

## Case Report

# Successful pregnancy following conservative treatment of massive ascites associated with acute *Chlamydia trachomatis* peritonitis

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It is well known that *Chlamydia trachomatis* causes acute and chronic pelvic inflammatory disease including salpingitis. We describe a case of successful pregnancy following conservative treatment of massive ascites associated with acute *Chlamydia trachomatis* peritonitis. In this present case, we conservatively treated a woman with acute chlamydial salpingitis accompanied with marked ascites and an adnexal mass that simulated a malignant neoplasm. Elevated CA125 and CA19-9 also suggested a malignancy at the time of diagnosis, however following treatment they decreased to below the cut-off value, and

were useful in identifying the efficacy of medical treatment. The patient subsequently became pregnant after infertility treatment and underwent a normal vaginal delivery. We conclude that the possibility of *Chlamydia trachomatis* peritonitis should be considered when a patient presents with ascites and an adnexal mass in sexually active women. (Reprod Med Biol 2004; 3: 217–221)

**Key words:** ascites, CA125, CA19-9, *Chlamydia trachomatis*, pelvic inflammatory disease.

## INTRODUCTION

IT HAS BEEN shown that *Chlamydia trachomatis* (*C. trachomatis*) infection can lead to severe reproductive complications. *C. trachomatis* is an important organism in pelvic inflammatory disease (PID), with sequelae including infertility, ectopic pregnancy and chronic pelvic pain.<sup>1–3</sup> Up to two-thirds of tubal factor infertility cases and one-third of ectopic pregnancy cases may be attributed to *C. trachomatis* infection.<sup>4</sup> Although *C. trachomatis* infection in women is usually asymptomatic, patients with acute salpingitis present with acute lower abdominal pain, tenderness on bimanual pelvic examination and infrequently with a palpable mass. Perihepatitis and peritonitis may accompany acute salpingitis, but marked ascites is rarely seen.

In this case report, we describe a successful pregnancy following conservative treatment of massive ascites associated with acute *C. trachomatis* peritonitis.

## CASE REPORT

A 29-YEAR-OLD woman, gravida 0, para 0, presented on 6 March 2001 with symptoms of lower abdominal pain. Her past medical history was scoliosis, diagnosed at 10 years of age, which was observed. There was no familial disease and she had received no blood transfusions. She had considered the pain to be dysmenorrhea, and had taken a non-steroidal anti-inflammatory drug. The following day the pain had not improved, and as she developed a fever of over 38°C she consulted our hospital.

Physical examination revealed left lower abdominal tenderness. The laboratory data are shown in Table 1. Clinical laboratory abnormalities included the following: white blood cells (WBC) 17 700/μL, C-reactive protein (CRP) 16.4 mg/dL, CA125 167 U/mL, CA19-9 CA19-9 255 U/mL. Other data were normal, including liver blood chemistry and renal function tests. *C. trachomatis* antibody titers in the sera were also examined. *C. trachomatis* antibody testing was performed using enzyme-linked immunosorbent assay (peptide chlamydia immunoglobulin G [IgG] and immunoglobulin A; Labsystems Oy, Helsinki, Finland). Antibody titers above 0.90 were considered positive. However, this result did not appear immediately. Computed tomography of the

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**Table 1** Laboratory data (7 March 2001)

Peripheral blood	
RBC (/μL)	500 × 10 <sup>4</sup>
Ht (%)	43.1
Hemoglobin (g/dL)	14.5
WBC (/μL)	17 700
Plt (/μL)	19.9 × 10 <sup>4</sup>
Biochemical data	
TP (g/dL)	7.3
BUN (mg/dL)	16
Cr (mg/dL)	0.61
AST (mU/mL)	17
ALT (mU/mL)	13
γ-GT (mU/mL)	15
C-reactive protein (mg/mL)	16.4
Tumor markers	
CA125 (U/mL)	167 (<35)
CA19-9 (U/mL)	255 (<36)
AFP (ng/mL)	1 (<7)
<i>Chlamydia trachomatis</i> antibody titer (ELISA)	
Immunoglobulin G	4.20 (<0.9)
Immunoglobulin A	0.78 (<0.9)

AFP, α-fetoprotein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Cr, creatinine; ELISA, enzyme-linked immunosorbent assay; γ-GT, γ-glutamyltransferase; Ht, hematocrit; Plt, platelets; RBC, red blood cell; TP, total protein; WBC, white blood cell. Values in parenthesis are cut-off values.

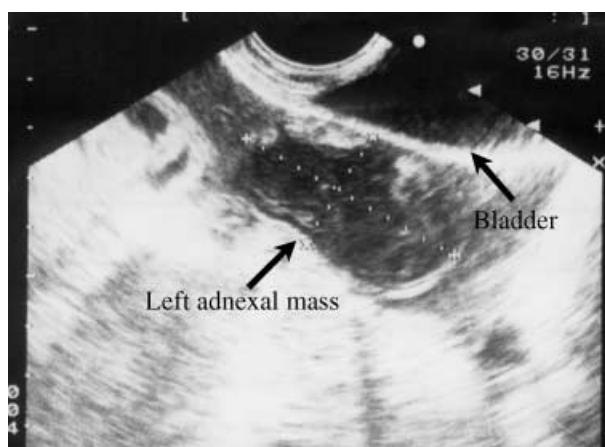
abdomen revealed massive ascites and an oval cystic mass measuring 4 × 3 cm in the left side of the uterus, which showed lower density compared with the uterus (Fig. 1).

As the physician diagnosed her with PID and suspected left ovarian tumor, the patient was admitted and a gynecologist was consulted. Transvaginal ultrasonography showed massive ascites and a left adnexal cystic mass with partial papillary growth similar to a malignant neoplasm (Fig. 2). We diagnosed her with PID and left adnexal tumor, which was not confirmed as malignant.

After hospitalization, the patient was immediately treated with cefazopran hydrochloride 2 g/day i.v. for 5 days, and levofloxacin 300 mg/day administered orally for 2 weeks to target the *C. trachomatis* infection. Follow-up examination showed a dramatic resolution of the pain and ascites. On 13 March 2001, the ascites was no longer detectable and we observed that the left adnexal mass did not seem to be derived from the ovary on transvaginal ultrasonography as the left ovary was adjacent. It then became clear that the *C. trachomatis* IgG titer was high, and we diagnosed left pyosalpinx.



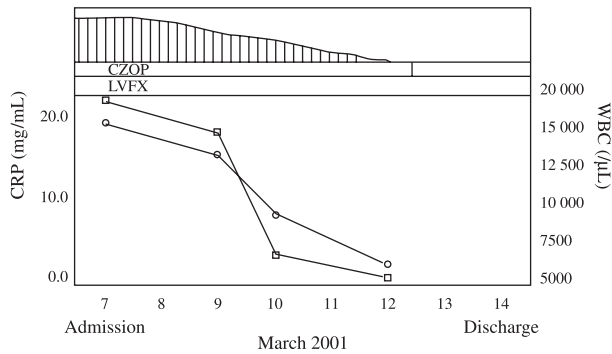
**Figure 1** Computed tomography reveals moderate ascites and a mass in the left side of the uterus, which showed low density compared with that of the uterus.



**Figure 2** Transvaginal ultrasonography showed ascites and a left adnexal cystic mass with partial papillary growth similar to a malignant neoplasm.

The clinical course of this patient is shown in Figure 3. The WBC count and the value of CRP had almost normalized by 12 March 2001, and she was discharged 2 days later.

On 4 April 2001, serum CA125 and CA19-9 were re-evaluated and they had decreased to 21 U/mL and 17 U/mL, respectively. However, left pyosalpinx was still detected on transvaginal ultrasonography. As she wanted to have a baby, we started an infertility evaluation. We were concerned about the recurrence of PID and decided to wait before confirming the tubal passage. Hormonal studies revealed that the pre-ovulatory estradiol value was low (114.1 pg/mL) and she was advised to start ovulation induction with cyclofenil. During the first treatment cycle, a pregnancy was established with timed intercourse at the time of ovulation



**Figure 3** After hospitalization, the patient was immediately treated with cefozopran hydrochloride (CZOP) 2 g/day i.v. for 5 days, and levofloxacin (LVFX) 300 mg/day administered orally for 2 weeks to target the *Chlamydia trachomatis* infection. Follow-up examination showed a dramatic resolution of the pain and ascites (▨). On 13 March 2001, the ascites was no longer detectable. The white blood cell (WBC) count (□) and the value of C-reactive protein (CRP) (○) had almost normalized by 12 March 2001. The patient was discharged on 14 March 2001.

from the right ovary. In February 2002, she underwent an uncomplicated vaginal delivery of a boy at 39 weeks' gestation. During pregnancy, and 8 months after delivery, the size of the left adnexal mass did not change remarkably.

## DISCUSSION

**P**ELVIC INFLAMMATORY DISEASE is a common and morbid intraperitoneal infection. The long-term implications of PID include higher rates of infertility, ectopic pregnancy and chronic pelvic pain. Chlamydial PID is the most preventable cause of infertility and adverse pregnancy outcome. After a single episode of PID, the relative risk for tubal factor infertility is approximately 10%. Each repeat episode of PID doubles the risk, so that it is approximately 20% after two episodes and almost 40% after three or more episodes.<sup>1-3</sup> Seroepidemiological studies suggest that chlamydial infection may account for a large population of cases of tubal factor infertility and ectopic pregnancy. These studies have demonstrated a strong link between serum antibodies to *C. trachomatis* and tubal factor infertility or ectopic pregnancy, both in women with or without a self-reported history of PID.<sup>5</sup>

The first study describing past chlamydial infection and tubal factor infertility was published in 1979.<sup>6</sup> In that study, the geometric mean antichlamydial antibody titer of patients with bilateral tubal obstruction

was significantly higher than that of patients with normal hysterosalpingograms (HSG). In a meta-analysis, the discriminative capacity of Chlamydia antibody titers in the diagnosis of any tubal pathology is comparable to that of HSG in the diagnosis of tubal occlusion.<sup>7</sup> However, many studies demonstrate a relationship between *C. trachomatis* antibody in the sera of infertile women and tubal subfertility.<sup>6,8-13</sup> High IgG antibody titers have been associated with inflammatory tubal damage, pelvic adhesions, and an increased relative risk for tubal pregnancy.<sup>14,15</sup> Using transvaginal hydrolaparoscopy (THL), our previous study demonstrated that *C. trachomatis* was highly associated with peritubal adhesion that was difficult to diagnose by HSG.<sup>16</sup> In another report, tubal occlusion diagnosed by THL in infertile women with past *C. trachomatis* infection was significantly associated with the *C. trachomatis* IgG antibody titer.<sup>17</sup> Laparotomy or laparoscopy was not performed in this case, however, as it was considered that tubal damage had occurred because of the high IgG antibody titer.

Hillis *et al.* reported that women with PID who delay seeking care are at increased risk for infertility and ectopic pregnancy.<sup>18</sup> Compared with women who sought care within the first 2 days of onset of pain, those who delayed 3-9 days were twice as likely to experience impaired fertility, and those who delayed for  $\geq 10$  days were 3.5-fold as likely to experience impaired fertility. Their data suggest that prompt evaluation and treatment of chlamydial PID can prevent these sequelae. In this present case, we suspected chlamydial infection, and immediately administered antibiotics sensitive to *C. trachomatis*. This treatment dramatically improved the peritonitis, and seemed to contribute avoiding severe damage to the right Fallopian tube. As the patient did not suffer tubal infertility, a pregnancy was established with timed intercourse at the time of ovulation from the right ovary.

As far as we know, ascites as a predominant feature of *C. trachomatis* infection has been described in 11 patients with chlamydial perihepatitis and/or salpingitis.<sup>19-26</sup> Exudative ascites with high-protein content is a common finding and the major cell components are lymphocytes, regardless of the number of leukocytes. The ascites had regressed before paracentesis in this present case, and we could not analyze the biological and cytologic features of the ascitic fluid.

Few patients with chlamydial infection have presented with both an adnexal mass and marked ascites.<sup>19,26,27</sup> In all three cases, chlamydial infection was not initially suspected. Laparotomy was performed in two cases, and pathological reports of resected tubes

suggested chlamydial infection.<sup>19,26</sup> In the remaining case, spontaneous regression of ascites was achieved and chlamydial infection was diagnosed retrospectively.<sup>27</sup>

In this present case, the tumor markers such as CA125 and CA19-9 in the sera were elevated. CA125 was initially thought to be specific for ovarian malignancies. Subsequently, it was found to be present in a variety of benign conditions, including pregnancy, pelvic inflammatory disease, endometriosis, tuberculosis and cirrhosis of the liver.<sup>28</sup> Moore and Soper reported that the degree of elevation of serum CA125 levels correlated with the severity of tubal inflammation noted at laparoscopy.<sup>29</sup> However, there was no report of elevated serum CA19-9 because of infection in the female upper genital tract. Ito and Gejyo described three possible mechanisms of elevated serum CA19-9 level in benign disease.<sup>30</sup> The inflammation or proliferation of non-cancerous tissues excretes CA19-9 in some benign diseases. Obstruction of the CA19-9 discharge pathway elevates the serum level. In addition, dysfunction of the organs that metabolize CA19-9 results in a high serum level. Many immunohistochemical studies have shown CA19-9 expression in various normal tissues, including the pancreas, gallbladder, stomach, colon, bronchial tree, salivary glands, prostate and endometrium.<sup>31,32</sup> We considered that the higher serum CA19-9 was probably due to hypersecretion from epithelial cells, including endometrium induced with inflammation.

Marked ascites, adnexal mass and elevation of these markers suggested the existence of malignancy at the time of diagnosis. We considered that PID was basically present, and the prompt treatment showed dramatic resolution of ascites and revealed that the ascites was absolutely derived from PID. To the contrary, these markers were useful to evaluate the efficacy of treatment for PID.

We conclude that *C. trachomatis* peritonitis should be considered when a patient presents with ascites and an adnexal mass in sexually active women.

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