Clinical Features of Fitz-Hugh-Curtis Syndrome in the Emergency Department

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Purpose: Fitz-Hugh-Curtis Syndrome (FHCS) is a clinical entity characterized by inflammation of the liver capsule associated with genital tract infection. The aim of this study is to provide physicians with clinical suggestions for diagnostic approaches based on a series of patients who were diagnosed with FHCS. Materials and Methods: We conducted a retrospective study of patients who were diagnosed with FHCS after presenting to the emergency department (ED). The symptoms, physical examinations, laboratory findings, radiological findings, and progress of the patients were reviewed. Results: During the four-year study period, a total of 82 female patients received a final diagnosis of FHCS in the ED. Chlamydia trachomatis was identified as a pathogen in 89% of the patients. Their clinical characteristics and laboratory findings were described. Fifty-two patients (63.4%) were admitted to the hospital. All of the admitted patients improved after treatment combining antibiotic therapy with conservative care. Conclusion: FHCS should be considered as a differential diagnosis for female patients of childbearing age with right upper abdominal pain. Timely diagnosis using biphasic computed tomography (CT) with arterial and portal phases may help ensure adequate medical treatment as well as avoid invasive procedures.

Key Words: Pelvic inflammatory disease, abdominal pain, computed tomography

INTRODUCTION

Fitz-Hugh-Curtis Syndrome (FHCS) is characterized by inflammation of the perihpatic capsules associated with pelvic inflammation, without involvement of the hepatic parenchyma.1,2 A definitive diagnosis can be made based on detection of violin string-like adhesions or identification of causative organisms in hepatic capsular lesion specimens, which requires laparoscopy or laparotomy.3,4 The use of noninvasive diagnostic procedures is desirable, considering that FHCS is a benign condition that can be completely cured by the oral administration of appropriate antibiotics.4

As the symptoms or physical findings of FHCS mimic other diseases, such as acute cholecystitis, a high index of suspicion is significant.5,6 Increased enhancement along the hepatic surface on computed tomography (CT) may suggest the diag-
nagnosis of FHCS. Recent studies demonstrated that dynamic abdominal CT, including an arterial phase scan, can significantly improve the depiction of perihepatic enhancement. Using this technique, the sensitivity and the accuracy of diagnosing FHCS can be markedly increased during the evaluation of female patients with acute right upper quadrant (RUQ) pain or suspicions of FHCS.

The aim of this study was to provide physicians with clinical suggestions for diagnostic approaches based on an analysis of patients who were diagnosed with FHCS at our institution over a four-year period.

MATERIALS AND METHODS

This was a retrospective study of patients diagnosed with FHCS after presenting to the emergency department (ED). The study was reviewed and approved by the institutional review board, and was conducted in an urban teaching hospital ED with an annual load of 40000 patients. All ED records of patients with a final diagnosis of FHCS from August 1, 2004 to July 31, 2008 were retrieved using the hospital information database and the Picture Archiving and Communications System. The exclusion criteria were: 1) patients with the diagnosis of FHCS without undergoing CT; 2) patients with increased enhancement in the arterial phase of CT, along with abnormal findings of the liver parenchyma, gall bladder and biliary system or any other accompanying diseases mimicking FHCS, as interpreted by the attending radiologist; 3) patients with only monophasic (portal phase set only) images without an arterial phase set; 4) patients who underwent surgery on the abdomen within six months; and 5) pediatric (<15 years) patients.

All CT scans were obtained with a multidetector CT (Sensation 16; Siemens Medical System, Forchheim, Germany) using the bolus tracking method. Precontrast CT scans were performed before contrast media injection. The contrast media (2 mL/kg iopromide 300 mgI/mL, Ultravist 300, Schering, Anseong, Korea) was given by a power injector (EnVision CT Injector, Medrad, Pittsburgh, PA, USA) at a rate of 3 mL/s through a 20-gauge catheter.

Late arterial phase images were obtained with a scan delay of 15 seconds after the Hounsfield unit of the abdominal aorta reached 100 HU. The portal venous phase was obtained 20 seconds after the end of the arterial phase. All obtained CT images were evaluated by the attending radiologists without any attempt of blinding. Testing of the collected endocervical swab specimens for detection of C. trachomatis was performed using the polymerase chain reaction (PCR) nucleic acid amplification technique and nucleic acid hybridization by the Roche COBAS® Amplicor™ (Roche Diagnostics, Mannheim, Germany).

We reviewed the symptoms, physical examinations, laboratory findings, radiological findings, progress, and prognoses recorded in medical records of the patients included in this study, all of whom were diagnosed clinically and radiologically.

All data are given as means (standard deviation) or medians [interquartile range (IQR)]. All statistical analyses were performed using SPSS software for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Characteristics of the patients

During the four-year study period, a total of 94 patients received a final diagnosis of FHCS in the ED. Among them, 11 patients were excluded according to the following criteria: concomitant abnormal pathology (n=9; 3 acute cystitis, 3 acute pyelonephritis, a renal stone, a gall stone, and a gall bladder polyp) and 3 patients who underwent CT without arterial phase. The 82 patients studied were all women, with a median (IQR) age of 27.5 (24.0-32.3) years (range 18 to 44). The last normal menstrual period occurred at a median of 15 (7.0-25.3) days prior to the ED visit. An intrauterine device was inserted prior to ED visit in 14 of 81 patients (17.3%). The percentage of patients who had a history of abortion were 63.4% (n=52), with a median of 1.0 (0.0-2.0) abortions. Past medical histories included pelvic inflammatory disease (PID) (n=9), appendectomy (n=6), tuberculosis (n=4), ectopic pregnancy (n=3), large loop excision of the transformation zone (n=3), cervical cancer (n=3), hepatitis (n=2), pyelonephritis (n=1), vaginitis (n=1), and ovarian cyst rupture (n=1). Eight (9.7%) patients had a history of treatment for PID within six months prior to presentation at the ED, with a median interval from PID treatment to the ED visit of 12.0 (7.0-18.5) days.

Patient symptoms and signs

The median interval from the development of the chief complaint to the ED visit was 3.0 (1.0-7.0) days. Chief complaints were: abdominal pain in 100% (n=82) of patients, fever in 14.6% (n=12), and urinary symptoms, such as
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Twenty of the 82 patients were lost to follow-up for reasons including discharged against medical advice (n=9), transfer to another hospital due to lack of beds in the ward (n=6), and change of medical facility due to location (n=5).

DISCUSSION

The incidence of FHCS has been reported to range from

Table 1. Clinical Manifestations of Abdominal Pain in Patients with Fitz-Hugh-Curtis Syndrome

| Chief complaints                  |       |
|----------------------------------|-------|
| RUQ pain                         | 70.7% (n=58/82) |
| Lower abdomen pain               | 6.1% (n=5/82) |
| Right flank pain                 | 4.9% (n=4/82) |
| Epigastric pain                  | 3.7% (n=3/82) |
| RLQ pain                         | 3.7% (n=3/82) |
| RUQ & RLQ pain                   | 3.7% (n=3/82) |
| RUQ & LUQ pain                   | 2.4% (n=2/82) |
| RUQ & LLQ pain                   | 1.2% (n=1/82) |
| LUQ pain                         | 1.2% (n=1/82) |
| Pleuritic pain                   | 1.2% (n=1/82) |
| Whole abdomen pain               | 1.2% (n=1/82) |

| Locations of abdominal pain      |       |
|----------------------------------|-------|
| RUQ only                         | 54.9% (n=45/82) |
| Whole abdomen                    | 2.4% (n=2/82) |
| Other area except RUQ            | 4.9% (n=4/82) |
| RUQ & low abdomen                | 32.9% (n=27/82) |
| RUQ & other abdomen              | 4.9% (n=4/82) |

| Locations of abdominal tenderness|       |
|----------------------------------|-------|
| RUQ only                         | 45.1% (n=37/82) |
| Whole abdomen                    | 1.2% (n=1/82) |
| Other area except RUQ            | 4.9% (n=4/82) |
| RUQ & low abdomen                | 43.9% (n=36/82) |
| RUQ & other abdomen              | 4.9% (n=4/82) |

RUQ, right upper quadrant; RLQ, right lower quadrant; LLQ, left lower quadrant; LUQ, left upper quadrant.

Fig. 1. Arterial phase scans revealed increased perihepatic enhancement (arrowheads) on the right and left lobes of the liver in this patient.
4% to 27% in patients with PID. In the present study, we identified 82 female patients diagnosed with FHCS during a four year period in an urban ED. The incidence of FHCS was 6.0% in adult (≥15 years) patients with PID in this study. The diagnosis rate of FHCS has increased perhaps due to the development of CT technology and availability. The pathogenesis of FHCS remains uncertain; however, several possible mechanisms have been proposed, including direct, hematogenous, and lymphatic spread. Exudative fluid can drain along the paracolic gutters from the pelvis to the diaphragm, causing perihepatitis followed by adhesions. However, because most patients show no evidence of generalized intra-abdominal infection between the pelvis and the liver, hematogenous or lymphatic spread are proposed. Rare cases of FHCS occurring in men also support these hypotheses.

An exaggerated immune response is also considered as a pathogenesis, because high titers of IgG antibody (1 : 512 to 1 : 1024) to C. trachomatis were found in all of the FHCS patients of a previous study. For many years, C. trachomatis was thought to be the sole causative agent of FHCS. Although the results of pelvic examination are subjective and somewhat dependent on a physician’s expertise, cervical motion tenderness and adnexal tenderness may suggest underlying PID. In this study, however, cervical motion tenderness and adnexal tenderness were reported as negative in 38% and 65% of patients, respectively. This lack of symptomatic presentation may be the result of visiting the ED during or after the recovery phase of PID. A previous study found that symptoms of acute and subacute PID such as fever, abdomen pain, and vaginal discharge are almost always present in patients with FHCS. However, in this study, only 15% of patients presented with a fever, and 41% of patients presented with vaginal discharge.

For many years, N. gonorrhoeae was thought to be the sole causative agent of FHCS. However, most experts now believe that C. trachomatis is the more common causative pathogen. In this study, using the PCR technique, C. trachomatis was found to be the main causative pathogen and was detected in 89% of patients. This was comparable to another study which reported that C. trachomatis was discovered in 82% of the FHCS patients. Culture studies are not useful in the ED because of time constraints and the need for special media for C. trachomatis. PCR for C. trachomatis may also not be available in most EDs, and the result of PCR cannot be confirmed on the spot. Accordingly, empirical antibiotics sensitive to C. trachomatis should be considered first in the ED.

Chlamydial infections may increase vulnerability to infection by other microbes, such as gram positive cocci and anaerobes. Therefore, even though the results of culture study are critical for diagnosing FHCS, cases in which expected pathogens are not identified still cannot be ruled out as indeed having the disease. Other causes such as genital

### Table 2. Results of Laboratory Tests of Patients with Fitz-Hugh-Curtis Syndrome

| Laboratory tests | Results | Range          | Normal range |
|------------------|---------|----------------|--------------|
| WBC counts (×10³/µL) (n=81/82) | 10404.0±2441.5 | 5290.0-16700.0 | 4.0-10.8 |
| Segment (%) (n=81/82)* | 75.7 (70.0-80.4) | 37.9-88.8 | 40.0-73.0 |
| CRP (mg/L) (n=74/82)* | 53.5 (22.4-91.2) | 0.8-260 | 0-5.3 |
| ESR (mm/hr) (n=67/82) | 63.8±31.9 | 2.0-158.1 | 0-20.0 |
| AST (IU/L) (n=80/82)* | 17.0 (15.0-21.0) | 11.0-319.0 | 13.0-37.0 |
| ALT (IU/L) (n=80/82)* | 11.0 (7.0-15.8) | 3.0-81.0 | 7.0-43.0 |
| Pregnancy test (n=82/82) | Negative (-); 100% (n=82) | Negative |
| C. trachomatis PCR (n=74/82) | Positive (+): 89.2% (n=66) | Negative |

PCR, polymerase chain reaction; SD, standard deviation; WBC, white blood cell; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; AST, Aspartate transaminase.

*Data are summarized as mean (SD) or median.
tuberculosis\textsuperscript{17} and laparoscopic surgery\textsuperscript{18} have recently been reported to be associated with FHCS.

We observed contrast enhancement of the hepatic capsules suggestive of perihepatitis on the arterial phase of dynamic CT scans from all patients of this study. Capsular enhancement on the arterial phase of CT imaging may reflect increased blood flow at the inflamed hepatic capsule, which is consistent with the laparoscopic findings of moist inflammation with injection of the vessels and exudate formations on the anterior surface of the liver. While enhancement on the portal or delayed phase images may reflect early events in capsular fibrosis, the most commonly enhanced area is the anterior surface of the right lobe, and the depth of enhancement is usually linear or less than 0.5 cm.\textsuperscript{9} The perihepatic enhancement can be shown as string, broadband, or mixed appearance.\textsuperscript{19} The inter-observer agreement for perihepatic enhancement is reported as substantial (weighted kappa=0.719) on the arterial phase image set.\textsuperscript{5}

However, perihepatic capsular enhancement can be shown not only in FHCS but also in various other conditions such as peritonitis, liver abscess, acute cholecystitis, and carcinomatosis. However, most of these can be differentiated correctly from FHCS using other CT image findings. For example, thickening of the gall bladder is observable in acute cholecystitis and the location of perihepatic capsular enhancement is adjacent to the inflamed gall bladder. Peritoneal carcinomatosis is frequently accompanied by nodular peritoneal thickening, while FHCS is usually seen as a thin enhancing line along the hepatic capsule. Severe fatty livers can also be differentiated from FHCS by reviewing non-contrast CT images which show pericapsular high attenuating lines.\textsuperscript{20} Therefore, it is important to search the entire abdominal CT image for other causes that can result in perihepatitis. It is helpful to also review the associated findings of PID, such as pelvic ascites, oophoritis, endometritis, cervicitis and tubo-ovarian abscess, for the diagnosis of FHCS.\textsuperscript{9} Perihepatitis is also a rarely diagnosed complication of systemic lupus erythematosus (SLE), requiring consideration in SLE patients with RUQ pain.\textsuperscript{21} First of all, the onset of symptoms is not always consistent with the onset of perihepatitis. Perihepatic capsular enhancement in the early phase may completely disappear in FHCS after improvement of symptoms with antibiotic treatment.\textsuperscript{8} Even though biphasic CT may not reveal intra-abdominal pathologic findings, such as perihepatitis, and pelvic inflammatory disease, FHCS in the early or recovery phase should be considered as a differential diagnosis for female patients of childbearing age with right upper abdominal pain.

Considering the risks of radiation exposure, the benefit of CT scan should be weighed against the potential risks. Abdominal CT scan of child bearing aged women should be performed cautiously after confirming the status of non-pregnancy. Ultrasonography may be a better approach to evaluate common etiologies such as acute cholecystitis in women with RUQ pain. There have been attempts to study the diagnosis of FHCS by ultrasonography; however this approach has limited utility even though FHCS can be diagnosed by detection of ascites and adhesions between the liver capsule and the abdominal wall.\textsuperscript{10,22} The detection of subtle thickening of the hepatic capsule is also subjective, and may be affected by the perceptions of the reviewer. In the present study, only one patient out of eight who underwent ultrasonography displayed subtle thickening of the hepatic capsule. Another 7 patients showed unremarkable findings. Magnetic resonance imaging may also be considered to detect perihepatitis, despite its high cost.\textsuperscript{19}

Antibiotic treatment is usually recommended for the treatment of FHCS. Intravenous or oral regimens can be used according to the guidelines for treating PID.\textsuperscript{10} In the present study, patients were treated with various combinations of antibiotics, including cephalosporin, aminoglycoside, metronidazole, and macrolides. Interestingly, clinical improvement was observed in patients treated with empirical antibiotics which are not effective for chlamydial infection. In the present study, macrolide was prescribed after several days to patients whose PCR results indicated chlamydial infection. Yang, et al.\textsuperscript{23} postulated that either chlamydial infection often resolves by itself or that it could not be the causative pathogen in FHCS, with other unknown microbes, such as several types of gram positive cocci or anaerobes, that cause pelvic inflammatory disease the more likely causes.

This study has several limitations. First, as a retrospective study, it may be affected by selection bias. Clinically diagnosed PID patients who underwent abdominal CT to evaluate abdominal pain were enrolled in this study. Second, even though laparoscopic examination is known as the gold standard for diagnosis of FHCS,\textsuperscript{3,4} this study was conducted for patients who were confirmed by clinical features, disease courses and typical findings of FHCS on biphasic CT. So, none of the patients underwent laparoscopic examination to confirm FHCS, nor was a follow-up CT scan performed to evaluate the correlation between clinical im-
provement and the absence of perihepatitis.

In conclusion, FHCS should be considered as a differential diagnosis for female patients of childbearing age with right upper abdominal pain. Timely diagnosis using biphasic CT with arterial and portal phases may help ensure adequate medical treatment as well as avoid invasive procedures.

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