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Case Report

Three cases of ovarian actinomycosis with literature review

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Abstract: Background: Actinomycosis is an actinomycete infection, a rare zoonotic disease characterized by chronic suppurative inflammation and granulomatous inflammation. When injury occurs to the mucosa where parasites are present, actinomycetes can invade the mucosa. Widespread use of intrauterine devices (IUDs) has increased the incidence rate of pelvic actinomycosis among women. The clinical manifestation of ovarian actinomycosis is mostly a solid or cystic ovarian mass, which can invade surrounding tissue and may be accompanied by elevated levels of the tumor marker cancer antigen 125 (CA125). Therefore, ovarian actinomycosis is easily misdiagnosed as a malignant ovarian tumor. Case Description: Three cases of ovarian actinomycosis diagnosed in the Department of Pathology of the West China Second University Hospital of Sichuan University from January 2020 to March 2022 were retrospectively analyzed. All 3 patients had a history of IUD implantation for more than 10 years. All patients presented with abdominal masses and abdominal pain. One patient had weight loss, and 2 patients had elevated tumor marker CA125. Imaging results showed that all patients had ovarian space-occupying lesions involving the surrounding tissue; therefore, all patients were suspected to have malignant ovarian tumors before surgery. All 3 patients underwent surgical treatment. Specifically, 1 patient underwent bilateral salpingo-oophorectomy, and 2 patients underwent total hysterectomy and bilateral salpingo-oophorectomy. All patients received high-dose antibiotic treatment after surgery, and thus far, relapse has not been observed. Postoperative pathologicexamination showed purulent inflammation and sulfur granules, consistent with ovarian actinomycosis. Anaerobic culture was positive for 1 patient. Conclusions: Ovarian actinomycosis is closely related to long-term IUD implantation. The clinical manifestations and imaging features of this disease are not specific; therefore, preoperative diagnosis is difficult. The disease is easily misdiagnosed as ovarian cancer. Sulfur granules are signs of ovarian actinomycosis, and thus, those with this manifestation should be carefully screened by pathologic examination. Surgery combined with antibiotic treatment is effective for ovarian actinomycosis, resulting in a good prognosis.

Keywords: Ovarian actinomycosis, sulfur granules, intrauterine devices (IUDs)

Introduction

Actinomycosis is a rare disease caused by actinomycotic infection, characterized by chronic suppurative inflammation and granulomatous inflammation. Actinomyces is an opportunistic pathogen that exists in the human nasopharynx, gastrointestinal tract, and genitourinary system. When parasitic sites are damaged, actinomyces can invade mucous membranes and cause diseases [1]. Actinomycosis is most common in the head and neck (60%), pelvic cavity (20%), chest and abdomen, and rarely occurs in the ovaries [2]. The clinical manifestation of ovarian actinomycosis are usually solid or cystic masses of the ovary, which can invade surrounding tissues and may be accompanied by elevated tumor marker CA125. Misdiagnosis is very common because its clinical manifestations are not specific, coupled with low incidence. Actinomycosis may easily be misdiagnosed as a malignant tumor of the ovary or other suppurative infection [3]. Therefore, it is particularly important to understand this disease and explore specific preoperative, intraoperative, and postoperative diagnostic methods. Here, we report 3 cases of ovarian actinomycosis admitted to our hospital from 2020 to 2022.

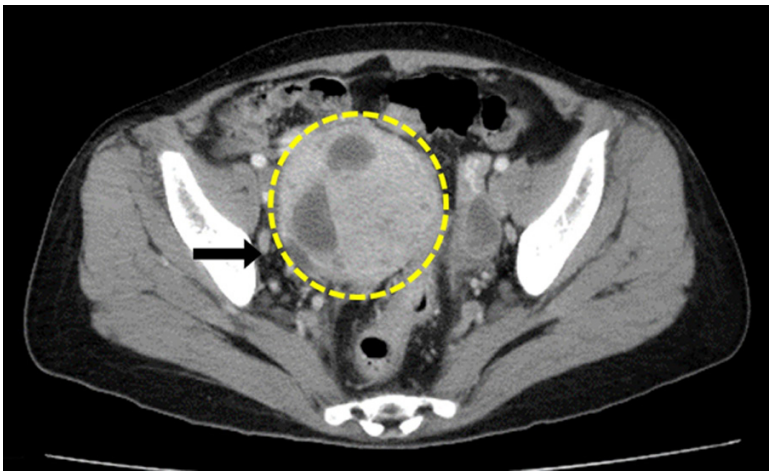

Figure 1. The cystic mass located in the right adnexal area with unequal-sized cystic lesions, "ovarian vascular pedicle sign" can be seen (CT scanning).

Case description

Case 1

A 48-year-old woman had idiopathic lower abdominal distension and discomfort for 4 months. She had a 10-year history of IUD implantation before the IUD was removed in 2018. The patient underwent laparoscopic myomectomy in 2019. At admission, tumor marker test results were unremarkable, and complete blood count (CBC) results showed increased C-reactive protein (CRP) and neutrophils (72.7%), a normal white blood cell count (6.7×10^9/L) and a normal CRP level. Ultrasound revealed a heterogeneous echogenic mass (7.6 cm × 6.3 cm × 4.9 cm), an anechoic mass (2.1 cm × 1.8 cm × 2.4 cm) in the right adnexal area, and a weak echogenic mass containing an irregular fluid-sonolucent area with no clear boundary to the posterior uterine wall. Hence, an ovarian malignancy was highly suspected before surgery. Bilateral salpingo-oophorectomy was performed. An enlarged right ovary was observed in the resected specimen, with a volume of approximately 7.2 cm × 6.5 cm × 5.0 cm. Multiple grayish-white nodular lesions were observed on the cut surface. Some of the nodular lesions had grayish-green purulent necrotic viscous fluid in their centers. Hemorrhage, cystic changes, and golden granules were observed in focal areas.

Case 2

A 47-year-old woman presented with idiopathic abdominal pain without metastatic pain for 1 month. She could palpate the abdominal mass on her own for the past 20 days. She lost approximately 5 kg of body weight in 1 month. An IUD was implanted in the patient 26 years prior. The tumor marker CA125 was elevated to 44.1 U/mL. CT revealed an ovarian space-occupying lesion invading the uterus and right ureter. A cystic mass located in the right adnexal area with unequal-sized cystic lesions, "ovarian vascular pedicle sign" was seen (**Figure 1**). The patient received transabdominal total hysterectomy, bilateral salpingo-oophorectomy, enterolysis, and ureterolysis. A 6-cm solid-cystic purulent mass with a foul smell was exposed in the right ovary during surgery. Pathologic examination of the specimen showed that the right ovary was enlarged (nodular shape), with a volume of 5.3 cm × 4.2 cm × 3.8 cm. The cut surface was cystic and solid, and the solid area was grayish-yellow with necrotic hemorrhage.

Case 3

A 50-year-old woman was admitted to the hospital due to abdominal distension for 20 days and an abdominal mass for 15 days. More than 20 years ago, an IUD was implanted in the patient. The tumor marker CA125 was elevated to 50.5 U/ml, and the proportion of neutrophils was increased to 77.8%. Ultrasound showed a heterogeneous weakly echogenic mass (approximately 4.3 cm × 3.9 cm × 5.5 cm) with ill-defined boundaries and irregular morphology in the rectouterine pouch. In the right adnexal area, a compartmentalized cystic mass (approximately 4.1 cm × 3.3 cm × 3.3 cm) was observed, with flocculent echoes inside, and the mass was not clearly demarcated from the weakly echogenic mass in the rectouterine pouch. The patient received transabdominal total hysterectomy, bilateral salpingo-oophorectomy, enterolysis, and bilateral ureterolysis. A mass (approximately 5 cm × 4 cm × 4 cm) with an uneven surface and a fragile texture was exposed during surgery. The mass patchily adhered to the tumors in the posterior uterine wall and the anterior wall of the rectum, and the left fallopian tube and the left ovary encased and fixed the mass at the bottom of

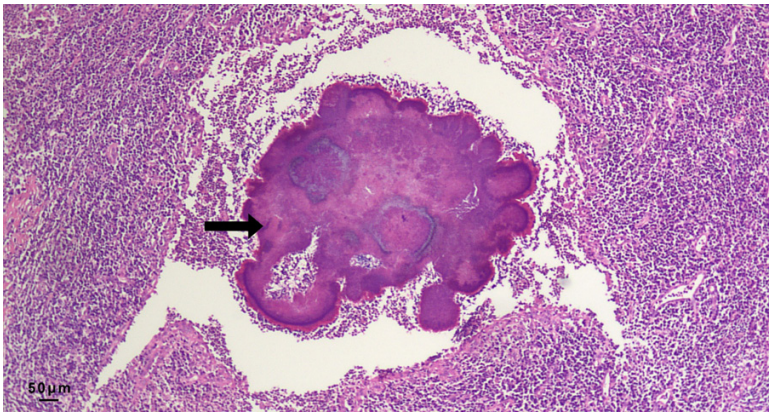

Figure 2. In a background of extensive suppurative inflammation, purple-blue mycelia were found in the center of the abscess, and the mycelia were arranged radially (Hematoxylin and eosin, ×200).

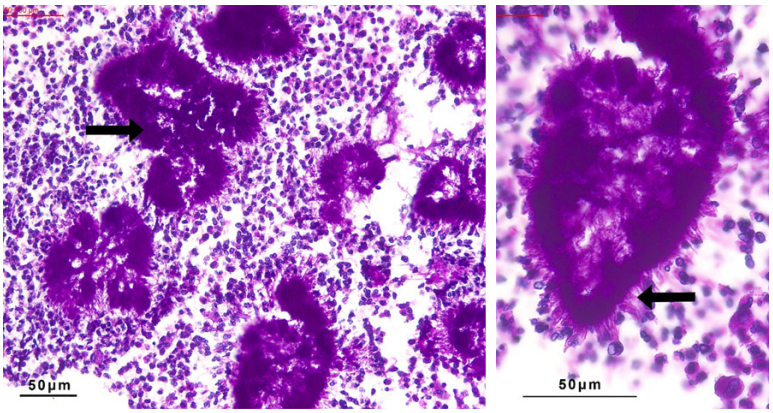

Figure 3. Periodic acid-Schiff staining was positive (left ×200, right ×400).

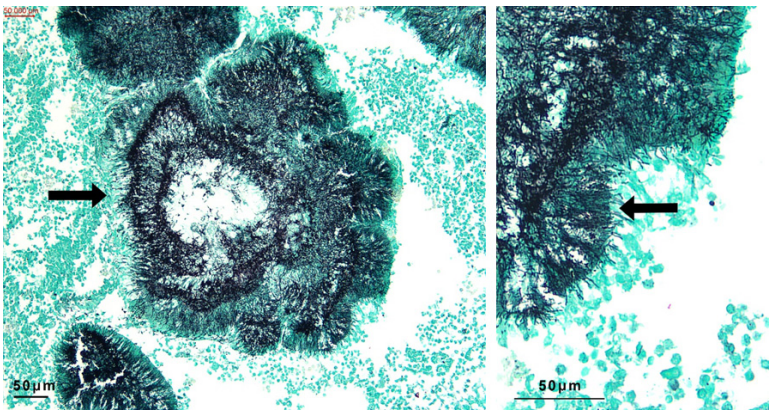

Figure 4. The mycelium is seen in a radial arrangement (methenamine silver staining, left ×100, right ×200).

the pelvis. The tumor in the anterior wall of the rectum (diameter of approximately 8 cm, with an uneven surface) involved approximately 10 cm of the middle and lower rectum and involved the uterus and local region of the posterior vaginal wall after penetrating the serosal surface.

The patients in cases 1 and 2 were sampled for anaerobic culture. The culture result was positive in case 2 and negative in case 1. Postoperative microscopic examination revealed extensive purulent inflammation and multiple abscess formation, histiocytosis, multinucleated giant cell reaction, fibrous tissue hyperplasia, and purplish-blue bacterial clumps with radial hyphae in the center of the abscess (**Figure 2**) in all three patients. Periodic acid-Schiff and methenamine silver staining were positive (**Figures 3**, **4**). Therefore, the patients were diagnosed with ovarian actinomycosis. All 3 patients received combined treatment with a sufficient amount of penicillin and metronidazole after surgery. All had a good prognosis and thus far no relapse.

Discussion

Ovarian actinomycosis is strongly related to the use of IUDs [4, 5]. The long-term stimulatory effect of the IUD on the lining leads to local damage of the endometrium, insufficient blood supply, and disorder of intrauterine microbiota, which provides the necessary conditions for the growth and spread of actinomyces. A long history of IUD use increases the risk of ovarian actinomycosis [2]. Some patients developed pelvic actinomycosis even 10 years after IUD removal [6]. In this study, all 3 patients had more than 10 years of IUD implantation history (26 years in Case 2). Ovarian actinomy-

cosis is generally manifested as solid or cystic solid masses of varying size in unilateral or bilateral ovaries, often involving the ipsilateral fallopian tube, and occasionally involving the bladder, intestine or other adjacent organs. Diseased tissue often adheres to the surrounding tissues, occasionally complicated by fistula and peritonitis. About 50% of cases of ovarian actinomycosis are accompanied by local lymphadenopathy. Some cases show focal invasion of surrounding tissue. Unfortunately, ovarian actinomycosis has no specific features by ultrasound, computerized tomography (CT), magnetic resonance imaging (MRI) or other imaging, so these cannot be used to distinguish ovarian actinomycosis from malignant tumor or other severe infections [7]. Patients with ovarian actinomycosis often present with abdominal pain, fever, weight loss, abnormal vaginal discharge and other symptoms. Patients often have high erythrocyte sedimentation rate, elevated C-reactive protein level, and some patients may have a slightly elevated CA125 level [8]. The course of the disease is a chronic history with slow onset, but some patients have severe complications such as septic shock, uterine perforation, intestinal perforation, or acute peritonitis. However, these clinical manifestations are not specific [9-11]. All three patients reported in this study were admitted to the hospital with suspected ovarian cancer based on imaging and clinical findings.

Ovarian actinomycosis is difficult to distinguish from ovarian malignant tumor, tuberculosis, and endometriosis due to unclear clinical manifestations and examination results [12-14]. This makes it difficult to diagnose preoperatively. One way of preoperative diagnosis is endometrial biopsy with culture to check whether there is actinomyces infection [1]. Although preoperative diagnosis is difficult, intraoperative frozen section diagnosis is of certain value. Although in many cases intraoperative frozen section cannot directly diagnose actinomycosis, it can at least eliminate the possibility of malignant tumor and reduce the risk of overtreatment. As for postoperative diagnosis, the traditional method is to perform bacterial culture. Actinomyces must be slowly cultured in a strict anaerobic environment of 37°C for at least 15-20 days, and actinomyces is highly sensitive to medium composition, sample type, previous antibiotic use, and microbial contamination. Therefore, the success rate of actinomyces culture is very low [15], which is also an important reason why microbial tests are rarely used for clinical diagnosis of actinomycosis. In this study, only case 1 underwent bacterial culture, of which the result was negative. In recent years, a number of new test methods have emerged, such as 16S rRNA sequencing, polymerase chain reaction (PCR), and fluorescence in situ hybridization (FISH), which have proven to be more accurate and faster in diagnosing actinomycosis than previous methods. 16S rRNA sequencing has 100% specificity and is used as a diagnostic standard for actinomycosis in some European countries. However, these diagnostic methods have not been widely used due to the high cost of equipment [16, 17].

Given the shortcomings and disadvantages of the aforementioned postoperative diagnostic methods, histopathologic examination is still the most commonly used diagnostic method for ovarian actinomycosis. The microscopic characteristics of ovarian actinomycosis are chronic granulomatous inflammation, chronic suppurative inflammation, structural destruction of the ovary, invasion of the lesion into the surrounding tissues, infiltration of neutrophils, lymphocytes, and plasma cells, and occasionally epithelioid cells, and multinucleated giant cells. Sulfur-containing granular abscess is sometimes visible to the naked eye. Sulfur granules are actinomycetes colonies, usually round or oval, in the shape of golden granules. Under the microscope, the sulfur particles are arranged radially, and the mycelium is intertwined with the basophilic rod-like end in a chrysanthemum shape. Sulfur particles are the characteristic finding to diagnose actinomycosis. Sulfur particles can be identified by methylamine silver staining, periodic acid-schiff (PAS) staining, Gram staining, acid-fast staining or other methods [16, 18, 19]. However, the diagnosis rate by histopathologic examination is less than 50% [15]. That means, about half of actinomycosis lacks pathologic evidence. Because of this, the pathologist needs to take more samples, more sections, more careful observation, or use special staining to improve the diagnostic rate. All 3 cases reported in this study were suspected to have ovarian malignancy before surgery. Intraoperative frozen section diagnosis showed suppurative inflam-

mation, no malignant tumor or sulfur granules. However, postoperative H&E staining and special staining detected specific sulfur particles which help to confirm the diagnosis.

Ovarian actinomycosis is mainly treated with a combination of surgery (salpingo-oophorectomy or hysterectomy and salpingo-oophorectomy) and antibiotic therapy. Surgery alone is not a cure. However, surgery can remove necrotic tissue, reduce the scope of lesions, help drainage, dissolve tissue adhesion and encapsulation, ameliorate hypoxia in the lesion and improve the effect of antibiotics [18]. Patients with ovarian actinomycetes have a good prognosis as long as they are treated early.

Conclusions

Ovarian actinomycosis is a rare infectious disease of the woman reproductive system. Because of nonspecific clinical and imaging findings, ovarian actinomycosis is easily misdiagnosed as ovarian cancer or other chronic infections. In view of the high correlation between ovarian actinomycosis and the history of IUD use, the possibility of ovarian actinomycosis should be routinely ruled out when a patient with a history of IUD use develops an ovarian space-occupying and infiltrating solid mass. This possibility should also be taken into account in pathologic examination, which requires careful microscopic observation for sulfur particles and bacterial clumps. Adequate sampling and continuous sectioning can increase the accuracy of diagnosis. In addition, more specific and reliable detection methods are needed.

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Disclosure of conflict of interest

None.

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