MEDICAL MGMT OF ECTOPIC PREGNANCY

FLAME LECTURE: 83

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LEARNING OBJECTIVES

- To describe medical treatment options including Methotrexate for ectopic pregnancies
- Medical management of ectopic pregnancies will be covered in this lecture
  - See FLAME LECTURE 82: Diagnosing an ectopic pregnancy
  - See FLAME LECTURE 84: Surgical management of ectopic pregnancies

MGMT OF ECTOPICS

- Ectopic pregnancies can be life-threatening, thus prompt diagnosis and treatment is imperative
- Ruptured ectopics must be treated surgically
- Stable (unruptured) ectopics can be treated either surgically OR medically with methotrexate (MTX)

MGMT OF ECTOPICS

- Before deciding on medical management, ensure the patient:
  - Is hemodynamically stable
  - Doesn't have a contraindication to MTX
  - And is both trustworthy and capable of complying with follow-up surveillance

WHAT IS METHOTREXATE?

- An antimetabolite that binds to the catalytic site of DIHYDROFOLATE REDUCTASE. This interrupts:
  - The synthesis of purine nucleotides → inhibiting DNA synthesis, DNA repair, and cell replication
  - The synthesis the amino acids serine and methionine
- MTX primarily affects actively rapidly proliferating tissues such as bone marrow, buccal/intestinal mucosa, respiratory epithelium, malignant cells, and trophoblastic tissue

MTX REGIMENS

- There are multiple different dosing regimens, however the two most common are single-dose and fixed multi-dose regimens
  - The regimens are posted to the right for reference, however they are above medical student level for the SHELF
- Notably, ectopics that are within the cervix or cesarean section scar are much more difficult to treat, thus fixed multi-dose regimens or even intra-sac injection of MTX can be used.

SINGLE DOSE PROTOCOL

1. MTX 50mg/m2 IM once (DAY 1)
2. Check bHCG levels on DAY 4 & DAY 7
3. Success measured as 15% bHCG decrease between DAY 4 and DAY 7
4. If decreased < 15%, give 2nd dose of MTX 50mg/m2 and repeat protocol
5. Follow bHCG to zero (on average takes 33.6 days[1])

FIXED MULTIDOSE PROTOCOL

1. MTX 1mg/kg IM (on DAY 1, 3, 5, etc).
2. Alternate with rescue folic acid 0.1mg/g IM (on DAY 2, 4, 6, etc)
3. Measure bHCG on MTX treatment days and continue therapy until bHCG has decreased by 15% from previous measurement
4. Follow bHCG to zero

MTX COUNSELING

- Efficacy
  - For single-dose MTX, if the bHCG is < 5000, success rate is 92-98%
  - If the bHCG > 5000, consider the multi-dose regimen or surgery
  - For patients concerned about fertility, MTX and tube-sparing surgery have shown no difference in future tubal patency, repeat ectopic pregnancy rates, or future IUP rates[1]
- Expectations / Side effects
  - Patients usually feel crampy abdominal pain for 2–3 days after MTX injection ("separation pain")
  - Vaginal bleeding is common
  - GI side effects are common (nausea, vomiting, and stomatitis)
  - Reversible alopecia, severe neutropenia, or pneumonitis are all rare side effects

MTX COUNSELING

- Instructions/Precautions
  - During therapy, DO NOT TAKE FOLIC ACID (including PNV), NSAIDs, or alcohol. AVOID sunlight exposure, sexual intercourse, and vigorous physical activity
  - There is an ongoing RISK OF TUBAL RUPTURE during treatment, thus strict precautions must be given to patients to return immediately for severe abdominal pain
  - Monitor for fever or respiratory symptoms as an early sign of pneumonitis
  - Taking MTX for the ectopic pregnancy has NOT been associated with any future risk of congenital anomalies

CONTRAINDICATIONS OF MTX

- Absolute Contraindications
  - Breastfeeding
  - Immunodeficiency
  - Pre-existing blood dyscrasias (bone marrow hypoplasia, leukopenia, thrombocytopenia, or significant anemia)
  - Alcoholism, chronic liver disease
  - Active pulmonary disease
  - Other hepatic (LFTs twice normal), renal (Cr > 1.3), or hematologic dysfunction
  - Peptic ulcer disease
  - Known sensitivity to methotrexate
- Relative Contraindications
  - Gestational sac > 3.5 cm
  - Fetal cardiac motion

Thus, before administering MTX, baseline labs should include:

- CBC, Cr, LFTs
- Repeat these labs DAY 7 after MTX to evaluate for impact on renal, hepatic, and hematologic function
- b-HCG at baseline, DAY 4 and DAY 7

EXPECTANT MANAGEMENT?!?

- Candidates who decline both surgical and medical management should be asymptomatic and have objective evidence of resolution (generally manifested by decreasing hCG levels)
- Patients must be compliant with surveillance → hCG +/- TVUS every 1-3 days
- Patients must be willing to accept the potential risks of: tubal rupture, internal hemorrhage, need for emergent surgery, and possible death
- Approximately 20–30% of ectopics are associated with decreasing hCG levels at the time of presentation.[1] In general, the lower the b-HCG, the better the prognosis for spontaneous resolution.
  - If the initial hCG level <200 mU/mL → 88% experience spontaneous resolution[2]
  - hCG >2,000 → 93.3% fail expectant management
- Reasons for abandoning expectant management include: intractable or significantly increased pain, failure of hCG levels to decrease, and evidence of tubal rupture (e.g. free fluid on TVUS).

IMPORTANT LINKS / SOURCES

- PRACTICE BULLETIN 94 – Medical Management of Ectopic Pregnancies
- Barnhart KT. *Ectopic Pregnancy*. N Engl J Med. 2009; 261:379-387
- Lipscomb GH, Bran D, McCord ML, Portera C, Ling FW. An analysis of 315 ectopic pregnancies treated with single-dose methotrexate. Am J Obstet Gynecol 1998;178:1354-1358