

## Actinomycotic Inflammatory Disease and Misdiagnosis of Ovarian Cancer. A Case Report

JALID SEHOULI<sup>1</sup>, JENS H. STUPIN<sup>1</sup>, ULRIKE SCHLIEPER<sup>1</sup>, SHERKO KUEMMEL<sup>1</sup>, WOLFGANG HENRICH<sup>1</sup>, C. DENKERT<sup>2</sup>, M. DIETEL<sup>2</sup> and WERNER LICHTENEGGER<sup>1</sup>

*University Departments of <sup>1</sup>Gynecology and Obstetrics and <sup>2</sup>Pathology, Charité University of Medicine, Virchow-Klinikum Campus, Berlin, Germany*

**Abstract.** *Actinomycosis in the pelvic region is an uncommon diagnosis. This infection is caused by *Actinomyces israelii*, a gram-positive anaerobic saprophyte bacterium that is a normal inhabitant of the upper intestinal tract in humans. Pelvic actinomycosis is difficult to diagnose pre-operatively and is diagnosed, in most cases, accidentally. Actinomycosis can mimic pelvic and abdominal malignancies. A case report of a 35-year-old female patient with a fixed pelvic mass is presented and the diagnosis and treatment of pelvic actinomycotic inflammatory disease in relation to ovarian cancer are discussed. Clinicians should be aware of this rare infection to spare women potential morbidity from excessive surgical procedures.*

Despite the broad use of tumor markers, sonography and computerized tomography, the differentiation between benign and malignant pelvic masses is still a clinical challenge. Accurate differential diagnosis is necessary because the treatment strategies vary greatly. A case of actinomycotic inflammatory disease, which was misdiagnosed as an advanced ovarian cancer, is reported.

### Case Report

A 35-year-old female, gravida 1, para 1, was referred with suspected ovarian cancer from an external hospital where she had received operative treatment 3 weeks previously. She complained of abdominal pain, increasing abdominal girth, adnexal masses, diarrhea, fever of 38.5°C and a 10-kg weight loss over the preceding 4 months. Additionally,

*Correspondence to:* Jalid Sehouli, MD, University Department of Gynecology and Obstetrics, Charité University of Medicine Berlin, Virchow-Klinikum Campus, Augustenburger Platz 1, D-13353 Berlin, Germany. Tel: ++ 4930 450564125, Fax: ++ 4930 450564910, e-mail: jalid.sehouli@charite.de

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hydronephrosis of the right kidney was diagnosed. In the history of the patient there had been no previous surgery or other severe disease. An intrauterine device (IUD) had originally been placed 9 years previously and had been changed every 2 years since then. Two months prior to admission, the IUD had been removed.

An exploratory laparotomy was performed, but was complicated by extreme adhesions, fibrosis (frozen pelvis) and cystic changes of the ovaries. Despite the fact that biopsies of the peritoneum showed no signs of malignancy, a diffuse peritoneal carcinomatosis was suspected. After receiving a right nephrostomy, in recovery, the patient was referred to our clinic for completion of the surgical management of her supposed advanced ovarian cancer. At this time the patient was afebrile. On pelvic examination, there was a solid, tender and fixed pelvic mass extending to both pelvic walls and to the posterior sacral region. The assessment of the lower abdomen by transvaginal and transabdominal sonography showed solid hypoechogenic-appearing adnexal masses with cystic components and without blood flow. Normal ovaries were not detectable. Ascites was not detected either in the pouch of Douglas or in the upper abdomen. The findings did not allow for the differentiation between a benign or malignant process (Figures 1a, 1b). The laboratory data revealed a slight leukocytosis of  $11.9 \times 10^3/\mu\text{l}$ , CRP (acute infection-related protein) of 4.1 g/dl (normal range <0.6 mg/dl) and hemoglobin of 9.8 g/dl. The tumor marker CA-125, at 49 U/ml, was slightly increased (normal range <35 U/ml).

A pre-operative cystoscopic placement of ureteral stents was followed by a median laparotomy. After lysis of the intestinal adhesions and careful mobilization of the colon, small bowel and sigmoid colon, severe bilateral tubo-ovarian abscesses were revealed. All the pelvic structures were covered with marked fibrosis. A bilateral salpingo-oophorectomy was performed. Drainage (easy-flow) was placed in the pelvic region.

The histopathological examination showed no evidence of malignancy, but the presence of sulfur granules

characteristic of *Actinomyces israelii* and led to the diagnosis of an extensive actinomycotic involvement of both ovaries and fallopian tubes (Figures 2a, 2b).

Immediately, the patient received a combination of Ampicillin and Sulbactam intravenously at a dose of 3 x 1.5 g/day for 2 weeks, followed orally for another 4 weeks. The post-operative period was without complications. The drain was removed after 5 days. After 8 days, the ureteral stents were removed and no hydronephrosis was detected. Fourteen days after surgery, the pelvic examination showed complete resolution of the induration and masses in the pelvis and the patient was discharged without any complaints. She is still without any symptoms 2 years after surgery.

**Discussion**

*Actinomyces israelii*, a filamentous, gram-positive bacillus, is a part of the microflora of the human oral cavity. *Actinomyces israelii* can not penetrate through the normally intact mucosal barrier (1). Actinomycotic disease is a rare diagnosis, the overall incidence being 1:100,000 to 1:300,000 annually, with rates 3 times as high for men as women (1). Most cases are seen in adolescents and middle-aged adults (1). Its manifestation in the pelvic region is rare. Furthermore, the incidence of IUD-associated cervicovaginal actinomycosis has been shown to be between 8 and 16% in most studies (2-4). Although rarely diagnosed, its important should be considered in the differential diagnosis of ovarian cancer (2). Fiorino reviewed the literature in 1996 and found 92 cases in 63 reports describing actinomycotic pelvic inflammatory disease simulating ovarian cancer (5). We analyzed an additional 7 reports of 8 patients published since 1996 (6-12).

Different symptoms can be compared between actinomycotic inflammatory disease (5-10) and ovarian cancer (13, 14) and the most common of these are summarized in Tables I and II, together with the corresponding difficulties in clinical discrimination.

It is clear from the database that findings of *Actinomyces israelii* can easily be confounded with ovarian carcinoma. Especially in women with an IUD, this differentiation should be made before laparotomy, as Chatwani and Amin-Hanjani showed in their study including 1,520 women with IUDs (2). In this study, the colonization rate increased with the duration of IUD use, reaching an overall colonization rate of 11.4%. These authors suggested that patients with IUDs should undergo annual cytological smears. Recently, Marwah and colleagues presented an unusual case of ovarian actinomycosis of a patient without an IUD (19).

Various other predisposing factors are discussed in the literature based on retrospective data and with limited evidence: neoplasia, dental caries, gastrointestinal tract

Table I. Differentiation between actinomycotic pelvic inflammatory disease (3-12) and ovarian cancer (13, 14).

Actinomycosis		Ovarian cancer
37 years	Median age	55 years
	Symptoms	
++	Abdominal pain	++
+	Weight loss	+
+	Abnormal vaginal bleeding	+
+	Anemia	+
++	Vaginal discharge	+/-
++	Fever	-
++	Leukocytosis	+
-	Ascites	++
+/-	Elevation of CA 125 (normal <35 U/ml)	++
approx. 8 years	Duration of IUD use	no association

frequent (++), sometimes (+), uncommon (-).

Table II. Symptoms of pelvic actinomycotic inflammatory disease (3-10).

Uni-/bilateral tumor involving the ovaries	>95%
Abdominal pain	>80%
Leukocytosis	>70%
Anemia	>60%
Fever	>55%
Weight loss	>40%
Vaginal discharge	>20%
Vaginal bleeding	>15%

perforation (necrosis), abdominal surgery, orogenital sex, compromised immune status (12).

Since the symptoms of both ovarian cancer and infection with *Actinomyces israelii* are very similar, non-invasive differentiation of the two diseases is particularly limited and can be achieved pre-operatively in only 10% of the cases. Some authors reported a diagnosis using ultrasound-guided biopsies (15). Lee and co-workers described a case using transcatheter computerized tomography-guided core needle biopsy in the diagnosis of pelvic actinomycosis (11). Culture methods are often too slow and relatively insensitive for the definitive diagnosis of infection with *Actinomyces israelii* (7). *In vitro* culture is difficult and requires microaerophile conditions and special culture media. Only 25% of actinomycotic cultures show positive results after a period of 3 to 4 weeks (1).

For solid-appearing masses and in early ovarian malignancy, Doppler sonography facilitates the pre-operative discrimination between benign and malignant processes (16). Adding color Doppler to conventional transvaginal sonography produces a specific and positive predictive value higher than that of conventional sonography alone in differentiating adnexal masses and can give additional information (17). In our case, however,

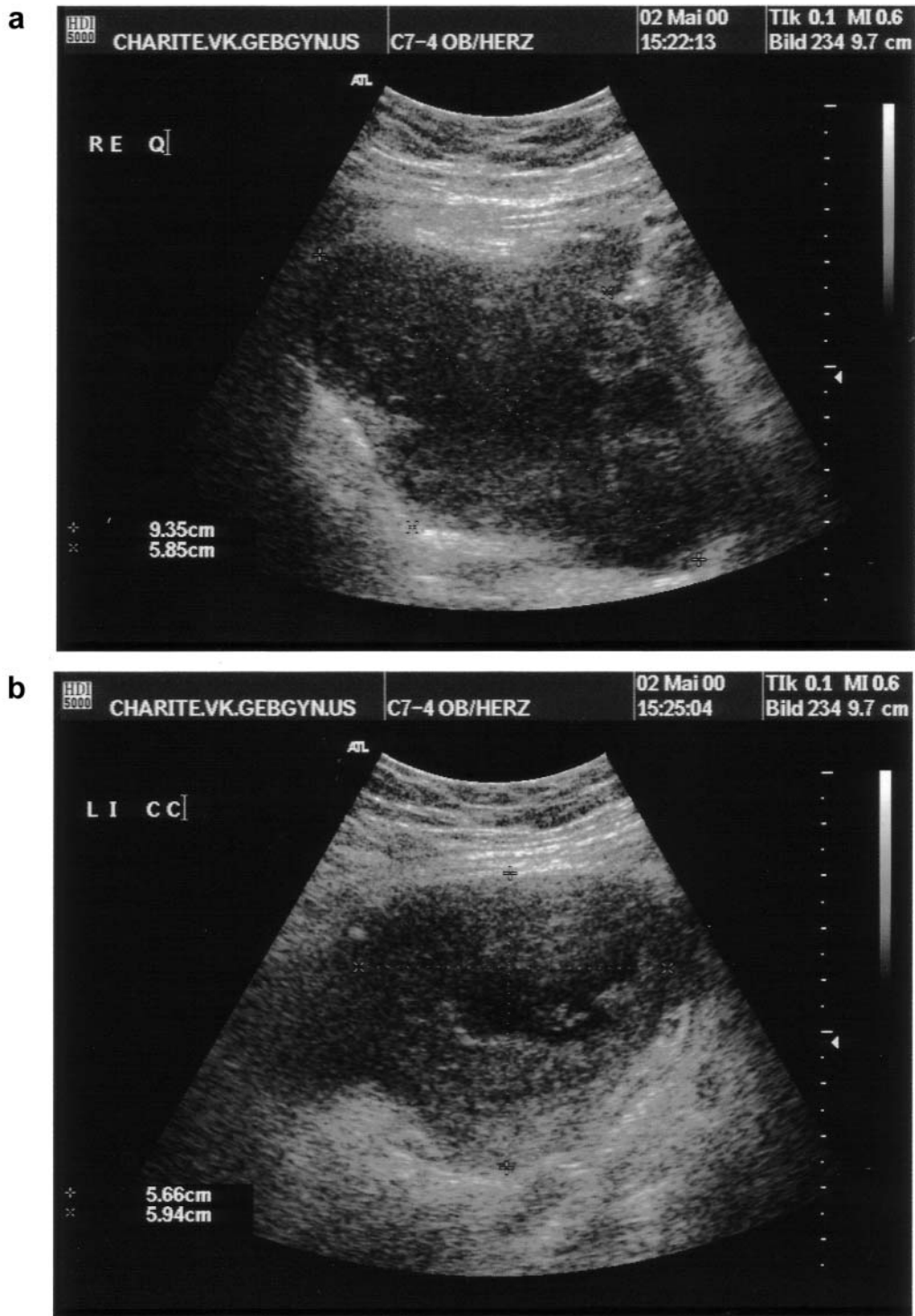


Figure 1. a) Transabdominal sonography of the right adnexal masses. b) Transabdominal sonography of the left adnexal masses.

transabdominal and transvaginal gray scale imaging and the use of color Doppler were not helpful in differentiating the bilateral adnexal masses. In the case of persisting symptoms, laparoscopy or laparotomy should be performed. Surgical

intervention should be limited to relieving obstructive symptoms and to removing necrotic tissues. To prevent post-operative fistulas, broad dissection of the intestines, ureter and bladder should be avoided. Drainage of pelvic

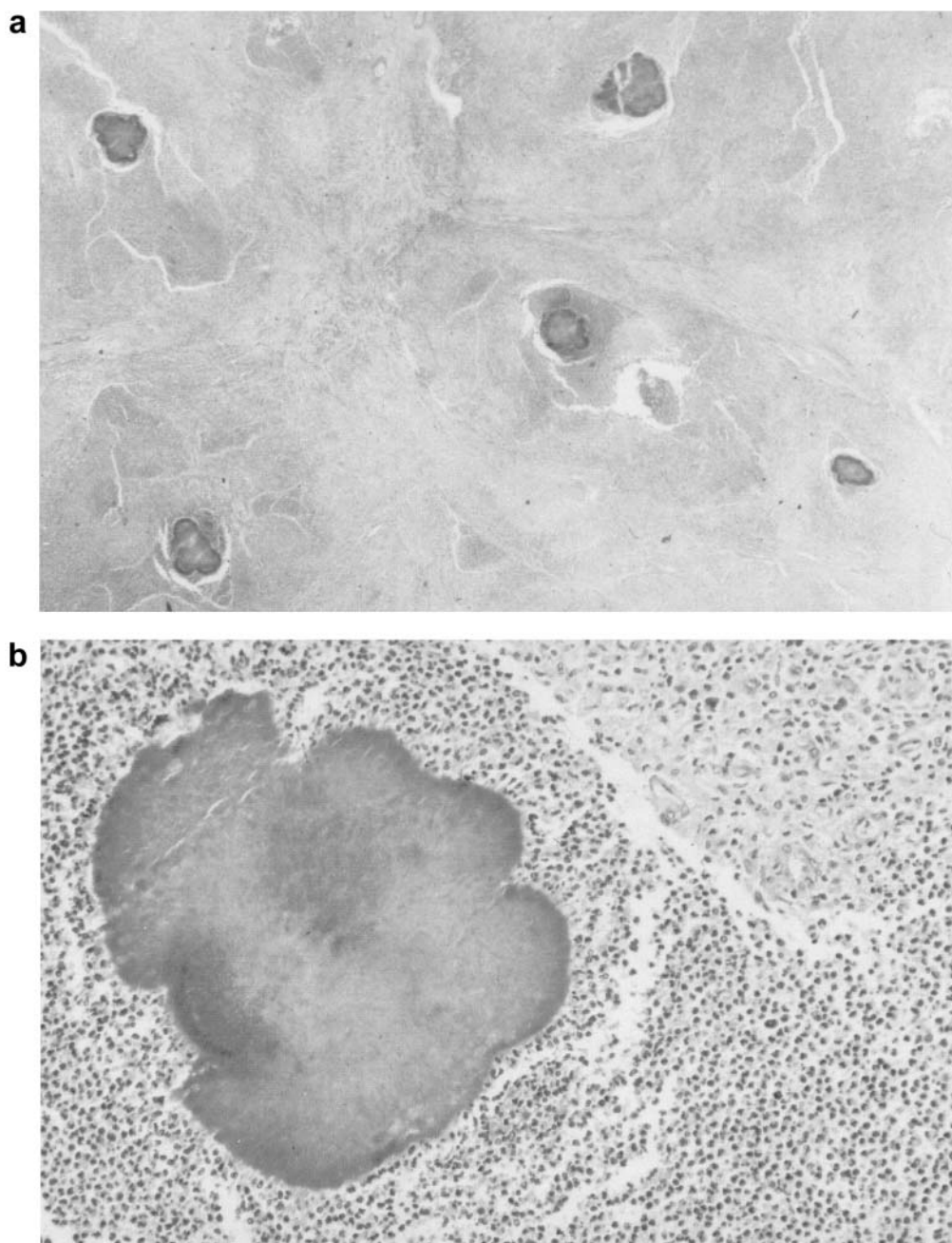


Figure 2. a) Multiple *Actinomycetes* embedded in microabscesses of the wall of the fallopian tube. H& E, x 3 (primary magnification). b) Sulfur granulum of *Actinomyces israelii* surrounded mainly by polymorphonuclear neutrophils and histiocytes. H&E, x 50 (primary magnification).

abscesses is the most beneficial procedure and helpful in most cases (4, 18).

The therapy of choice consists of surgical resection of the inflammatory, infected tissue and long-term penicillin-based antibiotic therapy. For a patient with an IUD, *Actinomyces israelii* in the cervico-vaginal smear, together with any of the symptoms mentioned above, primary antibiotic therapy is preferred.

## Conclusion

Pelvic actinomycosis is a rare inflammatory disease which mimics ovarian cancer. Differentiation is difficult, but a history of IUD use, *Actinomyces israelii* detection and absence of serum tumor markers should prompt the diagnosis of actinomycosis. To avoid invasive detection methods, all aspects of differentiation, including laparoscopy

with biopsies, should be considered in cases in which the diagnosis remains unclear or when symptoms persist.

## References

- 1 Gorbach SL, Bartlett JG and Blacklow NR: Infectious Diseases. Second Edition. WB Saunders, Philadelphia, 1998.
- 2 Chatwani A and Amin-Hanjani S: Incidence of actinomycosis associated with intrauterine devices. *J Reprod Med* 39: 585-587, 1994.
- 3 Cleghorn AG and Wilkinson RG: The IUCD-associated incidence of *Actinomyces israelii* in the female genital tract. *Aust NZ J Obstet Gynecol* 29: 445-449, 1989.
- 4 Evans DTP: *Actinomyces israelii* in the female genital tract: a review. *Genitourin Med* 69: 54-59, 1993.
- 5 Fiorino AS: Intrauterine contraceptive device-associated actinomycotic abscess and *Actinomyces* detection on cervical smear. *Obstet Gynecol* 87: 142-149, 1996.
- 6 Antonelli D and Kustrup JF Jr: Large bowel obstruction due to intrauterine device: associated pelvic inflammatory disease. *Am Surg* 65: 1165-1166, 1996.
- 7 Kirova YM, Feuilhade F, Belda-Lefrere MA and Le Bourgeois JP: Intrauterine device-associated pelvic actinomycosis: a rare disease mimicking advanced ovarian cancer: a case report. *Eur J Gynaecol Oncol* 18: 502-503, 1997.
- 8 Ko Kivok Yun P, Charasson T, Halasz A and Fournier A: Pelvic actinomycosis abscess and intrauterine device. *Contracept Fertil Sex* 25: 239-241, 1997.
- 9 Laurent T, de Grandi P and Schnyder P: Abdominal actinomycosis associated with intrauterine device: CT features. *Eur Radiol* 6: 670-673, 1996.
- 10 Nugteren SK, Ouwendijk RJ, Jonkman JG, Straub M and Dees A: Colitis and lower abdominal mass by *Actinomyces israelii* in a patient with an IUD. *Neth J Med* 49: 73-76, 1996.
- 11 Lee Y, Min D, Holcomb K, Buhl A, DiMaio T and Abulafia O: Computed tomography guided core needle biopsy diagnosis of pelvic actinomycosis. *Gynecol Oncol* 79: 318-323, 2000.
- 12 Lee LC, Lai TJ and Huang SC: Actinomycotic tubo-ovarian abscess mimicking advanced ovarian malignancy in a woman with tubal ligation. *Int J Gynaecol Obstet* 68: 157-158, 2000.
- 13 Schwartz PE: Surgical management of ovarian cancer. *Arch Surg* 116: 99-106, 1981.
- 14 Igoe BA: Symptoms attributed to ovarian cancer by women with the disease. *Nurse Pract* 22: 127-128, 1997.
- 15 Schmidt WA, Bedrossian CW, Ali V, Webb JA and Bastian FO: Actinomycosis and intrauterine contraceptive devices: the clinicopathologic study. *Diagn Gynecol Obstet* 2: 165-177, 1980.
- 16 Leeners B, Schild RL and Funk A: Colour Doppler sonography improves the pre-operative diagnosis of ovarian tumours made using conventional transvaginal sonography. *Eur J Obstet Gynecol Reprod Biol* 64: 79-85, 1996.
- 17 Buy JN, Gossain MA and Hugol D: Characterization of adnexal masses: combination of color Doppler and conventional sonography compared with spectral Doppler analysis alone and conventional sonography alone. *Am J Roentgenol* 166: 385-393, 1996.
- 18 Hoffmann MS, Roberts WS, Solomon P, Gunasekarin MD and Cavanagh D: Advanced actinomycotic inflammatory disease simulating gynecologic malignancy. A report of two cases. *J Reprod Med* 36: 543-545, 1991.
- 19 Marwah S, Marwah N, Singh I, Singh S, Gupta A and Jaiswal TS: Ovarian actinomycosis in absence of intrauterine contraceptive device: an unusual presentation. *Acta Obstet Gynecol Scand* 84: 602-607, 2005

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