Pelvic actinomycosis-like disease due to *Propionibacterium propionicum* after hysteroscopic removal of an intra-uterine device


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A female patient presented with episodes of fever and pain in the lower right abdomen after hysteroscopic removal of an intra-uterine device two months earlier. Pelvic actinomycosis originating from a tubo-ovarian abscess was suspected and antibiotic treatment consisting of doxycycline and metronidazol was administered. There

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A 38-year-old woman presented at the Emergency Department with complaints of periodic fever and pain in the lower right abdomen two months after hysteroscopic removal of an intra-uterine device (IUD). The temperature was 38 degrees Celsius. At gynecological examination, tenderness of the right lower abdomen was noticed with a bulging swelling in the recto-uterine pouch. Laboratory examinations showed a leukocytosis (13.4x $10^9/l; n=7.5-10^9/l$), an elevated C-reactive protein (129 mg/l; n=1-10 mg/l), an elevated erythrocyte sedimentation rate (45mm; n=0-25 mm) and a microcytic anemia (Hb= 11.4 g/dl; n= 12-16,1 g/dl), indicating the presence of a chronic infection. An abdominal-pelvic ultrasonography showed an enlarged right adnex measuring 9 cm in diameter with a multilocular circumscribed fluid collection with a small echodens area and a larger transonic area with some free fluid in the recto-uterine pouch (figure 1 A, B).

Pelvic inflammatory disease with a tubo-ovarian abscess was suspected and antibiotic treatment consisting of doxycycline and metronidazol was administered. There
was no clinical improvement after two days of treatment, and subsequently vaginal puncture of the abscess was performed. Gram stains of the abscess material showed a few gram-positive, filamentous rods with possible branching, positive cocci in chains and many polymorphonuclear leukocytes. Based on the results of the gram stain, doxycycline was switched to penicillin to treat a possible actinomycosis.

After two days of incubation, smooth white colonies were observed of branching gram positive rods and small colourless colonies of gram positive cocci on the anaerobic media, Columbia agar with 5% sheep blood (bioMérieux Benelux B.V., Boxtel, the Netherlands). The gram positive rods were katalase and oxidase negative and biochemical evaluation on the basis of the API rapid ID 32 A (bioMérieux Benelux B.V., Boxtel, the Netherlands), identified it as Propionibacterium propionicum formerly known as Arachnia propionica. The gram positive cocci were identified as P. micra and a Peptostreptococcus species using the same API rapid ID 32 A (bioMérieux Benelux B.V., Boxtel, the Netherlands). The P. propionicum and Peptostreptococcus species were confirmed with 16S rRNA sequencing and both showed >99.9% homology with representatives in Genbank. Sequence analysis of the P. propionicum resulted in 1061 base pairs of the 5’end from the 16S rRNA gene which was given the GenBank accession number HQ413290. The highest homology was observed with the partial 16S rRNA sequence of P. propionicum with accession number AF285117.

Two days after the antibiotic switch to penicillin, no clinical improvement was observed. A computed tomography (CT)-scan showed a multilocular lesion of 9 cm in diameter in the recto-uterine pouch (figure 1 C, D, E).
An open laparoscopic procedure was performed which showed an enlarged right ovary of approximately 9 x 5 cm that was located behind the uterus and reached into the recto-uterine pouch. Several adhesions between the uterus and right adnex were laparoscopically removed. The fallopian tube was also enlarged and during manipulation pus was released from the right ovary. The left adnex was partly a vue also due to adhesions, but was considered normal. The abscess of the right ovary was drained and a drain was left in situ in the recto-uterine pouch.

Gram stains of the abscess material again showed rare gram-positive, filamentous rods with possible branching suggestive for actinomycosis, positive cocci in chains, and many polymorphonuclear leukocytes. Culture grew no aerobic organisms, but after two days there was growth of smooth white colonies of branching gram positive rods and small colourless colonies of gram positive cocci on the anaerobic media, Columbia agar with 5% sheep blood (bioMérieux Benelux B.V., Boxtel, the Netherlands). Results of identification by API rapid ID 32 A (bioMérieux Benelux B.V., Boxtel, the Netherlands) revealed *P. propionicum*, *P. micra* and *Peptostreptococcus* species.

Patient showed a rapid clinical improvement after the operation and was released from the hospital one week later. All the cultured isolates were penicillin susceptible, determined by penicillin E-test (AB Biodisk, Solna, Sweden). The Minimum Inhibitory Concentrations (MICs) for penicillin were 0.094 µg/ml for *P. propionicum*, 0.047 µg/ml for the *Peptostreptococcus* sp. and 0.012 µg/ml for *P. micra*. The patient was treated for 4 weeks with 24 million units of penicillin intravenously, after which the treatment was continued with amoxicillin for 6 months orally. Follow-up of the right adnex was performed with ultrasonography. After 6 months, the patient was well and ultrasonography and gynecologic investigation showed a normal aspect of both adnexa.
Discussion. We report a patient with an actinomycosis-like pelvic process originating from a tubo-ovarian abscess two months after hysteroscopic removal of an IUD that was in situ for approximately eight years. *P. propionicum*, *P. micra* and *Peptostreptococcus* species were found as causative agents. Of these three *P. propionicum* is the most pathogenic species, causing actinomycosis-like disease. *P. propionicum* has been isolated from patients with lacrimal canaliculitis, osteomyelitis, brain abscess, endodontic infections, chronic tympanomastoiditis, renal abscess, pulmonary abscess, cervico-facial actinomycosis (2,4,6,10,21,23,30,33), in one case of chronic granulomatous disease with multiple episodes of chest trauma and micro-abscesses and granulomatous inflammation in lung tissue (26), and in one case of disseminated actinomycosis with a hepatic abscess (14). This case report represents the first finding of *P. propionicum* in association with pelvic disease.

Propionibacteria belong to the family of *Propionibacteriaceae* and are pleomorphic, slow-growing, nonsporeforming, gram-positive, anaerobic bacteria. Species of Propionibacteria can be found as members of commensal flora, especially on the skin, in the mouth, and in the gastro-intestinal tract. They are generally nonpathogenic but become pathogenic in patients with implantation of foreign bodies, immunosuppression and after surgery or trauma. Four clinical relevant species of Propionibacteria have been recognized; *P. acnes*, *P. avidum*, *P. granulosum*, and *P. propionicum* (20).

*P. propionicum* was first described by Pine and Hardin in 1959. At that time the organism was identified as *Actinomyces israelii* (27). Subsequent work by Buchanan and Pine, suggested this organism to represent a new species, *Actinomyces propionicus*, on the basis of differences in metabolism, physiology, and cell wall composition (7). The organism was later reclassified again and placed in a new genus, Arachnia, under the name of *Arachnia propionica* (2). Further research later classified the organism in the genus of Propionibacteirium, under the name of *P. propionicum* (8,11,35).

*P. propionicum* differs from *Actinomyces* species by production of propionic acid from glucose and by the presence of diaminopimelic acid in the cell wall that resembles those of other *Propionibacterium* species (15,24). Differentiation between the two different species can also be performed with 16S rRNA sequencing (1,28).
*P. propionicum* and *A. israelii* are difficult to distinguish because both bacteria are microaerophilic to anaerobic and grow optimally under anaerobic conditions. The most pronounced difference of *P. propionicum* and *A. israelii* are difference in growth rate and colony morphology on Columbia agar with 5% sheep blood (bioMérieux Benelux B.V., Boxtel, the Netherlands) incubated anaerobically. *P. propionicum* grows after 18-24 hours of incubation as very little smooth white colonies with branches originating from a single point, after 7-14 days of incubation the colonies get bigger and then resemble the colonies of *A. israelii* with its rough breadcrumb or molar structure. In contrast to *P. propionicum*, *A. israelii* only starts to grow after 7-10 days of incubation and its colony morphology immediately looks like a molar tooth.

*P. micra* and *Peptostreptococcus* species were also found in the actinomycosis-like pelvic lesions due to *P. propionicum*. We consider their presence as “companion microbes”. These concomitant bacteria may serve as copathogens enhancing the progress of the disease. *Actinobacillus actinomycetemcomitans, Eikenella corrodens, Fusobacterium* spp., *Bacteroides* spp., *Capnocytophaga* spp., *Staphylococcus* spp., *Streptococcus* spp. and *Enterobacteriaceae* have been commonly isolated in various combinations depending on the site of infection (13,16,25,29,31,32). The co-isolation of *P. micra* and *Peptostreptococcus* sp. in this case of an actinomycosis-like disease due to *P. propionicum* therefore is not unusual. We consider *P. propionicum* to be the main pathogen, because in this case it is the only isolate that can cause an actinomycosis-like disease (2,4,6,10,14,21,23,26,30,33). The contribution to the pathogenesis of *P. micra* and *Peptostreptococcus* sp. however is difficult to assess, and it seems reasonable to consider them as being copathogens when designing the therapeutic regimen. Therefore it is important to perform the identification and to determine the antimicrobial susceptibility of the concomitant bacteria in case of actinomycosis or actinomycosis-like disease.

The first two cases of pelvic actinomycosis associated with a contraceptive device where reported by Brenner and Gehring in 1967 (5) and Henderson in 1973 who reported a tubo-ovarian abscess associated with an IUD (17). There are a several studies reporting that pelvic actinomycosis is associated with prolonged use of an IUD (3,18,19,34). In general the risk of acquiring pelvic actinomycosis is significantly higher in women who use an IUD for a prolonged period, especially ≥5 years (9,12).
To our knowledge, only one study reported two cases of actinomycosis in association with an IUD which were considered to be associated with *P. propionicum*. Diagnosis was confirmed by immunofluorescence but no positive cultures were obtained (22). A literature search with *Arachnia propionica* and *Actinomyces propionicus* causing actinomycosis associated with an IUD delivered no results. This case-report thus represents the first finding of *P. propionicum* causing pelvic actinomycosis associated with an IUD.

Reference List


