Case 1 – Disseminated abdominopelvic actinomycosis mimicking infiltrating peritoneal carcinomatosis: a misdiagnosis of advanced ovarian malignancy

C. Scaffa[1], N.S. Losito[2]

Abstract
In cases of abdominopelvic actinomycosis – a rare suppurative and/or pseudotumoral syndrome sometimes simulating a peritoneal carcinomatosis – the misdiagnosis of advanced ovarian cancer is possible. The differential diagnosis of actinomycosis is very difficult and achieved post-operatively in most cases, often after demolitive debulking surgery. We report a case of a 49-year-old woman, an intrauterine device (IUD) user for 8 years, with clinical findings, diagnostic imaging and CA125 levels (238.7 IU/mL) suggesting an advanced ovarian malignancy. The patient underwent surgical exploration showing a widespread bilateral adnexal tumour with disseminated and bowel-infiltrating peritoneal carcinomatosis, after which a complete cytoreduction was performed with a definitive pathological diagnosis of abdominopelvic granulomatous and suppurative infection by *Actinomyces israelii*, and no evidence of malignancy.

Key words: differential diagnosis, ovarian cancer, pelvic actinomycosis, peritoneal carcinomatosis

Introduction

In developed countries, actinomycosis is a relatively rare disease generally caused by *Actinomyces israelii*, although at least 39 species have been described [1]. Actinomyces are anaerobic Gram-positive organisms normally present in the oropharynx, gastrointestinal tract, bronchus and, sometimes, in the female genital tract. These saprophytes become pathogens in particular conditions (e.g. in mucosal lesions, in low oxygen level etc.) and, in these cases, their penetration through mucosal membranes causes an inflammatory response leading to a suppurative and/or pseudotumoral syndrome, sometime mimicking a malignancy [2].

Among women, abdominopelvic actinomycosis is a rare condition (about 3% of all actinomycosis) generally associated with long-term use of an intrauterine device (IUD), whereas the colonization of the female genital tract in non-users is very rare [3-6]. In particular, *Actinomyces israelii* infects 2–12% of IUD users (commonly with more than 4 years of use, 8 years on average), usually at the time of insertion or withdrawal and, more rarely, some years after removal [3, 7].

Abdominopelvic actinomycosis can affect uterus and adnexa, bowel, liver, pancreas, kidney, greater omentum, retroperitoneum and abdominal wall. Clinical symptoms are not specific, with a wide range of presentation from chronic pseudotumoral syndrome with risk of bowel obstruction, to acute abdomen symptoms for abscess rupture (abdominal pain, body weight loss, fever, vaginal discharge, anaemia and leucocytosis) [3] and, in the presence of infiltrating adnexal masses with peritoneal involvement, a differential diagnosis with advanced ovarian cancer is hard to achieve [8] (Table 1). Neither computed tomography (CT) or magnetic resonance imaging (MRI) can distinguish between neoplasm, endometriosis, peritonitis, bowel inflammatory disease, complicated appendicitis or tuberculosis. Pre-operative microbiological culture, if possible, is also often false negative (in 76% of cases) as Actinomyces are slow-growing, acid-resistant, filamentous bacteria requiring incubation of fresh material and one week to grow [2]. Therefore, excision biopsy is frequently needed and

[1]Gynecologic Oncology Surgery, Istituto Nazionale Tumori IRCCS "Fondazione G. Pascale", Naples, Italy.
[2]Surgical Pathology, Istituto Nazionale Tumori IRCCS "Fondazione G. Pascale", Naples, Italy.

Correspondence to: Dr. Cono Scaffa, Chirurgia Oncologica Ginecologica, Istituto Nazionale Tumori IRCCS "Fondazione G. Pascale", Via M. Semmola, 80131 Napoli, Italy.
Phone: +39 081 5903369 – Fax: +39 081 5903851
E-mail: c.scaffa@istitutotumori.na.it

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Table 1. Clinical differentiation between abdominopelvic actinomycosis and ovarian cancer (modified from [8])

Actinomycosis	Characteristic	Ovarian cancer
37 years	Median age	55 years
++	Abdominal pain	++
+	Weight loss	+
+	Abnormal vaginal bleeding	+
+	Anaemia	+
++	Vaginal discharge	+/–
++	Fever	–
++	Leucocytosis	+
–	Ascites	++
+/–	Elevation of CA125	++
Approx. 8 years	Duration of IUD use	No association

IUD, intrauterine device; ++, frequent; +, sometimes; –, uncommon

pathological examination shows characteristic sulphur grains (0.1-5 mm) containing filamentous bacterial colonies in half of cases [2].

For all of these reasons, the diagnosis of abdominopelvic actinomycosis before the surgical exploration or demolitive debulking is very difficult [3, 9]. In this regard, we present a case of abdominopelvic actinomycosis, with increased CA125 levels, simulating a disseminated peritoneal carcinomatosis with bowel infiltration, as an advanced ovarian cancer.

Case presentation

A 49-year-old woman, gravida 4 para 2, was referred to our department with suspected diagnosis of advanced ovarian cancer. She was eumenorrhoeic (without abnormal vaginal bleeding and/or discharge), with an IUD inserted 8 years earlier and just removed. The patient complained of abdominopelvic pain for two months; vaginal examination revealed a solid mass attached to the pelvis and congregating uterus and adnexa; no fever and weight loss were reported (Eastern Cooperative Oncology Group [ECOG] performance status 0). Laboratory tests showed anaemia (haemoglobin 11.2 g/dL), leucocytosis (11,990 cells/μL), thrombocytosis (695,000 platelets/μL), hyperfibrinogenaemia (6.2 g/L), hypoalbuminaemia (3.07 g/dL) and elevated CA125 levels (238.7 IU/mL).

Contrast-enhanced CT of thorax, abdomen and pelvis revealed a heterogeneous and infiltrating pelvic mass in the anatomical location of the right ovary (max diameter 5.2 cm), not dissociable from uterus and contiguous bowel; the left ovary also appeared enlarged and inhomogeneous, and was infiltrating the sigma wall; the uterus was inhomogeneous with enlarged cervix. Finally, multiple abdominopelvic peritoneal nodules were described (max diameter 3.2 cm) [Figure 1]. Contrast-enhanced diffusion-weighted imaging (DWI)-MRI confirmed the bilateral adnexal tumour with peritoneal nodules, in particular at the mesocolon and caecum, with peritoneal effusion.

All of these findings suggested the presence of a disseminated peritoneal carcinomatosis as advanced ovarian malignancy; therefore, an exploratory surgery was performed.

At laparotomy, there was a widespread bilateral adnexal tumour (max diameter 4 cm) with disseminated peritoneal carcinomatosis in the pelvis and the right paracolic gutter, and deep invasion of the uterus, lesser omentum, ileum and sigmoid colon; superficial nodules were also present on the transverse colon. Intraoperative frozen sections gave an uncertain result, nevertheless, demolition debulking surgery was performed for the high suspicion of advanced ovarian cancer (clinical-instrumental, serological and explorative suspicion) and the high risk of obstructive complications. To remove the lesions, therefore, a complete cytoreduction was undertaken: total hysterectomy, bilateral salpingo-oophorectomy, radical omentectomy, ileum and sigmoid colon resection with reanastomosis (with protective loop ileostomy), excision of transverse colon nodules, partial peritonectomy and appendectomy.

The definitive pathological examination showed, in all surgical specimens, a disseminated granulomatous and suppurative condition with the characteristic sulphur grains of *Actinomyces israelii* infection, and no evidence of malignancy (Figure 2).

The post-operative period was uneventful and the patient was discharged at postoperative day 5. After pathologi-

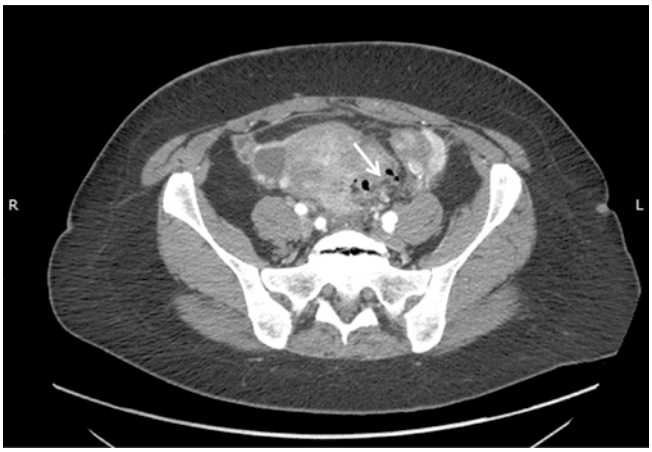

Fig. 1. Contrast-enhanced computed tomography (CT) scan showing a bilateral adnexal mass not dissociable from uterus and deeply infiltrating the sigmoid colon (arrow).

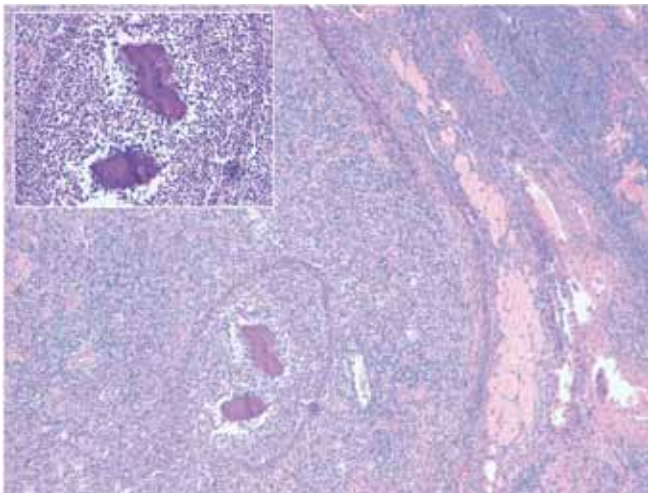

Fig. 2. Pathological examination showing suppurative and granulomatous infection by *Actinomyces israelii* in ovarian parenchyma (on the right, corpus albicans); in the inset, highlighting of characteristic sulphur grains surrounded by polymorphonuclear leucocytes (5xHPF H/E).

cal diagnosis, the patient received high-dose long-term penicillin therapy (first intravenous, then oral), and she is without any symptoms at the 6-month follow-up visit.

Conclusion

Abdominopelvic actinomycosis is a rare suppurative and/or pseudotumoral syndrome which could mimic an advanced ovarian cancer, with appearance of disseminated and infiltrating peritoneal carcinomatosis. Literature review shows that this misdiagnosis is not an exceptional condition because the primary diagnosis of actinomycosis is very difficult and achieved only post-operatively in most cases (in 83% of cases after a demolitive debulking surgery: hysterectomy, salpingo-oophorectomy, bowel resection etc.) [6-10].

The main challenge for the management of abdominopelvic actinomycosis is, therefore, to reach a diagnosis before surgery. This eventuality should be considered whenever examining long-term IUD users with abdominopelvic symptoms and infiltrating peritoneal lesions at imaging (eventually presenting with fever and leucocytosis) [10]. Nevertheless, in many cases, surgery is still necessary: 1) for differential diagnosis with a potential malignancy; 2) in the case of multiple and large lesions; and 3) in the case of the risk of pseudotumoral/obstructive and/or abscessual/perforative complications.

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Commentary

I read with interest the paper by Scaffa and Losito. In the present study, a case of intra-abdominal invasive actinomycosis, mimicking ovarian cancer and diffuse peritoneal carcinomatosis, was described. The authors provide further evidence suggesting that uncommon granulomatous/suppurative intra-abdominal infectious diseases may appear as gynaecological malignancies [1].

Accumulating data supported that intra-abdominal infections (e.g. tuberculosis, echinococcosis and actinomycosis) may be misdiagnosed as an invasive ovarian carcinoma [1, 2]. Differential diagnosis between these infections and malignancies are challenging and not always achievable pre- and intra-operatively [1, 2].

Interestingly, in the present case, histological analysis of frozen sections was unable to determine the

nature of the lesions. However, an important lesson learned from this experience is that histological diagnosis (at the time of frozen section or definitive histological examinations) should be available before carrying out demolition procedures, in order to exclude the presence of benign or non-gynaecological malignant disease (for which the value of extensive surgery remains unproved) [3].
We have to take into account that, although the occurrence of the aforementioned abdomino-pelvic infectious diseases is rare (especially in industrialized, non-endemic countries), their incidence is growing due to the increase in immigration flow from developing countries [1, 2]. Therefore, their knowledge and consequent awareness are paramount in the setting of gynaecologic oncology. Infectious diseases have to be considered in the diagnostic process in patients presenting with suspicious ovarian cancer, especially in women coming from endemic areas. Accurate anamnesis and frozen section analysis may reduce the rate of unnecessary demolition procedures, thus minimizing operative time and intra-and post-operative morbidity, as well as surgical costs. Further studies, aimed at providing more insight into the differential diagnosis between granulomatous invasive infections and intra-abdominal malignancies are warranted.

Francesco Raspagliesi
Gynecologic Oncology Surgery, Fondazione IRCCS,
Istituto Nazionale dei Tumori, Milano, Italy.
E-mail: francesco.raspagliesi@istitutotumori.mi.it

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