Diagnosis of Acute Pelvic Pain

Martin Quan, MD
Los Angeles, California

The diagnosis of acute pelvic pain in the woman of reproductive age represents a major clinical challenge. In approaching such a patient, the clinician must differentiate between pregnancy-related causes, gynecologic disorders, and nonreproductive tract causes. A careful history and physical examination, along with selective and knowledgeable use of diagnostic tests and procedures, are essential to the diagnostic process. Diagnostic laparoscopy represents the reference standard for diagnosis of many of its possible causes and can obviate the need for exploratory laparotomy. Once competing diagnoses have been adequately excluded, an empiric trial of antibiotic therapy for acute pelvic inflammatory disease, coupled with close clinical follow-up, should be considered in patients with acute pelvic pain found to have cervical motion tenderness and bilateral adnexal tenderness on examination.

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For the primary care physician providing services to women of reproductive age, the problem of acute pelvic pain represents a major diagnostic challenge. Numerous studies have shown the unreliability of a clinical diagnosis that is based solely on a patient's medical history and physical findings.[1–3] Much of the morbidity and mortality associated with acute pelvic pain can be attributed to misdiagnosis and delayed physician intervention.[3,4]

During the past decade, advances in pregnancy testing, pelvic ultrasound, and diagnostic laparoscopy have greatly enhanced the clinician's ability to make an earlier, more accurate diagnosis. This paper focuses on the clinical aspects of acute pelvic pain with a primary emphasis on the diagnosis of its reproductive tract causes.

Differential Diagnosis of Acute Pelvic Pain

The differential diagnosis of the patient with acute pelvic pain can be conveniently divided into three major categories: pregnancy-related causes, such as ectopic pregnancy and spontaneous abortion; gynecologic disorders, such as acute pelvic inflammatory disease (PID), endometriosis, and complications of ovarian cysts; and nonreproductive tract disorders, such as acute appendicitis and urinary tract infection (Table 1).

Numerous studies attest to the diagnostic challenge posed by the female patient presenting with acute pelvic pain. Jacobson and Westrom[1] examined by laparoscopy 814 women believed to have acute PID and were able to confirm the clinical diagnosis in only 65% of cases. A normal pelvis was seen in 23% of patients, and in 12%, another disorder was found. Conditions misdiagnosed as acute PID included ectopic pregnancy, endometriosis, acute appendicitis, and complications arising from ovarian cyst. Schwartz and DiPietro[2] reported on the clinical outcomes of 73 women presenting with the classic triad of ectopic pregnancy (namely, acute pelvic pain, abnormal uterine bleeding, and an adnexal mass) and found a tubal gestation in only 14% of patients; other more common diagnoses included pelvic pain of undetermined cause, ovarian cyst, and acute PID. Finally, Brenner and associates[3] reviewed the clinical histories of 300 consecutive patients with ectopic pregnancies at their institution. They found that one half of them had been seen and sent home at least once before a diagnosis was made at the time of laparotomy. Moreover, they discovered that 11% had been seen twice and 5% had been seen and sent home three times before the correct diagnosis was made.

History and Physical Examination

Obtaining a comprehensive medical history is the starting point in the evaluation of acute pelvic pain and can be

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From the Division of Family Medicine, University of California, Los Angeles. Requests for reprints should be addressed to Martin Quan, MD, UCLA Family Health Center, 220 UCLA Medical Plaza, Room #220, Los Angeles, CA 90024-1683.

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Table 1. Differential Diagnosis of Acute Pelvic Pain

- Pregnancy-related
  - Ectopic pregnancy
  - Abortion
    - Septic
    - Threatened
    - Incomplete
  - Intrauterine pregnancy with corpus luteum bleeding
- Gynecologic
  - Acute pelvic inflammatory disease
  - Endometriosis
  - Ovarian cyst
    - Hemorrhage
    - Rupture
  - Adnexal torsion
  - Mittelschmerz
  - Uterine leiomyoma
    - Degeneration
    - Torsion
  - Primary dysmenorrhea
  - Tumor
- Nonreproductive tract causes
  - Gastrointestinal
    - Acute appendicitis
    - Inflammatory bowel disease
    - Mesenteric adenitis
    - Irritable bowel syndrome
    - Diverticulitis
  - Urinary tract
    - Urinary tract infection
    - Renal calculus
- No evident organic abnormality

Table 2. Historical Data of Value in Evaluating Acute Pelvic Pain

- Age
- Obstetrical history
- Menstrual history
- Characteristics of pain
  - Onset, duration
  - Palliative/aggravating factors
- Associated symptoms
  - Urinary symptoms
  - Gastrointestinal symptoms
  - Fever
  - Abnormal bleeding
  - Vaginal discharge
- Contraceptive history
- Surgical history
- Gynecologic history
  - Acute pelvic inflammatory disease
  - Ectopic pregnancy
  - Sexually transmitted diseases
- Social history
  - Marital status
  - Number of sexual partners
  - Current sexual activity including type

the source of important diagnostic clues (Table 2). Historical items considered risk factors for acute PID include age between 15 and 25 years, use of an intrauterine contraceptive device, a male sexual partner with symptoms of urethritis, a prior history of acute PID, and a past history of gonococcal infection.[4,5] Similarly, a history of delayed menstruation or prior ectopic gestation suggests the possibility of an ectopic pregnancy.

The patient's method of contraception can also be of diagnostic value. A woman who has been sexually abstinent in the months preceding the onset of pain would be unlikely to have a pregnancy-related etiology. The risk of acute PID may be reduced by approximately 50% in patients taking oral contraceptives or using a barrier method of contraception.[6,7] Women reliably using combined oral contraceptives should not ovulate and thus are at decreased risk for an ectopic pregnancy or the complications of a functional ovarian cyst.[8,9] Although the presence of an intrauterine contraceptive device (IUD) is a well-established risk factor for acute PID,[7] it does not increase the absolute risk for developing an ectopic pregnancy. An IUD, however, is more effective at preventing intrauterine as opposed to extrauterine implantation, and thus a pregnancy that occurs accidentally with an IUD in place has an estimated 10-fold increased risk of being ectopic. Similarly, an accidental pregnancy that occurs in a woman who has undergone tubal ligation has a 30-fold increased risk (a one in six chance) of being ectopic.[8]

After the history, a careful physical examination should be performed. This examination should include evaluation for the presence of fever, orthostatic changes in blood pressure and heart rate, abdominal and pelvic tenderness and peritoneal signs, vaginal discharge, cervical erythema and discharge, cervical and uterine motion tenderness, uterine size, shape, and consistency, adnexal masses and tenderness, and nodularity of the uterosacral ligament.

Although the history and physical examination may suggest the diagnosis, they generally lack adequate sensitivity, specificity, or both. For example, not only can abnormal uterine bleeding, part of the classic triad of ectopic pregnancy, be absent in 50% of patients with tubal pregnancies,[10,11] but it can be present in 36% of patients with acute PID[1] and 11% of patients with acute appendicitis.[12] Cervical motion tenderness, the sine qua non of acute PID, is a sensitive sign of this disorder and can be elicited in up to 97% of cases[13]; however, it lacks specificity as it can also be found in 43% of ectopic pregnancies[11] and 28% of patients with acute appendi-

citis.[12] Finally, the presence of an adnexal mass, the hallmark of an ectopic gestation, can be absent in 50% of patients,[3] present in 69% to 98% of patients with adnexal torsion,[14,15] and present in 25% to 49% of patients with acute PID.[1,13]

It is evident that the laboratory must assume an important role in the evaluation of acute pelvic pain.

Laboratory Tests

Complete Blood Count

A complete blood count is frequently ordered in the evaluation of acute pelvic pain, but it lacks sensitivity and specificity. The hematocrit is low, or less than 30, in 28% of patients with ectopic pregnancy, but normal, or greater than 35, in 38%.[3] The finding of a leukocytosis would suggest an inflammatory process. A normal white blood count, however, can be demonstrated in 56% of patients with acute PID[13] and 37% of patients with acute appendicitis.[16] Conversely, an elevated white blood count has been reported in up to 15% of patients with ectopic pregnancy[3] and 63% of patients with a bleeding corpus luteum.[17]

Erythrocyte Sedimentation Rate

The erythrocyte sedimentation rate (ESR) is another nonspecific sign of inflammation. Although classically elevated in acute PID, it can be normal (less than 15 mm/h) in 25%.[1] In a series of 36 patients with acute appendicitis and 45 patients with acute PID, Bongard et al[12] reported the ESR to be of no value in differentiating these two disorders.

Urinalysis

The finding of pyuria on microscopic examination of the urinary sediment raises the possibility of a urinary tract infection. Pyuria can also arise, however, from inflammation contiguous to the ureter or bladder due to an inflamed appendix in a posterior (retrocecal or subcecal) position,[18] or from contamination of the urinary sediment by a purulent vaginal or cervical discharge.

Cervical Gram Stain

Although a cervical Gram stain for *Neisseria gonorrhoeae* is considered a poor screening test for gonococcal infection in the asymptomatic female patient, some investigators have found it to be of value in the setting of acute pelvic pain.[13,19] In such patients, a sensitivity for gonococcal infection of 68% and a specificity of 98% have been reported for the finding of gram-negative intracellular diplococci seen within three or more neutrophils on Gram stain. Although a positive result is considered supporting evidence for the diagnosis of acute gonococcal PID, the diagnostic accuracy of this finding will vary with the skill and experience of the microscopist.

A more recent and valuable application of the cervical Gram stain may be in confirming the presence of mucopurulent cervicitis. The finding of 10 or more polymorphonuclear leukocytes per microscopic field (at a magnification of 1000) in a Gram-stained endocervical smear is diagnostic of this clinical entity[20] and is considered by some investigators to substantiate the clinical diagnosis of acute PID.[21,22]

Nonculture Tests for Neisseria gonorrhoeae *and* Chlamydia trachomatis

Laboratory confirmation of endocervical infection with gonorrhea or *Chlamydia trachomatis* is regarded as supporting evidence for the diagnosis of acute PID. Although cultures remain the reference standard for diagnosis of both of these pathogens, nonculture methods have been developed and are now available. These methods offer several advantages including a more rapid turnaround time and wider clinical availability.

Nonculture tests for the laboratory detection of *N gonorrhoeae* include the enzyme immunoassay (EIA) and the DNA probe test. The EIA test for gonorrhea uses polyclonal rabbit antibodies to bind to gonococcal antigens in urogenital specimens and then adds peroxidase-conjugated anti-rabbit immunoglobulin and a peroxidase substrate to generate a color signal that is assessed with a photometer. Studies evaluating its performance in female populations with intermediate (7% to 10%) and high (12% to 28%) prevalence rates for gonorrhea have reported sensitivities ranging from 74% to 100% and specificities of 86% to 100%.[23] Lieberman and Wheelock[23] investigated its use in a female population with a low (3.6%) prevalence of infection and found a sensitivity of 92% and a specificity of 97%. A DNA probe test that binds with gonococcal ribosomal RNA is now commercially available and in two recent studies demonstrated a sensitivity of 86% and a specificity of 99% to 100% in women with a high disease prevalence.[24,25]

Nonculture systems for detecting chlamydia include the direct-smear immunofluorescent antibody (DFA) test, the enzyme immunoassay (EIA), and a DNA probe test. The DFA and EIA are both antigen-detection tests; the former uses fluorescein-tagged, species-specific monoclonal antibodies to *C trachomatis* to identify ele-

mentary bodies in infected secretions, whereas the latter is based on immunochemical detection of solubilized chlamydial antigens. When studied in female populations with intermediate and high infection rates, the DFA and EIA tests have been shown to have sensitivities ranging from 61% to 99% and 60% to 98%, respectively, and specificities of 89% to 99% and 86% to 98%, respectively.[21] In studies evaluating their use in asymptomatic women, a sensitivity and specificity of 81% to 96% and 98% to 99%, respectively, have been reported for the DFA test,[26,27] and 78% to 82% and 97% to 98%, respectively, for the EIA.[26,28] Clinical use of a commercially available DNA probe for *C trachomatis* was recently studied by Iwen et al,[29] and a sensitivity of 93% and a specificity of 98% were found in women with an intermediate disease prevalence.

Examination of the Male Partner

Examination of the male partner for the presence of urethritis can be of value in corroborating the diagnosis of acute PID. Since more than one half of men with gonococcal urethritis[30] and one third of men with chlamydial urethritis[31] may be asymptomatic, a urethral Gram stain and studies for detecting gonorrhea and chlamydia should be obtained even in the absence of symptoms. In a study by Wasserheit et al,[32] confirmatory evidence for the diagnosis of acute PID was present on evaluation of the male partner in over 50% of the patients with acute PID.

Pregnancy Tests

Pregnancy tests are of great potential value in the evaluation of acute pelvic pain since they enable the clinician to identify those patients with pregnancy-related causes. In most patients with acute pelvic pain, the question is really not whether a pregnancy test should be ordered but, rather, whether there is any reason why it should not. To use the available tests effectively, however, it is important to understand the capabilities and limitations of the test ordered.

Urine pregnancy tests

Traditional urine pregnancy tests, including the 2-minute latex particle agglutination-inhibition slide tests and the standard hemagglutination-inhibition tube tests, were generally believed not to be of value in the diagnostic evaluation of acute pelvic pain because of their lack of sensitivity.[33] Ultrasensitive tube tests became available during the past decade that were capable of detecting human chorionic gonadotropin (hCG) levels of 150 to 250 mIU/mL. These tests have been found to be positive in 80% to 85% of ectopic pregnancies.[34] Urine monoclonal antibody, enzyme-linked immunosorbent tests represent the most recent advancement in urine pregnancy testing and can detect hCG levels as low as 25 mIU/mL. Although Barnes et al[34] reported a false-negative rate of 10% in their series of 108 patients with tubal gestations, more recent studies have demonstrated that these tests are positive in up to 96% to 100% of ectopic pregnancies.[35–37]

Serum Pregnancy Tests

A major advancement in pregnancy testing has been the development of serological assays for hCG. Although generally regarded as less convenient and more costly, these tests afford a greater diagnostic accuracy than urine tests and are unaffected by the hydration status of the patient.[34] Serum tests are available as both qualitative and quantitative tests.

Qualitative serum pregnancy tests include radioreceptor assays (RRA) as well as serum monoclonal antibody tests and qualitative radioimmunoassays (RIA). The RRA was the first of these tests to be developed and was positive at hCG levels of 200 mIU/mL. In a study by Berry et al,[38] the RRA detected 94% of patients with ectopic pregnancies. The monoclonal antibody tests and the qualitative radioimmunoassays possess even a greater sensitivity and become positive at hCG levels of 10 to 25 mIU/mL. In a study reported by Olson et al,[39] the qualitative serum β-hCG assay detected 71 of 74 patients (96%) with tubal gestations.

The quantitative radioimmunoassay for the β-subunit of hCG is the most sensitive pregnancy test available, detecting hCG levels as low as 5 mIU/mL and becoming positive 7 to 9 days after conception. Studies have demonstrated a sensitivity for ectopic pregnancy ranging from 98.8% to 100%.[2,40] Thus, a negative test virtually excludes the diagnosis of ectopic pregnancy.

None of the pregnancy tests are specific for ectopic pregnancy and can be positive in any condition associated with hCG production. In addition to ectopic pregnancy, such conditions would include a normal intrauterine pregnancy, a threatened abortion, gestational trophoblastic disease, and recent spontaneous or voluntary abortion. In a study of first trimester pregnancies, Steier et al[41] found that hCG was still detectable 9 to 35 days (median 19 days) after a spontaneous abortion and 16 to 60 days (median 30 days) after an induced abortion. Thus, a positive pregnancy test still requires localization of the tissue responsible for the hCG production.

Serum Progesterone Levels

In the patient with acute pelvic pain associated with pregnancy, several investigators have found measurement of a serum progesterone level to be helpful in the differentiation of normal from abnormal pregnancy (ie, ectopic pregnancy, inevitable abortion). Although the optimal discriminatory level has yet to be determined, investigators have generally found serum levels above 20 to 25 ng/mL (64 to 80 nmol/L) to be most consistent with a normal pregnancy, and levels below 15 to 20 ng/mL (48 to 64 nmol/L) to be more indicative of an abnormal pregnancy.[42–45] In their series that included 67 patients with ectopic pregnancies, 128 patients with nonviable intrauterine pregnancies, and 387 patients with normal pregnancies evaluated in an emergency department, Stovall and associates[44] found progesterone levels below 15 ng/mL in 81% of ectopic gestations, 93% of nonviable intrauterine pregnancies, and in less than 11% of normal pregnancies. Levels exceeding 25 ng/mL were present in 61% of normal pregnancies, 4% of nonviable pregnancies, and fewer than 2% of ectopic pregnancies.

Effective clinical use of serum progesterone levels requires that several caveats be kept in mind. First of all, progesterone values can vary with the assay used, and thus each laboratory must determine its own discriminatory level on the basis of the methodology employed.[46] Second, progesterone levels can be influenced by agents used for ovulation induction and thus are of uncertain value in patients with a recent history of ovulation induction.[45] Finally, serum progesterone levels are generally not diagnostic and serve primarily to assess the likelihood of a pathologic pregnancy being present.[47]

Culdocentesis

Culdocentesis is a relatively simple, rapidly performed diagnostic test that detects and samples fluid present in the cul-de-sac of the pelvis. Hemoperitoneum, diagnosed when nonclotting blood is aspirated, confirms the presence of intraperitoneal bleeding and is found in 70% to 97% of patients with ectopic pregnancies.[48] If free-flowing clear or blood-tinged fluid is demonstrated, the diagnosis of a ruptured ovarian cyst would be corroborated. Aspiration of purulent fluid is indicative of an inflammatory process, such as acute PID, acute appendicitis, or a ruptured diverticular abscess. Culdocentesis is considered negative if a few milliliters of straw-colored peritoneal fluid is obtained and nondiagnostic if no fluid or clotting blood is found. Culdocentesis is contraindicated in a patient with a mass in the cul-de-sac.[49]

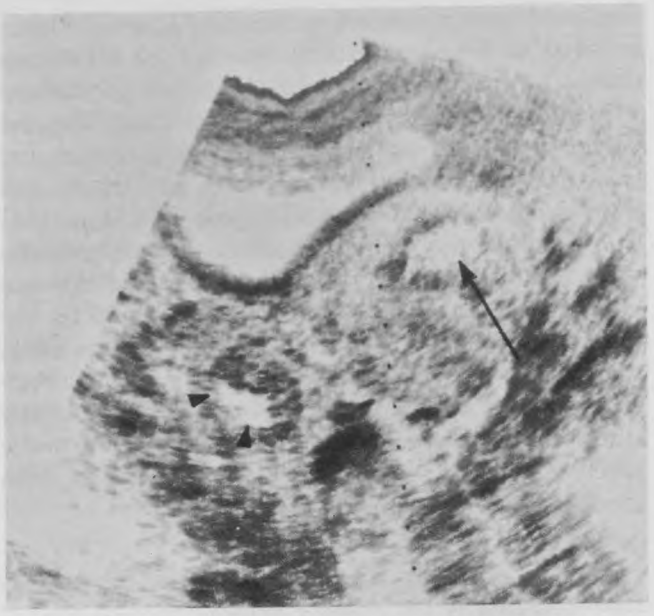

Figure 1. A transverse transabdominal ultrasound scan demonstrates an extrauterine gestational sac in the right adnexa (arrowheads) that confirms the diagnosis of ectopic pregnancy. In addition, a pseudogestational sac can be identified within the uterus (arrow).

Pelvic Ultrasonography

Pelvic ultrasonography has proved invaluable in the diagnosis of acute pelvic pain associated with pregnancy. The finding of an extrauterine gestational sac confirms the diagnosis of ectopic pregnancy but is seen on transabdominal sonography in only 15% of cases (Figure 1).[50] Ultrasonography is often of greater value in excluding the diagnosis of an ectopic pregnancy by its demonstration of an intrauterine gestation (Figure 2) since these conditions rarely coexist; estimates of the incidence of heterotopic pregnancy range from 1 in 4000 to 1 in 30,000 pregnancies.[51,52] Although the finding of an intrauterine gestational sac on a sonogram is typically accepted as being diagnostic of an intrauterine pregnancy, it has been shown that this sonographic appearance can be simulated by the appearance of a collection of blood within hyperplastic endometrium (the so-called pseudogestational sac) seen in 8% to 20% of ectopic pregnancies (Figure 1).[53] In light of this, it is recommended that, in the setting of acute pelvic pain, the diagnosis of an intrauterine pregnancy not be definitively made until such time that a "double decidual sac" sign (corresponding to the concentric decidua parietalis and decidua capsularis), a yolk sac, fetal heart activity, or a fetal pole can be identified within the intrauterine sac (Figures 2 and 3).[54–56]

In the pregnant patient with a sonogram showing a

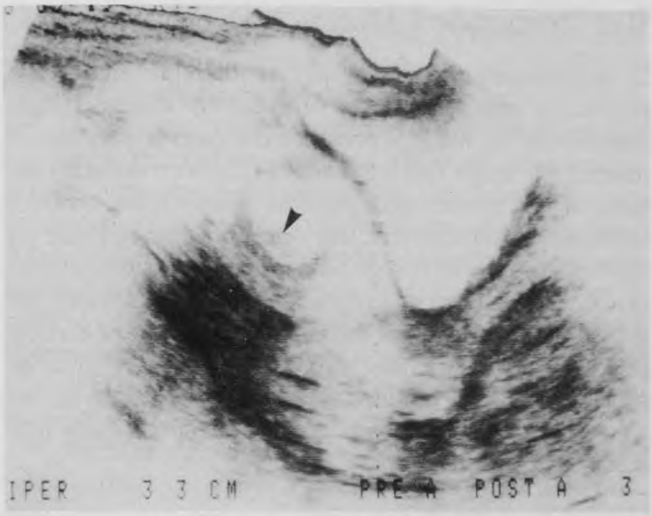

Figure 2. A transverse transabdominal ultrasound scan demonstrates an intrauterine gestational sac. On closer inspection, a fetal pole can be identified within the sac (arrowhead).

saclike structure within the uterus but lacking definitive evidence of an intrauterine pregnancy, correlation of the sac size with the quantitative hCG level can be of clinical value.[57–59] Nyberg et al[57] have demonstrated a strong correlation between gestational sac size and hCG determinations up to the 8th menstrual week in normal singleton pregnancies, and use of this relationship can assist in the differentiation of normal from abnormal pregnancy (ie, ectopic pregnancy and inevitable abortion). A

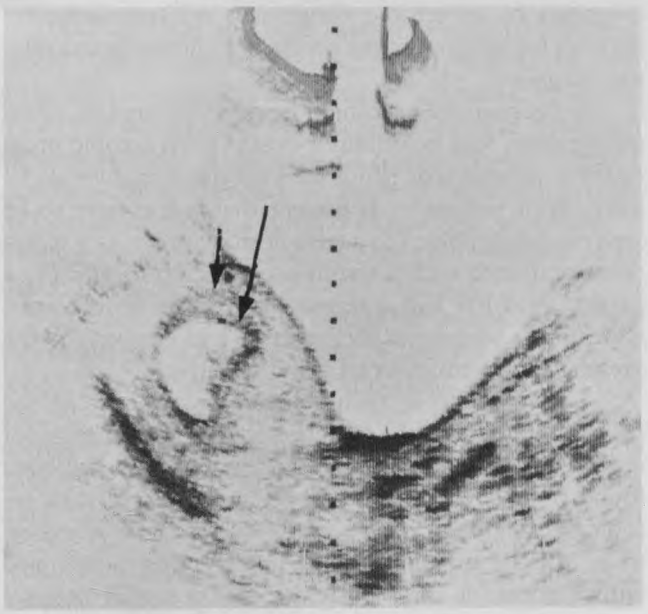

Figure 3. Pelvic ultrasonogram demonstrating the "double sac sign" indicative of an intrauterine gestation. The concentric echogenic rims correspond to the decidua capsularis (long arrow) and the decidua parietalis (short arrow).

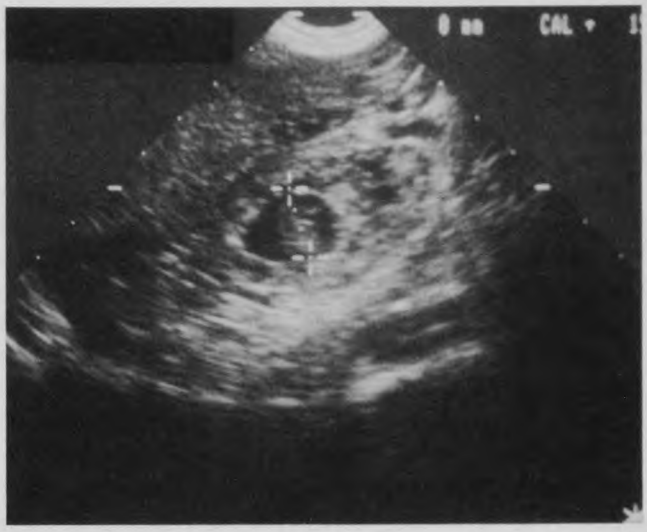

Figure 4. Transvaginal sonogram demonstrating an extrauterine gestational sac indicative of an ectopic pregnancy.

disproportionately low hCG level relative to gestational sac size would suggest the presence of an abnormal pregnancy, whereas appropriate correlation between the two measurements would be indicative of a normally developing intrauterine pregnancy and reduce the likelihood of a pseudogestational sac.[58]

Pelvic ultrasonography has traditionally been performed using a transabdominal approach. A relatively recent innovation in pelvic ultrasonography has been the development of transvaginal sonography. This technique is capable of providing improved picture resolution of pelvic structures by its use of a higher frequency, intravaginal transducer probe that obviates the need for a full bladder. A major advantage of the transvaginal technique is its ability to identify intrauterine pregnancies at an earlier stage and its greater diagnostic accuracy for ectopic pregnancy.[53,60] For example, on transabdominal sonography, the appearances of the intrauterine gestational sac and the fetal pole (with cardiac activity) are important landmarks that are usually imaged approximately 5 and 6½ to 7 weeks,[57] respectively, from the start of the last menstrual period. On transvaginal sonography, these same landmarks are typically seen 4⅘ and 5½ to 6 weeks, respectively, from the last menses.[53,61] In addition, an extrauterine gestational sac (Figure 4) can be identified on transvaginal sonography in as many as 65% of patients with ectopic pregnancies.[58]

Pelvic ultrasonography has not proved as valuable in the diagnosis of acute pelvic pain unassociated with pregnancy because of its lack of adequate sensitivity and specificity.[62] Sonography has a limited role in the evaluation of such patients and is best used on a selective basis. For the patient in whom pain or uncooperativeness with

the examination precludes an adequate pelvic examination, sonography may be of value in suggesting a diagnosis. In addition, an adjunctive diagnostic role has been proposed for patients with suspected acute PID, torsion of the adnexa, or acute appendicitis. For example, the finding of a tubo-ovarian abscess on sonography corroborates the diagnosis of acute PID.[4] Similarly, a unilaterally enlarged, hypoechoic ovary is indicative of torsion, particularly if engorged vessels (appearing as small, multiple cystic structures of uniform size) can be identified at its periphery.[63] Finally, in patients with acute, nonperforating appendicitis, the finding of an inflamed appendix (a tubular structure with an echo-poor center, a blind tip, and a root pointing to or contiguous to the cecum, which does not exceed 6 mm at its greatest diameter) has been found by some investigators to have a sensitivity as high as 80% and a specificity of 95%.[64]

Examination of Endometrial Tissue

Microscopic examination of the intrauterine contents is a diagnostic option for the patient with acute pelvic pain and a positive pregnancy test who desires termination of an undesired pregnancy or in whom it can be demonstrated that the pregnancy is abnormal and nonviable. The presence of chorionic villi in the material obtained on suction curettage would generally exclude the diagnosis of ectopic pregnancy, whereas the absence of such villi is strong presumptive evidence of ectopic pregnancy.

Diagnostic Laparoscopy

Diagnostic laparoscopy is an invaluable technique that provides direct visual access to structures within the peritoneal cavity. Although some investigators have advocated its routine use in all patients with acute pelvic pain,[1,65,66] logistical and economic considerations have limited its use. It is considered a safe procedure when performed by an experienced laparoscopist, but it is not without risk. There are an estimated 5 deaths per every 100,000 laparoscopies performed and 5 major morbid events per 1000 performed[67]; possible morbid events include blood vessel injury, penetration of a hollow viscus, bleeding, and gas embolism. Nevertheless, diagnostic laparoscopy is clearly indicated in the patient with acute pelvic pain in whom a diagnosis remains unclear despite a comprehensive evaluation, and the possibility of a surgical emergency, such as ectopic pregnancy or acute appendicitis, must be ruled out.

Recommended Diagnostic Approach

In approaching the female patient of reproductive age presenting with acute pelvic pain, the first differentiation that should be made is whether the pain is pregnancy-related. Although this has traditionally been done on the basis of the history and physical examination, modern management dictates that this determination be made on the basis of a serum pregnancy test or a sensitive monoclonal antibody urine pregnancy test. In addition, for those patients in whom the clinical suspicion of ectopic pregnancy is sufficiently high, culdocentesis should be considered as an adjunct to pregnancy testing in an attempt to more effectively exclude this potentially life-threatening disorder.

Acute Pelvic Pain Associated with Pregnancy

In the patient with acute pelvic pain associated with pregnancy, the next step is localization of the tissue responsible for the hCG production. Culdocentesis is a consideration (particularly if pelvic ultrasonography is not readily available) with the finding of hemoperitoneum strongly suggestive of the diagnosis of ectopic pregnancy and indicating the need for immediate laparoscopy or laparotomy. If hemoperitoneum is not found, pelvic ultrasonography should then be performed. Identification of an extrauterine gestation sac confirms the diagnosis of an ectopic pregnancy, whereas definitive findings for an intrauterine pregnancy effectively excludes this diagnosis.

If a gestational sac cannot be demonstrated on ultrasonography, four possibilities exist: (1) an ectopic pregnancy is present that is not seen on sonography; (2) an intrauterine pregnancy is present that is too early to be seen on sonography; (3) a false-positive pregnancy test, a rare occurrence with a serum pregnancy test; and (4) a patient who has had a recent induced or spontaneous abortion in whom insufficient time had elapsed for the pregnancy test to revert to being negative.

The first step in such a patient is to examine the pelvic sonogram for the presence of high-risk findings for ectopic pregnancy. A noncystic adnexal mass has been found by several investigators to be associated with ectopic pregnancy in 83% to 85% of cases.[68,69] Furthermore, the combination of fluid in the cul-de-sac coupled with a noncystic mass possesses even a higher positive predictive value, being associated with an ectopic pregnancy in 94% of cases.[68] In such patients, diagnostic laparoscopy has been recommended to rule out this diagnosis.

If no such findings are present, three management options should then be considered:

1. *Expectant management with close clinical follow-up.* This option would be appropriate for clinically stable patients with mild symptoms in whom the diagnosis of ectopic pregnancy remains a clinical uncertainty. Patients in whom this option is chosen demand close clinical follow-up with serial evaluations and instructions to seek medical attention immediately if symptoms worsen. In addition to serial pelvic and abdominal examinations, determination of the serum progesterone level, quantitation of the hCG titer, and serial pelvic ultrasound examinations may be of value in such patients.

The concept of the "hCG discriminatory zone," which correlates the hCG titer with sonographic findings, has great potential value in patients in whom expectant management is chosen. This concept was first proposed in 1981 by Kadar et al,[56] who postulated that there was an absolute hCG titer above which an intrauterine gestation sac should normally be seen. This concept was brought to fruition by Romero and associates[70] in 1985 when they found that 98% of normal intrauterine pregnancies with titers exceeding 6500 mIU/mL had a gestational sac demonstrable on transabdominal sonography. Furthermore, this study also revealed that among patients with hCG titers exceeding 6500 mIU/mL in whom no sac could be identified, 86% had ectopic pregnancies. Subsequent studies have suggested that the hCG discriminatory level may be actually as low as 3600 mIU/mL with transabdominal sonography[71] and as low as 1000 or 1600 mIU/mL with transvaginal sonography.[61,72] Since the hCG discriminatory zone for any given ultrasonography laboratory is a function of operator experience and sonographic technique and resolution capacity, proper application of this diagnostic concept demands that the clinician be aware of the discriminatory hCG zone at which a normal intrauterine pregnancy is routinely imaged at the ultrasonography laboratory to which he refers.[73]

For patients with hCG titers below the discriminatory zone, serial measurements of the hCG titer can be used to identify patients with abnormal, nonviable pregnancies. In viable pregnancies, serial hCG titers are expected to rise by 66% in 48 hours and by 114% in 3 days.[74,75] Although an abnormal change in hCG titers can be observed in 90% of ectopic pregnancies, it can also be seen in 12.5% of normal intrauterine pregnancies.[75] Since it is uncertain whether accurate prediction of the nonviability of a gestation is possible solely by analysis of early doubling time data, Cartwright and DiPietro[76] have recommended that operative intervention be considered only if the clinical situation deteriorates or if hCG levels plateau or fall. Ectopic pregnancy and inevitable abortion would be the major diagnostic considerations in such patients and can be differentiated by examination of the uterine contents or diagnostic laparoscopy.

2. *Examination of the endometrial tissue.* For pregnant patients desiring termination as well as those patients in whom it can be conclusively demonstrated that their pregnancy is abnormal and nonviable, performance of suction curettage with immediate histologic examination of the curettings is a diagnostic option. The finding of chorionic villi excludes the diagnosis of ectopic pregnancy, whereas the absence of such villi identifies a patient at high risk for ectopic pregnancy.

3. *Diagnostic laparoscopy.* This procedure is the most accurate and rapid way of establishing or excluding the diagnosis of ectopic pregnancy.

Acute Pelvic Pain Unassociated with Pregnancy

Acute PID is the leading diagnostic consideration in patients with acute pelvic pain unrelated to pregnancy. Although classically associated with bilateral pain, it can produce unilateral symptoms in 10% of cases.[13] Acute PID should be suspected in all patients with acute pelvic pain found to have cervical motion tenderness and bilateral adnexal tenderness. In light of the inaccuracy associated with its clinical diagnosis, however, many authorities have advised that a clinical diagnosis of acute PID be made only if a specified set of clinical criteria derived from laparoscopic studies are fulfilled.[22,77] Criteria required in the past included the presence of lower abdominal pain, cervical motion, and adnexal tenderness on examination, plus at least one of the following:

1. Fever exceeding 38°C
2. White blood count exceeding 10,500/mm^3
3. Purulent fluid obtained on culdocentesis
4. An inflammatory mass found on pelvic ultrasonography
5. Elevated erythrocyte sedimentation rate
6. Positive endocervical Gram stain for gonorrhea
7. Positive cervical culture or nonculture test for *C trachomatis*
8. More than 5 white blood cells per oil immersion field on five consecutive fields on Gram stain of the endocervical discharge.

Acute appendicitis is a potentially life-threatening disorder that demands consideration in all patients presenting with acute pelvic pain. Notorious for its protean manifestations, predictive factors for its diagnosis have

been identified by Alvarado[78] and include the presence of a leukocytosis, a history of a few hours of pain in the epigastrium or periumbilical area prior to migration of the pain to the right lower quadrant, a neutrophilia of more than 75%, slight temperature elevation exceeding 37.3°C, nausea and vomiting, anorexia, and direct rebound pain. Clinical skill and judgment remain the cornerstone of diagnosis for acute appendicitis (with a "negative" appendectomy rate of 15% to 20% considered appropriate),[12] although graded-compression ultrasonography may be of potential value in clinically ambiguous cases in which the need for surgery remains uncertain.

Torsion of the adnexa typically presents as unilateral pain but can produce bilateral pain in 25% of cases.[14] Although an infrequently encountered disorder, it nevertheless ranked 5th among 3772 gynecologic surgical emergencies reported by Hibbard.[79] The index of suspicion for this disorder is raised in patients with intense, progressive pain combined with a tense, tender, adnexal mass on examination, particularly if an antecedent history of repetitive, transitory pain is elicited. Pelvic sonography can be of value in confirming the diagnosis. An early laparoscopic diagnosis is important since surgical intervention before infarction may permit ovarian and adnexal preservation.

A ruptured or hemorrhagic corpus luteal cyst typically produces bilateral pain but can cause unilateral tenderness in 35% of cases.[17] The diagnosis of a ruptured ovarian cyst is corroborated by the finding of free-flowing clear or blood-tinged fluid on culdocentesis. In the patient in whom pregnancy has been excluded, the finding of hemoperitoneum on culdocentesis would be strongly suggestive of a hemorrhagic ovarian cyst.

Endometriosis is more commonly linked with chronic or recurrent pain but can be the cause of acute pelvic pain as well. Clinical clues suggestive of this diagnosis include a history of infertility, dysmenorrhea, and deep dyspareunia and the findings of fixed uterine retrodisplacement and tender uterosacral and cul-de-sac nodularity on pelvic examination. Although measurement of serum levels of CA 125 and pelvic ultrasonography may be of diagnostic value in selected patients with endometriosis (primarily those with more advanced disease), definitive diagnosis of this disorder generally requires the performance of laparoscopy.[80,81]

Despite these considerations, a significant subset of patients with acute pelvic pain will continue to have an unclear diagnosis. Such a group of patients would appear similar to a cohort of patients studied by Chaparro and associates in 1978.[65] In this study, diagnostic laparoscopy was performed in 229 patients with acute pelvic pain after first excluding those with obvious acute PID, a history of delayed menstruation, and a positive culdocentesis productive of blood or pus, as well as those with diffuse peritonitis. The most common final diagnoses in this group of patients were acute PID in 46%, a normal pelvis in 23%, a hemorrhagic follicular cyst in 14%, and an ectopic pregnancy in 11%. Since modern pregnancy testing would more effectively exclude ectopic pregnancy and since a hemorrhagic follicular cyst not actively bleeding is generally managed expectantly, management options in this remaining group of patients would include:

1. *Expectant management with close clinical follow-up.* These patients should be followed clinically until either the symptoms resolve or the diagnosis more clearly reveals itself clinically, or until laparoscopy is deemed necessary because of worsening or persistence of symptoms.

2. *Therapeutic trial of antibiotics for presumed acute PID with close clinical follow-up.* Recent Centers for Disease Control (CDC) guidelines[4] now recommend that treatment for PID be routinely instituted in patients who fulfill the minimum criteria for the diagnosis (ie, lower abdominal tenderness with cervical motion tenderness and bilateral adnexal tenderness) in the absence of competing diagnoses. In a comprehensive analysis of the literature on the diagnosis of PID, Kahn and colleagues[82] offered support for the CDC recommendation and endorsed the use of a lower clinical threshold for making a tentative diagnosis of mild PID and initiating an empiric trial of antibiotic therapy.

3. *Diagnostic laparoscopy.* Diagnostic laparoscopy warrants consideration in patients deemed at sufficient risk for having a surgical emergency, patients who fail a therapeutic trial of antibiotics for suspected acute PID, and patients with persistent or worsening symptoms.

Conclusions

Acute pelvic pain in women of reproductive age represents a major diagnostic challenge. In approaching such patients, the clinician must differentiate between pregnancy-related causes, gynecologic disorders, and nongynecologic conditions. A careful history and physical examination can be the source of important diagnostic clues. Although laboratory tests (particularly pregnancy testing, pelvic ultrasonography, and diagnostic laparoscopy) have proved of great value in the diagnostic process, optimal utilization of these tests demands that their capabilities and limitations be recognized and understood. Diagnostic laparoscopy represents the reference standard of diagnosis for many of the causes of acute pelvic pain, and its use often obviates the need for exploratory laparotomy. When competing diagnoses have been adequately excluded, an empiric trial of antibiotics

for a presumptive diagnosis of acute PID should be considered in patients with acute pelvic pain who have cervical motion tenderness and bilateral adnexal tenderness on examination.

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