

Review Article

Fitz-Hugh-Curtis Syndrome: A Comprehensive Review

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ABSTRACT

Fitz-Hugh-Curtis syndrome (FHCS) is a rare disorder that occurs in women. FHCS is a chronic manifestation of pelvic inflammatory disease (PID). It is characterized by inflammation of the membrane lining the stomach (peritoneum) and the tissues surrounding the liver (perihepatitis). The majority of cases occur in women of reproductive age between 15 and 30 years of age who have PID. Approximately 4–14% of women with PIDs develop FHCS. It occurs with greater frequency in adolescents with PIDs because they are more susceptible to infection. In extremely rare cases, it has occurred in men. PIDs are an ascending microbial infection involving the genital tract that affects sexually active. The United States experiences 750,000 cases of PID each year. FHCS is an uncommon manifestation of PIDs involving around 4% of adolescents. According to a case report, a 23-year-old girl found with FHCS at Bombay Hospital and Institute of Medical Sciences, Mumbai, Maharashtra, India. Many organisms are associated with FHCS, *Chlamydia trachomatis* is the most common pathogen involved. Common symptoms include severe pain in the upper right area (quadrant) of the abdomen, fever, chills, headaches, and a general feeling of poor health (malaise). There are insufficient data documenting the prognosis of FHCS as it usually responds to antibiotics very well. In one trial of triple therapy (penicillin-gentamicin-metronidazole) versus Augmentin for non-chlamydial salpingitis, only one patient in each treatment group had treatment failure.

Keywords: Fitz-Hugh-Curtis syndrome, Pelvic inflammatory disease, Reproductive age

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Introduction

Fitz-Hugh-Curtis syndrome (FHCS) or perihepatitis is a rare disorder that occurs almost exclusively in women.^[1] FHCS is a chronic manifestation of pelvic inflammatory disease

(PID).^[2] It is characterized by inflammation of the membrane lining the stomach (peritoneum) and the tissues surrounding the liver (perihepatitis). The muscle diaphragm which plays an essential role in breathing may also be affected. Common symptoms include severe pain in the upper right quadrant of the abdomen, fever, chills, headaches, and a general feeling of poor health.^[1]

The majority of cases occur in women of reproductive age who have PID. Approximately 4–14% of women with PID develop FHCS. It occurs with greater frequency in adolescents with PID because they are more susceptible to infection. In extremely rare cases, it has occurred in men.^[1] FHCS was first described in the medical literature in 1920 by Stajano. In 1930, Curtis described adhesions between the

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anterior surface of the liver and the abdominal wall found during laparotomies in patients with atypical gallbladder attacks. He found that while no other upper abdominal pathology was present, residual gonococcal tubal changes were frequently observed in the patient.^[3]

In 1934, Fitz-Hugh, Jr. reported similar cases which was presented with right upper quadrant abdominal pain. Laparotomy showed unusual, localized, peritonitis involving the anterior surface and edge of the liver and adjacent peritoneal surface of the diaphragm. After drainage, tube insertion smears from drained fluid showed Gram-negative, intracellular, biscuit-shaped diplococci. It is now known, however, that the syndrome is not exclusive to gonococcal infection and has been reported in both sexes.^[4]

Definition

FHCS is a rare disorder which is also called “gonococcal perihepatitis” or “perihepatitis syndrome” that happens when PID causes swelling of the tissue around the liver. PID is an infection of a woman’s reproductive organs. In some cases, this inflammation spreads to the covering of the liver or the tissues surrounding the liver in the abdomen. It can also spread to the diaphragm.^[6]

Causes

It is most often caused by sexually transmitted infections such as chlamydia and gonorrhea. It causes inflammation of the uterus, ovaries, fallopian tubes, cervix, or vagina.^[6] Researchers believed that more cases of FHCS are caused by infection with *Chlamydia trachomatis* than with *Neisseria gonorrhoeae*. Some researchers believed that it occurs because of infection of the liver and surrounding tissue, which may result from bacteria traveling from the pelvis directly to the liver or via the bloodstream or lymphatic system. Some researchers have speculated that FHCS may occur because of an improper immune system response to infection with *N. gonorrhoeae* or *C. trachomatis*. Several studies have demonstrated that individuals with FHCS have high levels of antibodies against *C. trachomatis*. More research is necessary to determine what role autoimmunity plays in the development of FHCS.^[1]

Epidemiology

PID is an ascending microbial infection involving the genital tract which affects sexually active women between 15 and 30 years of age. The United States experiences 750,000 cases of PID each year. FHCS is an uncommon manifestation of PID involving around 4% of adolescents. While many organisms are associated with FHCS, *C. trachomatis* is the most common pathogen involved.^[7] According to a case report by Sonavane and Rathi, a 23-year-old girl found

with FHCS at Bombay Hospital and Institute of Medical Sciences, Mumbai, Maharashtra, India.^[8]

Pathogenesis

As we know, FHCS is a complication of PIDs. Pathogenesis of the syndrome is still a confound because the mechanism that leads to FHCS is not fully understood. Many theories have been proposed over the years, and research is still ongoing.^[9]

In the year 1953, a research study suggested that pathogenic organisms spread through the peritoneal fluid from the pelvis to the diaphragm, especially if there has been recent use of an intrauterine device.^[10]

A different theory was suggested through a case report in which the spread of the infection could take place through the blood stream. The hematogenous spread was supported due to the finding of focal lesions in a patient with FHCS, which resolved with the use of antibiotics.^[11]

Another theory suggested the spread through the lymphatic tract, and this could explain the fact that most patients have no signs of an extensive intra-abdominal infection or disseminated bloodstream infection.^[12]

Further microorganisms associated with PIDs are spread:

- Through spontaneous ascending infection, microbes from the cervix or vagina travel to the endometrium, through the fallopian tubes, and into the peritoneal cavity. Complications include endometritis, salpingitis, tubo-ovarian abscess, pelvic peritonitis, and perihepatitis.
- Finally, the hematogenous spread is also possible such as with tuberculosis.^[7]

Signs and Symptoms

FHCS is associated with sudden, severe pain in the upper right area of the abdomen just below the ribs. The patient may also feel pain on the right shoulder and right arm. Moving usually makes it worse. Other symptoms are fever, chills, night sweat, nausea and vomiting, hiccups, headaches, and a general feeling of poor health (malaise). Symptoms of PID include pain in the lower belly and vaginal discharge.^[6]

Investigations

Laboratory tests

- Performing a pregnancy test will not only guide the choice of antibiotic therapy but also address the possibility of an ectopic pregnancy.
- Complete blood count to assess for leukocytosis. Know however that only up to 50% of women with PIDs has a clinically significant leukocytosis. Blood cultures can vary and are generally negative in the setting of PIDs.
- Complete metabolic panel to assess for any electrolyte, renal, or hepatic derangements.

- Vaginal secretions can be assessed for leukorrhea.
- Quantitative culture for chlamydia along with gonorrhea and chlamydial DNA probes can aid in diagnosis.
- Other tests to consider include rapid plasma reagin, hepatitis B and C, HIV, and urinalysis.^[6,13]

Radiological findings

- Computed tomography scan will show increased perihepatic enhancement in the arterial phase with a majority of patients also showing pelvic fat infiltration. Other findings associated with PID can be found: Pyosalpinx, tubo-ovarian abscess, and fluid collection in the pelvic cavity.
- Transvaginal ultrasonographic scanning is a favorable option for cases in which a clinical picture of PID may be unclear. Findings can include hydrosalpinx, pyosalpinx endometritis, tubo-ovarian abscess, oophoritis, and ectopic pregnancy.
- Magnetic resonance imaging can show tubo-ovarian abscess, edematous tubes, or free pelvic fluid collections.^[6,13]

Procedural findings

- Laparoscopy is the gold standard for diagnosing FHCS and PIDs. In the setting of PIDs, laparoscopy can show edema with exudates on tubal surfaces, ectopic pregnancy, or tubo-ovarian abscess. FHCS can be diagnosed directly through visualization of adhesions between the diaphragm and liver or liver and the anterior abdominal wall and these adhesions are called “violin-string” as shown in Figure 1.
- An endometrial biopsy can show endometritis.^[6,13]

Management

Since FHCS emerges from PID, the treatment of FHCS is directed toward the specific symptoms that are apparent in each individual. Antibiotic therapy is the mainstay treatment for individuals with FHCS. Different regimens of tetracycline, doxycycline, ofloxacin, metronidazole, and additional antibiotics may be prescribed to fight the infection. Pain medications (analgesics) such as acetaminophen and codeine may be used in some cases. The Centers for Disease



Figure 1: “Violin-string” adhesions of chronic Fitz-Hugh-Curtis syndrome^[5]

Control and Prevention has released guidelines on the treatment of PID.^[9]

A recent data published from a study, according to which a fourth-generation synthetic fluoroquinolone antibacterial agent, moxifloxacin is an ideal monotherapy for the treatment of PID.^[14]

Nevertheless, antibiotic therapy should be directed to the most likely pathogens, such as *N. gonorrhoeae* and *C. trachomatis* and microorganisms found in the endogenous flora of the vagina and cervix, such as anaerobic bacteria and facultative bacteria, many of which are associated with bacterial vaginosis.^[15]

The gold standard seems to be cefotetan 2 g IV every 12 hourly or cefoxitin 2 g IV every 6 hourly with doxycycline 100 mg orally or IV every 12 hourly for parenteral treatment and ceftriaxone 250 mg intramuscularly in a single dose with doxycycline 100 mg orally twice a day for 14 days, with or without metronidazole 500 mg orally twice a day for 14 days, for per os treatment. Clinical experience should guide decisions regarding transition to oral therapy, which usually can be initiated within 24 h of clinical improvement. Oral therapy can be considered for women with mild to moderately severe acute PID, as the clinical outcomes among women treated with oral therapy are similar to those treated with parenteral therapy. Women who do not respond to oral therapy within 72 h should be reevaluated to confirm the diagnosis and should be administered parenteral therapy on either an outpatient or inpatient basis.^[16]

In some cases, antibiotic therapy may not provide relief of symptoms and a surgical procedure known as a laparotomy may be performed. During a laparotomy, a small, thin instrument is inserted in the abdominal cavity through a small incision made in the abdomen. Physicians can then destroy any fibrous scar tissue found in the perihepatic region.^[1]

Hospitalization should be considered for patients with the following conditions:

- Uncertain diagnosis
- Pregnancy
- Severe illness
- Pelvic abscess on imaging
- Inability to tolerate anything by mouth
- Immunodeficiency
- Failure to improve after 72 h of therapy.

Patients with persistent symptoms of fever, chills, or cervical motion tenderness after 72 h of treatment should be reevaluated for possible surgical intervention.^[7]

Prevention

FHCS is concerned with PID, the best way to prevent it is to not get PID. To reduce the risk individual can:

- Wipe from front to back after using the bathroom to prevent infection^[6]
- Use condoms. Condoms are the best way to prevent sexual transmitted diseases. Because a man does not

need to ejaculate to give or get STIs, make sure to put the condom on before the penis touches the vagina or anus. Other methods of birth control, such as birth control pills, shots, implants, or diaphragms, will not protect from STIs.

- Get tested. Be sure both the partner is tested for STIs. Talk to each other about the test results before have sex.
- Be monogamous. Having sex with just one partner can lower the risk for STIs. After being tested for STIs, be faithful to each other. That means both the partners have sex only with each other and no one else.
- Limit your number of sex partners. Risk of getting STIs goes up with the number of partners a person have.
- Do not douche. Douching removes some of the normal bacteria in the vagina that protects from infection. Douching may also raise risk for PID by helping bacteria travel to other areas, such as uterus, ovaries, and fallopian tubes.
- Do not abuse alcohol or drugs. Drinking too much alcohol or using drugs increases risky behavior and may increase risk of sexual assault and possible exposure to STIs.

This work best when used together. No single prevention can protect from every single type of STI.^[17]

Differential Diagnosis

FHCS may mimic a number of other diseases. These include ectopic pregnancy, cholecystitis, viral hepatitis, renal colic, pyelonephritis, pulmonary embolism, and appendicitis.^[17]

Complications

One of the most common complications encountered in patients with FHCS is infertility. Another rarely seen complication is bowel obstruction due to adhesion formation in the peritoneal cavity.^[17]

Prognosis

There are insufficient data documenting the prognosis of FHCS as it usually responds to antibiotics very well. In one trial of triple therapy (penicillin-gentamicin-metronidazole) versus Augmentin for non-chlamydial salpingitis, only one patient in each treatment group had treatment failure.^[16]

Conclusion

FHCS is a common clinical entity connected with perihepatitis and PID that need to be treated with great attention. It is important that abdominal infections, especially those affecting the genital tract, should be diagnosed and treated

in early stages because the risk of occurrence of permanent damages and pelvic sepsis are high.

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