

# Pyogenic Liver abscess and Gastrointestinal Variant of Lemierre Syndrome in Patient with Crohn's Disease

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## Abstract

Crohn's disease (CD) has several intestinal and extraintestinal manifestations and complications, including fistulas, arthritis, and abscesses. Pyogenic liver abscesses are rare among the general population and also in patients with Crohn's disease. They are associated with high mortality when treatment is delayed. Although *Fusobacterium* bacteremia and thrombophlebitis are most commonly reported in head and neck infections, the abdominal form is also a well-defined entity due to gastrointestinal colonization. We describe a case of liver abscesses and hepatic vein septic thrombosis due to *Fusobacterium nucleatum* in an adult male patient with Crohn's disease.

**Keywords:** Abscess, Crohn's disease, Lemierre, liver, pyogenic

## INTRODUCTION

Crohn's disease is an idiopathic, gastrointestinal inflammatory disease characterized by granulomatous, transmural inflammation with numerous intestinal and extra-intestinal manifestations and complications. Primary sclerosing cholangitis is a hepatobiliary complication more prevalent in ulcerative colitis than in Crohn's disease. Conversely, Crohn's disease is associated with a higher incidence of pyogenic liver abscess, cholelithiasis, and granulomatous hepatitis.<sup>1,2</sup>

Pyogenic liver abscess is a very rare hepatobiliary manifestation of Crohn's disease (CD). Most cases of liver abscess in CD have been observed in young male patients with long-term and active disease.

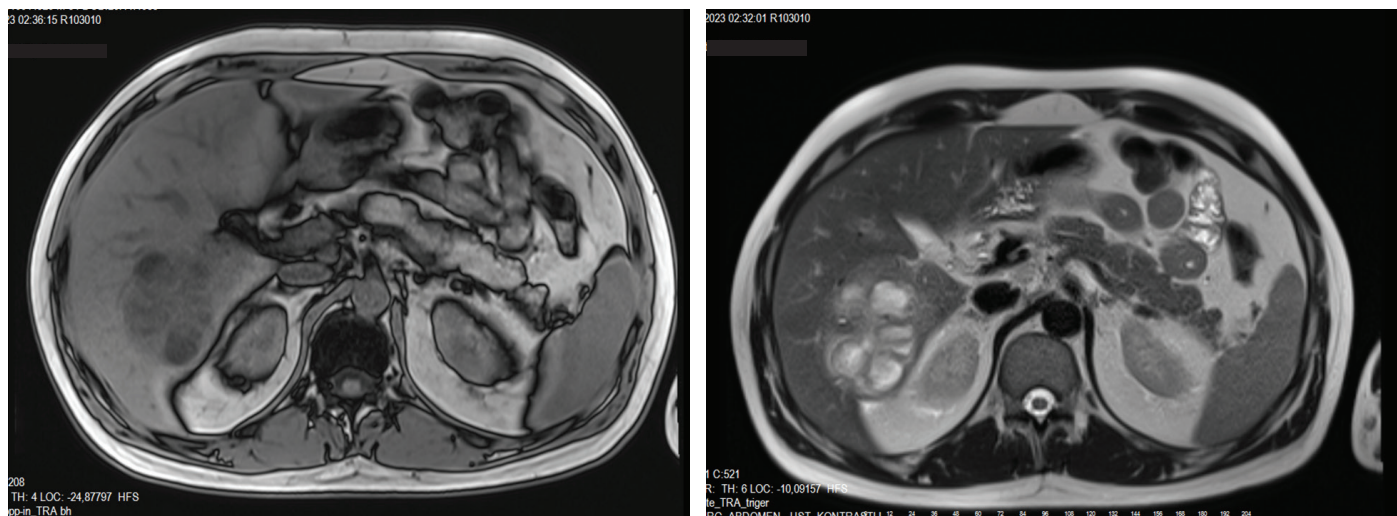
Lemierre's syndrome is characterized by bacteremia, internal jugular vein thrombophlebitis, and metastatic septic emboli secondary to acute pharyngeal infections. The most common causative agent of Lemierre's syndrome is *Fusobacterium necrophorum*, followed by *Fusobacterium nucleatum*.<sup>3</sup> A liver abscess is one of the less common presentations of metastatic disease.

In this report, we aim to present a rare case of a gastrointestinal variant of Lemierre's syndrome and liver abscess associated with *Fusobacterium nucleatum* in a Crohn's disease patient. This case was successfully treated with anticoagulation, antibiotic therapy, and percutaneous drainage.

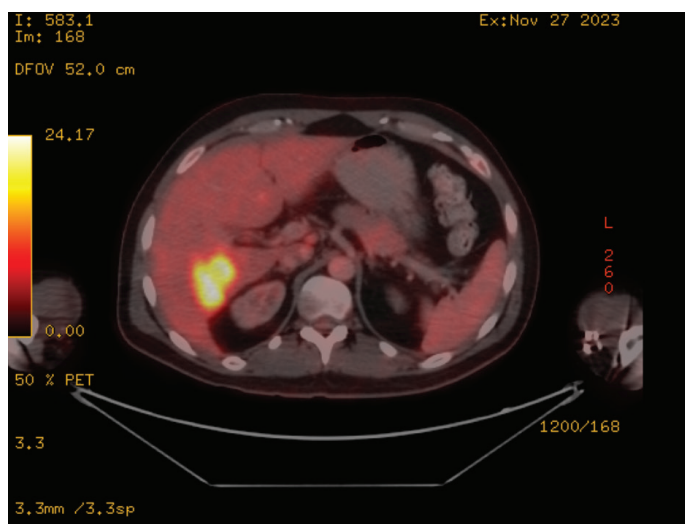
## CASE PRESENTATION

A 34-year-old male patient with a two-year history of Crohn's disease involving the ileum, previously treated with mesalamine, azathioprine, and adalimumab, was admitted to the hospital with abdominal pain and vomiting. His medical history included perianal abscess drainage and fistula surgery. After a CT enterography revealed increased mucosal thickness in the ileum and jejunum, his treatment was switched from adalimumab to ustekinumab without performing a colonoscopy. One month later, the patient was admitted to our clinic with a three-day history of abdominal pain and fever. His vital signs were as follows: temperature of 37.5 °C, heart rate of 110 beats per minute, respiratory rate of 14 per minute, and blood pressure of 120/80 mmHg. Physical examination revealed minor pain in the epigastric region with normal bowel sounds; there was no organomegaly or rebound tenderness.

Laboratory results revealed the following: Wbc: 16400 10<sup>3</sup>/μl, Hgb: 13 g/dL, Hct: %38 MCV: 86 fL, Plt:365000 10<sup>3</sup>/μl, neu:13600 10<sup>3</sup>/μl, lymph:1.53 10<sup>3</sup>/μl, AST:28,7 U/L, ALT:47 U/L, ALP:300 U/L, GGT:71 U/L, Creatinine: 0.8 mg/dL, Na: 135 mmol/L, K:4.63 mmol/L, Total Bilirubin: 1.41mg/dL, Direct Bilirubin: 0.39 mg/dL, albumin: 3.71 g/dL, INR:1,31,CRP: 347 mg/L,procalcitonin:0.99 ng/mL, Sedimentation Rate:89.



**Figure 1.** Abdominal MR/MRCP revealed a 67x69 mm T2A hyperintense, diffusion-restricted, and peripherally enhanced area compatible with an abscess in liver segments 5-6, along with an acute thrombus extending from the right portal vein to the periphery.



**Figure 2.** PET-CT revealed significant FDG uptake (SUVmax: 12.2) in a 54x40 mm heterogeneous dense mass lesion located medially at the broadest part of liver segment 5-6.

Abdominal MR/MRCP revealed a 67x69 mm T2A hyperintense, diffusion-restricted, and peripherally contrasted area compatible with an abscess in liver segments 5-6, along with an acute thrombus extending from the right portal vein to its peripheral branches, causing total lumen occlusion (Figure 1). Inflammatory markers, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), were remarkably elevated. A comprehensive diagnostic workup, including tests for *Clostridium difficile*, HIV, hepatitis, *Entamoeba*, *Giardia*, and fecal culture with toxin, yielded no definitive findings. Immunoglobulin levels (IgG and its subclasses, IgA, IgM, and IgE) were all within normal limits. Treatment was empirically started with intravenous piperacillin-tazobactam 3x4.5 g, metronidazole 500 mg iv 3x1, and enoxaparin sodium 0.6 ml 2x1. Thrombophilia investigations, including plasma concentrations of anti-thrombin III, anti-cardiolipin, anti-phospholipid, and antinuclear antibodies, as well as genetic testing for factor V Leiden mutation, revealed no abnormalities. No pathogens were detected in blood or urine samples. A PET-CT performed to rule out malignancy revealed significant FDG uptake (SUVmax:

12.2) in a 54x40 mm heterogeneous dense mass lesion medially at the level of liver segment 5-6 (Figure 2).

Colonoscopy revealed normal colonic segments; however, ulceration and stenosis across a 7-cm segment of the terminal ileum indicated active Crohn's disease. Control imaging post-procedure showed regression of the abscess following percutaneous hepatic abscess drainage conducted by interventional radiology. The patient was discharged after three weeks of hospitalization and continued oral antibiotic therapy for an additional four weeks. A culture of the abscess drainage material later grew *Fusobacterium nucleatum*, and acute phase reactants regressed.

## DISCUSSION

Pyogenic liver abscess can develop as a complication of bacterial, parasitic, and fungal infections. The most common causes include *Streptococcus*, *Klebsiella*, and *E. coli*.<sup>4</sup> In cases where there is no history of inflammatory bowel disease (IBD)-related cholelithiasis, primary sclerosing cholangitis, hepatobiliary intervention, or infection, determining the route of entry of the agent into the hepatic parenchyma can be challenging.<sup>5,6</sup> Crohn's disease is associated with bacterial translocation and portal venous bacteremia as a result of intestinal barrier impairment and complications such as fistulation, perforation, and abscess.<sup>7,8</sup> The occurrence of pyogenic liver abscess in the course of Crohn's disease is believed to be caused not only by intestinal inflammation but also by immunosuppressive therapy and malnutrition.<sup>9</sup>

*Fusobacterium nucleatum* has been identified as the causal pathogen in fewer than 50 pyogenic liver abscess (PLA) cases, and only two of these cases were associated with Crohn's disease.<sup>10</sup> The cases reported in the literature primarily involve periodontal disease, diverticulitis, and a few instances of colorectal carcinoma.<sup>11-13</sup>

In a study involving 59 biopsy specimens from individuals with inflammatory bowel disease (IBD) and healthy controls, *Fusobacterium* spp., traditionally associated with oral flora, was found in 26 isolates, with 18 identified as *F. nucleatum*. Interestingly, half of these *F. nucleatum* isolates were from patients with Crohn's disease, while 17% were from healthy controls.<sup>14</sup> *Fusobacterium* spp. binds to host plasminogen, causing plasma activation, local proteolysis, and tissue damage, which can lead to portal pyemia and thrombosis. There are only a few cases iden-

tified as *Fusobacterium*-related gastrointestinal Lemierre variant.<sup>15,16</sup> A correlation has been observed between prolonged active disease duration and a higher prevalence among males.<sup>17</sup> The most common symptoms include fever, upper right chest pain, itching, sweating, and dark-colored urine. The symptoms and findings of our patient were similar to those of previously published cases, and Crohn's disease was both endoscopically and clinically active.

The initiation and duration of anticoagulant therapy in Lemierre Syndrome or its gastrointestinal variant is based on personal experience rather than randomized clinical trials.<sup>18</sup> In high-risk individuals, if there are no contraindications, the general tendency is to initiate treatment.<sup>19</sup> In our case, despite the negative results from the hereditary thrombophilia screening, anticoagulant treatment was initiated due to the increased risk associated with active Crohn's disease. When *Fusobacterium nucleatum*-associated infections are identified in systems other than the head and neck, such as the gastrointestinal or urogenital systems, it is important to perform screening for underlying malignancy.<sup>20</sup>

This case is significant as it represents a rare, emerging, and under-recognized complication of stricturing Crohn's Disease. To the best of our knowledge, this is one of the rarest cases of *F. nucleatum*-related portal vein thrombosis and pyogenic liver abscess in Crohn's disease. Pyogenic liver abscess should be considered in patients with Crohn's Disease presenting with abdominal pain and fever. Lack of familiarity and delays in diagnosis increase rates of morbidity and mortality.<sup>21</sup>

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