Clinical outcome of Fitz-Hugh-Curtis syndrome mimicking acute biliary disease

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AIM: To analyze the clinical characteristics of patients diagnosed with Fitz-Hugh-Curtis syndrome.

METHODS: The clinical courses of patients that visited St. Mary’s Hospital with abdominal pain from January 2005 to December 2006 and were diagnosed with Fitz-Hugh-Curtis syndrome were examined.

RESULTS: Fitz-Hugh-Curtis syndrome was identified in 22 female patients of childbearing age; their mean age was 31.0 ± 8.1 years. Fourteen of these cases presented with pain in the upper right abdomen alone or together with pain in the lower abdomen, and six patients presented with pain only in the lower abdomen. The first impression at the time of visit was acute cholecystitis or cholangitis in 10 patients and acute appendicitis or pelvic inflammatory disease in eight patients. Twenty-one patients were diagnosed by abdominal computer tomography (CT), and the results of abdominal sonography were normal for 10 of these patients. *Chlamydia trichomatis* was isolated from 18 patients. Two patients underwent laparoscopic adhesiotomy and 20 patients were completely cured by antibiotic treatment.

CONCLUSION: For women of childbearing age with acute pain in the upper right abdomen alone or together with pain in the lower abdomen, Fitz-Hugh-Curtis syndrome should be considered during differential diagnosis. Moreover, in cases suspected to be Fitz-Hugh-Curtis syndrome, abdominal CT, rather than abdominal sonography, assists in the diagnosis.

Key words: *Chlamydia trichomatis*; Abdominal pain; Fitz-Hugh-Curtis syndrome

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INTRODUCTION

Acute abdominal pain is one of the most common symptoms experienced by patients visiting hospitals, particularly the emergency room. Pain in the right upper abdomen is a symptom of biliary diseases, such as gall bladder (GB) stones or cholecystitis, and it may also be present in duodenal ulcers, liver abscess, subphrenic abscess, herpes zoster infection, etc. In addition, pain in the right upper abdomen, alone or together with pain in the lower abdomen, is associated with Fitz-Hugh-Curtis syndrome, although this condition is infrequent among hospital patients.

Fitz-Hugh-Curtis syndrome is characterized by inflammation in perihepatic capsules with concomitant pelvic inflammatory disease without involvement of hepatic parenchyma[1-3]. Most Fitz-Hugh-Curtis syndrome patients are women of childbearing age who visit hospitals because of acute pain and tenderness in the right upper abdomen. The pain in the right upper abdomen is caused by adhesion of the anterior hepatic surface and the abdominal wall[4]. The pain tends to...
We retrospectively reviewed the records of 22 patients who were diagnosed with Fitz-Hugh-Curtis syndrome. Patients’ medical records, disease histories, physical and systemic examinations, and first impression by the clinicians that performed the initial diagnosis were examined. Laboratory tests, blood chemistry, serological tests, direct smears of specimens, and bacterial culture tests were performed. For radiological tests, the results of ultrasound tests and CT were examined. Diagnostic and therapeutic laparoscopic surgery, antibiotic treatments after diagnosis, and prognosis were examined for each patient.

RESULTS

Characteristic of patients
Our study sample included 22 Fitz-Hugh-Curtis syndrome patients diagnosed at our hospital. The patients were all women of childbearing age with a mean age of 31.0 ± 8.1 years (range 19-49 years). Their most recent sexual activity was between 3 d and 1 mo prior to the visit and the frequency of sexual activity was also provided. Except for two patients for whom symptoms were relatively meager and who were thus admitted through outpatient clinics, 20 patients visited the emergency room because of acute abdominal pain. The interval from the development of symptoms to a hospital visit was diverse, ranging from the same day to 2 wk, with an average of 5.8 ± 4.5 d (Table 1).

Chief complaint
The chief complaint requiring a visit to the hospital was pain in the right upper abdomen in seven patients (32%), pain in the right upper abdomen and pain in the lower abdomen in seven cases (32%), pain in the lower abdomen in six cases (27%), fever in one case (4.5%), and epigastric pain in one case (4.5%). With the exception of one case, fever was absent in the patients (Table 1).

First impression
After the first impression of the clinicians that examined the patients initially, 10 patients were diagnosed with acute cholecystitis or a GB stone, eight patients were diagnosed with acute appendicitis or pelvic inflammatory disease, and four patients were diagnosed with acute pyelonephritis, acute hepatitis, acute gastritis, or peptic ulcer disease (Table 1).

Test results
Various test methods were used for diagnosis. In 21 patients (95.5%), an abdominal CT scan was performed and Fitz-Hugh-Curtis syndrome was diagnosed according to its characteristics, the finding of contrast enhancement in the hepatic capsules. One of the patients was diagnosed as having Fitz-Hugh-Curtis syndrome by an abdominal CT scan and was treated; however, due to deterioration in her symptoms, laparoscopic surgery was performed and adhesion between the anterior side of the liver and the abdominal wall was confirmed. The remaining patient developed acute peritonitis during
pregnancy and was diagnosed by laparoscopic surgery without abdominal CT scan. Among the 21 patients diagnosed by abdominal CT scan, abdominal sonography was performed in 10 of them prior to abdominal CT scan and the results were normal in all cases.

According to blood chemistry tests, the number of leukocytes averaged 11.532/mm³, which was slightly higher than normal. Liver function test results were within the normal range in most patients, with the exception of 1 patient with a result 4 times greater than the upper normal limit. ESR averaged 51.3 mm/h which was elevated five times more than normal (normal value, 0-10 mm/h). C-reactive protein (CRP) averaged 52.3 mg/L, which was over 10 times higher than normal (normal value, less than 5 mg/L). The serological antibody tests to \textit{C. trichomatis} and PCR tests to six common sexually transmitted disease pathogens indicated the presence of \textit{C. trichomatis} in 18 patients, \textit{T. vaginalis} in one patient, \textit{U. urealyticum} in one patient, and \textit{M. hominis} in one patient. One patient was diagnosed during emergency surgery and, thus, the serology tests were not performed. Direct specimen smears were all negative. A cell culture test was performed for seven patients (three cases for \textit{Streptococcus agalactiae}, one case for \textit{U. urealyticum}, one case for \textit{Staphylococcus aureus}, one case for \textit{Candida albicans}, and one case for \textit{Escherichia coli}) and the findings concurred with the results of the serological chlamydia antibody tests of and PCR tests performed to determine the presence of pathogens (Table 2).

**Treatment and progress**

Of 22 patients, 20 patients (91%) improved following general or combinatorial antibiotic therapy and conservative care. One patient did not respond to antibiotic therapy; her pain became more severe but her symptoms improved after adhesiotomy by laparoscopic surgery. One patient developed acute peritonitis during pregnancy and, thus, laparoscopic surgery was performed for the purpose of diagnosis and treatment; she improved after adhesiotomy. Doxycycline was administered as a single antibiotic to five patients, and in combination to 14 patients. For those patients that received combination therapy, triple drug therapy consisted of metronidazole and aminoglycoside with ampicillin/sulbactam or cephalosporin and dual drug therapy consisted of an aminoglycoside with ampicillin/sulbactam or metronidazole with cephalosporin. Three patients received 2 drug therapy for 1 wk and their clinical symptoms were improved (Table 3).

**DISCUSSION**

\textit{Curtis} syndrome is characterized by perihepatic inflammation appearing with pelvic inflammation primarily in women of childbearing age. It occurs in 12.0%-13.8% of pelvic inflammation cases\cite{8,9}. In 1930, \textit{Curtis}\cite{10} reported the violin-string appearance between the anterior hepatic surface and the abdominal wall in gonorrhea patients. Furthermore, in 1934, \textit{Fitz-Hugh}\cite{11} reported gonococcal peritonitis accompanied by pain in the right upper abdomen. Previously, \textit{N. gonorrhoeae} was considered to be the major pathogen of this syndrome; however, in 1985, Lopes-Zeno et al.\cite{4} showed that \textit{C. trachomatis}, not \textit{N. gonorrhoeae}, was the major pathogen. In the past, the definitive diagnosis was made using methods that confirmed adhesion in the vicinity of the liver by laparoscopic surgery or open abdominal surgery. Recently, the disease was diagnosed and experienced infrequently as it was diagnosed by non-invasive methods such as serological tests for specific antibodies to pathogens that induce pelvic inflammation,
PCR, and abdominal CT scan.

It has been suggested that the mechanisms of development of Fitz-Hugh-Curtis syndrome include inflammation in hepatic capsules caused by inflammation in the reproductive system through the peritoneal cavity; migration of pathogens from the peritoneal membrane to the liver via blood; migration of pathogens from the peritoneal membrane to the liver through lymph ducts; and a hyperimmune response to *C. trichomatis*; nonetheless, the precise mechanism has not been elucidated yet[10].

The pain in the right upper abdomen that appears as the main symptom during the acute phase develops as a sudden sharp pain that becomes more severe in response to deep breathing, body movements, coughing, etc, and it develops as a result of congestion of hepatic capsules, spotted hemorrhage, and fibrous exudates. Occasionally, the pain may radiate to the right shoulder. Lower abdominal pain may appear simultaneously with the right upper abdomen pain or intermittently with the abdominal pain. If pain progresses to a chronic state without pain in the lower abdomen, the pain in the right upper abdomen generally appears continuously or may become dull.

In our study, 14 of 22 patients (64%) showed right upper quadrant (RUQ) pain; the typical symptom of Fitz-Hugh-Curtis syndrome. Seven of 14 patients displayed only RUQ pain, and in the other seven patients RUQ pain was accompanied by pain in the lower abdomen. The other eight patients (36%) had no typical RUQ pain symptom but experienced pain in the epigastrium or only in the lower abdomen, or they had fever and other systemic symptoms. Even when there is no pain in the right upper abdomen, which is the characteristic of Fitz-Hugh-Curtis syndrome when it occurs as perihepatic inflammation, the possibility of Fitz-Hugh-Curtis syndrome can not be ruled out completely[11,12]. Though it is not typical, diagnosis of Fitz-Hugh-Curtis syndrome with the major symptom of pain in the lower abdomen with pelvic inflammation or systemic symptoms should be considered. It has been reported that cases in which pain in the upper abdomen develops without pain in the lower abdomen are rare[13,14]; however, in this study, seven patients (32%) developed pain only in the right upper abdomen. This takes place in patients who have recovered from an acute episode of pelvic inflammatory disease without appropriate treatment[10]. These cases have to be cautiously differentiated from diseases for which the major symptom is pain in the right upper abdomen, such as acute cholecystitis. Although our study did not explore this, there are cases that display pain in the left upper abdomen by perisplenitis as the main symptom of Fitz-Hugh-Curtis syndrome. Hence, we think that cases of non-typical symptoms should be fully considered[13].

For the diagnosis of Fitz-Hugh-Curtis syndrome and the earlier findings of laboratory tests, the only method for definite diagnosis used to be assessment of adhesions in the vicinity of the liver by invasive laparoscopic surgery; however, diagnosis has recently been made possible by a non-invasive abdominal CT scan resulting in contrast enhancement in hepatic capsules caused by perihepatic inflammation during the acute phase of Fitz-Hugh-Curtis syndrome[7,16,17]. In this study, 21 cases (95.5%) were diagnosed by abdominal CT scan. Laparoscopic surgery was performed in only two patients for the purpose of diagnosis and

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**Table 3 Clinical characteristics of 22 patients with Fitz-Hugh-Curtis syndrome**

| No. | Age  | Symptom (pain)       | Duration | Impression | Diagnosis               | Treatment                        | Prog  |
|-----|------|----------------------|----------|------------|-------------------------|----------------------------------|------|
| 1   | 39   | Low abdomen          | 5        | PID        | CT                      | Doxycycline                       |      |
| 2   | 23   | RUQ                  | 7        | Cholecystitis | CT                     | Doxycycline                       |      |
| 3   | 35   | RLQ                  | 5        | Appendicitis | CT + Sono              | Cepha + Amino + Metro             |      |
| 4   | 19   | Low abdomen          | 5        | Appendicitis | CT + Sono              | Doxycycline                       |      |
| 5   | 22   | RUQ                  | 7        | Cholecystitis | CT + Sono              | Cepha + Amino + Metro             |      |
| 6   | 29   | RUQ + low abdomen    | 6        | Appendicitis | CT + Sono              | Cepha + Amino + Metro             |      |
| 7   | 26   | RUQ                  | 3        | Cholecystitis | CT + Sono              | Cepha + Amino + Metro             |      |
| 8   | 21   | Epigastrium          | 3        | Gastric ulcer | CT + Sono              | Cepha + Amino + Metro             |      |
| 9   | 37   | Fever                | 10       | Hepatitis   | CT                      | Doxycycline                       |      |
| 10  | 41   | RUQ                  | 14       | Cholecystitis | CT                      | Amp + Amino + Metro               |      |
| 11  | 49   | Low abdomen          | 10       | PID         | CT                      | Amp + Amino + Metro               |      |
| 12  | 33   | RUQ + low abdomen    | 0        | Cholecystitis | CT                      | Doxycycline                       |      |
| 13  | 45   | RUQ                  | 1        | Cholecystitis | CT + Sono              | Cepha + Metro                     |      |
| 14  | 32   | RUQ                  | 5        | GB stone    | CT + Sono              | Amp + Amino + Metro               |      |
| 15  | 34   | RUQ + low abdomen    | 14       | PID         | CT + Sono              | Cepha + Amino + Metro             | Lapa |
| 16  | 27   | RUQ + low abdomen    | 2        | GB stone    | CT + Sono              | Cepha + Amino + Metro             |      |
| 17  | 31   | Low abdomen          | 14       | Pylonephritis | Amp + Amino              | Amp + Amino + Metro               |      |
| 18  | 25   | RUQ + low abdomen    | 1        | Cholecystitis | CT                      | Amp + Amino + Metro               |      |
| 19  | 38   | RUQ + low abdomen    | 1        | Appendicitis | CT + Sono              | Amp + Amino + Metro               |      |
| 20  | 33   | RLQ                  | 4        | Appendicitis | CT                      | Amp + Amino + Metro               |      |
| 21  | 22   | RUQ + low abdomen    | 1        | Cholecystitis | CT                      | Amp + Amino + Metro               |      |
| 22  | 27   | RUQ pain             | 10       | Gastritis   | CT                      | Amp + Amino + Metro               |      |

RUQ: Right upper quadrant abdominal; RLQ: Right lower quadrant abdominal; PID: Pelvic inflammatory disease; GB: Gallbladder; CT: Computed tomography; Sono: Ultrasonography; Cepha: Cephalosporin; Amino: Aminoglycoside; Metro: Metronidazole; Amp: Ampicillin/sulbactam; Prog: Prognosis; Lapa: Laparoscopic adhesiolysis.
treatment. In addition, differential diagnosis of Fitz-Hugh-Curtis syndrome from hepatobilary diseases was performed for patients presenting with pain in the right upper abdomen by abdominal sonography. In our study, abdominal sonography was performed on 10 patients in the emergency room. All of these patients showed normal findings. Because abdominal sonography observations are mainly concentrated on the GB or liver, which are usually considered major causes of pain in the right upper abdomen, there is a failure to notice pelvic inflammatory disease which can be observed in the pelvic cavity. There may also be discrepancies in the expertise of different sonographers. Although abdominal sonography is of great help as a primary diagnostic tool to prove the causality of pain in the right upper abdomen, there are clear limitations in using only abdominal sonography to diagnose Fitz-Hugh-Curtis syndrome. Therefore, in sexually active women of childbearing age presenting with pain in the right upper abdomen or pain in the right upper abdomen together with pain in the lower abdomen, that have normal liver function test results and for whom Fitz-Hugh-Curtis syndrome is strongly suspected, an abdominal CT scan may diagnose the syndrome more rapidly and accurately.

For the identification of causative pathogens, uterine cervical specimens have been used most frequently, although rectal, urinary tract and salivary specimens can be used. To confirm the presence of the major pathogen, a culture test is widely applied and, more recently, ligase chain reaction (LCR), PCR, and a specific antibody test have been used to identify the pathogen. In our study, PCR and specific antibody tests were performed to identify the pathogen; tests were positive for *C. trichomatis* in 18 patients (82%), and testing for *N. gonorrhoeae*, which has been known to be the most prevalent pathogen in the past, was negative. Other pathogens were detected in the remaining three patients and it is thought that pathogens other than *C. trichomatis* that induce pelvic inflammation could be causative of Fitz-Hugh-Curtis syndrome. Lactobacilli maintain normal vagina flora, but if normal vagina flora is altered, an inflammation is usually induced by *G. vaginalis*, *C. albicans*, *T. vaginalis*, *M. hominis*, and the cervix becomes inflamed due to *C. trichomatis*, *N. gonorrhoeae*, and *N. gonorrhoeae*. In our study, the major causative pathogen *C. trichomatis* was not identifiable by culture tests. *C. trichomatis* cannot be identified in general bacterial culture tests as culture tests for *C. trichomatis* require special media that is not used in general bacterial culture. Therefore, for cases suspected to be Fitz-Hugh-Curtis syndrome, culture tests should be performed using the special media for *C. trichomatis* to enable accurate diagnosis. Hepatic enzyme values are normal or slightly elevated in Fitz-Hugh-Curtis syndrome, which is of help in differentiating it from hepatitis.

In Fitz-Hugh-Curtis syndrome, the liver function test is normal or slightly elevated and the ESR, although still controversial, has been reported to be increased in some cases. Recently, CRP has been reported to be a marker that reflects the clinical course of this disease. In most of our cases, the results of liver function tests were normal except for one patient with a result four times greater than the upper normal limit, and leukocyte values were slightly increased. ESR were elevated five times and CRP was elevated over 10 times more than the normal in our study. However, it is difficult to diagnose Fitz-Hugh-Curtis syndrome definitely by serum biochemistry and serological tests; therefore, they are only partially able to aid in the diagnosis of Fitz-Hugh-Curtis syndrome.

Antibiotics against the identified causative bacteria were administered as treatment and, for cases that were unresponsive to antibiotic therapy, surgery was performed to remove the adhesion in the vicinity of the liver. Standardized treatments were not available so antibiotics targeting *C. trichomatis*, *N. gonorrhoeae*, gram negative bacilli, and anaerobic bacteria were administered. Oral antibiotics were administered for 2 wk and non-oral antibiotics were administered for 48 h after the improvement of clinical symptoms. It has been reported that treatment reactions in most patients are good. This was the case in our study, with the exception of one case in which laparoscopic surgery was performed following the deterioration of symptoms. Most patients improved following antibiotic treatment. Moreover, the lesions were absent on abdominal CT scan performed after the treatment (Figure 1).

The diagnosis rate of Fitz-Hugh-Curtis syndrome has increased due to the recent development of
imaging tests. Most patients recover completely after treatment with appropriate antibiotics. Nevertheless, this syndrome is often misdiagnosed as other diseases with similar clinical symptoms which results in unnecessary treatment and hospital stays. Therefore, if sexually active women visit a hospital because of pain in the right upper abdomen or pain in the right upper abdomen and pain in the lower abdomen, Fitz-Hugh-Curtis syndrome should be considered. For patients suspected to have Fitz-Hugh-Curtis syndrome, an abdominal CT scan, rather than abdominal sonography, may be helpful since it provides a more rapid and accurate diagnosis.

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