

ECTOPIC PREGNANCY

Evaluating a patient with possible ectopic pregnancy early in pregnancy is often problematic. Symptoms often appear between six and eight weeks following the last menstrual period but this is not invariable. Missed period (amenorrhea), abdominal / pelvic pain and vaginal bleeding are the most common symptoms presenting with the breast tenderness and nausea which accompany normal early pregnancy. [1]

Risk factors for ectopic pregnancy have been stratified. Women at highest risk for ectopic pregnancy have had prior tubal surgery, prior tubal sterilization, prior ectopic pregnancy or currently use an IUD. Women at high risk have infertility, prior Chlamydia infection, prior pelvic inflammatory disease, multiple sexual partners or use tobacco. Prior abdominal surgery and early age of first intercourse also elevate chance for ectopic somewhat.

Prior endothelial tubal injury is the common risk factor for tubal ectopic pregnancy.

Diagnosis of early, un-ruptured ectopic pregnancy is complicated as the symptoms are usually subtle and intermittent. Once rupture occurs intense pain, signs of acute abdomen on physical examination and significant free fluid on imaging often contribute to making the diagnosis easier, however, option to intervene and conserve the tube is limited. The goal is to make the diagnosis prior to tubal rupture.

In a woman with abdominal pain and a positive pregnancy test other conditions including ruptured corpus luteum cyst, torsioned ovary, appendicitis, nephrolithiasis, pelvic inflammatory disease, endometriosis, infarction of a fibroid or ovarian tumor must be excluded in the work up.

Pregnancy Hormone Testing—

Human chorionic gonadotropin, HCG, is made by trophoblastic cells in the placenta. In a normal pregnancy hCG levels increase geometrically over the first six to seven weeks doubling between 1.4 and 2.1 days. A steep slope of increase is then observed until about ten weeks gestational age. [2,3]

Often Quantitative hCG levels do not increase as rapidly in ectopic pregnancies or abnormal intra-uterine pregnancies. Failing pregnancies, whether in or out of the uterus, are associated with spontaneously decreasing hCG levels.

Quantitative hCG levels should be monitored on an every other day basis beginning when concern over possibility of ectopic pregnancy is entertained. A single positive blood hCG level can not establish the well being of a pregnancy although a single negative test can exclude pregnancy from the differential diagnosis.

Ultrasound—

By itself ultrasound can substantially decrease the likelihood of ectopic pregnancy when an intra-uterine gestational sac is identified, although the chance of hetero-ectopic pregnancy is 1 / 4000 –

5000 pregnancies (separate pregnancies in and out of the uterus). Hetero-ectopic pregnancy is strongly associated with assisted reproductive technologies and specifically with super-ovulation.

Ultrasound can suggest ectopic pregnancy in various circumstances: 1.) pregnancy is seen outside of the uterus or in an abnormal location in the uterus (cervix or cornua); 2.) substantial free fluid is noted in the cul-de-sac; or, 3) large adnexal mass is noted.

Discriminatory Zone—

Early ectopic pregnancy is best diagnosed using blood testing and transvaginal, high frequency ultrasound. The relationship of hCG levels and ultrasonic findings holds the highest level of precision for diagnosing ectopic pregnancy. Kadar in 1981 developed this paradigm. [4] Discriminatory Zone is defined as a serum hCG level above which one should always detect an intra-uterine gestational sac on ultrasound. In 1981 the hCG level was 6,500 mIU/ml used when transabdominal, transvesicle scanning was standard. With development of high frequency transvaginal scanning the discriminatory zone fell to 1,500 to 2,000 mIU / ml. With current equipment the number is now about 1,000 mIU/ml. [5,6]

The higher the discriminatory zone is set the lower the likelihood of interrupting a normal intra-uterine pregnancy. The lower the discriminatory zone is set the lower the likelihood of missing an ectopic pregnancy prior to potential rupture. Specificity at three hCG levels was evaluated in the literature: 1.) 1000 mIU/ml was 87.3%, 2.) 1500 mIU/ml was 93.4%, and, 3.) 2000 mIU/ml was 95.2%. [7]

At Desert Women's Care we use 1,500 mIU / ML as the discriminatory zone. The absence of an intra-uterine gestational sac at or above this level strongly suggests the probability of ectopic pregnancy or abnormal intra-uterine pregnancy. The goal of the work-up is to exclude the likelihood of a viable intra-uterine pregnancy. Work-up does not always demonstrate the location of an abnormal pregnancy. Diagnosis of ectopic pregnancy most commonly is made by exclusion.

If a mass is noted outside of the uterus, color Doppler may enhance diagnostic precision. A "Ring of Fire" with increased blood flow is noted surrounding an ectopic pregnancy. [8]

Some variability is introduced because there is no clear-cut discriminatory zone for multiple gestations.

Diagnostic Possibilities—

Abnormal Intra-uterine pregnancy: Declining hCG levels or levels not increasing appropriately are most commonly associated with failed intra-uterine pregnancies. Twenty to thirty percent of all pregnancies fail. D&C can be performed but chorionic villi are not always found on pathology. If curettage is performed, serum hCG levels can be followed post curettage if histopathology does not confirm the clinical impression. When an intrauterine pregnancy has been evacuated, hCG levels should drop by at least 15 percent the day after evacuation. [9]

Tubal Ectopic pregnancy: Well over 90% of all ectopics are within the fallopian tube. The most common location in the tube is the ampulla (70%), with 15% in the isthmus and 15% in the fimbria. [10]

Cervical Ectopic pregnancy: These pregnancies account for 1 – 2% of all ectopic pregnancies. Because of their proximity to the uterine artery significant bleeding can result either spontaneously or as a consequence of surgical removal.

Ovarian Ectopic pregnancy: About 1% of all ectopics are located within the ovary. To be a true Ovarian Ectopic the following four criteria must be met: 1.) The gestational sac is located in the region of the ovary; 2.) The ectopic pregnancy is attached to the uterus by the ovarian ligament; 3.) Ovarian tissue in the wall of the gestational sac is proved histologically; and 4.) The tube on the involved side is intact. Ovarian ectopic pregnancies are not associated with conventional risk factors for ectopic pregnancy. [11]

Cornual Ectopic pregnancy and Angular Ectopic pregnancy: Pregnancies in these locations can lead to uterine rupture with significant blood loss. Casual ultrasound can often mistake these pregnancies for normal intra-uterine pregnancies.

Abdominal Ectopic pregnancy: These pregnancies occur within the abdomen and, hence, can expand significantly without extrinsic compression. Therefore, abdominal pregnancies can go undetected until an advanced age and often result in catastrophic hemorrhage and maternal mortality rates of up to 20%. [12,13]

Management—

If left unchecked an ectopic pregnancy will either rupture, abort or spontaneously resolve. Because of the potentially catastrophic implications of rupture benign neglect is not an option for women suspected of having ectopic pregnancy.

Ectopic pregnancy can be medically or surgically managed. The level of hCG, size of the lesion and presence of fetal heart tones in the adnexae are used to choose an appropriate option. Patients in whom surgical management is required include those with hemodynamic instability, suspected ectopic rupture, lack of proximity to or inability to reach the hospital in a timely manner and suspected lack of compliance with care plan. Women who fail medical management will also need surgical therapy.

Specific exclusion criteria include:

- a. hCG greater than 5,000 mIU / ml [14]
- b. presence of fetal cardiac activity [15]
- c. mass greater than 3.5 cm [16,17]
- d. elevated free fluid

Medical Management—

Medical treatment with either methotrexate or luovorin is acceptable. Treatment with methotrexate was first reported in the 1980's. About one third of women are candidates for methotrexate management of ectopic pregnancy. [18]

Of women undergoing medical management, about 90% are successfully managed. [19]

Methotrexate is a folic acid antagonist and is particularly effective against trophoblast and fetal cells. The dose of MTX used to treat ectopic pregnancy is almost 1 / 10th the dose when used in chemotherapy and, therefore, most of the unpleasant side effects are not experienced when used for ectopic pregnancy.

At Desert Women's Care we use a single dose treatment strategy for medical management of ectopic pregnancy. We use a single, 50 mg/m² in a single intra-muscular dose. Body surface area is calculated as follows: BSA = square root ((cm X kg)/3600). [20]

With Day 1 being the day of injection, quantitative hCG is again drawn on Day 7. If Day 7 hCG has not declined by at least 25% a second dose of methotrexate is administered. If the hCG levels increase failure of medical management is diagnose treatment failure. If hCG levels decrease they are drawn on a weekly basis until a negative result returns.

Studies show no benefit from single or serial ultrasound examinations during methotrexate treatment. [21]

Paradoxical pain can result from methotrexate injection and persist up to a week. This can often be confused with impending tubal rupture and lead to unnecessary surgical intervention. We prescribe narcotic analgesics because motrin and other non-steroidal anti-inflammatory drugs can lead to adverse reactions in combination with methotrexate.

Surgical Management—

Surgical treatment of tubal ectopic pregnancies include removal of the tube, removal of the affected segment of tube (with conservation of fimbria and proximal tube for later re-anastomosis) or linear salpingotomy with enucleation of the ectopic. Surgery can be performed open or laparoscopically based on the skill of the surgeon and the presentation of the patient.

At Desert Women's Care we define the patient's expectations preoperatively and act accordingly. In a woman with ectopic pregnancy after failed sterilization removal of both tubes is recommended. Oppositely, in women trying to conceive normally, linear salpingotomy and enucleation of ectopic is recommended. In this procedure a linear incision with needle-point electro-cautery is created on the anti-mesenteric border of the tube. The suction-irrigation device is insinuated into the defect and hydro-dissection is used to separate the ectopic from the wall of the tube. Bleeding is assessed and the tube closed as necessary. Both salpingectomy and salpingotomy are performed with the laparoscope and are considered out-patient procedures. If there was significant bleeding related to ectopic rupture replacement with Intra Venous fluids, blood and blood products may all be necessary prior to discharge.

Recurrence—

In women desiring to conceive after a previous ectopic pregnancy there is a likelihood of recurrence. Chance of recurrence is dependent on method of treatment. Women who either have salpingectomy (with the contralateral tube intact) or methotrexate therapy have an 8% recurrence rate for ectopic gestation. [22]

The similarity confirms the concept that pre-existing tubal disease, often related to chlamydial infection, predisposes to ectopic.

With linear salpingotomy, the incidence of recurrent ectopic pregnancy is approximately 15 percent [23] but recurrence risk rises to 30 percent following two ectopic pregnancies. [24]

Blood Type and Antibodies

Women who are Rh negative and antibody negative must receive Rhogam to minimize the chance of Sensitization and potential compromise to future pregnancies. At Desert Women's Care we administer one ampule of Rhogam in Rh negative, un-sensitized women after surgery for ectopic pregnancy.

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