Abdominal/Pelvic Mass in a 55-Year-Old Intrauterine-Contraceptive-Device User

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A 55-year-old woman without significant medical history presented to the emergency department with a chief complaint of weakness, weight loss, and abdominal tenderness for several months. She also noted a tender palpable mass in the left inguinal area for five days. Six months prior to presentation, she was seen by a psychiatrist, diagnosed with depression and anxiety, and started on paroxetine. Over the next several months, she began to experience fatigue, indigestion, decreased appetite, alternating diarrhea and constipation, weight loss of approximately 25 pounds, and an increase in urinary frequency. She denied dysuria, nausea, vomiting, dizziness, shortness of breath, or chest pain. She noted that she had an intrauterine contraceptive device (IUCD) in place for the past 24 years.

The patient denied any significant surgical history. Her gynecological history revealed that her last menstrual cycle was 15 years prior. She had no history of sexually transmitted diseases or abnormal PAP smears (last PAP was ten years ago). Her obstetric history revealed three spontaneous vaginal deliveries at full term without complications. There was no significant family history. Her social history included a 35-pack-year history of smoking and occasional alcohol use. She denied any history of illicit drug use. She was a former bartender but had been unable to work secondary to her illness. She had no primary care physician and had not been seen by a doctor in ten years.

Physical examination revealed a thin woman in no apparent distress. Vital signs on admission included a blood pressure of 115/54 mm Hg, a heart rate of 124 beats per minute, a respiratory rate of 15 breaths per minute, and a temperature of 36.9 °C. Her calculated body-mass index was 20. Further examination revealed poor dentition and no cervical lymphadenopathy. Cardiovascular exam demonstrated a tachycardia with a regular rhythm. There was no appreciable murmur, and her apical impulse was located in the fifth intercostal space in the left midclavicular line. Auscultation revealed clear lung fields. The patient's abdominal exam disclosed a nondistended abdomen with normally active bowel sounds. Palpation of the left lower quadrant revealed a tender, fixed, firm mass. There was no evidence of rebound, guarding, or CVA tenderness. On pelvic examination there were no vulvar lesions, vaginal lesions, or discharge. An IUCD string was

CME INFORMATION

TARGET AUDIENCE

The January/February Clinical Case of the Month is intended for family physicians, general internists, medicine subspecialists, general practitioners, obstetricians-gynecologists, emergency medicine physicians, pediatricians, dermatologists, radiologists, and psychiatrists.

EDUCATIONAL OBJECTIVES

The Clinical Case of the Month is a regular educational feature presented by the Louisiana State University in New Orleans. Medical students, residents, postdoctoral fellows, and faculty collaborate in the preparation of these discussions. After reading this article, physicians should be able to identify and understand better the pathophysiology, microbiology, clinical presentation, diagnosis, and treatment of pelvic actinomycosis.

CREDIT

The LSMS Educational and Research Foundation designates this educational activity for a maximum of one (1) category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

DISCLOSURE

Dr. Wardlaw has nothing to disclose.
Dr. Ejedepang-Koge has nothing to disclose.
Dr. Beech has nothing to disclose.
Dr. Lopez discloses that he is a member of the LSMS *Journal* Board and the LSMS *Journal* Editorial Board.

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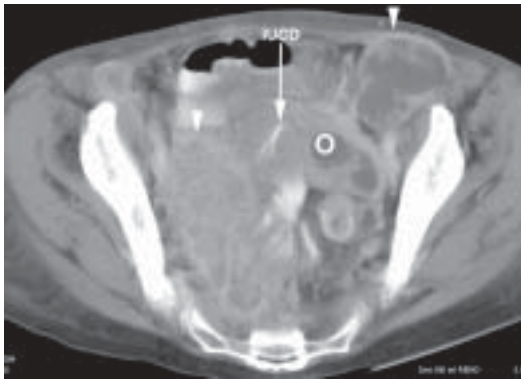


Figure 1. Computed tomographic scan of the pelvis. An IUCD is seen within the uterus (arrow). A complex mass is seen in the left adenexa consistent with a tubo-ovarian abscess (O). In addition, abnormal lymphadenopathy is seen within the left inguinal region and along the right pelvic sidewall (arrow heads).

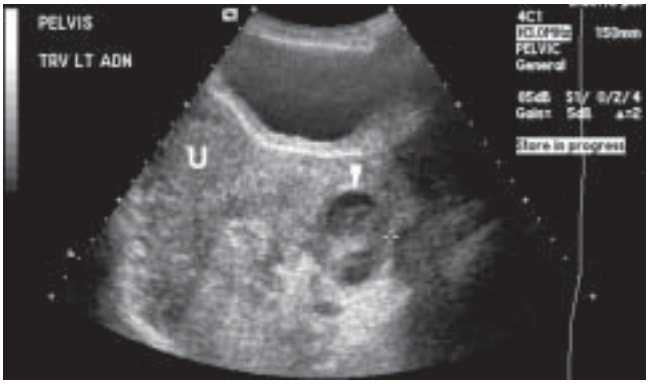


Figure 2. This transverse view of the pelvis by ultrasound further demonstrates the complex nature of the left ovary (arrow head) by highlighting its cavitary nature and its associated fluid-fluid levels. (U = uterus).

visible at the cervical os. No cervical lesion, discharge, or motion tenderness on motion was appreciated. The uterus was fixed and difficult to assess. No rectal masses were palpated, and stool examination did not reveal the presence of blood. Skin examination revealed multiple nonprofessional tattoos.

The patient's laboratory test results were significant for a slightly decreased serum sodium of 133 mmol / L (normal range, 135-146 mmol / L) and a minimally elevated serum creatinine level of 1.3 mg / dL (normal range, 0.7-1.2 mg / dL). The patient's peripheral white blood cell count was 16.3 $x10^3$ / μL (normal range, 4.5-11.0 $x10^3$ / μL) with a differential of 83% neutrophils, 11% lymphocytes, and 6% monocytes. The platelet count was increased to 866 $x10^3$ / μL (normal range, 130-400 $x10^3$ / μL). A microcytic anemia with a MCV 79.7 fL (normal range, 80-100 fL), hemoglobin of 6.1 g / dL (normal range, 12.0-16.0 g / dL) and hematocrit of 19.0 % (normal range, 35-46%) was appreciated. The patient's iron studies were abnormal and consistent with an anemia of chronic inflammatory disease: serum iron of 8 μg / dL (normal range, 40-160 μg / dL), serum total iron-birthing capacity of 229 μg / dL (250-425 μg / L), and serum ferritin of 418.6 μg / L (normal range, 20-210 μg / L).

The patient was admitted for further evaluation and management. A computed tomographic scan of the abdomen and pelvis performed with contrast revealed marked distortion of the normal uterine morphology. An IUCD was seen within the uterus (Figure 1). There were complex masses of the left adnexal and inguinal regions that demonstrated an irregular central fluid component. In addition, a predominantly solid right adnexal mass was seen which was indistinguishable from the pelvic sidewall. A transverse image of the pelvis by ultrasound further demonstrated the complex nature of the left adnexal mass (Figure 2). This highlighted the cavitary features of the left adnexal mass which had fluid-fluid levels. There were no lesions noted on a chest CT scan that was obtained to evaluate for metastatic disease. The IUCD was removed. The patient was referred to a specialist in gynecology-oncology for further evaluation of a suspected ovarian malignancy.

Ultimately, the patient underwent surgery. Intra-operative findings revealed severe pelvic adhesive disease, a 6 x 6 cm necrotic mass along the left anterior abdominal wall, an 8 cm necrotic mass involving the omentum, a large mass encasing a portion of the small bowel, tumor involvement of both ovaries, and a large infiltration of tumor in the right posterior cul-de-sac. Sub-total hysterectomy, bilateral salpingo-oophorectomy, tumor debulking, lymph node dissection, and cystoscopy were performed. Cystoscopy demonstrated that the bladder dome was normal and free of disease. Indigo carmine injection revealed good flow from the right ureteral orifice. The left ureteral orifice was severely scarred with minimal flow. Histopathology revealed no evidence of malignancy, but did reveal extensive inflammatory changes with evidence of sulfur granules and *Actinomyces* species (Figure 3 & 4). Bilateral ureteral stents were placed for hydronephrosis. The patient received a six-week course of intravenous penicillin G to be followed by an extended course of oral penicillin. She is currently doing well.

ACTINOMYCOSIS – DISCUSSION

Actinomyces species are Gram-positive filamentous bacilli which are often misclassified as fungi. Actinomycosis is the term used to refer to chronic granulomatous inflammatory conditions caused by infections with these organisms.[1-3] These bacteria are normal inhabitants of the human oropharnynx, gastrointestinal tract, and the female genitourinary tract and usually do not cause disease. However, an opportunistic infection can occur if the mucosal barrier is disrupted by trauma, surgery, dental procedures, gastrointestinal perforations or aspiration, appendicitis, foreign bodies, neoplasia, or IUCDs.[3-7] The infection can spread in multiple ways, such as direct extension by moving across connective tissue planes, aspiration, and, rarely,

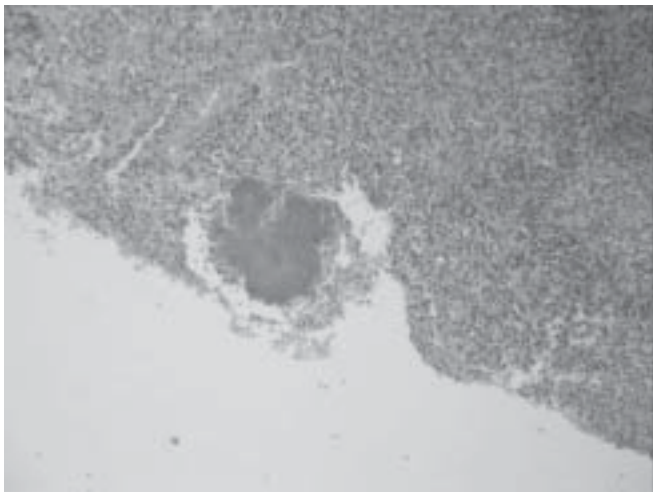
hematogenously. An anaerobic or microaerophilic environment is required for the organism's growth. The disease process is indolent in nature and is characterized by tissue destruction, fibrosis, and the formation of abscesses and fistulas. In turn, fistulas may develop into sinus tracks that drain characteristic sulfur granules. *Actinomyces israelii* is overwhelmingly the most common human pathogen, but infection has been reported with other species.[5, 6]

Making an accurate diagnosis of actinomycosis is an important yet challenging task. Unfortunately, a preoperative diagnosis is made in less than 10% of cases.[8] The diagnosis is suggested by finding the characteristic sulfur granules in tissue sections, but confirmation requires anaerobic cultures which are positive in only 24 to 50 percent of cases.[6] Definitive diagnosis can also be obtained by species-specific antibodies; however, this is of limited clinical value.[9] Other pathogens can develop the appearance of sulfur granules such as *Nocardia*, *Streptomyces*, and *Botryomycosis*.[5] It is important to differentiate *Actinomyces* from *Nocardia* because antimicrobial therapy is different. Though morphologically similar on gram and acid-fast staining, they can be distinguished with the Kinyoun stain, a modified acid-fast staining technique, ie, *Nocardia* stains positive while *Actinomyces* does not.[6,10]

Actinomycosis infections usually are polymicrobial and include organisms such as *E. coli*, *Bacteroides*, *Fusobacterium*, *Streptococcus*, *Staphylococcus*, and *Candida* species.[9] A diagnosis by histopathological methods is difficult because many tissue sections contain only a few sulfur granules. Therefore, both hematoxylin and eosin (H&E) staining and gram staining are performed to assist with the histological evaluation. On H&E staining, the organism and sulfur granules are seen together as round or oval basophilic masses with radiating arrangements of eosinophilic projections usually surrounded by inflammatory cells (Figure 3). The bacteria can be further distinguished from the sulfur granules by highlighting the organism's filaments with special stains: Gomori's methanamine-silver, periodic acid-Schiff, Brown-Brenn, or MacCallen-Goodpasture (Figure 4).[6]

Actinomyces infections have been categorized into four main clinical manifestations including cervicofacial, thoracic, central nervous system, and abdominopelvic.[6] The most common clinical presentation is cervicofacial actinomycosis which accounts for approximately 40 to 50 percent of cases.[11] Risk factors include dental manipulation and facial trauma which result in direct extension to nearby structures. The submandibular space, parotid gland, and mandible are commonly involved, whereas spread to the tongue, lips, hard palate, or gingiva is rare.[6] Thoracic involvement, which occurs in about 15 percent of all cases, has the poorest prognosis of these clinical entities.[6,11] The lung, mediastinum, or chest wall may be involved. Resulting in a chronic pneumonia, empyema, or even a fistulous tract draining through the chest wall, these infections are often mistaken for other lung processes such as tuberculosis or malignancy.[6] Central nervous system involvement represents 3 percent of all cases.[11] Infections usually present as a space-occupying lesion, typically in the frontal or temporal lobes, with resultant focal neurological involvement and increased intracranial pressure. Other presentations include chronic meningitis, meningoencephalitis, subdural empyema, actinomycetoma, and spinal and cranial epidural abscesses. In one study of 70 cases, the overall mortality was 28%, and over one-half of the patients that survived went on to have persistent neurological sequelae.[10]

Abdominopelvic actinomycosis occurs in 20 percent of all cases and may represent the most indolent form of infection.[11] The appendix and ileo-cecal valve are common sites of involvement that are often confused for inflammatory bowel disease, appendicitis, or intestinal tu



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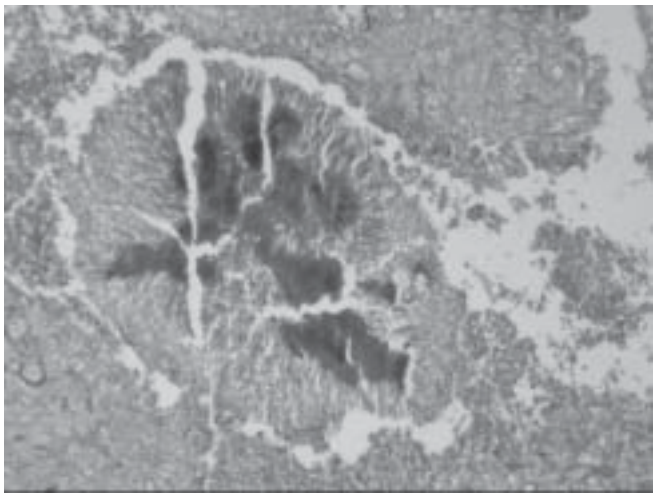

Figure 4. The bacteria are further distinguished from the sulfur granules by highlighting the organism's filaments with periodic acid-Schiff stain.

berculosis.[5] Pelvic involvement has increased in the past two decades secondary to IUCD usage, and there is a direct correlation between the duration of IUCD use and the risk of infection from *Actinomyces*. One proposed mechanism suggests that the IUCD facilitates the ascension of *A. israelii* from the vagina to the fallopian tubes and ovaries.[12] One study of 92 cases of pelvic actinomycosis revealed that the average patient was 37 years old and had an IUCD in place for eight years.[9] The clinical presentation may include abdominal pain, weight loss, vaginal discharge, and fever along with laboratory studies showing anemia, leukocytosis, and an elevated erythrocyte sedimentation rate.[1,5] Pelvic actinomycosis may result in endometritis, salpingo-oophoritis, tubo-ovarian abscess, or a pelvic mass.

As was the case in our patient, pelvic actinomycosis is often misidentified initially as ovarian cancer. Most women with ovarian malignancies are either asymptomatic or experience only mild nonspecific gastrointestinal symptoms or pelvic pressure. Advanced ovarian malignancy may present with abdominal pain, bloating, urinary symptoms, a palpable mass, and ascites. The major risk factor for ovarian cancer is family history. Other noteworthy associations include infertility, nulliparity, frequent miscarriages, and ovulation-inducing drugs such as clomiphene. Our patient did not have any known risk factors for ovarian carcinoma but had worrisome symptoms of weight loss, progressive weakness, abdominal tenderness, and a large abdominopelvic mass.

Since *Actinomyces* are normally indigenous in the female genital flora, the relationship of genital colonization with this organism in asymptomatic patients and the subsequent development of pelvic actinomycosis is unclear.[3] The presence of bacteria found by PAP smear, even in the presence of IUCD usage, does not predict the risk of development of active infection. The evidence suggests that removal of the IUCD is not required in asymptomatic patients and that antibiotic therapy is not necessary in those without evidence of pelvic infection.[4] Some authors argue, however, that if a PAP smear demonstrates *Actinomyces* species, the IUCD should be removed and the patient treated with antibiotics in order to prevent a potentially more chronic, extensive infectious course.[12] One study of 43 patients reported that treatment with antibiotics and IUCD removal in asymptomatic patients with colonization was 100% effective in eliminating *Actinomyces* versus an elimination rate of 66.7% when antibiotics alone were given and the IUCD was left in place.[7] Of note, the incidence of colonization with *Actinomyces*-like organisms depends on the type of IUCD being used. For example, the incidence of colonization with the multiload copper IUCD (ML375) is 20% as compared to 2.9% with the levonorgestrel-releasing IUCD (LNG-IUD). Our patient had a copper IUCD in place for greater than two decades.

The treatment of actinomycosis depends on the severity of the involvement. For mild cases, cure may be achieved with medical therapy alone. However, surgical intervention is often needed in addition to medical management for complicated disease processes or when malignancy cannot be excluded.[1] Some authors suggest that an extended course of antibiotics may reduce the amount of surgical intervention needed or even eliminate the need for surgery.[9] However, others argue that effective surgical removal of pelvic abscesses can allow for a successful shorter course of antibiotics.[13-15] Ultimately, clinical judgment on a case-by-case basis should be used to direct therapy. The drug of choice for actinomycosis is intravenous penicillin G at doses of 18-20 million units/day for four to six weeks followed by oral penicillin V for six to twelve months. In patients with a penicillin allergy or who are intolerant of penicillin, the following antibiotics can be used: chloramphenicol, clindamycin, erythromycin, tetracycline, imipenem, streptomycin, and cephalosporins with anaerobic activity.[1,5,6,9] A prolonged course of antibiotics is essential in order to decrease the chance of recurrence. In addition, serial radiological imaging is recommended to assess the response to therapy.[1] If a favorable response is not seen within four weeks, a superinfection from another bacterial source should be considered.[5] The prognosis of actinomyces is generally good when treated expeditiously; however, if the treatment is delayed, extensive local involvement and complications can develop.[11]

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CME QUESTIONS

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For each question, choose the one answer that is most correct.

1. All of the following anatomical areas are commonly involved in *Actinomyces* infections except:
   a) Cervicofacial
   b) Central nervous system
   c) Thoracic
   d) Bone Marrow
   e) Abdominopelvic

2. True or False. *Actinomyces* species are normal inhabitants of the human oropharynx, gastrointestinal tract, and female genitourinary tract.

3. True or False. Pelvic actinomycosis is often misidentified initially as ovarian cancer.

4. All of the following statements are true except:
   a) Pelvic actinomycosis has increased in the past two decades secondary to IUCD usage, and there is a direct correlation between the duration of IUCD use and the risk of infection from *Actinomyces*.
   b) The antibiotic of choice for actinomycosis is penicillin G.
   c) A prolonged course of antibiotics is essential in order to decrease the chance of recurrence.
   d) Pelvic actinomycosis is more common than cervicofacial actinomycosis.
   e) Clindamycin, erythromycin, tetracycline, chloramphenicol, and imipenem are alternative antibiotics that can be used to treat actinomycosis.