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Fitz-Hugh-Curtis Syndrome Caused by Gonococcal Infection in a Patient with Systemic Lupus Erythematosus: A Case Report and Literature Review

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Conflict of interest: None declared

Patient: Female, 22
Final Diagnosis: Fitz-Hugh-Curtis syndrome – disseminated gonococcal infection
Symptoms: Abdominal pain • fever • polyarthritis
Medication: —
Clinical Procedure: —
Specialty: Infectious Diseases

Objective: Rare co-existence of disease or pathology
Background: Fitz-Hugh-Curtis (FHC) syndrome is a perihepatitis linked to inflammatory pelvic disease. It can be caused by *Neisseria gonorrhoeae* or *Chlamydia trachomatis* infections. FHC syndrome usually presents with pain in the right hypochondrium and fever, associated with symptoms and signs of pelvic infection in women.
Case Report: We present the case of a 22-year-old woman with systemic lupus erythematosus (SLE) who presented with polyarthritis, cutaneous lesions, and abdominal pain. The diagnosis of FHC syndrome was based on the findings of abdominal computerized tomography (CT) and the isolation of *Neisseria gonorrhoeae* (NG) in blood cultures. The association of arthritis and cutaneous lesions was diagnosed as a syndrome of arthritis-dermatitis, also caused by systemic NG infection. The patient had a favorable outcome with antibiotic treatment.
Conclusions: FHC syndrome should be considered in sexually active young patients, mainly women, with pelvic infection and perihepatitis. It may be caused by disseminated gonococcal infection. An important risk factor is the serum complement deficit, which may predispose to severe forms. Low serum complement level is a frequent manifestation of active SLE. CT images showing the typical findings of perihepatitis allow making the correct diagnosis.

MeSH Keywords: Gonorrhea • Lupus Erythematosus, Systemic • Peritoneal Diseases

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/906393>

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Background

Disseminated gonococcal infection (DGI) is a consequence of the bacteremic spread of *Neisseria gonorrhoeae* (NG). It is estimated to affect 0.5–3% of patients infected with gonococcus [1].

The World Health Organization (WHO) estimated that in 2008 there were 106 million new cases of gonorrhea worldwide, an increase of 21% over 2005. In the United States, gonorrhea is the second most prevalent sexually transmitted disease after Chlamydia, with more than 300 000 cases reported in 2011 [2].

In Argentina in 2016, the National Surveillance System of the Ministry of Health reported 3193 cases, with an incidence rate of 7.96 per 100 000 inhabitants in 2013. [3] DGI has many forms of presentation, the most common being arthritis-dermatitis syndrome. It should be considered in young, sexually active patients with joint symptoms and skin lesions. Less frequently, it may present with perihepatitis, constituting Fitz-Hugh-Curtis syndrome. It has been reported that up to 13% of patients with DGI have complement deficiencies [1]. SLE, as an immune complex-mediated disorder, frequently presenting low serum complement levels in the active phases of the disease, favoring the development of *Neisseria* infections. [4]

We present the case of a patient with SLE and DGI with perihepatitis and arthritis-dermatitis syndrome, which teaches the clinical difficulty of differentiating gonococcal bacteremia from a lupus flare, and the diagnostic clues to distinguish both entities.

Case Report

A 22-year-old woman with a history of SLE (diagnosed 3 years before) was admitted to our institution complaining of fever with rigors, arthralgias and arthritis in knees, ankles, and wrist joints, starting 24 h before. She had noticed increased vaginal discharge 2 weeks earlier and received intravaginal antibiotic treatment, with complete resolution of her symptoms. One year before, she had presented with lupus enteritis and received treatment with steroid, with complete resolution. She was receiving treatment with prednisone 10 mg/day, azathioprine 100 mg/day, and hydroxychloroquine 200 mg/day.

On admission, physical examination revealed: blood pressure 110/70 mmHg, heart rate 115 bpm, axillar temperature 39.2°C, SatO₂ 97% (0.21), and arthritis signs in knees, ankles, and wrist joints. One skin pustular lesion on the left leg was observed, as well ulcerative palatal lesions (Figures 1, 2). Abdominal examination revealed peritoneal tenderness in the hypogastrium, right hypochondrium, flank, and right iliac fossa. Pelvic examination results were normal.



Figure 1. Skin pustular lesion on left leg.

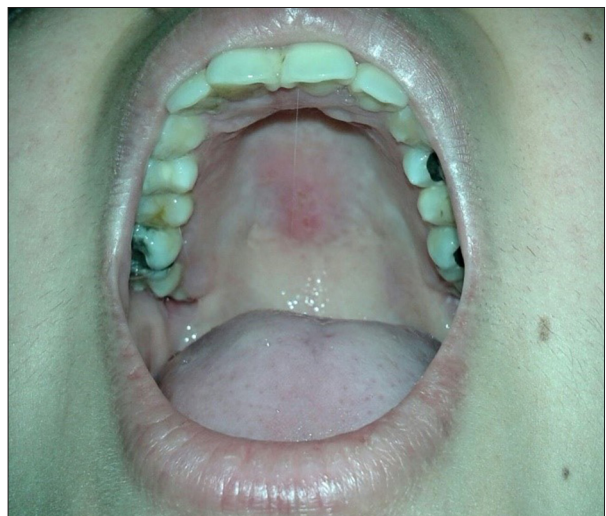


Figure 2. Ulcerative palatal lesions.

The electrocardiogram showed sinus tachycardia. Her hemoglobin level was 9.8 gr/dL (VN: 13–16 gr/dL), white blood cell count was $26.9 \times 10^9/L$ (NV: $5-10 \times 10^9/L$) with neutrophilia and immature forms, and platelet count was $382 \times 10^9/L$ (NV: $150-400 \times 10^9/L$). C-reactive protein (CRP) was 21 mg/dl (NV: 0.1–0.5 mg/dl), erythrocyte sedimentation rate (ESR) was 35 mm/h, and serum ferritin 42 ng/dl. Plasma creatinine, urea, and liver function tests (LFT) were normal. Serum proteinogram: total proteins 7.4 g/dl; albumin 3.80 g/dl; alfa1 0.37 g/dl, alfa 2 0.78 mg/dl, beta 0.72 mg/dl, gamma globulin 1.72 g/dl. Serum C3 complement 67 mg/dl, and C4 9 mg/dl. ANA positive 1/320, homogeneous, anti-DNA antibodies: negative. Urine sediment showed: protein +, erythrocytes 10–20, dysmorphic. Serologic assays for HIV, HCV, HVB, VDRL, and *Chlamydia trachomatis* were negative.

A pelvic ultrasound yielded normal results and a CT scan of the abdomen and pelvis with intravenous contrast demonstrated

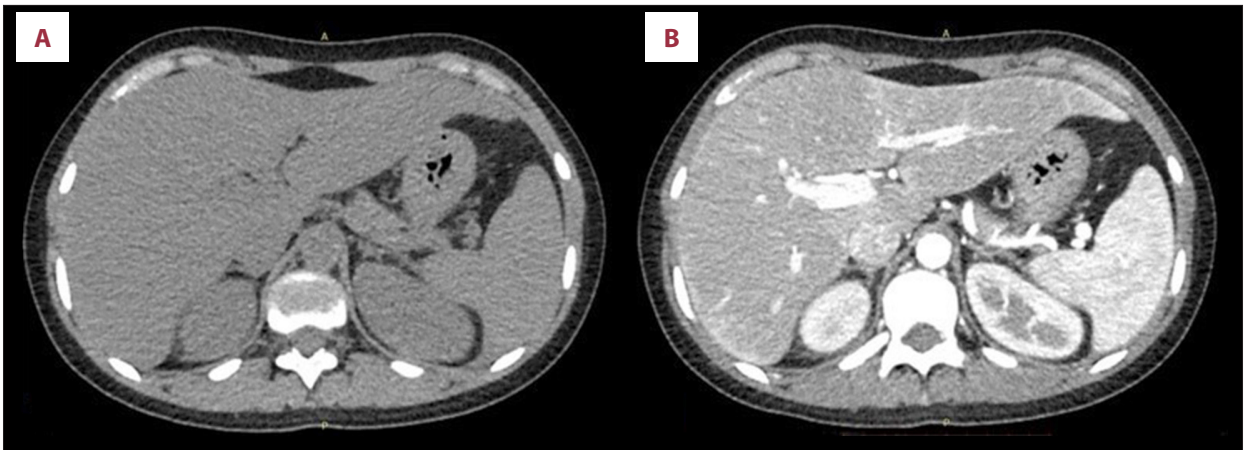


Figure 3. (A, B) Abdominal CT. Contrast enhancement of hepatic capsule.

early enhancement of hepatic capsule (Figure 3A, 3B). These CT findings were interpreted as perihepatitis due to FHC syndrome. She was started on antibiotic treatment with intravenous ceftriaxone 2 gr/day and doxycycline 200 mg/day. The prednisone dose was increased to 60 mg/day. At 48 h after admission, blood cultures were positive for NG. The patient completed 14 days of antibiotic treatment with complete resolution of clinical and laboratory manifestations related with infection. She continued ambulatory control and treatment of SLE.

Discussion

Gonorrhoea is a sexually transmitted infection caused by the NG microorganism. It mainly affects adolescents and young adults. DGI is a consequence of bacteremia and dissemination.

Although previously estimated to affect 0.5–3% of infected patients, the rate of DGI is currently lower [1].

As a predisposing factor, it has been reported that up to 13% of patients with DGI have complement deficiencies [5]. Other risk factors associated with dissemination are female sex and menstruation [1]. About half of the women with DGI start their symptoms within 7 days after menstruation or during the third trimester of pregnancy, possibly due to an increase in vascularization and a decrease in the mucosal and endometrial barrier, facilitating bacterial dissemination [2]. Our patient presented her menstrual period on day 2 of hospitalization, which may have facilitated gonococcal bacteremia.

SLE involves a deregulation of the immune system. The T and B lymphocytes are activated, leading to the production of autoantibodies and the formation of immune complexes, with a decrease in serum complement [4–6]. In these patients, the decrease in serum levels of complement increases the risk

of infections by certain bacteria that depend on the complement system for their opsonization and subsequent lysis [4].

In an earlier work, Ellison concluded that the prevalence of inherited or acquired complement deficiency among patients with disseminated gonococcal infection is higher than in the general population and is an important factor predisposing to systemic infection by NG [5]. In the series by Mitchell et al. of *Neisseria* infection in SLE, it was reported that young women with renal disease and acquired or congenital hypocomplementemia are most affected [4].

The clinical spectrum of DGI is very broad, and includes: polyarthritides, tenosynovitis (generally asymmetrical), septic arthritis, mucocutaneous involvement, perihepatitis, endocarditis, meningitis, and even septic shock [1,2,7–9]. Arthritis-dermatitis syndrome is the most frequent form of presentation of DGI [1,2]. Skin lesions occur in 60–75% of patients, and are most frequently located on the hands, feet, and distal third of the extremities. They are usually painless and vary in appearance from petechiae or erythematous papules to isolated pustules in which gonococci can be found [1,2,8,10,11].

Pain in the upper right quadrant of the abdomen in the context of pelvic inflammatory disease (PID) is suggestive of perihepatitis. This process has been called Fitz-Hugh-Curtis syndrome (FHC), although it was the Uruguayan surgeon Carlos Stajano who, for the first time in 1920, observed adhesions between the hepatic capsule and the anterior abdominal wall in patients with gonococcal infection [12].

In 1930, Arthur Curtis and Thomas Fitz-Hugh established the connection between the acute pain syndrome in the right hypochondrium after a pelvic infection and the “violin string” adhesions found in women with evidence of previous salpingitis. In 1934, they suggested that *Neisseria gonorrhoeae* was the causative agent when they succeeded in isolating

it from a smear of the hepatic capsule in a patient with this syndrome [13].

In 1978, Müller-Schoop serologically demonstrated an acute infection by *Chlamydia trachomatis* (CLT) in 9 of 11 patients who had undergone a laparoscopic evaluation of peritonitis, 6 of whom also had perihepatitis [14]. At present, most experts believe that CLT is more frequent than NG as the causative agent of FHC [13,15].

Estimates of the incidence of FHC depend on the diagnostic criteria used. The incidence ranges from 4% to 14% in women with PID, but it is as high as 27% in adolescents with PID, whose anatomy makes them more susceptible to infection [13].

Among the pathogenic mechanisms proposed, the most accepted is the direct extension of NG from the fallopian tubes, through the paracolic spaces to the hepatic capsule and overlying peritoneum. Other possible pathways are hematogenous or lymphatic propagation and an exaggerated immune response to CLT infection [1,13].

On admission, our patient did not present clinical manifestations of PID, and had normal results of pelvic examination and ultrasound study. The presentation of FHC syndrome without PID manifestations has been described. Normal gynecological evaluation may be insufficient to rule out FHC in a young woman with pain in the abdominal right upper quadrant [16].

Peri-hepatitis has also been reported as a manifestation of SLE [17–19]. In our case, it could be an important differential diagnosis, but the documentation of gonococcal infection confirmed causal etiology. The association of SLE and FHC caused by gonococcal or chlamydial infections has not been previously reported.

Disseminated gonococcal infection should be considered in all young, sexually active patients with SLE and perihepatitis, not only because the clinical picture of these 2 processes have a significant similarity, but also because these patients have an increased risk of severe infection, as reported in the literature [7,8,10,20–22].

Our patient had marked leukocytosis with left-sided deviation and immature forms, disproportionate elevation of CRP compared to ESR, and a ESR/CRP ratio of 1.45. These findings led to considering the presence of infection in patients with SLE. An ESR/CRP ratio <2 is suggestive of infection in patients with SLE [23].

For the definitive diagnosis of FHC, laparoscopy or laparotomy are traditionally required. With these surgical procedures, “violin strings” adhesions may be observed to demonstrate the

presence of the microorganisms involved. However, at present, contrast-enhanced CT has emerged as an important diagnostic modality prior to surgery and is the most widely used method at present [15,21,24]. The characteristic image is a subcapsular perihepatic enhancement in the contrast-enhanced arterial phase, which reflects the increase in blood flow in the inflamed hepatic capsule [15,16,21,22]. Other findings in CT are thickening of the peritoneum, adhesion bands, and liquid collections. In addition to allowing an early diagnosis of perihepatitis, it excludes other causes of abdominal pain and avoids invasive procedures [21].

Parenteral antibiotic therapy with a third-generation cephalosporin, which should be accompanied by azithromycin or doxycycline to provide additional coverage for *Chlamydia*, is currently recommended as a treatment for DGI [1,2,25].

If the pain persists despite proper treatment, a laparoscopic examination should be performed to determine if there are perihepatic adhesions. Laparoscopy provides a less invasive therapy than laparotomy when lysis of adhesions is necessary for the relief of symptoms [13,21].

Conclusions

Disseminated gonococcal infection occurs in 0.5–3% of gonococcal infections. It usually causes tenosynovitis, arthritis, cutaneous involvement, and perihepatitis.

An important risk factor is the serum complement deficit, which may predispose to severe forms.

Systemic lupus erythematosus, when it presents with exacerbations, may cause consumption of the complement and predisposition to infections by *Neisseria*.

We present the case of a patient with SLE who presented with a disseminated gonococcal infection that was manifested by arthritis-dermatitis syndrome and Fitz-Hugh-Curtis syndrome.

To the best of our knowledge, the association of SLE and FHC caused by gonococcal infection has not been previously reported.

Although SLE may be a cause of perihepatitis, disseminated gonococcal infection should be considered in all young, sexually active patients with SLE and arthritis-dermatitis syndrome or with perihepatitis.

Conflict of interest

None.

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