

Pylephlebitis Complicated by Hepatic Abscesses due to *Fusobacterium Nucleatum*: A Case of Lemierre's Syndrome Variant and Literature Review

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ABSTRACT

In gastrointestinal-variant Lemierre syndrome, *Fusobacterium nucleatum* can cause pylephlebitis and liver abscesses. We report a 62-year-old woman presenting with abdominal pain and altered mental status. Abdominal computed tomography showed hepatic lesions and thrombosis in the superior mesenteric and portal veins. Magnetic resonance cholangiopancreatography showed multiple cystic hepatic masses suspicious for abscess vs metastases. Malignancy workup was unrevealing. *F. nucleatum* grew on both blood and ultrasound-guided liver aspirate cultures. Twelve weeks of antibiotics and anticoagulants resolved her condition. Given the high mortality rates, prompt detection and treatment of gastrointestinal-variant Lemierre syndrome is critical to delivering quality, patient-centered care.

KEYWORDS: Lemierre's syndrome; GI variant Lemierre's syndrome; *Fusobacterium nucleatum*; Fusobacterial liver abscess; *F. nucleatum*

INTRODUCTION

Fusobacterium necrophorum is known to cause a life-threatening septicemic condition known as Lemierre syndrome. This disease is characterized as septic thrombophlebitis of the internal jugular vein, with distant metastatic spread to lungs, joints, and bone.¹ A lesser known strain common in the gut flora, *Fusobacterium nucleatum*, can cause portal vein thrombophlebitis leading to liver abscesses.¹ This presentation is known as the gastrointestinal (GI) variant of Lemierre syndrome. We report a rare case of *F. nucleatum* septicemia with septic pylephlebitis and multiple liver abscesses mimicking liver metastases.

CASE REPORT

A 62-year-old woman with a medical history of hypertension and heart failure presented with malaise, confusion, low-grade fever, and myalgia. She had left-sided cramping abdominal pain with decreased appetite and intermittent hematochezia in the previous 1–2 months.

On admission, the patient was hemodynamically stable. Physical examination was remarkable for tenderness to palpation in the right upper quadrant and epigastrium, without guarding or rebound. Laboratory studies showed a white blood cell count of 12 K/ μ L with 81% neutrophils, hemoglobin 8.8 g/dL, mean corpuscular volume 78, alkaline phosphatase 128 U/L, creatinine 1.3 mg/dL (baseline 0.6 mg/dL), and blood urea nitrogen 28 mg/dL.

Abdominal and pelvic computed tomography (CT) with intravenous contrast (Figure 1) demonstrated hepatic lesions up to 9 cm, subocclusive thrombus in the superior mesenteric and portal veins, enlarged para-aortic lymph nodes, and thickened colon consistent with chronic diverticulitis. An infectious workup was significant for blood cultures that grew *F. nucleatum*. Enoxaparin

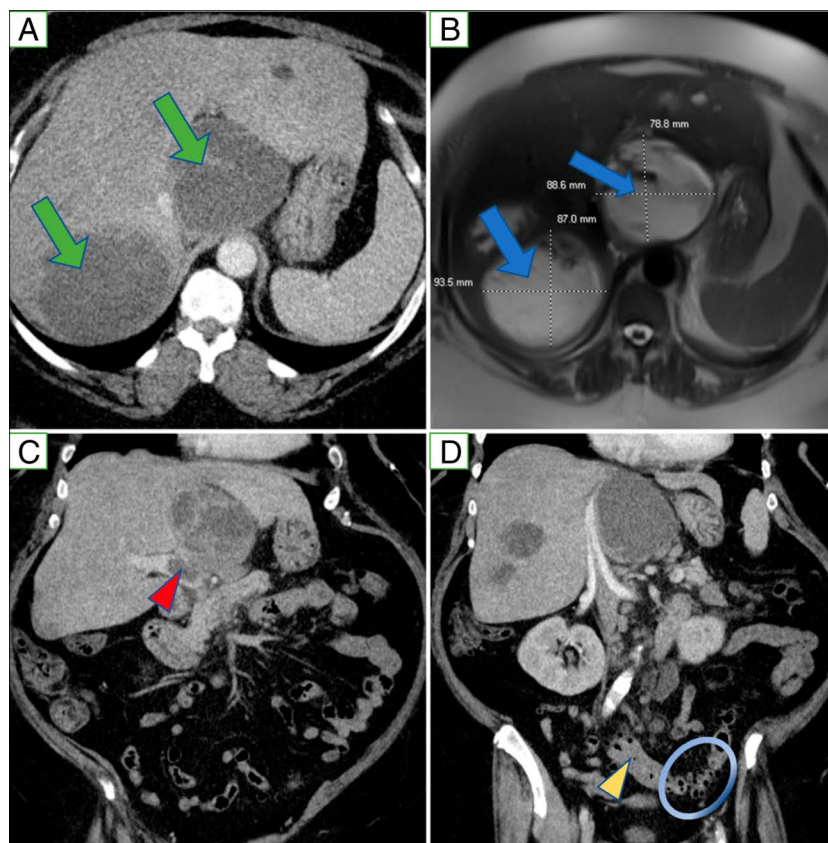


Figure 1. (A) Abdominal and pelvic CT with IV contrast showing 2 large hepatic abscesses (green arrows) up to 9 cm in size. (B) Abdominal MRI T2 showing the 2 large hepatic abscesses (blue arrows). (C) Abdominal and pelvic CT with IV contrast showing subocclusive thrombus in the portal vein (red arrow head). (D) Abdominal and pelvic CT with IV contrast showing thickening of the sigmoid colon wall (yellow arrow head) and colonic diverticula (encircled). CT, computed tomography; IV, intravenous; MRI, magnetic resonance imaging.

and ampicillin-sulbactam were initiated. Magnetic resonance imaging (MRI)/cholangiopancreatography (Figure 1) redemonstrated multiple predominantly cystic hepatic masses suspicious for abscess vs metastatic disease. Transthoracic echocardiogram was negative for any valvular vegetation. Malignancy workup was unrevealing and included chest CT, brain MRI, carcinoembryonic antigen, alpha-fetoprotein, and cancer antigen 19-9. Colonoscopy (Figure 2) showed a benign-appearing, intrinsic 10 cm long stenosis of the distal sigmoid that was traversed, 5 mm sessile polyp in the mid-sigmoid that was not resected, extensive diverticula, and internal hemorrhoids, with no observed masses.

Interventional radiology performed aspiration and drain placement of the 2 largest hepatic lesions. Aspiration yielded purulent fluid consistent with abscess and negative for malignancy. Aspirate culture grew *F. nucleatum*. By day 12, her abdominal pain had improved significantly and she was switched to ertapenem and apixaban and then discharged.

She continued to follow-up with infectious disease with abdominal CT every 4 weeks. After 6 weeks, drains were removed and she was switched to amoxicillin-clavulanate for an additional 6 weeks. She continued anticoagulation for a total of 12 weeks. An

abdominal and pelvic CT scan (Figure 3) after 12 weeks showed near-complete resolution of the hepatic abscesses and mild residual nonocclusive thrombus in the superior mesenteric and portal veins. She lost to follow up with the GI clinic.

DISCUSSION

Pylephlebitis, suppurative thrombophlebitis of the portal vein, is a rare but life-threatening complication of intra-abdominal or pelvic infections.² *Fusobacterium* species are among the infectious causes precipitating thrombosis, which can present as internal jugular thrombophlebitis in Lemierre syndrome and as portal and superior mesenteric vein thromboses in the GI variant of Lemierre syndrome. The thrombogenic ability of the *Fusobacterium* species is because of its ability to aggregate platelets and vascular compression from inflammation and edema.³

PubMed and Scopus databases were searched for case reports or case series in English reporting pylephlebitis complicated by liver abscess due to *Fusobacterium* up to January 2023. Keywords used in the search included Lemierre syndrome, GI-variant Lemierre syndrome, pylephlebitis, *Fusobacterium*, and liver abscess. The search yielded 9 cases⁴⁻¹² (Table 1). Including our case, the mean age was 51.2 years (19-69 years), with a 1:1

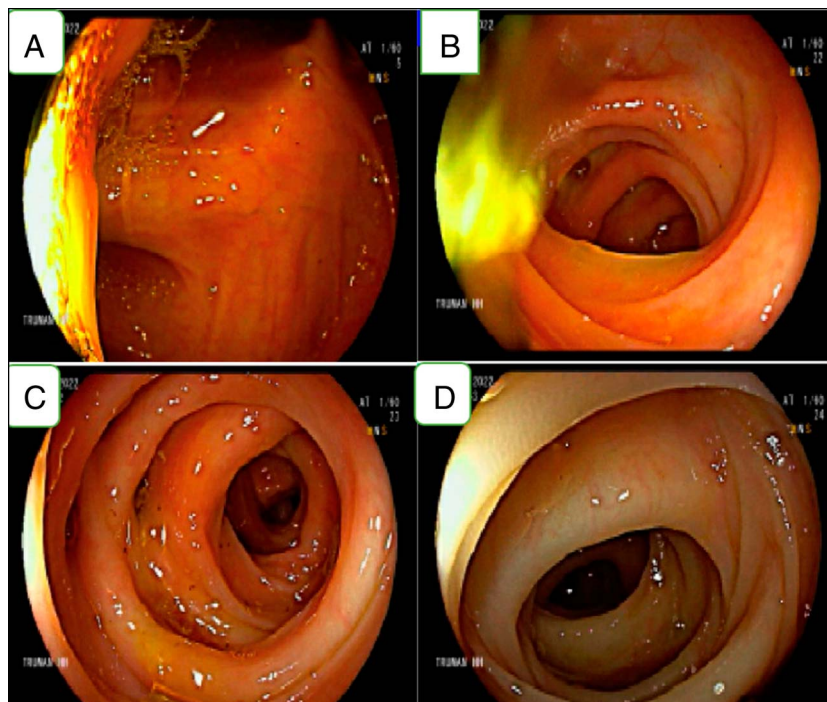


Figure 2. Colonoscopy showing (A, B) extensive diverticula with a mixed opening in the entire colon and (C, D) moderate benign-appearing intrinsic 10 cm length stenosis in the distal sigmoid.

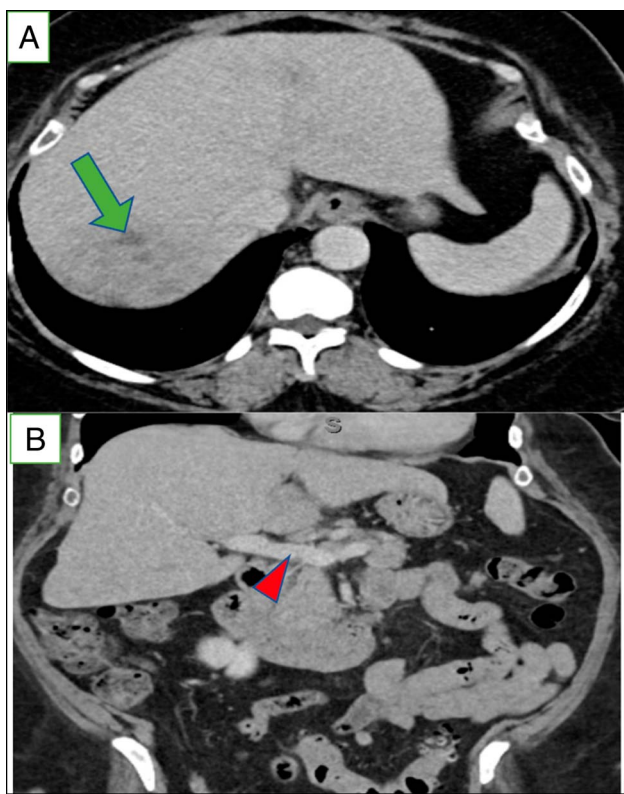


Figure 3. Repeat abdominal and pelvic computed tomography with intravenous contrast after 12 weeks showing (A) near-complete resolution of hepatic abscess on the right lobe (green arrow) and complete resolution of hepatic abscess on the left lobe and (B) near-complete resolution of thrombus in the portal vein (red arrow head).

male-to-female ratio. Four cases^{4,5,9,10} were *F. necrophorum*; 3 cases^{6,11,12} along with our case were *F. nucleatum*; and 2 cases^{7,8} were of unspecified Fusobacterium species. In our literature review, all infections were monomicrobial and community-acquired. The source of infection was GI sources in 5 cases (4 diverticular diseases, 1 pancreatitis), an oropharyngeal source in 2 cases, and post-GI procedure sources in 2 cases. The source could not be identified in 1 case (Table 2). We believe that diverticulitis is the source in our case, based on the left lower abdominal pain before presentation, signs of chronic diverticulitis on CT, and narrowing in the sigmoid colon on colonoscopy, which was likely diverticular stricture. Recent literature has shown that patients with *F. nucleatum* bacteremia have an increased risk of colorectal cancer.¹³ We emphasize that age-appropriate cancer screening in GI-variant Lemierre syndrome, including colonoscopy, should be considered to rule out malignancy.

Clinical diagnosis of pylephlebitis is often challenging, requiring confirmation of thrombus formation in the portal vein or its branches and positive blood cultures.¹⁴ Six cases in the review had positive blood cultures while 7 had positive liver aspirate cultures (Table 2). Patients typically presented with a triad of dull right upper quadrant or epigastric pain, fever, and leukocytosis. The most common enzyme abnormality in our review was alkaline phosphatase (60%) (Table 1).

A prompt multidisciplinary approach is required to treat pylephlebitis, including a combination of antibiotics, abscess

Table 1. Demographic data from all 10 case reports included in the literature review

Study	Country	Age (sex)	Medical history	Underlying hypercoagulable diseases	Symptoms		Laboratory findings				
					Abdominal pain	Fever	LC	AST (U/L)	ALT (U/L)	ALP (U/L)	TB (mg/dL)
Current study, 2022	United States	62 (F)	HTN and HFrEF	None	Present	Present	Present	Normal	Normal	High	Normal
Furuncuoglu et al, 2021 ⁴	Turkey	54 (F)	Pancreatic adenocarcinoma	None	Present	Present	Present	High	Normal	High	High
Radovanovic et al, 2020 ⁵	United States	69 (M)	Asthma, BPH, and SCC of the tongue	None	Present	Present	Present	Normal	Normal	High	N/A
Tariq et al, 2019 ⁶	United States	48 (F)	Roux-en-Y bypass	None	Present	None	Present	High	High	High	High
Rahmati et al, 2017 ⁷	United States	59 (F)	Multiple sclerosis	None	Present	Present	Present	High	High	High	High
Buelow et al, 2013 ⁸	United States	65 (M)	N/A	None	Present	Present	N/A	N/A	N/A	N/A	N/A
Kröll and Sendi, 2012 ⁹	Switzerland	34 (M)	Healthy	None	Present	Present	Present	N/A	N/A	N/A	N/A
Shahani and Khardori, 2011 ¹⁰	United States	34 (M)	Chronic pancreatitis	None	Present	None	Present	Normal	Normal	Normal	Normal
Clarke et al, 2003 ¹¹	United Kingdom	19 (F)	Healthy	None	Present	Present	Present	N/A	High	High	High
Etienne et al, 2001 ¹²	France	68 (M)	TB	None	None	Present	No	High	High	N/A	N/A

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; BPH, benign prostatic hyperplasia; CT, computed tomography; F, female; HTN, hypertension; HFrEF, heart failure with reduced ejection fraction; LC, leukocytosis; M, male; N/A, not available; SCC, squamous cell carcinoma; TB, tuberculosis; TB, total bilirubin.

drainage, and anticoagulants.¹⁴ Coverage for *Fusobacterium* with combinations of penicillin/beta-lactamase inhibitors, metronidazole, cephalosporins, carbapenems, or clindamycin should always be pursued.⁵ Most regimens included an initial 2–4-week course of intravenous therapy, followed by oral therapy.⁵ The duration of treatment in the reported cases was variable and ranged from 2–12 weeks (Table 2). Source control and abscess drainage with culture are recommended in cases of liver abscess to confirm etiology and guide therapy.^{2,6,15} Abscess drainage was performed in 8 of the 10 cases in our review.

The role and duration of anticoagulant use remain controversial.¹⁶ Some authors recommend the universal use of anticoagulation because of higher recanalization rates while others suggest the selective use of anticoagulation.¹⁶ Anticoagulants were used in 7 of 10 of the reviewed cases, and the duration varied from 2 to 6 months. There is no definitive rule for testing for hypercoagulable diseases (HCDs). All the cases did not report a history of HCD, and 1 case tested for underlying hypercoagulable disease. Follow-up imaging is usually performed to confirm the resolution of liver abscess and portal vein thrombosis. Follow-up imaging with ultrasound, CT, or MRI of the abdomen was pursued in 8 of 10 cases. Cavertous transformation of the portal vein, a complication of long-standing portal vein thrombosis, was noticed in 2 cases.

In conclusion, the GI variant of Lemierre syndrome can mimic metastatic liver lesions with portal vein thrombosis. Therefore, excluding malignancy and rapidly recognizing distinctive clinical features is critical. With a mortality rate of 11%–35%,^{2,14} early detection and prompt treatment of GI-variant Lemierre syndrome is crucial to delivering quality, patient-centered care.

DISCLOSURES

Author contributions: F. Jaber: writing the draft and manuscript, project administration, and is the article guarantor. S. Alsakarneh: writing the manuscript and literature review. J. Campbell: reviewing and editing the manuscript and figure organization. A. Awad: writing the manuscript and organizing the table. WT Mohamed: reviewing and editing the manuscript and literature review. K. Wittler: reviewing and editing the manuscript and supervision. H. Ghaz: reviewing and editing the manuscript, resolving points of conflict, and supervision. W. Clarkston: reviewing and editing the manuscript and supervision.

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Table 2. Extracted diagnosis, management, and prognosis data from all 10 case reports included in the literature review

Study	Workup								Management				Outcome (liver abscess)	Outcome (PVT)
	Infection source	Imaging	Thromboses site	Blood culture	Organism	Liver abscess	Aspiration culture	Gene PCR and/or sequence analysis	Abscess drainage	Antibiotics (total duration)	Anticoagulation (total duration)	Follow-up (duration)		
Current study, 2022	Diverticulitis	CT and MRI	PV and SMV	Positive	<i>F. nucleatum</i>	Yes	Positive	No	Yes	Ampicillin/sulbactam > ertapenem > amoxicillin-clavulanic acid (12 wk)	Enoxaparin and then apixaban (12 wk)	CT	Near-complete resolution	Near-complete resolution (mild residual)
Furuncuoglu et al, 2021 ⁴	Pancreatic adenocarcinoma status post surgery	MRI	PV	Positive	<i>F. necrophorum</i>	Yes	N/A	No	No	Cefaperazone-sulbactam (1.5 wk)	None	MRI	Complete resolution	Complete resolution
Radovanovic et al, 2020 ⁵	Unknown	US, CT, and MRI	PV	Positive	<i>F. necrophorum</i>	Yes	Positive	No	Yes	Ceftriaxone and metronidazole > amoxicillin-clavulanic acid (5 wk)	Enoxaparin and then warfarin (N/A)	N/A	N/A	N/A
Tariq et al, 2019 ⁶	Surgical site	CT and MRI	PV	N/A	<i>F. nucleatum</i>	Yes	Positive	No	Yes	Ceftriaxone and metronidazole (6 wk)	Enoxaparin and then rivaroxaban (6 mo)	CT (4 mo)	Complete resolution	No resolution and formation of collaterals
Rahmati et al, 2017 ⁷	Diverticulosis	CT and MRI	PV	Positive	Fusobacterium	Yes	Positive	Yes	Yes	Ampicillin-sulbactam > ertapenem > ceftriaxone and metronidazole > amoxicillin-clavulanic acid (8 wk)	Enoxaparin (8 wk)	CT (4 mo)	Near-complete resolution	Cavernous transformation of portal vein
Buelow et al, 2013 ⁸	Diverticulitis	CT	PV	Negative	Fusobacterium	Yes	Positive	No	Yes	Ciprofloxacin and metronidazole > ceftriaxone and metronidazole (N/A)	Heparin > enoxaparin (N/A)	N/A	N/A	N/A
Kröll and Sendi, 2012 ⁹	Oropharyngeal	US and MRI	PV	Negative	<i>F. necrophorum</i>	Yes	Negative	Yes	Yes	Ceftriaxone and metronidazole (N/A)	Was given, but not specified	Done but not specified (1 year)	Complete resolution	Complete resolution
Shahani and Khardori, 2011 ¹⁰	Pancreatitis	CT	PV, SMV, and SV	Positive	<i>F. necrophorum</i>	Yes	Positive	No	Yes	Vancomycin and meropenem > tigecycline and meropenem > tigecycline (4 wk)	None	CT (2 mo)	Complete resolution	Cavernous transformation of the portal vein and formation of collaterals
Clarke et al, 2003 ¹¹	Oropharyngeal	CT and US	PV and SMV	Positive	<i>F. nucleatum</i>	Yes	Positive	No	Yes	Benzyl-penicillin, metronidazole and ciprofloxacin (6.5 wk)	Warfarin (N/A)	US (7 wk)	Partial resolution	Portal hypertension, and formation of collaterals
Etienne et al, 2001 ¹²	Diverticulosis	CT and US	PV	Positive	<i>F. nucleatum</i>	Yes	N/A	No	No	Cefotaxime and metronidazole > metronidazole (5 wk)	None	US (5 wk)	Complete resolution	N/A

CT, computed tomography; MRI, magnetic resonance imaging; N/A, not available; PCR, polymerase chain reaction; PV, portal vein; PVT, portal vein thrombosis; SMV, superior mesenteric vein; SV, splenic vein; US; ultrasound; >, switch to.

Informed consent was obtained from the patient.

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