



An atypical presentation of lemierre syndrome of urogenital source

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ARTICLE INFO

Article history:

Received 31 August 2021

Received in revised form 18 October 2021

Accepted 18 October 2021

Available online xxxx

Keywords:

Lemierre

Urogenital

Fusobacterium

Necrophorum

Bartholin

Thrombophlebitis

ABSTRACT

Lemierre syndrome has classically been described as septic thrombophlebitis of the internal jugular veins resulting from primary oropharyngeal disease caused by *Fusobacterium necrophorum*. However, many cases have been reported of the syndrome originating from other primary sites of infection, resulting in limited utility of the diagnostic criteria and increased difficulty in making the diagnosis. We describe a 22-year-old female who developed the syndrome through a *Fusobacterium* infection which originated from a Bartholin gland abscess, a phenomenon that has not yet been described in the literature. Understanding and recognizing the variable forms of Lemierre syndrome allows us to better define the condition and provide optimal care to patients.

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Introduction

Lemierre syndrome is a form of septic thrombophlebitis classically resulting from primary infection of the head and neck most commonly by the pathogen *Fusobacterium necrophorum*. Individuals with the syndrome typically develop thrombotic disease within the jugular veins in addition to other systemic findings including pulmonary and hepatic abscesses. What are much more under-recognized, however, are the atypical presentations of the syndrome that do not involve diseases of the oropharynx, despite a plethora of reports in the literature of infections originating from the gastrointestinal and genitourinary tracts. Here we present a case of a young patient who developed complications of Lemierre syndrome resulting from an infected Bartholin gland cyst.

Case presentation

A 22-year-old previously healthy East Asian female initially presented to an outside hospital with the complaint of one week of general malaise, myalgia, and dyspnea. At presentation her review of systems was also notable for subjective fevers, anorexia, nasal discharge and congestion, and abdominal pain. She also reported having increased vaginal pain and dysuria for the past few days. She denied having cough, sore throat, throat pain, or hoarseness.

The patient was initially from Australia and came to the United States eight years ago to pursue her educational goals. She recently traveled back to Australia in the spring of 2020 for a short period of time. She was a student at a nearby university. The patient denied any recent outdoor activities or exposures to farm animals. She was functionally independent, very rarely smoked cigarettes, and denied any alcohol or drug use. She denied any sick contact but admitted to having unprotected sex approximately one month ago.

On presentation (day 1) to the outside hospital (OSH) the patient was found to be afebrile, tachycardic, and hypotensive. She was admitted to their intensive care unit where her oxygen requirement gradually increased. Her initial bloodwork revealed white blood cell count 6200/ μ L (eventually increasing to 19,500/ μ L) and platelet count 23,000/ μ L at admission. Her metabolic panel was notable for a creatinine 1.33 mg/dL (which improved to 0.5 mg/dL after administration of IV fluids), alanine transaminase 36 U/L, aspartate transaminase 59 U/L, alkaline phosphatase 466 U/L, and total bilirubin 2.9 mg/dL. Her serum lactic acid level was initially 4.9 mmol/L.

Imaging at OSH (Fig. 1) included a chest radiography which revealed small bilateral pleural effusions with right side greater than left. Computerized tomography (CT) of abdomen and pelvis was notable for the liver consisting of multiple cystic lesions throughout measuring approximately 1.7 cm in diameter with intrahepatic and extrahepatic bile duct dilatation, mild splenomegaly, and evidence of a right sided Bartholin gland cyst. An ultrasound of the abdomen performed revealed findings consistent with hepatic abscesses and reactive gall bladder thickening. Her blood cultures from admission resulted in growth of *Fusobacterium necrophorum* in both sets. She

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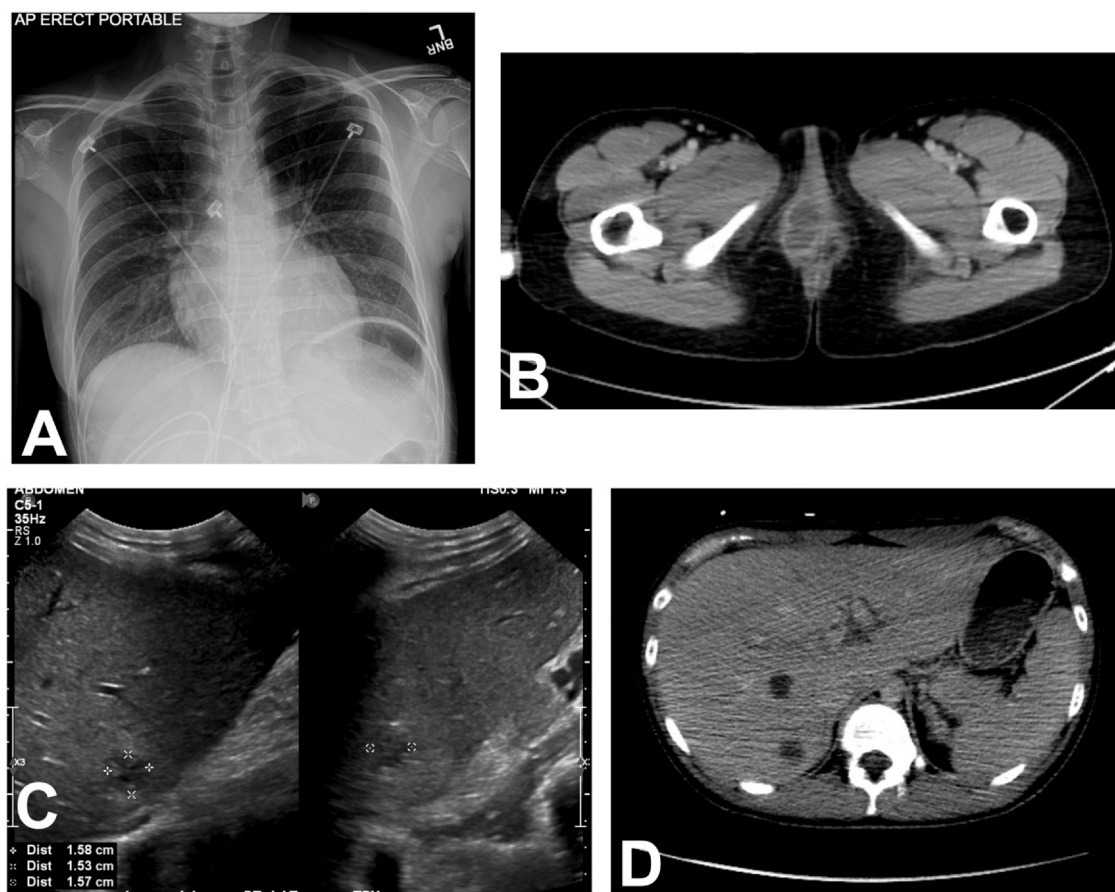


Fig. 1. Title: Imaging during initial presentation at outside hospital (Day 1). Description: A. Chest x-ray showing interstitial opacities as well as bilateral pleural effusion, right side greater than left. B. Computerized tomography (CT) scan of abdomen showing possibly infected right Bartholin gland cyst. C. Ultrasound of liver showing hepatic abscesses. D. CT scan of abdomen showing hepatic abscesses.

was started on meropenem and arrangements were made to have her transferred to our hospital for further management.

On arrival to our institution's intensive care unit on day 3 the patient was febrile (102.4° F), tachycardic, tachypneic with a blood pressure of 157/97 and an oxygen saturation of 100%, however now on 60 L/min, 65% FiO₂ high flow nasal cannula. Her physical exam was notable for a lung exam revealing scattered crackles with normal respiratory effort on high flow nasal cannula, cardiac exam revealing tachycardia, and abdominal exam demonstrating mild right upper quadrant abdominal tenderness. On genitourinary exam, the patient had erythema and edema of the labia without drainage. There was no evidence of poor dentition or gingivitis on oral exam. Initial labs were notable for white blood cell count 14,700/ μ L (absolute neutrophil count 11,560/ μ L), hemoglobin 11 g/dL, platelet count 16,000/ μ L, erythrocyte sedimentation rate 31 mm/h, serum lactate dehydrogenase 323 U/L, alkaline phosphatase 129 U/L, c-reactive protein 17.05 mg/dL, fibrinogen 349 mg/dL, and haptoglobin was 59 mg/dL. COVID-19 PCR was negative, as were the HIV antibody screening and urine gonorrhea and chlamydia PCR tests. CT of the neck (Fig. 2) showed no evidence of abscess formation, and initial CT of chest showed multiple nodular foci throughout the right lung fields, concerning for septic emboli, multifocal pneumonia, and bilateral pleural effusion, right greater than left, with collapse of adjacent lung tissue. Interval worsening of hepatic abscess burden was also noted. Infectious disease was consulted and her antibiotic regimen was transitioned from meropenem to piperacillin-tazobactam. The patient's respiratory status improved with diuresis, and she was transferred to the general medicine ward on day 6 on nasal cannula.

The patient subsequently underwent an ultrasound guided thoracentesis of the right lung on day 9 with removal of 800 mL of maroon colored pleural fluid. Analysis of the pleural fluid revealed evidence of exudative fluid by Light criteria given a fluid LDH/serum LDH of 3.48, a fluid protein/serum protein of 0.61, and a fluid LDH that was greater than two thirds the upper limit of normal for serum LDH at our lab. Additional findings included a fungal smear with no growth, a negative acid-fast stain, a gram stain with no organisms and with 4+ granulocytes, and no aerobic or anaerobic bacterial growth.

Repeat CT of chest, abdomen and pelvis (Fig. 3) on day 10 revealed evidence of bilateral multifocal pneumonia with pleural effusions as well as concerns for necrotizing pneumonia or developing pulmonary abscess, the presence of hepatic abscesses, and subcutaneous right perineal region fluid collection concerning for infected Bartholin gland cyst. Given the findings of persistent pleural effusions and the vulvar cyst, cardiothoracic surgery and gynecology were consulted at this time.

On day 11, the patient underwent a video-assisted thoracoscopic surgery (VATS) washout and decortication to relieve the persistent right pleural effusion. Pleural rind acid fast staining was negative, biopsy revealed fibrinous and organizing pleuritis with fibrinopurulent exudate consistent with empyema, and cultures revealed 1+ granulocytes with no organisms. She simultaneously underwent a pelvic examination by the gynecology team while sedated which revealed a right labial abscess with swelling. Incision and drainage were performed resulting in the drainage of clear serous fluid followed by thick white caseous material. Gram stain

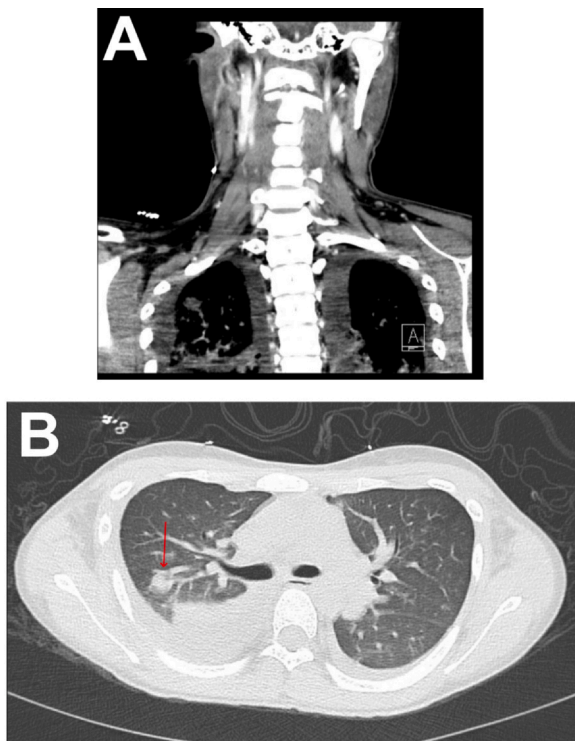


Fig. 2. Title: Imaging during initial presentation to our hospital (Day 3). Description: A. Contrast-enhanced computerized tomography (CT) of neck, coronal view, which showed no evidence of abscesses or thrombotic disease. B. CT of chest showing nodular foci (red arrow) in right lung concerning for septic emboli. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

revealed no organisms with 3+ granulocytes, and bacterial culture grew two colonies of *Candida albicans*.

The patient additionally had a contrast-enhanced CT of her abdomen and pelvis done on day 15 which noted (Fig. 4) a nonocclusive thrombus within the right common iliac vein extending into the internal iliac

vein and possible right distal external iliac vein nonocclusive thrombus. Both transthoracic and transesophageal echocardiography done during the admission were performed and neither revealed any evidence of valvular vegetations. She was not anticoagulated during this admission. After extensive work up and evaluation of the clinical picture and lab/imaging findings, the diagnosis of atypical Lemierre syndrome of urogenital origin was made.

The patient continued to clinically improve as her oxygen requirement and dyspnea decreased, in addition to her vulvar pain. None of several repeat blood cultures since the initial sets at OSH grew organisms. The patient was subsequently transitioned to intravenous ceftriaxone and oral metronidazole and discharged on day 17 with an infectious disease follow up appointment. Three weeks later at follow up the patient reported improvement of symptoms (including breathing and vaginal pain), appetite, energy, and weight. She was transitioned to amoxicillin-clavulanate with another future infectious disease follow up appointment.

Discussion

Lemierre syndrome, first described in 1936 by French bacteriologist André-Alfred Lemierre, is a syndrome of septic thrombophlebitis classically and usually involving the internal jugular veins in the setting of recent oropharyngeal infection [1]. The condition is most caused by the bacterium *Fusobacterium necrophorum* with other culprits including other *Fusobacteria*, *Staphylococcus*, *Streptococcus*, *Enterococcus*, *Bacterioides*, and *Peptostreptococcus* [2].

The pathogenesis of Lemierre syndrome involves a primary infection, usually pharyngitis, which leads to bacterial translocation into pharyngeal spaces and subsequent jugular vein involvement resulting in thrombophlebitis. As the disease progresses, metastatic involvement from septic emboli can occur and most commonly involves the lungs (in the form of abscesses, cavitary lesions, and effusions), but also joints, spleen, liver, and kidneys. On clinical presentation, patients are typically young (16–30 years old) and otherwise healthy. They may present with symptoms of pharyngitis (sore throat, neck pain) as well as nonspecific symptoms of infection

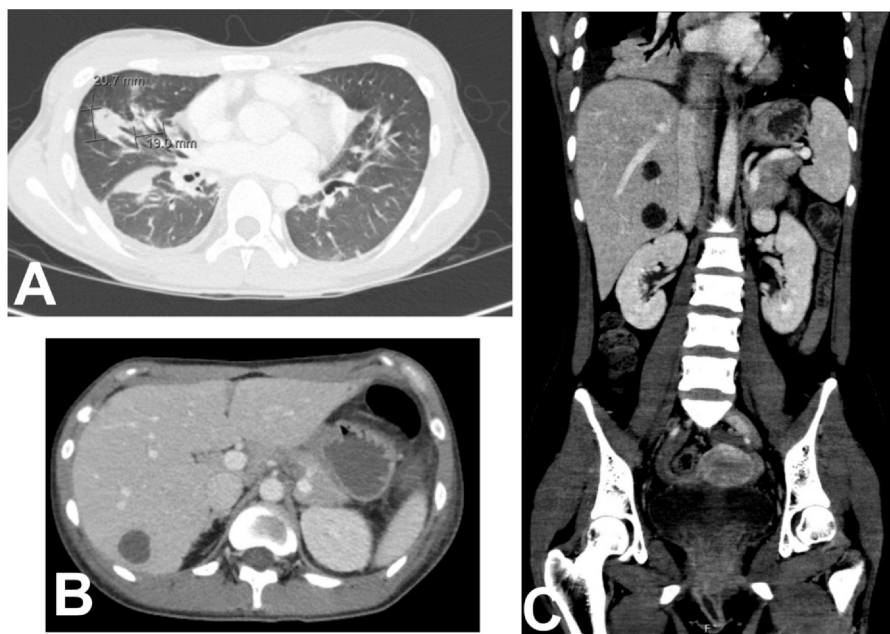


Fig. 3. Title: Repeat imaging on Day 10 after thoracentesis was performed. Description: Repeated computerized tomography of chest of the abdomen and pelvis showing A. multifocal pneumonia with nodular opacities in transverse view, B. hepatic abscess in transverse view, C. hepatic abscesses and right vulvar lesion consistent with Bartholin's gland cyst in coronal view.

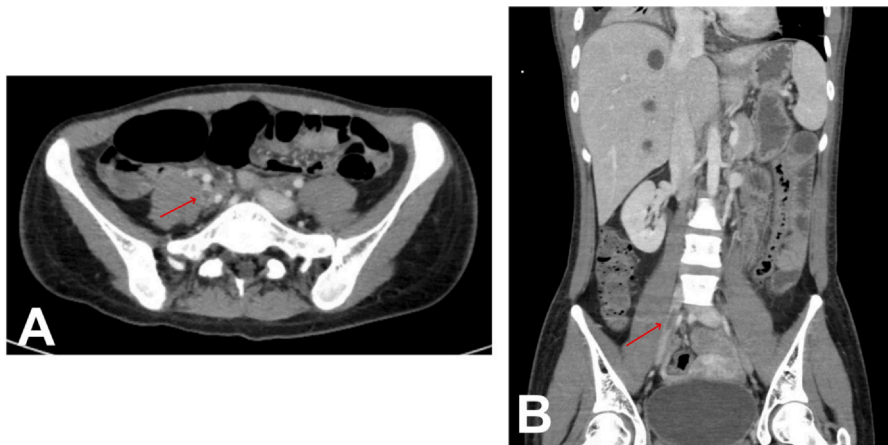


Fig. 4. Title: Repeat computerized tomography of the abdomen and pelvis with contrast on Day 15. Description: A. thrombosis in right iliac vessels (red arrow) in transverse view, B. thrombosis in right iliac vessels (red arrow) in coronal view. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

including fever, abdominal pain, nausea, and vomiting. Patients may be febrile, hypotensive, tachycardic, tachypneic possibly with pharyngeal hyperemia and exudate on presentation.

Diagnosis involves the identification of the organism in blood cultures, the evaluation of jugular vein thrombophlebitis with imaging (CT scan of head and neck with IV contrast, ultrasonography as alternative), and the additional evaluation of metastatic disease with imaging and cultures based on clinical signs of involved systems (such as lung imaging or joint aspiration). Historically, criteria for diagnosis included: 1. A primary head/neck infection, 2. Thrombotic disease of the internal jugular vein or other vein of the head/neck or metastatic lesions, 3. *F. necrophorum* isolated from blood culture or normally sterile sites [3]. Treatment focuses on early and aggressive antibiotic therapy typically with beta lactamase resistant beta lactam (such as empiric therapy with piperacillin-tazobactam, carbapenem, or ceftriaxone) with clindamycin and metronidazole as alternatives based on sensitivity data [4]. Surgical incision and drainage or washout may be necessary for adequate source control in the setting of abscesses. The use of anticoagulation therapy for thrombosis, while controversial, may be beneficial if extensive clot is present especially into the cerebral sinuses.

Our patient's presentation and clinical findings were quite atypical for Lemierre syndrome. She did not present with the classic head or neck complaints (sore throat, throat pain, neck swelling) but rather with vulvar pain and generalized signs and symptoms of infection. While her initial blood cultures did grow *Fusobacterium necrophorum*, CT evaluation of neck did not show any evidence of abscess or thrombophlebitis. Rather, extensive thrombotic disease was seen in the iliac veins. Metastatic disease to the lung and liver, which is typical of Lemierre syndrome, was seen in our patient. Interestingly, she had evidence of an inflamed Bartholin gland cyst consistent with her vulvar pain.

Our patient likely had translocation of *F. necrophorum* through her infected Bartholin gland cyst resulting in thrombophlebitis of her right common iliac, internal iliac and external iliac veins. Disease progression resulted in the development of pulmonary and liver abscesses. Unfortunately, the incision and drainage of her Bartholin gland cyst was performed post-antibiotics and did not grow any bacterial organisms. Given that *F. necrophorum* is part of the normal bacterial flora in the pharynx, gastrointestinal tract, and the female genital tract, it is reasonable to assume that the origin of infection for our patient was genitourinary in source given the overall clinical picture [4].

Various atypical presentations of Lemierre syndrome have been described as case studies in the literature, including one here of an infection likely of gastrointestinal source (colonic bleed) [5]. Several cases have been reported of the female urogenital tract as the source including: a postcoital wound [6]; an intrauterine device related endometritis from *F. necrophorum* [7]; uterine necrosis in setting of caesarian section [8]. A more recent case was published of a 28-year-old female with pelvic peritonitis without thrombophlebitis due to *F. necrophorum*, however of unclear source [9]. Ocular and central nervous system manifestations of the syndrome has also been described [10,11]. On our literature review, there has been no prior report of atypical Lemierre syndrome resulting from Bartholin gland infection. While presentations of atypical Lemierre syndrome of suspected urogenital source are quite diverse, generally patients tend to have thrombophlebitic disease of iliac/ovarian vessels and pulmonary/hepatic abscesses. This was true in the case of our patient as well.

The historical diagnostic criteria for Lemierre syndrome described above have been controversial in the field as many patients have variant forms of the classic syndrome. Our patient for example had no head/neck symptoms or findings on head/neck imaging, however carried many other features of the syndrome. Additionally, Lemierre syndrome can be caused by pathogens other than *F. necrophorum*, further limiting the validity and utility of the criteria. Given that such variety in presentations have been reported, it is reasonable to examine these case reports further and allow for re-definition of the syndrome. It is quite possible that the low prevalence of these systemic manifestations of Lemierre syndrome may be attributed to the fact that they are underrecognized and under-reported. Here, we present this case to add to current literature on atypical Lemierre syndrome and to increase awareness among practitioners so they may consider this diagnosis. This is especially important as the disease is quite life threatening if early evaluation and diagnosis are not made and prompt treatment is not administered.

Conclusion

Lemierre syndrome in its classic form is described as thrombophlebitis of the internal jugular veins in the setting of *Fusobacterium necrophorum* infection of the oropharynx. Less recognized are the atypical forms of the syndrome and their variations in presentation. Here we describe a case of a young female with

pulmonary, hepatic and thrombophlebitic diseases in the setting of *F. necrophorum* bacteremia likely of urogenital source (Bartholin gland cyst). Similar presentations have been described in literature, however they are largely underrecognized. Better understanding in the medical community of such variants of Lemierre syndrome can allow for prompt diagnosis, early treatment, and better outcomes.

Author contribution

Abhishek Thakur: Data collection, Data analysis, Writing, Final review and Submission. **Wenjing Chen:** Data collection, Data analysis, Writing and Final review.

Acknowledgements

The authors would like to thank Drs. Pinky Jha, MD (Medical College of Wisconsin) and Natasha Kesav, MD (University Hospitals Cleveland Medical Center) for their assistance in review and editing of the manuscript.

Declarations of Interests

None.

Informed Consent

Informed consent was obtained from the individual participant included in the study.

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