CASE REPORTS

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Tubo-ovarian Actinomycosis and the Use of Intrauterine Devices

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ACTINOMYCOSIS, a chronic suppurative disease caused by an anaerobic actinomycete, most commonly involves the face, thorax or abdomen.[1] The pelvis is an unusual location for infection with actinomycetes. Twenty cases of pelvic actinomycosis associated with use of an intrauterine device (IUD) have been reported[2-10]; three were diagnosed by culture and histology, one by culture and histology of an accompanying subphrenic abscess and 17 by histology alone. We recently cared for a patient with IUD-associated pelvic actinomycosis, in which the organism was identified by histologic testing and culture. Because the number of women using IUD's is growing it is likely that more cases of this infection will occur. Thus, a review of methods of diagnosis and management of IUD-associated pelvic actinomycosis should be useful.

Report of a Case

A 29-year-old woman, gravida 2, para 1, had a therapeutic abortion in March 1971. She used an IUD (Dalkon Shield) from 1971 until April 1975, when it was removed because of menometrorrhagia. At the time of its removal, the physician observed that the IUD had been lying transversely. In June 1975 the patient noted pain in the lower left quadrant of her abdomen. A mass in the left ovary was palpated on pelvic examination. However, she refused further evaluation at that time.

In August 1976 the patient complained of continued abdominal pain. On physical examination she had a firm, slightly tender, 7-cm mass in the left adnexa, contiguous with the uterus. A physical examination showed no other abnormalities. There were 11,200 peripheral blood leukocytes

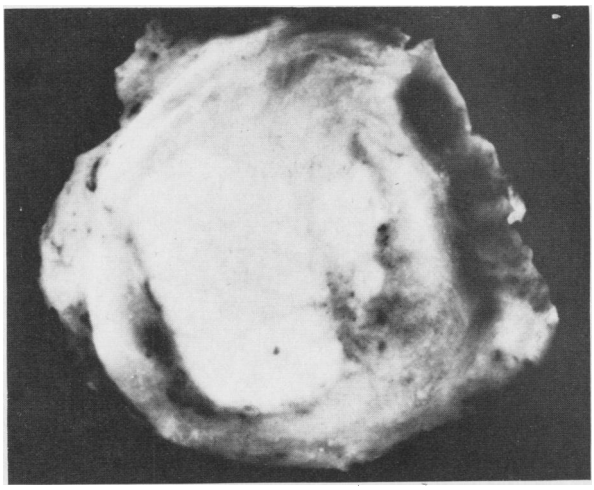

Figure 1.—Tubo-ovarian abscess, 5 by 2.5 cm.

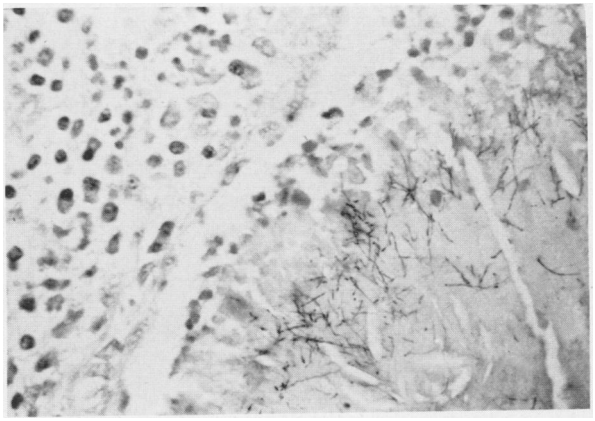

Figure 2.—Microscopic section of tubo-ovarian abscess. Gram-stained preparation with Gram-positive, filamentous, branching rods and acute and chronic inflammatory cells within a fibrous matrix.

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TABLE 1.—*Diagnosis, Treatment and Outcome of Therapy in 21 Patients With Endometrial or Tubo-ovarian Actinomycosis*

Case No.	Method of Diagnosis*	Site	Treatment					Outcome—Follow-up When Patient Reported Well (yrs)
			Antibiotic	Dose (grams/day)	Route	Duration	Surgical or Other Procedure	
1[2]	H(+),C(−)	Right	Penicillin	2.5	IM	about 8 days postop	TAH-BSO	2
			Penicillin	2	PO	6 months postop		
			Streptomycin	NA	NA	NA postop		
			Sulfisoxazole	4	PO	6 months postop		
2[3]	H(+),C(+)	Bilateral	Penicillin	3.75	IM	6 weeks postop	Bilateral excision of abscess followed by TAH (a year later)	2.75
3[3]	H(+)	Bilateral	Co-trimoxazole	4 tablets/day	PO	8 days preop	TAH-BSO	0.58
			Tetracycline	1	PO	8 days preop		
			Penicillin	1	PO	3 months postop		
4[4]	H(+),C(−)	Bilateral	Ampicillin	1	PO	3 days preop	TAH-BSO	1
			Penicillin	3.125	IV	1 dose during operation		
			Penicillin	9.375	IV	3 days postop		
			Penicillin	4	PO	5 days postop		
			Penicillin	2	PO	1 year postop		
			Kanamycin	1	IM	1 dose during operation		
			Kanamycin	1	IM	5 days postop		
5[5]	H(+),C(+)	Bilateral	Cephalothin	NA	NA	NA preop and postop	TAH-BSO	3
			Gentamicin	NA	NA	NA preop and postop		
			Clindamycin	NA	NA	3 weeks postop		
6[5]	H(+),C(+)†	Left	Ampicillin	NA	NA	NA preop	TAH-BSO	2
			Penicillin	NA	NA	NA postop		
			Clindamycin	NA	NA	NA postop		
			Penicillin	NA	PO	6 months postop		
7[6]	H(+)	Left	Penicillin	2	PO	30 days postop	TAH-BSO	0.67
8[7]	H(+),C(+)	Bilateral	Lincomycin	NA	Parenteral	NA postop	BSO	1
			Gentamicin	NA	Parenteral	NA postop		
			Penicillin	NA	Parenteral	NA postop		
			Penicillin	NA	PO	3 months postop		
9[8]	H(+),C(−)	Left	Penicillin	NA	NA	NA	TAH-BSO	NA
10[8]	H(+),C(−)	Bilateral	Penicillin	NA	NA	NA	TAH-BSO	NA
11[8]	H(+),C(−)	Endometrial	Erythromycin	NA	NA	NA	IUD removed	NA
12[8]	H(+),C(−)	Endometrial ? adnexal	Penicillin	NA	IV	20 days§	IUD removed	NA
			Kanamycin	NA	NA	NA		
13[8]	H(+),C(−)	Endometrial	Penicillin	NA	NA	NA	IUD removed	NA
14[8]	H(+),C(−)	Endometrial	Penicillin	NA	NA	NA	IUD removed	NA

16[6] .. H(+),C(−)	Left	Penicillin	NA	NA	NA	TAH-BSO	NA
17[8] .. H(+),C(−)	Endometrial ? adnexal	Ampicillin	NA	NA	NA	IUD removed	NA
18[8] .. H(+),C(−)	Endometrial	Penicillin	NA	NA	NA	IUD removed	NA
19[9] .. H(+)	Left	Penicillin	12.5	IV	2 weeks postop	TAH-BSO	0.75
		Clindamycin	0.6	PO	9 months postop		
20[10] .. H(+),C(−)	Bilateral	Cephalothin	4	IV	7 days preop	TAH-BSO	3
		Kanamycin	1	IM	7 days preop		
		Chloramphenicol	3	IV	14 days preop		
		Chloramphenicol	2	IV	NA preop		
		Tetracycline	1.5	IV	14 days preop and postop		
		Tetracycline	2	PO	30 days postop		
21‡ .. H(+),C(+)	Bilateral	Penicillin	18.75	IV	2 days after 1st operation	Left salpingo-oophorectomy followed by TAH and right salpingo-oophorectomy (51 days later)	0.5
		Penicillin	2	PO	30 days after 1st operation		
		Gentamicin	0.24	IV	2 days after 1st operation		
		Penicillin	12.5	IV	10 days before 2nd operation		
		Penicillin	12.5	IV	7 days after 2nd operation		
		Penicillin	2	PO	14 days after 2nd operation		

IM = intramuscular; IUD = intrauterine device; IV = intravenous; NA = not available; PO = by mouth; postop = postoperatively; preop = preoperatively; TAH-BSO = total abdominal hysterectomy and bilateral salpingo-oophorectomy

*H(+) = *Actinomyces* identified in histologic preparation; C(+) = *Actinomyces* identified in culture; C(−) = *Actinomyces* not identified in culture.
†Subphrenic, not pelvic.
‡Present case.
§Time of administration unknown.

per cu mm with 73 percent polymorphonuclear cells and 6 percent band forms; the hematocrit was 30 percent and sedimentation rate was 59 mm per hour ((Wintrobe). Vaginal culture and culdocentesis were not done. A laparotomy was carried out in August 1976, and a 5- by 2.5-cm tubo-ovarian abscess on the left side was found (Figure 1). Adhesions and clubbing of the right fallopian tube were also noted during the operation. The left ovary and fallopian tube were excised. Although inflammatory disease involving the right ovary and fallopian tube was evident, the right adnexa was left in place in accordance with the patient's preoperative request. Treatment consisted of 30 million units per day of aqueous penicillin given intravenously for two days, 80 mg of gentamicin given intravenously every eight hours for two days and 2 grams per day of penicillin V given orally for the following 30 days. Histologic examination of the excised tubo-ovarian abscess disclosed Gram-positive, filamentous, branching rods, with acute and chronic inflammatory cell infiltrates within a fibrous matrix (Figure 2). Culture of the tubo-ovarian abscess showed a pure growth of *Actinomyces israelii.*

At a subsequent clinic visit in September 1976, the patient felt mild lower abdominal pain on palpation of the right adnexal area; a pelvic examination and sonogram showed a mass in the right adnexa. The leukocyte count was 6,400 per cu mm, and sedimentation rate was 46 mm per hour (Wintrobe). She was admitted to hospital and treated with 21 million units of penicillin G given intravenously each day for 17 days (10 days before the operation and 7 days afterwards). In October a second laparotomy was done, and inflammation and fibrosis of the right adnexal area with adhesions and clubbing of the fallopian tube were noted. A 5-cm cyst involving the right ovary was noted, and the ovary, the right fallopian tube and the uterus were removed. Histologic examination and culture showed no evidence of actinomycetes in any of these tissues, although extensive acute and chronic salpingitis was noted. The patient was given 500 mg of penicillin orally four times per day for two weeks after discharge from the hospital. She was well six months after the second surgical procedure.

Comment

This case illustrates certain typical epidemiologic features of tubo-ovarian actinomycosis and

the problem of establishing a preoperative diagnosis.

It is often difficult to distinguish the clinical presentation of tubo-ovarian actinomycosis from that of chronic pelvic inflammatory disease caused by other organisms. As in the case reported above, pelvic actinomycosis usually presents as a chronic indolent disease with symptoms persisting from months to years. The average time from onset of symptoms to diagnosis in one series was 19 months.[11] In our patient, weight loss, lower abdominal and pelvic pain, and clinical course were more consistent with a pelvic tumor than with an acute infectious process.

Tubo-ovarian actinomycosis generally occurs in distinct clinical situations: following appendicitis or abdominal surgical procedures,[10,12] and in the presence of an IUD.[2-10] Actinomycosis is thought to occur in these circumstances because intestinal or uterine mucosal barriers are disrupted due to inflammation or mechanical trauma, thereby allowing colonization with *A israelii,* a species of bacteria normally present in humans in the vagina or gastrointestinal tract.[3,10,13] Recent reports have described organisms in histologic and cytologic preparations of smears, stained with Gram and acid-fast stains, from the genital tract of women who have used IUD's.[14] Data concerning identification of the organism by culture, however, have not been provided.

The specific location of pelvic actinomycosis appears to depend on predisposing factors. For example, tubo-ovarian actinomycosis described in the earlier literature occurred on the right side in 38 percent of cases, on the left side in 18 percent and bilaterally in 44 percent.[11] The predominance of disease on the right side over the left was attributed to earlier appendicitis or appendectomy in many cases. In our review of the 21 cases of IUD-associated pelvic actinomycosis (20 previously reported cases and the present case), 7 patients had endometrial infections documented by histologic examination alone. Of the remaining 14 cases, the lesions were on the right side in 7 percent (one of 14), on the left side in 36 percent (five of 14), and bilateral in 57 percent (eight of 14) (Table 1). Although the number of cases is small, there are more cases of IUD-associated pelvic actinomycosis on the left side than in earlier series[4,11] in which the development of disease was thought to be related to previous appendiceal disease.

Diagnosis of actinomycosis is generally based on histologic evidence of classic sulfur granules and Gram-positive, nonacid-fast, branching, filamentous bacteria (Figure 2 and Table 1). Cultures are frequently negative, possibly because the organism is fastidious or because anaerobic specimens are often handled improperly. Because the organism may be difficult to culture and other organisms may produce similar histologic features,[15] additional diagnostic techniques have been developed.

A serologic test that assays for precipitating antibody to actinomycetes by counterimmunoelectrophoresis is being evaluated to diagnose actinomycosis; thus far, it has been reported to be sensitive and specific.[16] Presence of antibody, measured by this assay, is reported to persist for six months in the absence of exacerbations of actinomycosis.

A fluorescent antibody technique has been reported to be useful in identifying actinomycetes in tissue.[17] In a recent study, 36 women had evidence of actinomycetes in Papanicolaou-stained cervicovaginal smears; 9,191 smears were analyzed.[18] Actinomycetes were identified exclusively in patients wearing an intrauterine device or vaginal foreign body (IUD's and pessaries). By using fluorescein isothiocyanate-labeled antiserum, the organisms were shown to be *A israelii* in eight randomly selected smears. Nine of the 36 patients (25 percent) had pelvic inflammatory disease, a rate that appears to be much higher than the already high rate among all IUD users. The authors of the report concluded that this observation underscored the importance and clinical significance of finding actinomycetes in the vaginal smears of IUD users and that Papanicolaou-stained cervicovaginal smears provided a relatively easy, inexpensive, fast and highly specific method for the morphologic diagnosis of actinomycetes. They also suggested that these smears permit recognition, at a relatively early stage, of a group of patients who are potentially at risk for the development of pelvic inflammatory disease and its associated more severe complications.

In an attempt to establish guidelines for treating our patient, we reviewed the available literature (Table 1). Removal of the IUD and administration of 8 million units of penicillin G over two weeks (personal communication, M. A. Schiffer, January 1979) probably constitutes adequate treatment of endometritis caused by actinomycetes.[8] All cases of IUD-associated tubo-ovarian

abscess reported in the literature have been treated by abdominal hysterectomy, salpingo-oophorectomy and, in addition, administration of penicillin or a cephalosporin (Table 1, patient 5). The mode of administration and the dose of penicillin given have varied widely. The smallest dose of penicillin given to any patient was 1 gram per day of penicillin V for three months; this patient was reported to be well seven months after therapy began.[3] It is noteworthy that one patient with tubo-ovarian actinomycosis secondary to appendicitis was treated with a total of 86.8 million units of penicillin over approximately three months and a total of 9.5 grams of sulfadiazine, and subsequently had a normal pregnancy and delivery.[12] Data derived from in vitro sensitivity testing as well as treatment of actinomycosis in other sites[19-21] provide evidence that erythromycin, tetracyclines and clindamycin, as well as cephalothin and chloramphenicol, are reasonable alternative drugs for treatment of tubo-ovarian actinomycosis in patients who are allergic to penicillin.

Summary

Tubo-ovarian actinomycosis was diagnosed in a woman who had been using an IUD. The organism was identified by histologic analysis and culture. This case and 20 previously reported cases of IUD-associated pelvic actinomycosis are reviewed. Methods of diagnosis and management are emphasized because this infection is more likely to occur in view of the increasing use of IUD's.

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Post-*Yersinia* Arthritis

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REACTIVE ARTHRITIS is the term used at present for a sterile arthritis following infection in a part of the body that is remote from the joints.[1-4] Reiter syndrome is an example. The arthritis is usually of abrupt onset, involves relatively few joints and, characteristically, occurs after a latent period of a few days to two or three weeks. The antecedent infections are bacterial or chlamydial. By custom, the term excludes viral-associated arthritides. This report describes the cases of four patients in Northern California with arthritis following gastroenteritis caused by *Yersinia enterocolitica*. This syndrome was first described by Ahvonen and colleagues[1] in a report of 11 patients in Finland with erythema nodosum, including arthritis in two patients, following *Yersinia* enteritis. A similar syndrome may be associated

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