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CASE REPORT

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Lemierre's syndrome complicating influenza A virus infection

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Abstract

We report a 24-year-old previously healthy woman with Lemierre's syndrome following influenza A virus infection. One week after influenza A was diagnosed by rapid antigen test and treated by oseltamivir, she developed multiple cavitary lung lesions, and a left internal jugular vein thrombosis. The blood culture grew Fusobacterium necrophorum. We administered ampicillin-sulbactam and unfractionated heparin to which she responded very well. Although viral infections have been related to Lemierre's syndrome, influenza virus rarely implicated. Lemierre's syndrome should be included in the differential diagnoses of rare complications of influenza virus infection.

KEYWORDS

influenza, Lemierre's syndrome

1 | INTRODUCTION

Lemierre's syndrome is a rare disease characterized by an oropharyngeal infection followed by a septic thrombophlebitis of the internal jugular vein with metastatic septic emboli to the lungs and other organs including joints, muscle, bone, and liver. In the pre-antibiotic era, this syndrome was almost always fatal.[1] The clinical presentation of Lemierre's syndrome is so distinct that it cannot be missed if the physician is aware of the syndrome.[2]

We report a classic case of Lemierre's syndrome with positive blood cultures with *Fusobacterium necrophorum* that developed following influenza A virus infection. Although viral infections, including Epstein-Barr virus (EBV), have been implicated in the pathogenesis of Lemierre's syndrome, influenza has only rarely been reported in association with this syndrome.[3,4]

2 | CASE REPORT

A 24-year-old previously healthy woman presenting with acute fever and sore throat was seen by her primary care physician and found to have influenza A virus infection diagnosed by rapid antigen test two weeks prior to the admission, for which oseltamivir was administered. One week later, the patient visited the same physician because of dyspnea, persistent fever, new right knee pain, and left neck pain. The primary care physician transferred the patient to a community hospital where they began antimicrobial therapy with meropenem and transported the patient to our tertiary medical center for further management. On physical examination, she had a blood pressure of 102/64 mm Hg, heart rate of 92 beats per minute, a respiratory rate of 26 per minute, and a temperature of 38.9° centigrade. She was alert and had no focal neurological deficits or nuchal rigidity. Chest auscultation revealed bilateral coarse crackles. The left neck was tender but not swollen, and her right knee was red, tender, and swollen.

The results of a laboratory investigation showed a white blood cell count of 26 770 per microliter (normal range 4000-8000) and a C-reactive protein level of 21 mg per deciliter (normal range: <0.3). The right swollen knee was aspirated revealing turbid fluid with numerous neutrophil-dominant leukocytes with negative gram-staining and culture results presumably due to already initiated meropenem treatment.

Computed tomography (CT) of the chest demonstrated multiple pulmonary septic emboli with cavities, and CT of the neck indicated left internal jugular vein thrombosis (Figure 1A,B).

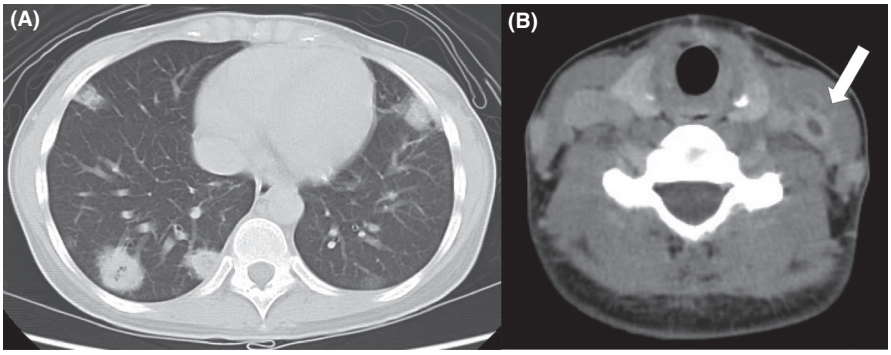

FIGURE 1 A, Computed tomography (CT) of the chest showed multiple cavitary lung lesions suggesting septic emboli. B, CT of the neck with contrast enhancement revealed left internal jugular vein thrombosis

On the day of her transfer to our medical center, we tentatively diagnosed her with Lemierre's syndrome without central nervous system involvement based on the characteristic presentation. We discontinued meropenem and started her on 12 g per day of ampicillin-sulbactam. For the internal jugular vein thrombosis which caused so severe stenosis that the vein became almost occluded, we initiated anticoagulation therapy with unfractionated heparin despite lack of controlled trials favoring anticoagulation in this setting, which was changed to warfarin and continued for a total of 3 months. The blood culture sent at the previous hospital reportedly grew gram-negative rods that were subsequently identified as *Fusobacterium necrophorum*. She was continued on the intravenous antimicrobial therapy with ampicillin-sulbactam for a total of 4 weeks. The blood cultures became negative by the third day of admission. After completion of the parenteral antibiotic therapy, all her symptoms improved and she was discharged home with oral clindamycin that was continued for another 8 weeks until the multiple cavitary lung lesions resolved. She was doing very well at the last visit.

3 | DISCUSSION

Viral infections such as Epstein-Barr virus have been related to Lemierre's syndrome,[5] although influenza virus has been very rarely reported in association with this syndrome.[3,4]

The primary event in the pathogenesis of Lemierre's syndrome is oropharyngeal infection, and less common are other infections of the head and neck such as mastoiditis, otitis media, and sinusitis.[6] Primary oropharyngeal infections caused by *Fusobacterium necrophorum* or other bacteria subsequently spread to the para-pharyngeal space and internal jugular vein. How this spread occurs is poorly understood. Possible mechanisms of spread include hematogenous spread through the tonsillar vein, lymphatic spread, and direct spread into the loose para-pharyngeal tissue.[7] Another possible mechanism is that oropharyngeal mucosa damaged by other bacterial or viral organisms during a primary infection enables *Fusobacterium necrophorum* to spread from a local infection or colonization, to adjacent para-pharyngeal tissue, gaining access to the internal jugular vein where the thrombus forms. EBV has a reported association with Lemierre's syndrome, although the pathogenesis is not clearly understood.[5]

3.1 | Secondary bacterial infections following influenza virus infection

Influenza virus is one of the most important human pathogens associated with significant morbidity and mortality. Although most influenza infections are self-limited in immunocompetent patients, it has been associated with severe primary viral pneumonia and secondary bacterial and fungal infections, especially in those with pregnancy and underlying diseases including cardiac, respiratory, and immunocompromising conditions.[8] Possible mechanisms of predisposition to secondary bacterial infection in patients with influenza include an altered mucosal structure, aberrant immunological response, increased bacterial colonization of the respiratory tract, and loss of barrier to inhibit bacterial invasion. From the immunological perspective, investigators have agreed that influenza-induced type I and II interferons (IFNs) at least in part are responsible for pathogenesis of superinfection after influenza virus infection. The involvement of T-cell immunity in the superinfection is likely to be temporally regulated. Early during influenza virus infection, interleukin-13 (IL-13) is produced which is beneficial due to its inhibition of IFN-gamma, whereas approximately 1 week into influenza virus infection, IL-13 production becomes reduced with resultant increased production of IFN-gamma that contributes to impaired innate antibacterial activity possibly leading to predisposition to severe bacterial infections.[9] During the influenza pandemic in 1918, most deaths were attributed to secondary bacterial infections mainly due to gram-positive cocci including *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Streptococcus pyogenes* with *Fusobacterium necrophorum* not being implicated.[10]

3.2 | Possible reasons why Lemierre's syndrome has only rarely been reported in patients with influenza virus infection

The influenza virus replicates in the epithelial cells throughout the respiratory tree and is able to damage any part of the tree leading to secondary bacterial infections that most frequently occur in patients with underlying comorbidities. Non-fatal influenza viral infections predominantly involve the upper respiratory tract, while fatal cases have been associated with lower tract infections.[11] This

may explain why influenza has rarely been related to Lemierre's syndrome which typically occurs in cases with precedent infections of the upper respiratory tract, an area that is only mildly involved by influenza virus infection. Another possible explanation is that Lemierre's syndrome often affects young adults[1] who often lack the underlying chronic diseases associated with poor prognoses in influenza viral infection.

4 | CONCLUSION

We described a typical case of Lemierre's syndrome with blood cultures positive for *Fusobacterium necrophorum* following influenza A virus infection. Lemierre's syndrome should be included in the differential diagnoses of rare complications of influenza virus infection.

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CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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