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Abstract

Right pleural effusion was diagnosed in a 36-year-old woman with right upper quadrant pain and fever. Enhanced pelvic computed tomography performed because of irregular genital bleeding revealed the pelvic inflammatory disease. Upon further questioning, the patient confirmed that she had recently undergone therapy for *Chlamydia trachomatis* infection. Therefore she was given an injection of tetracycline because we suspected Fitz-Hugh-Curtis syndrome (FHCS), a pelvic inflammatory disease characterized by perihepatitis associated with chlamydial infection. A remarkable clinical response to antibiotics was noted. The right upper quadrant pain was due to perihepatitis, and the final diagnosis was FHCS. Right pleural effusion may be caused by inflammation of the diaphragm associated with perihepatitis. Once chlamydial infection reaches the subphrenic liver, conditions in the closed space between the liver and diaphragm due to inflammatory adhesion may be conducive to chlamydial proliferation. The possibility of FHCS should be considered in patients and carefully distinguished from other abdominal diseases.

KEYWORDS: perihepatitis, right pleural effusion, Fitz-Hugh-Curtis syndrome, chlamydial infection, pelvic inflammatory disease

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Case Report

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Right pleural effusion was diagnosed in a 36-year-old woman with right upper quadrant pain and fever. Enhanced pelvic computed tomography performed because of irregular genital bleeding revealed the pelvic inflammatory disease. Upon further questioning, the patient confirmed that she had recently undergone therapy for *Chlamydia trachomatis* infection. Therefore she was given an injection of tetracycline because we suspected Fitz-Hugh-Curtis syndrome (FHCS), a pelvic inflammatory disease characterized by perihepatitis associated with chlamydial infection. A remarkable clinical response to antibiotics was noted. The right upper quadrant pain was due to perihepatitis, and the final diagnosis was FHCS. Right pleural effusion may be caused by inflammation of the diaphragm associated with perihepatitis. Once chlamydial infection reaches the subphrenic liver, conditions in the closed space between the liver and diaphragm due to inflammatory adhesion may be conducive to chlamydial proliferation. The possibility of FHCS should be considered in patients and carefully distinguished from other abdominal diseases.

Key words: perihepatitis, right pleural effusion, Fitz-Hugh-Curtis syndrome, chlamydial infection, pelvic inflammatory disease

The incidence of *Chlamydia trachomatis* (*C. trachomatis*) infection in sexually active women has gradually increased. The chief symptoms are gynecologic in nature, but a few of these patients suffer sudden onset of pain in the right upper quadrant and epigastralgia [1–3]. In the past, laparotomy was performed in some patients with intensive abdominal tenderness [4, 5]. Fitz-Hugh-Curtis syn-

drome (FHCS) is believed to arise directly from the spread of pelvic inflammation associated with sexually transmitted disease. However, no distinct pathway from the pelvic space to the perihepatic region has been reported. Other pathways are suspected, such as lymphatic or vascular pathways, from the rectal mucosa because gonococcal perihepatitis has been reported in a homosexual man [6–8]. It is also unclear why the inflammation occurs only around the liver. We report herein a case of FHCS with right pleural effusion in a young woman and review some of the literature on FHCS [9–11].

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Case Report

The patient was a 36-year-old woman who complained of right upper quadrant pain and fever (40 °C), and was treated by analgetic injection by a local physician. Two days later, she visited the emergency room of our hospital because the abdominal pain had not improved. Physical examination upon admission revealed no abnormalities, except marked tenderness from the right upper quadrant to the dorsum and abdominal surgery scars due to an appendectomy. No neurological signs were observed. The patient underwent X-P radiography study because of a 3-day history of constipation, but chest and abdominal X-P ray findings were almost normal, except for slight dilatation of the large intestine due to gas (Fig. 1A, B), and there was no evidence of ileus. However, physical examination revealed marked tenderness from the right upper quadrant to the dorsum. Abdominal ultrasonography (US) showed no evidence of cholecystitis, choledocholithiasis, or renal stone, but indicated minor right pleural effusion. The patient was admitted to our hospital, to the Division of Internal Medicine, for investigation of the right upper quadrant pain. Her history included appendicitis at age 26; there had been no pregnancy or child

birth. Both her mother and sister had suffered from a ureteral stone. Laboratory data upon admission are shown in Table 1.

Clinical course after admission. Our staff urologist was consulted because of the patient's intensive right quadrant pain during palpation and blood in the urine (1+), but there was no clear evidence of a renal or ureteral stone. Endoscopic examination of the upper gastro-intestinal tract showed no evidence of an ulcerated lesion. The patient was treated with third-generation cephem antibiotics (CPR; Broact 2 g/day) because an infection of unknown focus was suspected. However, the tenderness and fever didn't improve with treatment. Non-contrast computed tomography (CT) of the chest revealed a small pleural effusion in the right thoracic cavity (indicated by an arrow in Fig. 2). Enhanced abdominal CT revealed localized hepatic capsular thickness (Fig. 3), which corresponded to the site of tenderness, suggesting perihepatitis, because the laboratory data of serum hepato-biliary systems were normal. The antibiotic was changed to penicillin (SBT/ABPC; Unasyn-S 6 g/day) by injection because early-stage pleuritis was suspected, but the clinical response to penicillin was not remarkable on the fifth day after admission. The patient underwent enhanced

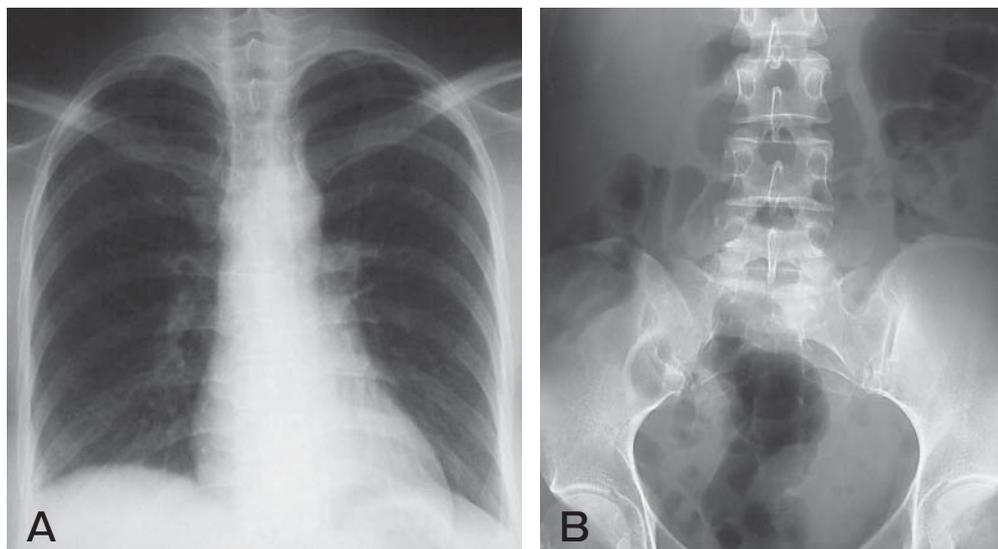


Fig. 1 Initial radiographic chest and abdominal findings.

A, Chest radiograph obtained with the patient in a standing position appears almost normal; **B**, Abdominal radiograph obtained with the patient in the supine position shows gas in the large intestine and no urinary tract stones.

Table 1 Laboratory data on admission.

Peripheral blood		Blood chemistry		Feces and urine chemistry	
WBC	9,500/ul	T-P	7.1 g/dl	Urinal blood	1 +
neutro	82.20%	Alb	3.9 g/dl	Urinal protein	(-)
eosi	0.20%	Glu	87 mg/dl	Urinal glucose	(-)
baso	0.10%	BUN	5.0 mg/dl	Occult blood	(-)
mono	6.50%	Cre	0.56 ng/ml		
Lymph	11%	Na	139 mEq/l	Virus markers	
RBC	$368 \times 10^4/\mu\text{l}$	Cl	104 mEq/l	HBs Ag	(-)
Hb	12.0 g/dl	K	3.3 mEq/l	HCV Ab	(-)
Ht	35.00%	Ca	8.9 mg/dl		
PLT	$20.4 \times 10^4/\mu\text{l}$	γ -GTP	18 IU/l	Syphilis qualitative	
		T-Bil	0.56 mg/dl	RPR	(-)
		GOT	13 U/l	TPHA	(-)
		GPT	10 U/l		
		LDH	142 U/l	Candida Ag	4 (2 <)
		Al-P	118 U/l		
		s-AMY	56 U/l	Anti- <i>C. trachomatis</i> IgG EIA	(+) 10.01
		CK	54 U/l	Anti- <i>C. trachomatis</i> IgA EIA	(-) 0.37
		T-Cho	120 mg/dl	Anti- <i>C. trachoma</i> IgM EIA	(-)
		CRP	7.26 mg/dl	PCR (<i>C. trachomatis</i>)	(+)
		ADA	28.6 IU/L		
				Tuberculosis reaction	9 × 9 mm
		Tumor marker			
		CA125	131 ng/ml		

ADA, adenosine deaminase; APTT, activated partial thromboplastin time; CA125, carbohydrate antigen 125; EIA, enzyme immunoassay; INR, international normalized ratio; PCR, polymerase chain reaction; PT, Prothrombin time; RPR, rapid plasma reagin; s, second; TPHA, Treponema pallidum hemagglutination test.

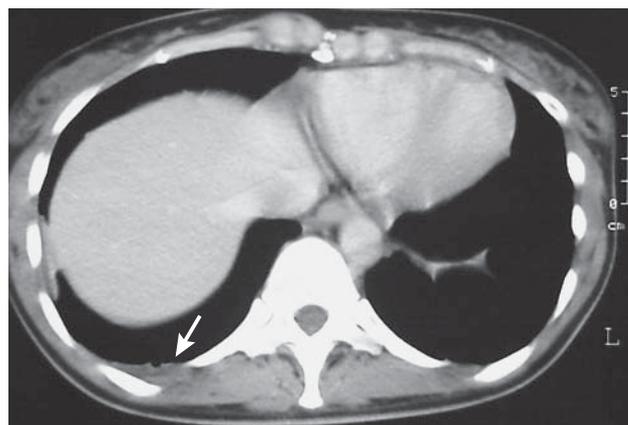


Fig. 2 Non-contrast chest computed tomography scan image reveals a small pleural effusion in the right thoracic cavity (arrow).

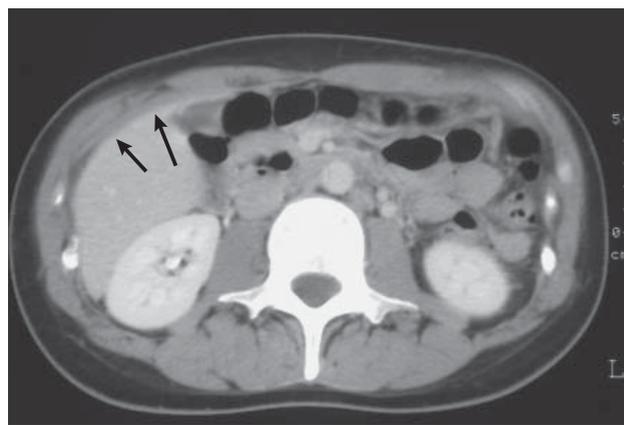


Fig. 3 Contrast-enhanced computed tomography scan image of the abdomen shows thickening of the hepatic surface (arrows).

pelvic CT because of irregular genital bleeding and lower abdominal pain. Enlargement of the uterus, serous fluid in the pouch of Douglas, bilateral swelling and dilatation of the adnexa and thickening of the peritoneum were revealed, indicating pelvic inflam-

matory disease (Fig. 4). We interviewed the patient again and confirmed that she had recently received medication from a gynecologist near her home for *C. trachomatis* infection, but she had not continued the treatment. Therefore, the gynecologist in our hospi-

tal was consulted. Gynecologic examination revealed that the uterus and ovaries were slightly enlarged, and there was marked tenderness. The uterine cervical secretions were mucinous, yellowish and odorous, strongly suggesting uterine cervicitis, endometritis or adnexitis. The laboratory data of the peripheral blood showed the specific IgA antibody against *C. trachomatis* was negative, but the titer of specific IgG antibody was high. Taken together with the result of the polymerase chain reaction (PCR) assay that revealed *C. trachomatis* in the uterine cervical secretion, these data suggested a past history of *C. trachomatis* infection and also a recent infection [12–13]. Also the localized hepatic capsular thickness, an elevated C-reactive protein level and white blood cell count, the inefficiency of cephem antibiotics, the history of *C. trachomatis* infection, and clinical symptoms such as the upper quadrant pain were typical findings of FHCS. Also, cytological findings in the uterine cervix were not specific. The nature of the treatment provided by the gynecologist near the patient's home was not precisely known. Tetracycline (MINO; Minomycin 200 mg/day) for the therapeutic assessment was injected according to the recommendation of our staff gynecologist. Laboratory serum data on the tenth day after admission showed that the white blood cell count had improved to 3,900/ μ l and the C-reactive protein level to 0.54 mg/dl. The results of Gram staining and *Neisseria gonorrhoea* culture of a cervical fluid were negative. Thickening of the hepatic surface and right-sided pleural effusion had disappeared (data not shown). The observation

of perihepatitis caused by *C. trachomatis* made it possible to diagnose FHCS without any aggressive examinations in this case. The patient was discharged on the twelfth day and contributed to receive medication as an outpatient.

Discussion

FHCS has generally been described as an unusual complication of pelvic inflammatory disease related to *C. trachomatis* infection; it is characterized by right upper quadrant pain due to perihepatitis associated with adhesions between the abdominal wall, liver surface and diaphragm [14, 15]. It was originally described in 1930 by Curtis, a gynecologist, who reported "violin string" adhesion between the anterior surface of the liver and anterior abdominal wall in association with gonococcal salpingitis. In 1934, Fitz-Hugh described 3 cases of intensive right upper quadrant peritonitis or perihepatitis, also associated with gonococcal salpingitis [5, 6]. In the present case, other pelvic inflammatory diseases that should be distinguished from *C. trachomatis* infection were as follows [16–17]: the infectious diseases such as gonorrhea and genital tuberculosis, infectious endometriosis, torsion of the ovarian tumor or cyst, severe appendicitis and ectopic pregnancy. Gonorrhea was excluded because *Neisseria gonorrhoea* were unidentified in the uterine cervical secretion and the tuberculin reaction was negative. An infectious endometriosis was excluded because no findings of chocolate cyst or lower abdominal pain associated with menstruation were observed. Also, no signs to suggest torsion of an ovarian tumor were observed. Severe appendicitis was excluded because of the patient's past history of an appendectomy, and there were no possibilities of ectopic pregnancy because pregnancy reaction was negative.

In FHCS, fibrotic-appearing inflammatory tissue between the hepatic surface and peritoneum is a cause of adhesion and leads to abdominal pain. In previous cases, invasive examinations such as laparoscopy were required for the definitive diagnosis of FHCS because it was necessary to find "violin string" adhesions between the abdominal wall and liver capsule and to isolate *C. trachomatis* from the liver capsule [18–20]. However, laparoscopic examination for the diagnosis of FHCS in young women is not

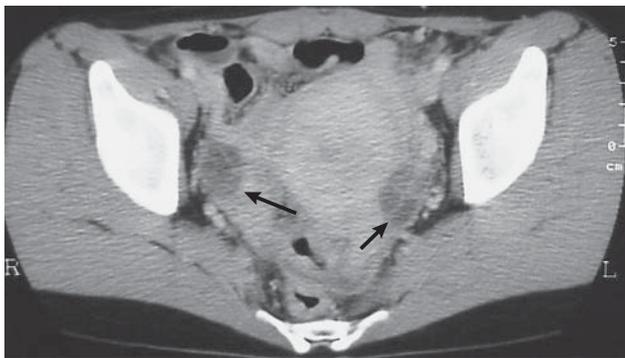


Fig. 4 Contrast-enhanced computed tomography scan image of the pelvis shows enlargement of the uterus and bilateral swelling of the fallopian tubes (arrows).

always recommended because of the risk of general anesthesia and the appearance of a scar. In our case, it was possible to diagnose FHCS on the basis of the clinical data and abdominal CT findings. In the present case, the possibility of recent *C. trachomatis* infection had to be considered even though specific IgA antibody against *C. trachomatis* was negative, because the PCR assay of *C. trachomatis* in the uterine cervical secretion was positive. Fibrous inflammatory adhesion of the liver to the diaphragm can be relieved by quick therapy against *C. trachomatis* infection. In our patient, however, incomplete therapy by not continuing the treatment against *C. trachomatis* by a gynecologist near her home caused progressive perihepatitis leading to FHCS.

Yoshitake *et al.* reported pathologic findings of perihepatitis in FHCS vary between the acute and chronic clinical phases [3]. Mild exudative inflammation of the hepatic capsule is characteristic of the acute clinical phase; capsular congestion, punctuate hemorrhage and fibrinous exudation are associated with the increased blood flow due to acute perihepatitis. In contrast, a fibrous adhesion between the anterior surface of the liver and the abdominal wall, with what is known as a violin-string appearance, develops in the chronic phase [3]. In our case, the hepatic capsular thickness in the enhanced CT examination was revealed, indicating the capillary proliferation due to an acute inflammation. Although there are some reports of ascites and peritonitis associated with FHCS, the chest CT scan in our case revealed a small pleural effusion in the right thoracic cavity, probably caused by inflammation of the diaphragm associated with perihepatitis, because there were no apparent findings of pneumonia or pleuritis diagnosed by the imagings such as chest CT scan and X-P or indicated by physical signs such as cough or sputum. There were also no findings to suggest pleural effusion such as pulmonary congestion, congenital heart failure or low nutrition. Together with the finding of perihepatitis in the CT scan, the pleural effusion was localized on the right side but not in the left side, suggesting that the right pleural effusion was caused by perihepatitis and inflammation of the diaphragm. The effusion was not of sufficient size to warrant examination for the presence of micro organisms. A slightly elevated concentration of tumor marker CA125 may be caused by pleural effusion.

In a search of the PUBMED database, we found only 1 case reported outside Japan that showed pleural effusion [7]. However, the mechanism of pleural effusion in that case was not described in detail. There were no documented case reports in which right pleural effusion was confirmed by CT as in our case. Enhanced CT provided us with a useful clue for the diagnosis of FHCS. The mechanism by which the inflammation occurs only around the liver has never been described in detail, but once a chlamydial infection has reached the subphrenic liver conditions in the closed space between the liver and diaphragm made by the fibrous and inflammatory adhesion, conditions may be conducive to chlamydial proliferation. Although FHCS is a gynecological disease, the patient may first consult a physician and undergo a standard medical examination. A general physician should keep the possibility of FHCS in mind when examining patients with right upper quadrant pain, because the incidence of FHCS will probably increase in the future.

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