus anticoagulant or moderate-to-high titer ACA (ie. > 20-50 GPL or MPL Units) repeated on two separate occasions at least 6 weeks apart

The risk of thromboembolism during pregnancy and postpartum is 5.5 times greater than for nonpregnant controls.

Thromboembolism

Antenatal Deep Venous Thrombosis

- Untreated
  - 24% incidence of PE
  - 15% mortality
- Treated
  - 4% incidence of PE
  - <1% mortality

Vascular anomalies basics

Classified according to flow characteristics:

- Fast
- Slow

Vascular channel components:

- Capillary
- Venous
- Lymphatic
- Arterial
- Combined

Venous malformations of the female pelvis

- Most common site: perineum (especially labia majora)
- Can affect all tissue layers- may be focal, multifocal, or diffuse
- Symptoms include: swelling, pain
  - Worsened by prolonged standing, walking, or excercising
  - Often worse with menses or pregnancy

Rectal venous malformations

- Presence of rectal bleeding
- May develop thrombosis of hemorrhoidal veins with resultant portal vein thromboembolism and hepatic infarction

Uterine and ovarian venous malformations

- Typically associated with ovarian vein insufficiency
- Forms a subtype of “pelvic congestion syndrome”

Extensive venous malformations

- May develop localized intralesional coagulopathy leading to systemic DIC, especially in association with surgery

Lymphatic malformations of the female pelvis

- Can occur as a focal or diffuse anomaly and are composed of:
  - Macrocysts (thin collections > 2 cm diameter)
  - Microcysts (< 2 cm diameter)
  - Combination of both
- Cystic lymphatic malformations often associated with localized enlargement of adjacent conducting veins or with persistent embryonic veins (lymphaticovenous (LVM)) or capillary-lymphaticovenous malformations (CLVM)
  - When it involves the adjacent limb with overgrowth – Klippel-Trenaunay Syndrome (KTS)

Fast-flow vascular malformations of the female pelvis

- Arteriovenous malformations (AVM)/arteriovenous fistuli (AVF)
- Change from asymptomatic to active shunting , venous engorgement, and venous hypertension
- Evolution secondary to
  - Trauma
  - Hormonal (puberty, pregnancy)
- Symptoms range
  - Mild discomfort/pelvic pressure
  - Vaginal/rectal bleeding
  - Cardiac volume overload/congestive heart failure (CHF)

Intra-uterine arteriovenous malformations

- Those that arise after pregnancy or uterine trauma
  - If retained products of conception returns, NOT true AVMs
- AVM presenting with uterine hemorrhage
  - Embolization has high success rate
  - Pregnancy post-uterine embolization reported successful in several series
- Uterine AVM reported in Hereditary Hemorrhagic telangiectasia

Klippel-Trenaunay Syndrome (KTS): basics

- First described in 1900
- Rare congenital malformation (M1:F1)
- Heterogeneous phenotypic expression
- Genetic inheritance – somatic mutation in *PIK3CA*

Klippel-Trenaunay Syndrome: classic diagnosis triad

Diagnosis is based on 2 out of 3 features:

- Capillary malformations (usually port wine stains)
- Soft tissue or bony hypertrophy (or both)
- Varicose veins or venous malformations

Klippel-Trenaunay Syndrome prenatal diagnosis

Detectable by 16-18 weeks with Color flow Doppler- TA
21 cases reported in literature

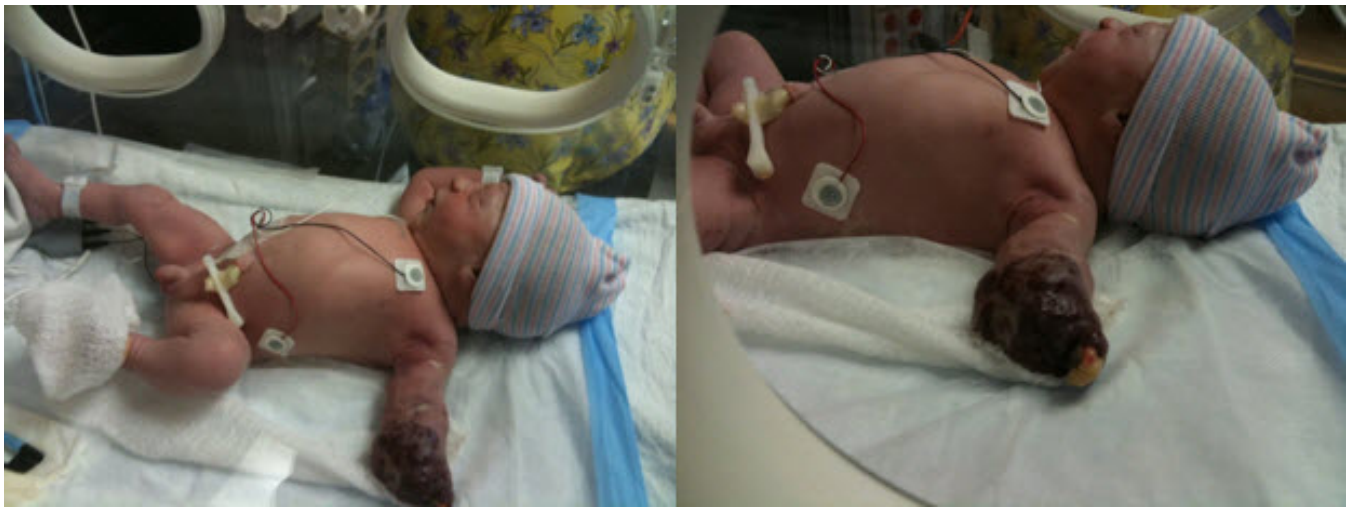
- Raised mass of significant size
- Limb asymmetry
- Polyhydramnios
- Cardiomegaly
- Placental thickness
- Hydrops

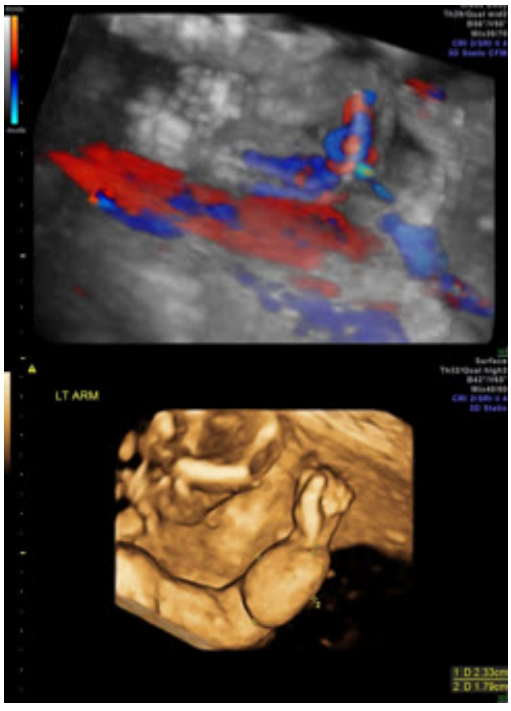
Pregnancy management in fetal Klippel-Trenaunay Syndrome

- Consider amniocentesis for chromosome analysis
- Fetal echocardiography
- Serial growth scans
- Maternal administration of digoxin in cases of hydrops may improve cardiac output
- Size and location of vascular malformation may require cesarean section
- Neonatology and pediatric surgery consultation

IN UTERO LIMB AVM

- 35-year old, P7 uncomplicated radiofrequency ablation (RFA) procedure at 17 weeks' gestation for selective termination of the donor twin in a case of Stage III twin–twin transfusion syndrome (TTTS)
- Three-dimensional ultrasound image of the fetus at 21 weeks' gestation, showing a 2.0×1.5-cm mass on the volar surface of the left forearm
- At 37 + 4 weeks, the patient delivered a vigorous male neonate, weighing 2570 g, via Cesarean section
- Vascular mass engulfing the left arm from the forearm to the axilla





Klippel-Trenaunay Syndrome in pregnant patients

Case Study 1: 21 yo P0000 presented for prenatal care

- Left leg capillary hemangioma, limb hypertrophy
- At 11 weeks gestation, patient complained of worsening shortness of breath upon exertion. Leg Doppler studies inconclusive due to lack of a deep venous system with multiple superficial leg varicosities. Ventilation/perfusion scan revealed multiple pulmonary emboli. Heparin anticoagulation was therapeutic. Emergent placement of a Greenfield filter was performed in the inferior vena cava.
- Induced at 38 weeks gestation due to intrauterine growth restriction by ultrasound evaluation. Normal spontaneous vaginal delivery of a male infant weight 2940 gms with APGARS 9/9. Postpartum course complicated by endomyometritis, urinary tract infection, and bacteremia. Sent home on the 8th postpartum day.

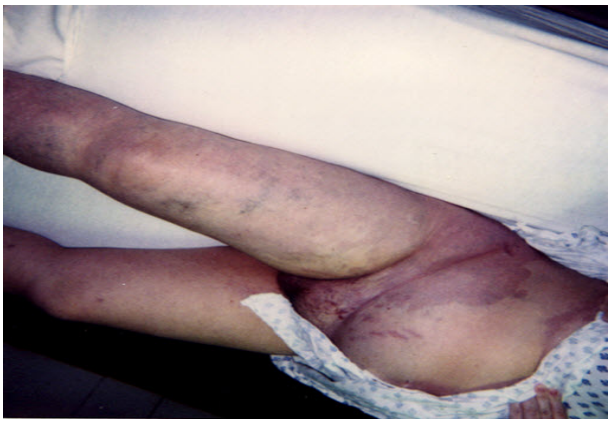
K-T Syndrome in pregnant patients (2)

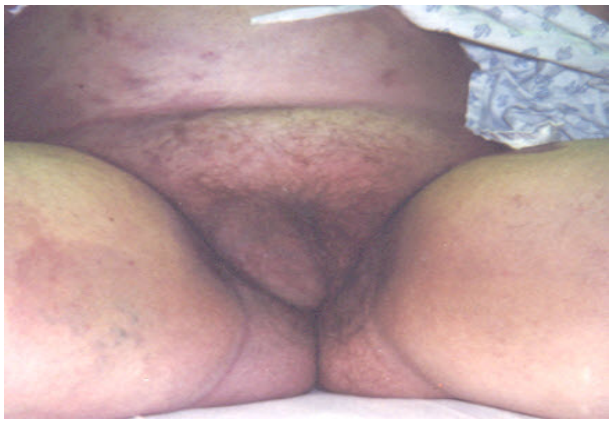
Case Study #2: 32- year old P0050 presented for preconception counseling

- Right leg and breast capillary hemangioma, limb hypertrophy, multiple thromboembolic events
- Right breast reconstruction, toe amputations, right leg vein strippings, Hickman catheter placement.
- Chronic Percocet use due to worsening leg pain throughout pregnancy. Heparin use throughout pregnancy- + Prothrombin gene mutation
  - Delivered at 36- weeks gestation by primary cesarean section due to vulvovaginal varicosities. Female infant appropriate weight for gestational age. No postoperative complication noted.

Second pregnancy uneventful but patient was noncompliant with leg stocking placement and administration of LMW heparin therapy

- Postpartum chronic leg pain with dependant edema and perfusion problems; possible need for amputation

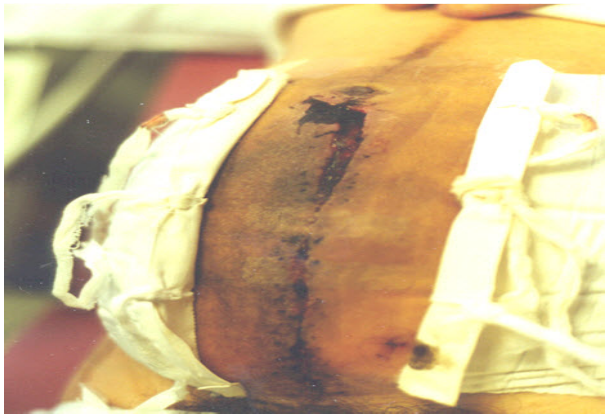


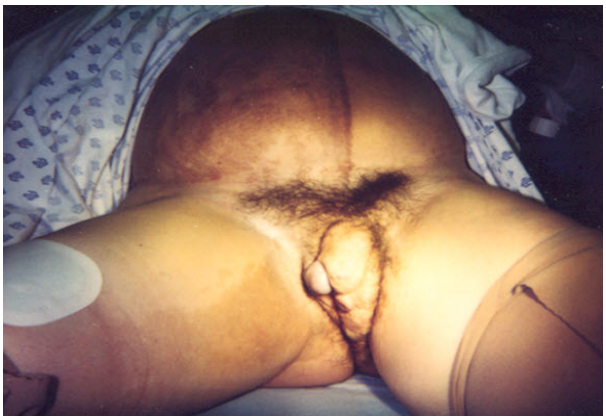


Klippel-Trenaunay Syndrome in pregnant patients (3)

Case Study 3: 29-year old P0000 presented for preconception counseling.

- Left leg and breast capillary malformation, left limb hypertrophy leading to multiple thromboembolism, splenic arteriovenous malformations, pelvic vein engorgement
- Left leg below the knee amputation, splenectomy, hemorrhoidectomy, pelvic vein embolization, right ovarian cystectomy for endometrioma, greenfield filter placed, inferior vena cava wall stenting due to filter obstruction
- + Prothrombin gene mutation
  - Delivered at 36- weeks gestation by primary cesarean section due to vulvovaginal varicosities. Superficial wound separation due to thrombosed capillary hemangioma bordering right aspect of the incision





Klippel-Trenaunay Syndrome in pregnancy questionnaire

- Why do it?
  - Provide better counseling to patients
  - Improve treatment/management
  - Improve medical database
- Limitations of the study design
  - Susceptible to errors caused by:
    - Selection bias
    - Imperfect memory- recall bias
    - Limited powers of observation
    - Respondent’s desire to give socially acceptable answers
- Advantages of the study design
  - Economical
  - Standardized

Klippel-Trenaunay Syndrome survey: 2004 obstetrical database, 147 pregnancies reviewed 7/25/04

In collaboration with the KT Support group. here are the findings:

- Age of respondents
  - Mean 26 yo (range 16-38 yo)
- Gestational age at delivery
  - Mean 38.52 weeks (range 26-42 weeks)
  - 5 pregnancies information not available
- Mode of delivery
  - 27% Cesarean sections rate
  - 17 pregnancies, elective terminations
  - 23 spontaneous miscarriages (16%)
  - 1 ectopic pregnancy
  - 1 stillbirth
  - 3 surveys returned with incomplete information
  - 103 live births in 50 patients
  - 73% vaginal delivery

Klippel-Trenaunay Syndrome in pregnancy questionnaire

Table 2: Sites of involvement in pregnant patients with K-T

Site	No. Patients
lower extremity	16
bilateral	2
unilateral	14
right	8
left	6
lower extremity only	4
upper extremity	2
bilateral	0
unilateral	1
right	0
left	1
upper extremity only	0
upper and lower extremities	3
bilateral	1
unilateral	2
thorax	7
pelvis or abdomen	11
head and neck	2

Klippel-Trenaunay Syndrome survey 2004: obstetrical complications (2)

- 15% preterm delivery
- 11.6% preterm labor
- 0.4% preeclampsia
- 0% intrauterine growth restriction
- **7.7% thromboembolism (not including 4 patients describing superficial phlebitis)**
- 1 patient with oligohydramnios
- 1 patient with placenta previa

COMPLICATIONS OF KLIPPEL-TRENAUNAY SYNDROME

- 48.5% NONE
- **10.6% postpartum hemorrhage**
- 2.9% antepartum hemorrhage
- 18.5% lower extremity swelling (3 patients also noted ulceration)
- 1.9% severe nausea
- 2.9% low platelets

MISCELLANEOUS COMPLICATIONS

- Pain
- Wound dehiscence
- Ruptured cyst with internal hemorrhage
- Spinal cord hemangioma
- Kidney surgery at 20 weeks
- Prescribed bedrest
  - 22% Yes, 78% No
- Obstetrical care providers
  - 18% family practitioners
  - 6.8% midwives
  - 58% Ob/Gyn
  - **17.4% maternal fetal medicine**

KLIPPEL-TRENAUNAY SYNDROME TREATMENT DURING PREGNANCY

- 3.9% Bedrest
- 3.9% Bedrest and leg elevation
- **10.6% Compression stockings**
- **29.1% Compression stockings and leg elevation**
- 4.9% Bedrest and compression stockings and leg elevation
- 7.8% Leg elevation
- 40% NO advice

Advice provided during pregnancy

- **49.5% NO ADVICE**
- 5.8% NO EFFECT
- 33% may worsen
- 9.7% will worsen

Medication treatments

- **76% NONE**
- 8.7% Aspirin
- 7.8% Heparin
- 7.8% low molecular weight heparin

Start of anticoagulation

- 1st tirmester 7.8%
- 2nd trimester 5.8%
- Postpartum 5.8%
- Misc: 1 patient started at 20-26 weeks and a second started at 32-37 weeks

Klippel-Trenaunay Syndrome and pregnancy: OUR current recommendations

- Compression stockings
- Thrombophilia work-up
- MRI spine and brain
- Heparin therapy (LMW); prophylaxis CASE BY CASE BASIS
- Serial growth scans
- Cesarean section – if significant vulvar varicosites obstructs vaginal delivery
- Anesthesia & vascular team consultation

ACOG Practice Bulletin (Sept 2013): Inherited thrombophilia in pregnancy

“Decision to treat with thromboprophylaxis, anticoagulant therapy, or no pharmacologic treatment (antepartum surveillance) is influenced by the venous thromboembolism history, severity of inherited thrombophilia, and additional risk factors.”

Risk of thrombotic events post partum

- 1.7 million women with first recorded delivery
- Within 6 weeks after delivery compared with 1 year later
  - 411 events vs. 38 events
  - Absolute risk difference of 22.1 events (95% CI, 19.6-24.6) per 100,000 deliveries
  - Odds ratio of 10.8 (95% CI, 7.8-15.1)
- Within 7-12 weeks after delivery compared with 1 year later
  - 95 vs. 44 events
  - Absolute risk difference of 3.0 events (95% CI, 1.6 -4.5) per
  - 100,000 deliveries Odds ratio of 2.2 (95% CI, 1.5-3.1)

Vascular malformations & pregnancy: future directions

- Establishing a pregnancy registry
- Improve counseling
- Provide improved quality of care

Gynecologic considerations & Klippel-Trenaunay Syndrome

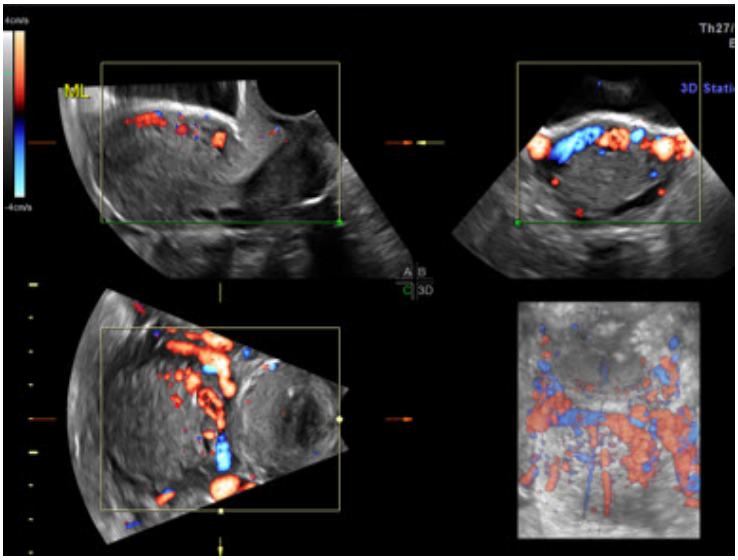
- Contraception
- Intercourse
- Uterine AVMs- menometrorrhagia

Oral contraceptives: 62 responders

- 13 unknown
- 20 used OCP’s
  - 6 SVT/DVT (32%)
  - 1 increased BP (5%)
  - 4 increased pain/edema/varicosity of effected site (20%)
  - 1 increased breast tenderness
  - 8 no complications
- 29 used other forms of birth control

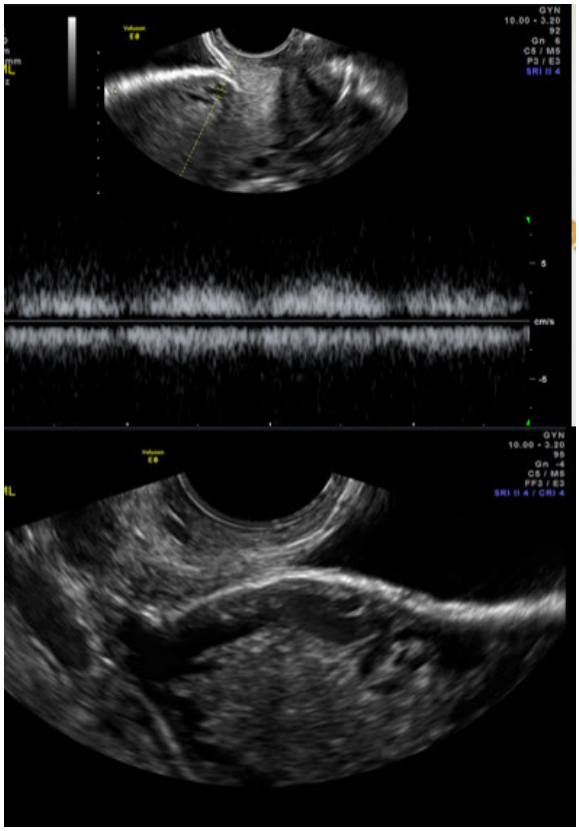
Uterine AVM

50-year old P3 postmenopausal bleeding



TREATMENT OF UTERINE AVMS (NON-PREGNANT)

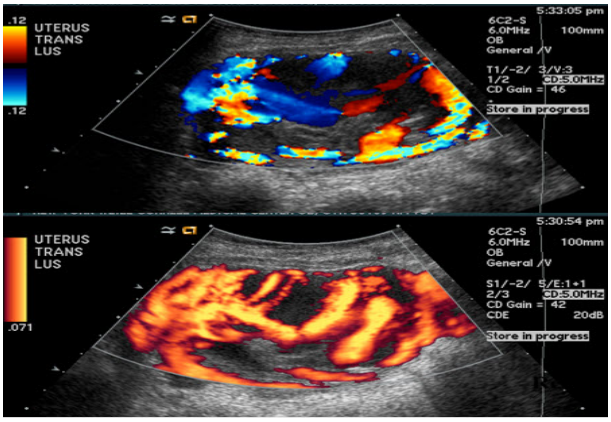
- Conservative management – spontaneous regression
  - Particularly for pregnancy- related uterine AVMs (Lee TY, et al Acta Radiologica 2014)
  - High PSV associated with increased failure rate
- Uterine artery embolization
- Hysterectomy

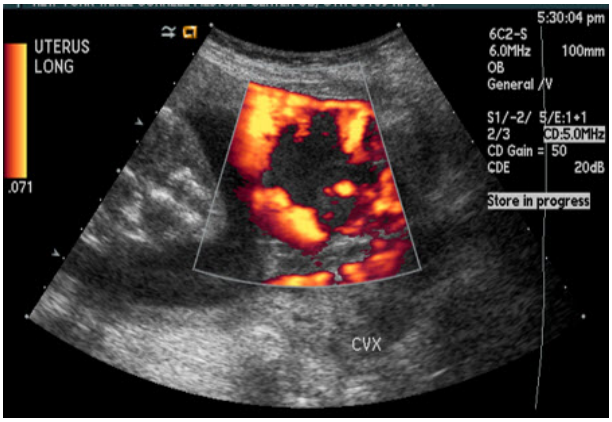


AVM of the lower uterine segment in pregnancy

- 34- year old G4, P3, T3, PT0, LC4, Ab0 IVF pregnancy
- Transferred due to a LUS vascular anomaly with a viable singleton gestation at 19+ weeks for attempt at “conservative management”
- OB hx
  - Pregnancy #1: 1995, 37- weeks twin gestation, Cesarean section, male-male, 6lbs 3oz / 6lbs 6 oz . IVF(done in Belgium)
  - Pregnancy #2: 1998, 40- weeks gestation, vaginal birth after Cesarean, female, 7lbs, PPH -10 U PRBC. Vaginal repair of lacerations
  - Pregnancy #3: 2002 37- weeks gestation, Cesarean, female, 5lbs 14oz
- Repeat Cesarean for breech uterine window, 2/3 of LUS repaired – ADVISED AGAINST FUTURE PREGNANCY

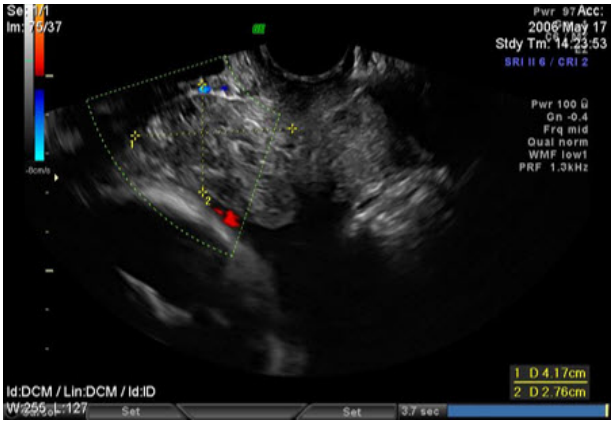
LUS AVM in pregnancy

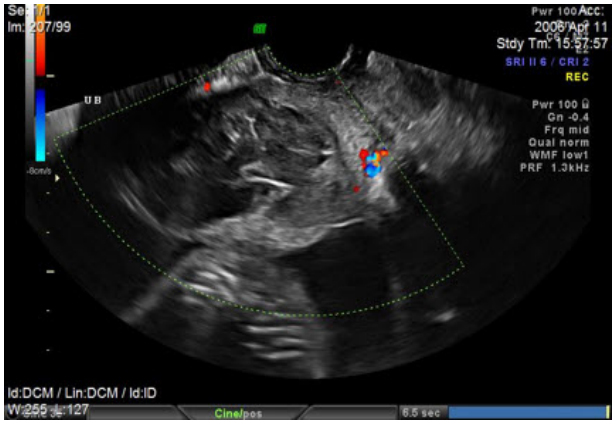




LUS AVM in pregnancy (2)

After embolization (22+ weeks)





EMBOLIZATION TECHNIQUE

- Right common femoral approach used
- Vasospasm was treated with administration of 100 mcg of nitroglycerin
- Glue embolization with 1 cc glue and 1 cc Ethiodol in left uterine artery and in several vessel branches
- Total rad exposure estimated to be 2-3 rads
- Fetal cardiac activity monitored throughout the procedure with ultrasound

PREGNANCY/POSTPARTUM COURSE

- Intermittent episodes of vaginal bleeding
- Late onset IUGR
- Preterm labor at 35 weeks leading to Cesarean Section
- Liveborn male infant, 1,820 grams, APGARS 9/9
- LUS necrotic avascular mass 3 cm x 5 cm left in situ
- Placental pathology: < 10th percentile weight for GA, NO micro or macroinfarcts
- 2 months PP: Saline Infusion Sonogram NORMAL UTERINE CAVITY

PREGNANCY/POSTPARTUM COURSE

Intermittent episodes of vaginal bleeding
Late onset IUGR
Preterm labor at 35 weeks leading to Cesarean Section
Liveborn male infant, 1,820 grams, APGARS 9/9
LUS necrotic avascular mass 3 cm x 5 cm left in situ
Placental pathology: < 10th percentile weight for GA, NO micro or macroinfarcts
2 months PP: Saline Infusion Sonogram NORMAL UTERINE CAVITY

AVM of the lower uterine segment in pregnancy (3)

2 MORE PREGNANCIES

- Pregnancy # 5
  - Delivery date: 07/01/2010
  - Weeks gestation: 32.4
  - Preterm labor: no
  - Delivery type: Cesarean section
  - Anesthesia type: spinal
  - Delivery location: MSSM (AR)
  - Infant sex: male x2
  - Birth weight: 4/7, 4/4
  - Name: Isaac, Eziel
  - Comments: admitted at 28 weeks due to absence of lower uterine segment visualization by MRI and ultrasound. Elective delivery due to concern about uterine rupture. Uterine window encompassing the entire LUS was visualized. Babies stayed in NICU x 2 weeks both A&W.
- Pregnancy # 6
  - Delivery date: 06/19/2013
  - Delivery type: Cesarean secrion
  - Anesthesia type: spinal
  - Delivery location: MSSM (AR/SM)
  - Infant sex: female
  - Birth weight: 6.1
  - Comments: IVF / ICSI

COURSE 15 QUIZ

1. All of the following are risk factors for Thromboembolism II (pregnancy related phenomenon) except:

   A. Advanced paternal age (greater than 35 years old)
   B. Operative vaginal delivery
   C. Cesarian section
   D. Advanced maternal age (greater than 35 years old)

2. A woman with a large vascular malformation of the leg and a prior history of a DVT wishes to get pregnant. Once pregnant, should she be:

   A. Placed on baby ASA
   B. Placed on Coumadin
   C. Placed on low molecular weight heparin prophylaxis
   D. Placed on low molecular weight heparin therapeutic

3. A woman with an extensive vascular malformation of her arm and chest comes for a preconception visit and wishes to know what special precautions she should take prior to getting pregnant. What would you tell her?

   A. Advise her to obtain a Maternal Fetal Medicine Consult
   B. Obtain a thrombophilia work-up
   C. Counsel her regarding the potential for worsening pain and swelling in the affected area
   D. No special advice
   E. a, b and c

4. Limb asymmetry, polyhydramnios, cardiomegaly, and a raised mass with or without a cutaneous stain may describe which syndrome:

   A. Cowden's Syndrome
   B. Klippel-Trenaunay Syndrome
   C. Dandy Walker Syndrome
   D. Sturge-Weber Syndrome

5. Physiological changes in pregnancy include all of the following except:

   A. Femoral venous pressure increases by 2-2.5x non-pregnant state
   B. Increase in cardiac output
   C. Cardiac output and venous pressure increase and arterial pressure initially falls
   D. Arterial pressure rapidly rises during first 24 weeks gestation

6. Symptoms of fast-flow vascular malformations of the female pelvis include all of the following except:

A. Mild discomfort
B. Pelvic pressure
C. Bradycardia /slow heart rate
D. Vaginal or rectal bleeding

7. Which of the following is not a risk factor for Thromboembolism I during pregnancy?

A. Cancer
B. Obesity
C. 1% weight loss during first trimester
D. Dehydration

8. Adolescent with a large vascular malformation of the leg with no prior history of a DVT wants to start on Oral Contraceptives (OCP). Should she:

A. Low estrogen/progesterone combination pill
B. Oral contraceptives are contraindicated
C. Take any OCP
D. Progesterone only pill

9. A woman with an extensive vascular malformation of her arm and chest comes for a preconception visit and wishes to know what special precautions should she take prior to getting pregnant. You would:

A. Advise a Maternal Fetal Medicine Consult
B. Obtain a thrombophilia work-up
C. Counsel regarding the potential for worsening pain and swelling in the affected area
D. All of the above

10. Which of the following vascular malformations can result in adverse complications during pregnancy?

A. Rectal VMs
B. Uterus and Ovarian VMs
C. Extensive and/or complex VMs outside of the female pelvis
D. All of the above

AUTHOR
PROFILES

Andrei Rebarber, M.D, Maternal-Fetal Medicine

Dr. Rebarber is a board certified Obstetrician / Gynecologist with subspecialty certification in Maternal-Fetal Medicine. He completed his MFM fellowship training at Yale University and was a member of the New York University School of Medicine faculty where he served in numerous leadership positions prior to his current role.

BIBLIOGRAPHY

A Foundation in Vascular Anomalies
Course 15: OB/GYN Management of Vascular Anomalies

Burrows, P. E., Mitri, R. K., Alomari, A., Padua, H. M., Lord, D. J., Sylvia, M. B., … & Mulliken, J. B. (2008). Percutaneous sclerotherapy of lymphatic malformations with doxycycline. Lymphatic Research and Biology, 6(3-4), 209-216.

Children's Hospital Boston. Vascular Anomalies Center. http://www.childrenshospital.org/clinicalservices/Site1964/mainpageS1964P0.html

Fishman, S. J., Shamberger, R. C., Fox, V. L., & Burrows, P. E. (2000). Endorectal pull-through abates gastrointestinal hemorrhage from colorectal venous malformations. Journal of Pediatric Surgery, 35(6), 982-984.

Kulungowski AM, Fishman SJ. (2011) Management of combined vascular malformations. Clinics in Plastic Surgery, 38(1):107–120.9.

Kulungowski AM, Fox VL, Burrows PE, Alomari AI, Fishman SJ. (2010) Portomesenteric venous thrombosis associated with rectal venous malformations. Journal of Pediatric Surgery, 45(6):1221–1227.10.

P. Burrows, R. Mitri, A. Alomari, H. Padua, D. Lord, M. Sylvia, S. Fishman, J. Mulliken. (2008). Percutaneous sclerotherapy of lymphaticmalformations with doxycycline. Lymphatic Research and Biology, 6(3-4): 209-216.

COURSE 15 QUIZ ANSWER KEY

1. A
2. C
3. E
4. B
5. D
6. C
7. C
8. D
9. D
10. D