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Lemierre Syndrome Without Pharyngitis: An Atypical Case Posing a Diagnostic Challenge

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Abstract

Atypical presentations of Lemierre syndrome can delay diagnosis, particularly in patients without preceding oropharyngeal symptoms. We present a case of a 61-year-old woman with poor dentition who presented with confusion, lethargy, headache, and hyponatremia without antecedent pharyngitis. Blood cultures grew *Streptococcus constellatus*, and cerebrospinal fluid (CSF) analysis demonstrated neutrophilic pleocytosis and elevated protein. Persistent severe headaches, high fever, right eye pain, decreased right distant visual acuity, and photophobia prompted venous imaging, which revealed a near-occlusive thrombus of the proximal left internal jugular vein with extension into the dural venous sinuses. Chest computed tomography (CT) demonstrated a moderate-to-large left pleural effusion. Treatment included intravenous ceftriaxone, metronidazole, therapeutic anticoagulation, chest tube placement, and intrapleural fibrinolytic therapy. Her neurologic status returned to baseline, and she was discharged after a 20-day hospitalization to complete antimicrobial and anticoagulation therapy. This case highlights the importance of considering Lemierre syndrome in older patients with unexplained bacteremia and neurologic or pulmonary findings, even in the absence of classic oropharyngeal symptoms.

Categories: Pulmonology, Internal Medicine, Infectious Disease
Keywords: atypical presentation, diagnostic challenge, fusobacterium necrophorum, internal jugular vein, lemierre syndrome, pulmonary septic emboli, septic thrombophlebitis

Introduction

Lemierre syndrome is a rare but potentially life-threatening form of septic thrombophlebitis classically characterized by internal jugular vein thrombosis, bacteremia, and metastatic septic emboli following an acute oropharyngeal infection. First described by André Lemierre in 1936, the syndrome became known as the “forgotten disease” after the widespread use of antibiotics decreased its incidence [1]. Classically, Lemierre syndrome affects otherwise healthy adolescents and young adults after pharyngitis or tonsillitis, most commonly due to *Fusobacterium necrophorum* [2]. The typical clinical course involves persistent fever, unilateral neck pain or tenderness, and pulmonary septic emboli developing days after the initial pharyngeal illness [1].

Contemporary literature, however, suggests that the clinical spectrum of Lemierre syndrome is broader than the traditional pharyngitis-associated presentation. In an analysis of 712 reported cases, 27% of patients had no signs or recent history of acute oropharyngeal infection, and 53% did not meet the restrictive definition of typical Lemierre syndrome [3]. Additional case reports and series have documented presentations in older adults, infections involving non-*Fusobacterium* organisms, and atypical complications, including intracranial venous thrombosis [4,5]. These nonclassic presentations can obscure the diagnosis and delay vascular imaging, antimicrobial optimization, and multidisciplinary management [1,2].

We report an atypical case of Lemierre syndrome in a 61-year-old woman who presented with encephalopathy and was subsequently found to have *Streptococcus constellatus* bacteremia, elevated cerebrospinal fluid (CSF) leukocyte count and protein, left pleural effusion, and internal jugular vein thrombosis with dural venous sinus extension. Although an odontogenic source was suspected, the primary focus of infection was not definitively established. This case highlights the importance of considering Lemierre syndrome in patients with unexplained bacteremia and neurologic or pulmonary manifestations, even in the absence of preceding pharyngitis.

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Case Presentation

A 61-year-old woman with a past medical history significant for poor dentition, alcohol use disorder, and 40 pack-year smoking history was brought to the emergency department for evaluation of progressive altered mental status. Her partner provided the history as the patient was somnolent during questioning. He

reported two to three days of worsening confusion, lethargy, generalized weakness, poor oral intake, and subjective fever. She had become increasingly sedentary, spending most of the day in a recliner. Her gait had changed from baseline to slow and shuffling. She had one episode of vomiting, which she attributed to food poisoning. She also endorsed sharp right periorbital pain and severe headaches. Alcohol consumption was noted to be several times per week. Her history was especially notable for multiple tooth extractions within the past year, after which she continued to use bicarbonate mouth rinses for dental pain.

On arrival at the emergency department, she was tachycardic at 114 beats per minute with a fever of 102.1 °F. Her blood pressure was 126/87 mmHg. On initial examination, the patient was somnolent and oriented to person and place but not to time, with a shuffling gait, nuchal rigidity, and a negative Brudzinski sign. On subsequent evaluation by neurology, she was alert and fully oriented, with intact memory, attention, and language. Pupils were equal and reactive to light, extraocular movements were intact, and visual fields were full to confrontation. However, she reported decreased distant visual acuity in the right eye. The remaining cranial nerves were intact. Motor examination demonstrated normal muscle tone and 5/5 strength in all extremities without pronator drift. Sensation was intact bilaterally, deep tendon reflexes were symmetric and normal, and plantar responses were downgoing bilaterally. Finger-to-nose testing was intact without dysmetria. An oropharyngeal inspection demonstrated no pharyngeal erythema, tonsillar swelling, or cervical lymphadenopathy. Initial laboratory studies were notable for multiple electrolyte derangements: hyponatremia, hypokalemia, and hypochloremia. She also presented with leukocytosis, transaminitis, and hyperbilirubinemia. Urinalysis demonstrated pyuria and bacteriuria, with positive nitrites and leukocyte esterase, and subsequent urine cultures growing *Escherichia coli*.

During the early hospital course, the patient received intravenous fluid resuscitation and empiric ceftriaxone for suspected urosepsis based on her initial urinalysis findings. At the time, she was also presenting with tremulousness, diaphoresis, and tachycardia, raising concern for concomitant alcohol withdrawal. A Clinical Institute Withdrawal Assessment for Alcohol score (CIWA-Ar) of 18 was obtained, for which she received symptom-triggered lorazepam and high-dose thiamine [6]. The patient's encephalopathy was initially considered multifactorial, with sepsis-associated encephalopathy, metabolic disturbances related to hyponatremia, and alcohol withdrawal included in the differential diagnosis. However, the combination of fever, altered mental status, and severe headache also raised concern for a central nervous system infection, particularly meningitis, despite the absence of meningeal signs. Therefore, a lumbar puncture was performed on hospital day 1, revealing CSF with 267 leukocytes/mm^3 with neutrophilic predominance, protein 105 mg/dL, and glucose 40 mg/dL. The BioFire Meningitis Panel was negative for all tested pathogens, including six bacterial targets (*Escherichia coli K1, Haemophilus influenzae, Listeria monocytogenes, Neisseria meningitidis, Streptococcus agalactiae, and Streptococcus pneumoniae*), seven viral targets (cytomegalovirus, enterovirus, herpes simplex virus types 1 and 2, human herpesvirus 6, human parechovirus, and varicella-zoster virus), and one fungal target (*Cryptococcus neoformans/gattii*). However, a CSF culture was not obtained. A summary of critical serum, CSF, and pleural fluid findings, as well as microbiological results, is provided in Table *1*.

Category	Test	Patient result	Reference range or expected finding	Interpretation
Serum chemistry	Sodium	124 mmol/L	135-145 mmol/L	Low
	Potassium	2.8 mmol/L	3.5-5.0 mmol/L	Low
	Chloride	86 mmol/L	98-107 mmol/L	Low
	Glucose	155 mg/dL	70-110 mg/dL	Elevated
	Total protein	5.6 g/dL	6.0-8.3 g/dL	Low
	Lactate dehydrogenase (LDH)	169 U/L	125-243 U/L	Normal
Serum osmolality	Serum osmolality	264 mOsm/kg	275-295 mOsm/kg	Low
Urine studies	Urine osmolality	812 mOsm/kg	50-1,200 mOsm/kg	Inappropriately concentrated urine
	Urine sodium	54 mmol/L	No fixed normal range	Elevated in the setting of hypotonic hyponatremia
Liver studies	Aspartate aminotransferase	63 U/L	10-40 U/L	Elevated
	Alanine aminotransferase	51 U/L	7-56 U/L	Normal
	Total bilirubin	2.5 mg/dL	0.1-1.2 mg/dL	Elevated
Hematology	White blood cell count	13.8 × 10^9/L	4.0-11.0 × 10^9/L	Elevated
Urinalysis	Nitrites	Positive	Negative	Abnormal
	Leukocyte esterase	Positive	Negative	Abnormal
	Bacteriuria	Present	Absent	Abnormal
Urine culture	Bacterial culture and colony count	Escherichia coli, >100,000 CFU/mL	No significant bacterial growth	Positive urine culture
Cerebrospinal fluid	Leukocytes	267 cells/mm^3	0-5 cells/mm^3	Elevated
	Differential	Neutrophil predominant	No neutrophilic predominance	Abnormal
	Protein	105 mg/dL	15-45 mg/dL	Elevated
	Glucose	40 mg/dL	40-70 mg/dL	Low-normal; low relative to serum glucose
	BioFire PCR	Negative	Negative	No organism detected
Microbiology	Blood cultures	Streptococcus constellatus	No growth	Abnormal
Pleural fluid	Total Protein	3.0 g/dL	Interpreted with Light's criteria	Consistent with exudative effusion
	LDH	1,530 U/L	Interpreted with Light's criteria	Consistent with exudative effusion
	Fluid-to-serum protein ratio	0.54	≤0.5 (does not meet exudative criterion)	Exudative
	Fluid-to-serum LDH ratio	9.05	≤0.6 (does not meet exudative criterion)	Exudative

TABLE 1: Initial laboratory findings, cerebrospinal fluid analysis, microbiology, and pleural fluid diagnostic thoracentesis.

LDH, lactate dehydrogenase; PCR, polymerase chain reaction

By hospital day 4, the patient continued to demonstrate sluggish recovery. Despite displaying improved attention and orientation, she continued to report severe headaches, neck pain, right eye pain, decreased right distant visual acuity, and photophobia. Blood cultures grew *Streptococcus constellatus*, prompting infectious disease consultation given the discordance between blood and urine culture results. Ceftriaxone was continued at 2 g intravenously every 12 hours. As her mental status improved and a more complete history and examination became possible, meningitis was considered less likely, and her neck pain was thought to be chronic. However, her persistent neurologic symptoms prompted magnetic resonance

venography (MRV) to evaluate for dural venous sinus thrombosis. Imaging demonstrated filling defects involving the left sigmoid and transverse venous sinuses, jugular bulb, and jugular vein (Figure *1*).

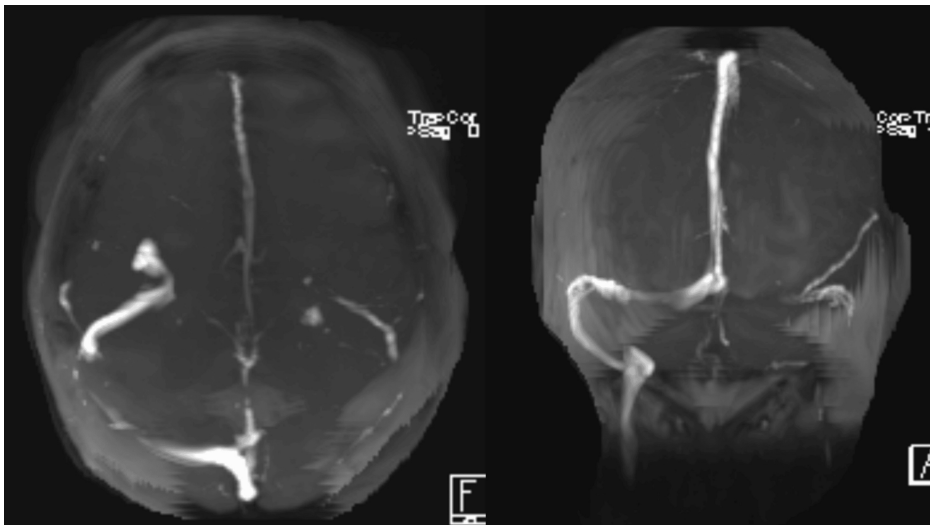


FIGURE 1: Magnetic resonance venography demonstrating left sigmoid and transverse venous sinus filling defect.

Subsequent computed tomography venography (CTV) confirmed a nearly occlusive thrombus within the proximal left internal jugular vein and jugular foramen, with an additional nonocclusive thrombus involving the left sigmoid sinus extending to the junction of the transverse sinus (Figure *2*). In the setting of *Streptococcus constellatus* bacteremia, these findings were best explained by Lemierre syndrome with left-sided septic thrombophlebitis and dural venous sinus extension. Therapeutic anticoagulation with intravenous heparin was initiated, and metronidazole was added to the antibiotic regimen, as anaerobes are frequently implicated in this pathology. Neurology agreed with continuation of full-dose anticoagulation and intravenous antimicrobial therapy.

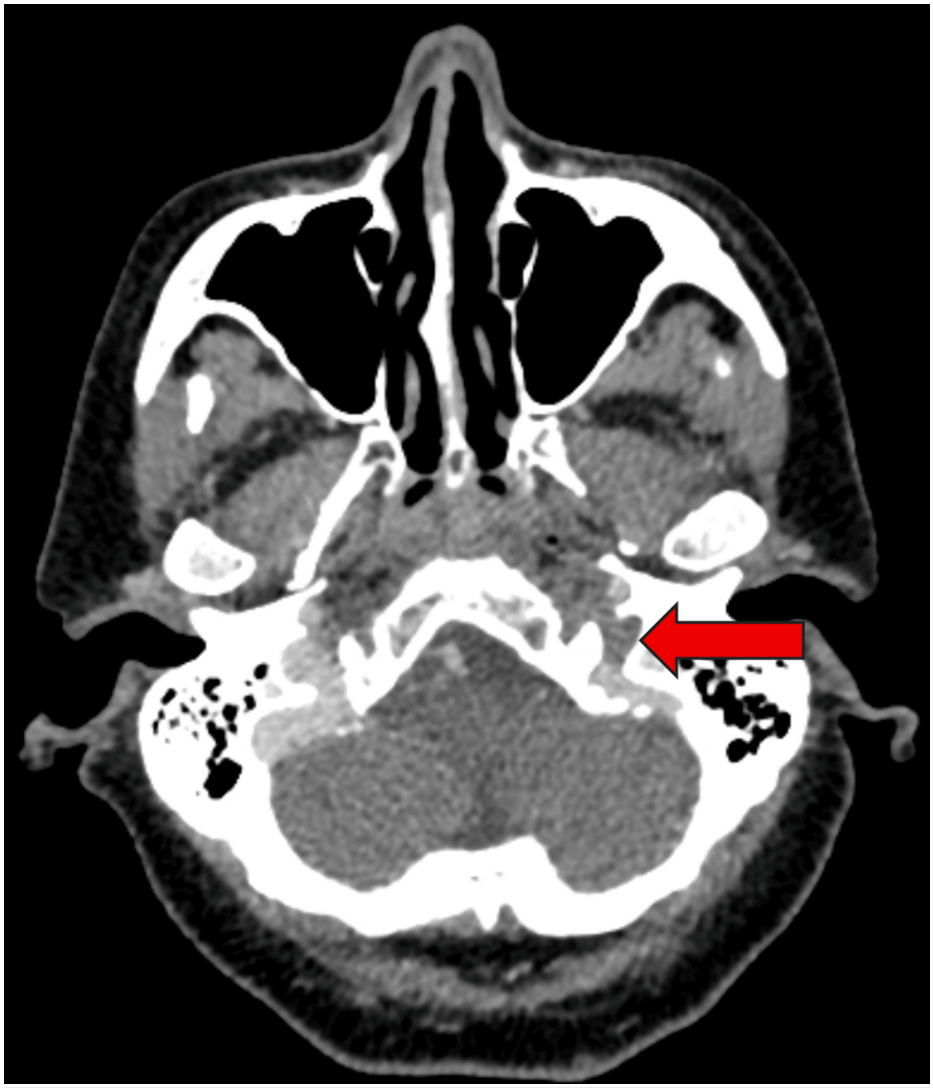


FIGURE 2: Computed tomography venography demonstrating near-occlusive left internal jugular vein thrombosis with dural venous sinus extension.

Computed tomography venography demonstrating a filling defect in the left internal jugular vein as it passes through the jugular foramen. The red arrow indicates the filling defect, consistent with internal jugular vein thrombosis.

On hospital day 8, the patient developed new-onset hypoxemia. CT of the chest demonstrated a moderate-to-large left pleural effusion with partial collapse/atelectasis of the left lower lobe (Figure *3*), which had not been present on admission. Interventional radiology was consulted for chest tube placement. Pleural fluid analysis revealed a total protein concentration of 3.0 g/dL and LDH of 1,530 U/L, compared with a serum total protein of 5.6 g/dL and serum LDH of 169 U/L. The pleural fluid-to-serum protein ratio was 0.54, and the LDH ratio was 9.05, both exceeding the respective Light's criteria thresholds of 0.5 and 0.6. Light's criteria distinguish exudative from transudative pleural effusions based on the relative protein and LDH concentrations in pleural fluid and serum [7]. These findings confirmed an exudative effusion, supporting an inflammatory or infectious process. The pleural effusion was suspected to represent pulmonary infectious involvement associated with Lemierre syndrome. The loculated pleural effusion required intrapleural fibrinolytic therapy with tissue plasminogen activator (tPA) and dornase alfa (DNase), administered via the chest tube with the assistance of pulmonology. The chest tube was removed on hospital day 14 following clinical improvement and decreased drainage.

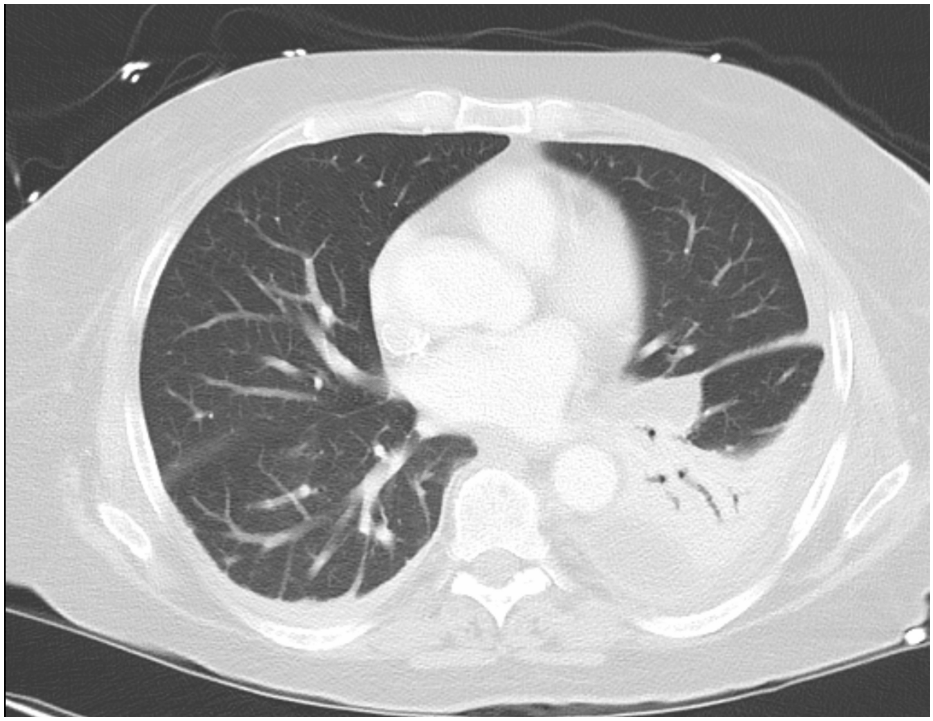


FIGURE 3: Computed tomography of the chest demonstrating moderate-to-large left pleural effusion with left lower lobe atelectasis.

The patient rapidly improved otherwise with return to baseline neurologic status and full orientation by day 6. Headache and blurry right vision improved gradually throughout the hospital course. Further evaluation of her hyponatremia revealed a serum osmolality of 264 mOsm/kg, urine osmolality of 812 mOsm/kg, and urine sodium of 54 mmol/L. These findings demonstrated hypotonic hyponatremia with inappropriately concentrated urine and elevated urinary sodium, suggestive of syndrome of inappropriate antidiuretic hormone secretion (SIADH), potentially related to her central nervous system infection. Her hyponatremia was considered multifactorial, with possible contributions from sepsis and volume depletion. She was managed with fluid restriction and salt tablet supplementation, with normalization of serum sodium prior to discharge. Her UTI due to *Escherichia coli* resolved after a seven-day antibiotic course. Transaminitis and hyperbilirubinemia were attributed to alcohol use and hepatic steatosis seen on ultrasonography. Alcohol withdrawal resolved with supportive care. Repeat blood cultures confirmed clearance of bacteremia.

After a 20-day hospital stay, the patient was discharged home in stable condition. She was afebrile, hemodynamically stable, and neurologically intact at discharge. Given the diagnosis of Lemierre syndrome complicated by internal jugular vein septic thrombophlebitis with dural venous sinus extension, infectious disease recommended prolonged antimicrobial therapy. Treatment with ceftriaxone 2 g intravenously every 12 hours was continued, and metronidazole 500 mg orally every eight hours was added for a six-week course to provide anaerobic coverage in the setting of persistent headaches and possible anaerobic involvement with Lemierre syndrome. Weekly complete blood count and comprehensive metabolic panel monitoring were arranged. If intravenous therapy became infeasible, an alternative oral regimen of levofloxacin 750 mg daily was recommended. She completed two weeks of inpatient intravenous heparin therapy and was transitioned to apixaban to complete a six-week total course of anticoagulation. Pulmonology recommended repeat chest imaging in six weeks with outpatient follow-up. She was referred for dental evaluation and counseled on alcohol and tobacco cessation.

Discussion

Atypical presentations of Lemierre syndrome may involve variations in the affected venous territory, causative pathogen, or primary site of infection [4]. Although internal jugular vein thrombosis is a characteristic finding, Lemierre-like syndromes involving other venous structures, including the facial, external jugular, and iliac veins, have been reported [4]. Microbiologic diversity further broadens this clinical spectrum. In an individual patient-level analysis of 712 cases, *Streptococcus* or *Staphylococcus* species were identified in 108 of 574 patients with positive bacterial cultures, with these organisms more frequently reported among older patients than *Fusobacterium* species [8]. Other reports have identified pathogens such as *Klebsiella pneumoniae*, further demonstrating that this syndrome is not restricted to *Fusobacterium* infections [5]. Atypical disease may also involve extracervical sites, as illustrated by Radovanovic et al., who described an abdominal variant characterized by *Fusobacterium necrophorum* bacteremia, septic portal vein

thrombosis (pylephlebitis), and hepatic abscess [9]. These variations underscore the challenges of defining Lemierre syndrome and its overlap with the broader spectrum of bacteria-associated thrombophlebitis [2].

Our patient's presentation illustrates the diagnostic challenges associated with this broader clinical spectrum. Unlike the typical presentation, this 61-year-old female had no reported antecedent pharyngitis and presented primarily with encephalopathy, severe headache, photophobia, abnormal CSF findings, and hyponatremia suggestive of SIADH, later developing a pleural effusion. Her confusion, lethargy, generalized weakness, and gait disturbances were potentially attributable to hypotonic hyponatremia, whereas tremulousness, diaphoresis, tachycardia, and an elevated CIWA-Ar score raised concern for concurrent alcohol withdrawal. The initial differential also included urosepsis and meningitis, suggesting a multifactorial cause of encephalopathy and complicating recognition of the underlying septic thrombophlebitis.

Pulmonary involvement is a recognized complication of Lemierre syndrome and may include pleural effusions, pneumonia, and empyema [1]. Shefa et al. described a 22-year-old man with *Fusobacterium necrophorum* bacteremia, necrotizing pneumonia, and bilateral empyema with the organism detected by pleural fluid molecular testing, despite the absence of internal jugular vein thrombosis [10]. In contrast, our patient had *Streptococcus constellatus* bacteremia with internal jugular vein thrombosis extending into the dural venous sinuses and subsequently developed a unilateral, loculated exudative pleural effusion requiring chest tube drainage and intrapleural fibrinolytic therapy. Although infectious pleural involvement was suspected, empyema and septic pulmonary emboli were not confirmed. Additionally, *Streptococcus constellatus* is part of normal oral and oropharyngeal flora and has been associated with odontogenic infections, deep neck space infections, abscess formation, and contiguous spread to adjacent anatomic compartments [11-13]. An odontogenic source was considered given the patient's poor dentition and history of dental infections; however, the primary source of infection remained unidentified.

The patient’s 40 pack-year smoking history may have further contributed to this suspected odontogenic pathway. Cigarette smoking is an independent risk factor for periodontal disease, dental caries, alveolar bone loss, and tooth loss, and has been associated with impaired salivary flow, altered gingival immune response, and increased biofilm formation [14-16]. Smoking also promotes oral microbial dysbiosis, including enrichment of anaerobic and pathogenic organisms such as *Fusobacterium* and *Streptococcus* species, while reducing protective commensal flora [16]. In this context, smoking-related periodontal disease and oral dysbiosis may have increased the risk for an occult odontogenic infection serving as the nidus for septic thrombophlebitis.

Management of Lemierre syndrome requires a multidisciplinary approach involving prolonged antimicrobial therapy and surgical drainage of abscesses when indicated. Antibiotic treatment typically extends for three to six weeks, with regimens commonly including metronidazole for anaerobic coverage [1]. This patient required high-dose ceftriaxone, metronidazole, chest tube placement with intrapleural fibrinolytic therapy, and multidisciplinary care involving infectious disease, neurology, pulmonology, interventional radiology, and cardiothoracic surgery. The role of anticoagulation remains controversial in isolated internal jugular vein thrombosis, and shorter courses of 6-12 weeks have been suggested when anticoagulation is used in this setting [17]. However, when thrombosis extends into the dural venous sinuses, management more closely mirrors cerebral venous sinus thrombosis (CVST). Specifically, in infection-associated CVST, treatment includes acute anticoagulation followed by transition to oral therapy and a typical duration of 3-12 months depending on infection resolution and interval imaging [18,19]. In this case, therapeutic anticoagulation was initiated because of near-occlusive internal jugular vein thrombosis with dural venous sinus extension.

A strength of this case report is its detailed characterization of an atypical presentation of Lemierre syndrome in an older adult, integrating microbiologic findings, CSF analysis, and venous imaging to illustrate the diagnostic challenges associated with the absence of pharyngitis. However, as a single case report, its findings have limited generalizability. The primary source of infection remained unidentified, and the absence of CSF culture limited microbiologic confirmation of central nervous system involvement. Additionally, long-term clinical outcomes and follow-up imaging were not reported, limiting assessment of thrombus resolution and sustained treatment response.

Conclusions

This case highlights the diagnostic challenge of Lemierre syndrome in an older adult without preceding pharyngitis and with *Streptococcus constellatus* rather than classic *Fusobacterium necrophorum*. Her presentation with encephalopathy, hypotonic hyponatremia suggestive of SIADH, neutrophilic CSF pleocytosis, dural venous sinus extension, and pleural effusion illustrates the broader clinical spectrum of Lemierre syndrome beyond the traditional presentation of a young patient with pharyngitis and neck pain. Physicians should consider Lemierre syndrome in older patients with unexplained bacteremia, persistent neurologic symptoms, pulmonary findings, or septic thrombophlebitis, even when classic oropharyngeal symptoms are absent. In patients with compatible clinical findings, timely vascular imaging and multidisciplinary evaluation may facilitate earlier recognition and help guide antimicrobial therapy and source control when indicated.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Critical review of the manuscript for important intellectual content: Megan A. Talamante, Spencer Messina, Laceyahna Winland, Ali Kia

Supervision: Megan A. Talamante, Spencer Messina, Laceyahna Winland, Ali Kia

Disclosures

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