

Pelvic Actinomycosis and Usage of Intrauterine Contraceptive Devices

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Pelvic inflammatory disease (PID) is one of the most commonly encountered serious infectious disease entities in gynecology. The past decade has witnessed many advances in our understanding of the pathogenesis of PID. It is now evident that such pelvic infections are largely polymicrobial in origin, with major involvement by anaerobic organisms.

Salpingo-oophoritis is a part of the spectrum of PID. Included among this group of infections are tubo-ovarian abscesses, traditionally referred to as either gonococcal or non-gonococcal in origin. Within the latter group of infections the importance of anaerobic organisms has also been elucidated. Of particular interest is the reported observation of an increased frequency of salpingo-oophoritis among users of intrauterine devices (IUDs). These reports have noted the specific occurrence of serious pelvic infections due to *Actinomyces* species, and this will be the topic of the infectious disease conference.

Our patient presented with a chronic illness characterized by lethargy, back pain, fever, and anemia; subsequently evaluation disclosed the presence of a large pelvic mass which was confirmed as a tubo-ovarian abscess at surgery. Histological evaluation demonstrated involvement by *Actinomyces* species. This patient's illness is discussed as a complication of chronic IUD usage with reference to specific management for this emerging problem.

CASE HISTORY

DR. JOHN KELLY (*Infectious Disease Fellow*): A 29-year-old woman, who had previously been in excellent health, was admitted to the medical service of Yale-New Haven Hospital for evaluation of back pain and anemia. She was a professional person who visited the Orient during the fall months, at which time she freely partook of native cuisine, but apparently did not become ill. In December she developed symmetrical polyarthritides of undetermined etiology, and responded to a two-week course of oral salicylates. In January, several months after her trip, she developed low back pain, which was more severe on the right side and which radiated down the right posterior thigh. A diagnosis of sciatica was entertained by her private physician and she was placed on a non-narcotic analgesic, with relief of symptoms.

In February she saw her gynecologist for evaluation of a vaginal discharge. A pelvic examination was normal, and an intrauterine device (IUD) was present in situ. However, hypochromic, microcytic anemia with a hematocrit of 26 percent was

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noted. Oral iron therapy was begun, and the vaginal discharge soon resolved upon application of a vaginal cream. In March, while in London, she became quite fatigued and her hematocrit was noted to be 23 percent. Stool examination for occult blood was negative, and sedimentation rate was elevated at 105 mm/hr (normal, < 15mm/hr). She returned to New Haven and was admitted to the medical service at Yale–New Haven Hospital. Her only complaints on admission were those of lethargy, moderate dyspnea on exertion, and continued low back pain. The patient was sexually active. She had been pregnant twice in the past, but with no live deliveries secondary to therapeutic abortions on both occasions. On exam she had a temperature of 101°F, angular cheilosis and a smooth tongue. She had a systolic flow murmur and no organomegaly. There was tenderness to the right of the lumbar spine and pain on straight leg raising to about 45 degrees. Her WBC count on admission was 21,000 cells/ul, the differential was shifted leftward, and the hematocrit was 19 percent. A reticulocyte count of 2 percent, a platelet count of 1,100,000 per ul, a mean corpuscular volume of 65, a sedimentation rate of 70 mm/hr, and a prothrombin time of 16.4 seconds (control 12 seconds) were noted. Liver function tests, including alkaline phosphatase, were mildly elevated but her bilirubin was normal at that time, as was her urinalysis. House officers who saw this patient went through a very extensive differential diagnosis including that of malignancy, collagen vascular disease, and the possibility of subacute bacterial endocarditis. The question of possible IUD perforation was not raised. An exhaustive work-up was begun. Dr. Aaron will review the X-rays with us. Is there any other data you would like to have?

DR. VINCENT T. ANDRIOLE (*Chief, Infectious Disease Section*): At the onset of her symptoms, four to six weeks after her trip, when she had polyarthritis, was there any history of rashes, and was there any objective evidence of arthritis?

DR. KELLY: She did have objective evidence of arthritis. There was swelling of most of her metacarpo-phalangeal and proximal interphalangeal joints, in addition to her knees and ankles, with some associated erythema and tenderness of motion. She did not have a rash and was afebrile.

DR. ANDRIOLE: She had no lymphadenopathy or blood loss noted?

DR. KELLY: Lymphadenopathy was not noted and there really had been no evidence of blood loss. She was seen by her private physician on three different occasions and the stool was reportedly negative for occult blood. An investigation into her menstrual history did not suggest menorrhagia. Indeed, her menses were generally scant, in terms of blood loss. So there was no obvious reason for this young woman's hematocrit to be low, and everyone's concern shifted towards a myeloproliferative problem or bone marrow failure.

A PHYSICIAN: She really didn't have a history of fever?

DR. KELLY: None was documented, although in retrospect she had intermittent sweats and perhaps even a moderate degree of weight loss. Hence, because of the concern over anemia, one of the first tests performed was a barium enema.

DR. JANICE AARON (*Department of Radiology*): This lumbo-sacral spine series was the first radiographic exam performed (Fig. 1). Pertinent findings include normal bones, no evidence of sacroileitis, and an IUD is in place. Her uterus is displaced to the left, which can be a normal finding. However, this patient has a soft tissue density in the right pelvis suggestive of a mass which is displacing the uterus.

A PHYSICIAN: Can you outline her uterus?

DR. AARON: Not exactly. We see the IUD and realize that it should be inside the uterine cavity. The second examination was the barium enema (Fig. 2). Again, one can see the IUD markedly displaced to the left, and a soft tissue density in the right



FIG. 1. On this lumbo-sacral spine film there is a right pelvic mass (M) displacing the uterus containing an IUD (open arrow) to the left.

side of the pelvis. The terminal ileum is normal. There is a large mass displacing the sigmoid colon. The mass slightly deforms the terminal ileum and the cecum (Fig. 3). The sigmoid view of the colon shows spiculations and tethering of the sigmoid colon, which are suggestive of an inflammatory process.

A PHYSICIAN: Is there any pathology intrinsic to the bowel wall?

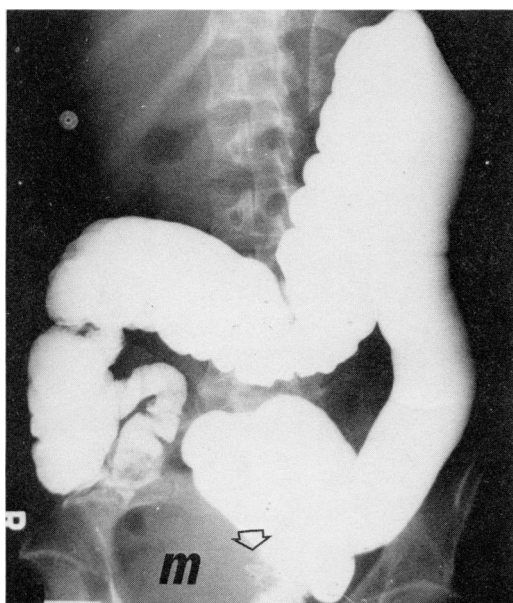


FIG. 2. A right pelvic mass (M) is displacing the barium-filled sigmoid colon and the uterus containing the IUD (open arrow).



FIG. 3. Spiculations and tethering of the barium-filled sigmoid colon (*open arrows*) suggest an inflammatory process related to the mass.

DR. AARON: No, the mass is extrinsic. The mucosa is intact and the angle formed by the mass with the bowel wall is obtuse. One definitely gets the impression that it is both an extrinsic and probably an inflammatory mass.

DR. KELLY: Does the mass appear to be circumferential in the rectosigmoid area?

DR. AARON: Yes, it does. When one views the lateral projection (Fig. 4), the barium-filled rectum should normally be near the sacrum. She has a large presacral space indicating a mass posterior to the rectum. In summary, we see a large mass in the right pelvis which extends posteriorly. Differential diagnoses at this point would include an ectopic pregnancy or tubo-ovarian infection (especially with an IUD in place), an adnexal tumor, or an infectious process arising in the appendix. Crohn's disease with a pelvic abscess would be unlikely with a normal terminal ileum.

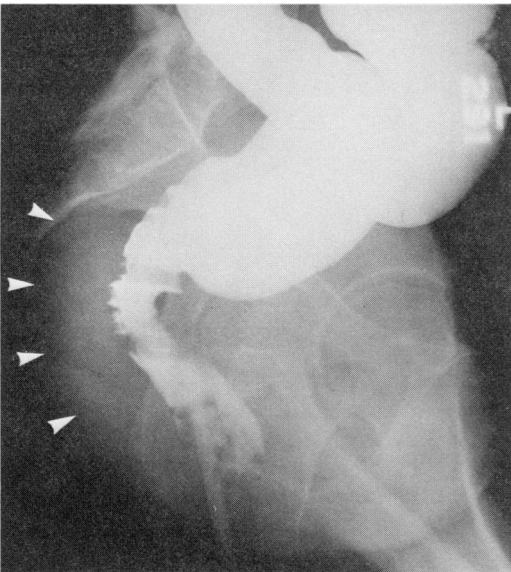


FIG. 4. A lateral view of the barium-filled rectum demonstrates a large presacral space (*arrows*) indicating mass posterior to the rectum.

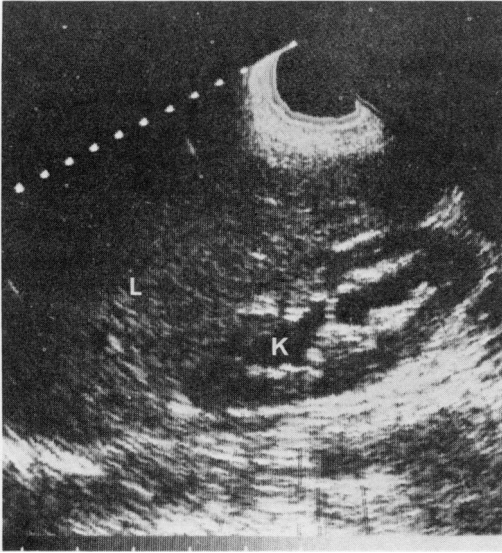


FIG. 5. Ultrasound examination of the right upper abdomen [liver (L), kidney (K)] shows centrally located large echo-free areas in the right kidney characteristic of a dilated collecting system.

DR. KELLY: Surprisingly, she had no gastrointestinal complaints. Her stools were well formed. A rectal exam was repeated on the day of the barium enema and a constricting band-like firmness was described 4 to 5 centimeters above the anal verge. The patient was then sent for an ultrasound examination.

DR. AARON: Normally on ultrasound (Fig. 5) the renal pelvic sinus appears white, with intense echoes. Seen on the ultrasound of this patient's right kidney are large, black holes (echo-free areas) in the center of the kidney. This is characteristic and diagnostic of an obstructed collecting system. This finding was confirmed by an excretory urogram (Fig. 6). On the transverse ultrasound sections (Fig. 7), looking

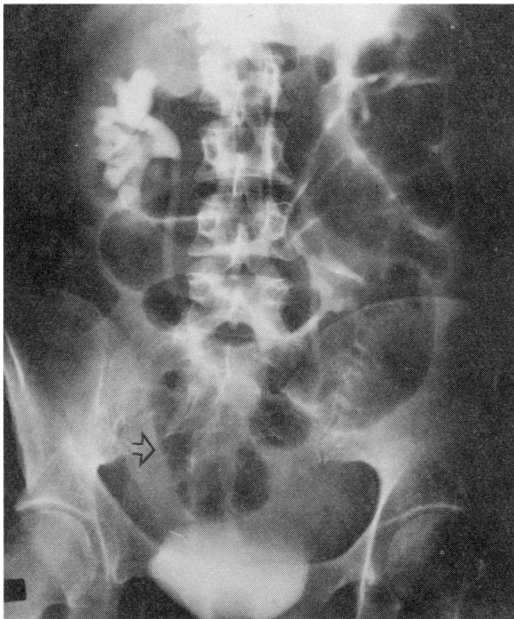


FIG. 6. The excretory urogram shows the right ureter partially obstructed in the pelvis (*open arrow shows point of compression*).

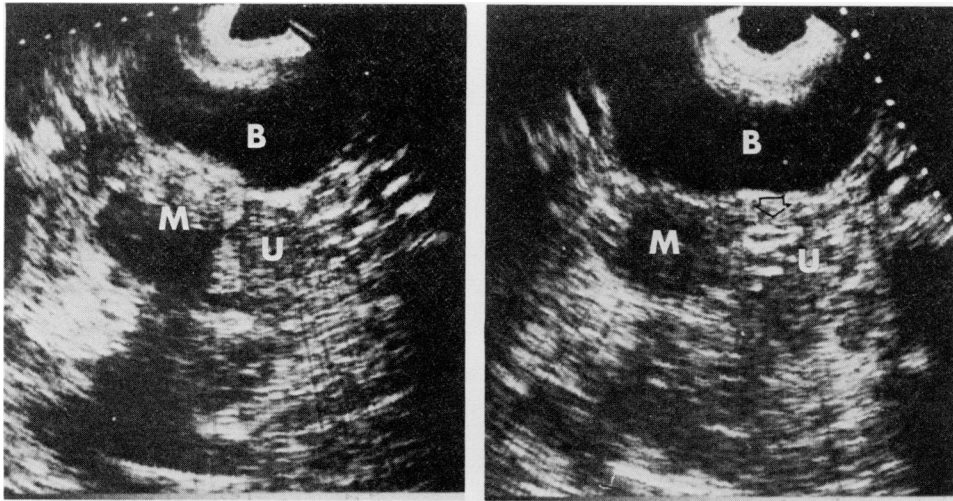


FIG. 7. Ultrasound of the pelvis shows the bladder (B), the uterus (U), the IUD (*open arrow*), and a right complex pelvic mass (M).

cephalad one sees a large, echo-free area which is the bladder. The little, white, spring-like object is the IUD, and it is inside the uterus. To the right is a large complex mass. It is complex because part of the mass is cystic or echo-free and the rest of it is solid, or echogenic. This could be the classic picture for a dermoid, where both cystic and solid elements are present; however, there is no shadowing from bones, teeth, or an air-fluid level. Could this be an ectopic pregnancy? A gestational sac compatible with an ectopic pregnancy is not present, but if rupture has occurred one would not see a sac.

DR. KELLY: What about tubo-ovarian abscess? Could it look like this?

DR. AARON: It certainly could look like this. In fact the main differential diagnoses now are tubo-ovarian or pelvic abscesses, a dermoid, some other ovarian tumor, or ruptured ectopic pregnancy. The sagittal sections are also helpful (Fig. 8). They

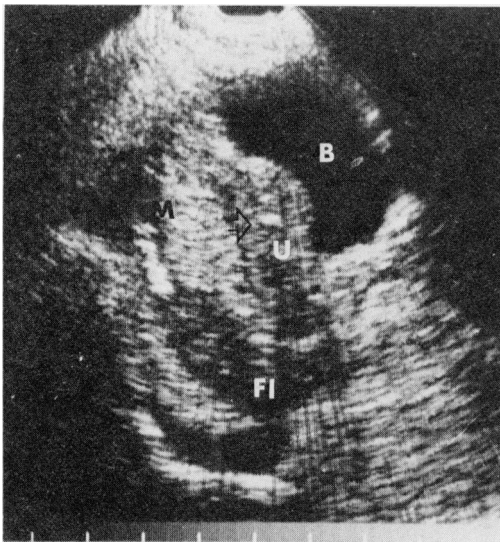


FIG. 8. The longitudinal ultrasound of the pelvis shows the bladder (B) indented by the uterus (U) containing the IUD (*open arrow*). There is fluid in the cul-de-sac (Fl.). The mass (M) is seen posterior to the uterus.

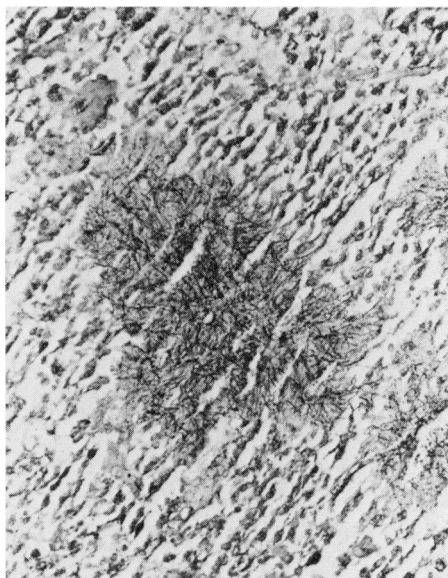


FIG. 9. Section of ovarian tissue taken at surgery demonstrating a central mass of actinomycetes within tissue (Grocott stain 400 \times).

show the IUD in the uterus, and the large complex mass indenting the bladder. In one view there is fluid present in the cul-de-sac.

DR. KELLY: To continue the clinical history, a pelvic exam confirmed the presence of a large right adnexal mass. A β -human chorionic gonadotrophin assay was negative. The mass was tender and growing increasingly so. The evening on which the ultrasound was done, raising the question of an abscess, the patient was begun on parenteral antibiotics, cephalothin, gentamicin, and clindamycin, and transferred to the gynecology service. There was a question of allergy to penicillin and they chose to use cephalothin rather than penicillin. Cefoxitin in combination with an aminoglycoside might have been a better alternative because cefoxitin covers anaerobes such as *Bacteroides fragilis*, and I'm sure some of you would have used clindamycin and gentamicin alone. The working diagnosis at that point was tubo-ovarian abscess, or an infected malignancy. Because of everyone's concern with regard to preserving fertility, the gynecologists thought the best approach would be to reduce some of the inflammation prior to operating. She improved significantly on antibiotics and was taken to the operating room in early April. A very large right tubo-ovarian abscess was found with extensive fibrosis involving both bladder and recto-sigmoid colon with destruction of the right ovary and fallopian tube, both of which were removed. However, they were able to preserve the uterus and left adnexa. The purulent material found at that time was described as foul smelling. It was cultured, but no organisms grew, possibly because the patient had been on antibiotics for three weeks. However, the histopathology of the surgical specimen revealed gram-positive branching rods consistent with actinomycosis. The final diagnosis of this patient's illness was an actinomycotic tubo-ovarian abscess of the right adnexa in association with an intrauterine device. Her anemia was attributed to chronic inflammation and probable intra-abdominal blood loss. Her polyarthritis remained unexplained and possibly unrelated to her present illness.

DISCUSSION

Data from the National Fertility Study conducted in 1973 indicated that nearly

two million married women, ages 15 to 44, were using IUDs. Scott [1] called attention to serious and potentially fatal complications associated with IUD use, including pelvic inflammatory disease (PID), uterine perforation, ectopic pregnancy, and spontaneous or septic abortion. The relative risk of PID among IUD users has been reported to be increased two- to 12-fold over controls [2-4]. The risk of infection appears to increase as the period of IUD use lengthens, but the risk associated with the use of copper IUDs may be slightly less than with plastic devices [4]. Actinomycosis has traditionally been described in three anatomical regions, the cervicofacial, thoracic, and abdominal areas, but pelvic and genital disease has been recognized with increasing frequency over the past decade. The common denominator associated with the latter syndrome appears to be the concurrent presence of an IUD [5,6,7]. The *Actinomyces* are gram-positive, non-acid fast, anaerobic, obligate parasites which are classified somewhere between the true bacteria and the complete fungi. They are commonly found associated with other organisms in dental caries, tonsillar crypts, and in the colon. *Actinomyces* species are not generally considered part of the normal vaginal flora, but rather are associated with the presence of a foreign body, most often an IUD. It is thought that the IUD causes the initial tissue injury which permits subsequent colonization by these organisms. It is not known whether orogenital contact is a means of transmission of *Actinomyces* to the lower genital tract of sexual partners.

In 1976 Gupta reported finding organisms resembling *Actinomyces* in the cervical smears of women using IUDs and he identified a majority of these organisms as *A. israelii* [5,7]. The prevalence of infection in women using IUDs varies from 8 percent among women attending a private gynecology service to approximately 25 percent of women evaluated in public clinics [8]. One might estimate that the overall rate of cytological detection of *A. israelii* in cervical smears of IUD users at about 10 percent. This incidence increases sharply in patients being evaluated for symptomatic pelvic infection; conversely, in women with IUDs in place and *Actinomyces* demonstrable in cervical smears, pelvic inflammatory disease is up to four times as common as in those who have negative smears [9]. The type of IUD employed may not be as relevant as the length of time it is in use; the longer the time of usage, the greater the incidence of infection [3,10].

The identification of *A. israelii* in cervical specimens at present is best determined by a sensitive and specific immunofluorescent assay. However, the specific antiserum is not yet widely available. A comparable degree of accuracy can be obtained by use of the Papanicolaou-stained vaginal smear which attains a sensitivity of approximately 70-95 percent, whereas attempts to utilize anaerobic cultures for diagnosis have not been productive [9].

Editor's note: The case of pelvic actinomycosis presented by Drs. Kelly and Aaron illustrates some new and important information for physicians and patients concerned about the health of women using intrauterine contraceptive devices. IUDs appear to predispose the wearer to colonization and tissue invasion with *Actinomyces* species. The majority of these women appear to be asymptomatic and the actual incidence of infection varies with the type of device used. The clinical spectrum of illness reported in the literature ranges from low-grade endometritis to fatal tubo-ovarian abscesses. Women whose cervical smears demonstrate actinomycetes-like organisms should have the device removed and be followed sequentially. Antibiotic treatment should probably be dictated by the clinical setting. As a general rule, the threshold for treatment should be low, since the therapy is relatively benign and we do not really know the extent to which colonization and tissue invasion may have occurred

in any given case. The organism is generally sensitive to penicillins, tetracyclines, and clindamycin. Pure infection with *Actinomycetes* is probably rare, and infection would be expected instead to occur in association with other anaerobic bacteria as part of a mixed suppurative process. In this situation, coverage for other anaerobes such as *Bacteroides fragilis* would have to be an additional consideration.

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