A rare case of *Achromobacter Xylosoxidans* infection presenting as Lemierre's syndrome complicated with bilateral lung empyema in a young boy

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ABSTRACT

Background: In the recent decades, Lemierre's syndrome (LS) has been increasingly diagnosed with a wide range of causative organisms, especially with increased awareness of such an entity.

Case Presentation: We report an unusual case of LS in a previously healthy 15-year-old boy who presented initially with high-grade fever, nonspecific gastrointestinal symptoms, and unilateral purulent otorrhea. Patient subsequently deteriorated requiring intensive care and exhibited altered mental status prompting an urgent contrast enhanced computed topography brain which clinched the diagnosis. Patient underwent mastoidectomy followed by IV antibiotics that were streamlined according to his pus culture. He also developed bilateral lung empyema requiring bilateral chest tube drainage. Anticoagulation was commenced for the thrombosis and patient was discharged home well.

Conclusion: This was an intriguing case in view of the unusual organism causing LS, initial diagnostic dilemma, and challenges in management.

Keywords: *Achromobacter Xylosoxidans*, Lemierre syndrome, IJV thrombosis, leptospirosis, lung empyema, case report.

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Background

Achromobacter Xylosoxidans is an aerobic, Gram negative rod which commonly inhabits aquatic environments [1]. Such bacteria have been recently implicated as an emerging cause of infection in both immunosuppressed and immunocompetent populations. Lemierre's syndrome (LS) was first described by Andre Lemierre in 1936 following a published case series of 20 patients with a primary oropharyngeal infection who developed bacteremia complicated with internal jugular vein (IJV) thrombosis caused classically by *Fusobacterium necrophorum*, an anaerobic Gram-negative bacillus [2]. This syndrome had decreased in prevalence since the advent of antibiotics, but now has been reported more frequently, especially in the past 20 years [3] Plausible explanations would be delayed antibiotics in view of limited access to healthcare as well as poor awareness and knowledge of need for treatment. If undiagnosed and left untreated, mortality was up to 90% during the pre-antibiotic era, and even with antibiotics mortality can still be around 5% currently [3].

We would like to report a case of LS with emphasis on the diagnostic challenges and the management.

Case Report

A previously healthy 15-year old Chinese gentleman presented to a rural health clinic with main complaints of fever associated with rigors accompanied by diarrhea for 1-week duration. He had no myalgia, arthralgia, or rashes. Patient denied any smoking, alcohol consumption, illicit drug use, or recent travel. During assessment, he was dehydrated, febrile with 40.4±C, had a blood pressure (BP) of 139/66 mmHg and was tachycardic at 150 beats per minute with electrocardiogram showing supraventricular tachycardia (SVT). However, the SVT failed to resolve with vagal manoeuvres and IV Adenosine. Patient was also given IV Ceftriaxone 2 g and fluid bolus of up to 1.5 l of normal saline. He was then transferred to our Emergency Department (ED) in Miri Hospital.

During assessment in ED, patient was still dehydrated, not tachypnoeic, and had a BP of 123/69 mmHg, pulse of 140 beats per minute and temperature of 38.2±C. Preliminary blood tests revealed leukocytosis (White blood cells: 29.6 × 10^9/mm^3) with predominant neutrophilia, thrombocytopenia (Platelets: 112 × 10^9/mm^3), elevated creatine kinase (2493), mild transaminitis (Aspartate transaminase: 155), and electrolytes imbalance (Na^+: 124, K^+: 2.9). He was subsequently admitted to the general medical ward and treated as leptospirosis in view of the endemicity of the tropical disease with IV Crystalline Penicillin and hydration. Leptospirosis IgM serology was still pending.

Unfortunately, patient deteriorated in the ward. He was still normotensive at 124/62 mmHg and less tachycardiac at 129 beats per minute; however, he became hypoxic with oxygen saturation of 96% even with Venti Mask 60% 28 litres, and more tachypnoeic with respiratory rate of 40 breaths per minute. Initial chest radiograph demonstrated left lower lobe consolidation and pleural effusion with subtle left upper lobe loculation and minimal right lower zone haziness (Figure 1). An echocardiogram performed showed good left ventricular systolic function, no pericardial effusion, and no vegetations. In view of severe sepsis and rapid deterioration, intravenous ceftazidine was added to cover for possible meliodosis. Leptospirosis IgM came back as negative.

Patient was then admitted into the Intensive Care Unit on Day 2 of admission for non-invasive ventilation and close monitoring. During re-examination, there was pus discharge from the left ear. He then divulged that he had left ear discharge for the past 1 week but dismissed it earlier. At that time, patient started having auditory and visual hallucinations but no other signs of meningism. Contrast enhanced computed tomography (CECT) of the brain (Figure 2) did not demonstrate meningeal enhancement, intracranial abscess nor empyema. However, soft tissue densities within the left external, middle ear cavities, and mastoid air cells were suspicious of left otomastoid infection. Incidentally, there was complete luminal occlusion of the visualized left IJV by rim enhancing central low attenuation thrombus with cranial extension into left jugular foramen and sigmoid sinus. The otorhinolaryngology team was consulted and the revised diagnosis was left acute otitis media complicated with left mastoid and subperiosteal abscess and left IJV thrombosis. This startling revelation was consistent with the diagnosis of LS.

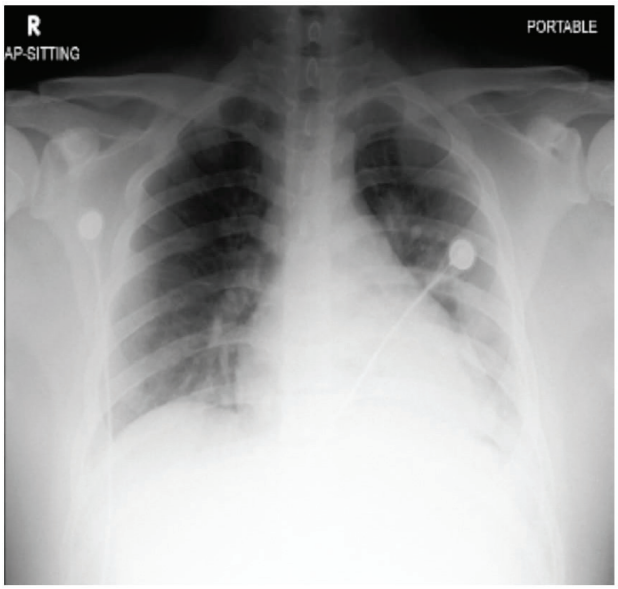

Figure 1. *First chest radiograph (AP view) showing left lower lobe alveolar consolidation and left subtle loculation. Minimal right lower zone haziness is also seen.*

In view of the recent development, antibiotics were streamlined to intravenous ceftriaxone as broad spectrum and intravenous metronidazole to cover for anaerobic infections. Low molecular weight heparin was also started for the thrombosis. As patient did not show any marked improvement clinically, a high resolution computed tomography of the temporal bone was performed followed by left cortical mastoidectomy. The surgery was uneventful. Subsequently, patient's fever subsided. Pus obtained from the surgery grew *Achromobacter xylosoxidans* and was sensitive to ceftazidime, carbapenems, tazocin, and polymycin B. Blood culture had no growth. Antibiotics were then changed back to ceftazidime. Blood glucose was within normal range.

Despite using appropriate antibiotics with surgical intervention, patient remained mildly breathless with a respiratory rate of 22 breaths per minute with oxygen saturation of 95% under room air. He was persistently tachycardic (130–140 beats per minute) as well. Serial

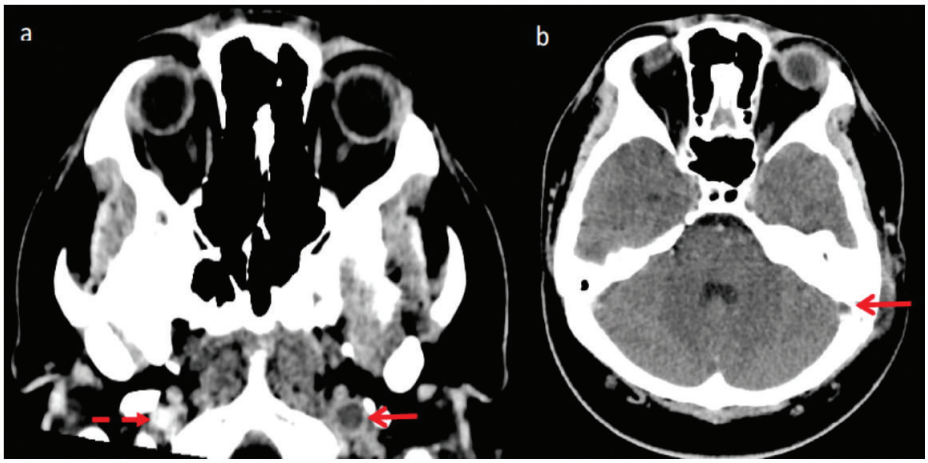

Figure 2. *Transverse contrast-enhanced CT Brain shows (a) Left IJV complete luminal occlusion by low attenuation thrombus with rim enhancement (solid arrow) as compared to the normally opacified right IJV (dashed arrow). (b) Left partial sigmoid sinus thrombosis.*

chest radiographs demonstrated worsening bilateral lung alveolar opacities with pleural effusions, worse on the left with increasing loculation. Subsequent CECT Thorax (Figure 3) revealed bilateral rim enhancing pleural effusions with loculations on the left, suggestive of bilateral empyemas, especially after echogenic mobile debris and septations were noted on complimentary thorax ultrasound. In addition to this, CT findings of right middle and lower lobe cavitating lung lesions (0.5 × 0.6 cm and 0.7 × 0.7 cm respectively) were suspicious of septic embolization. Bilateral ultrasound guided pleural drainage was performed, draining pus. Post procedural chest radiograph demonstrated near resolutions of bilateral pleural effusions and improvement of bilateral alveolar haziness.

Patient then completed 6 weeks of intravenous antibiotics and made a remarkable recovery. He was then discharged well with warfarin after achieving target INR of 2–3. Anticoagulation was planned for 3 months with follow-up imaging to reassess resolution of thrombosis.

Discussion

Nowadays, it is rare to see LS, especially with the rampant usage of antibiotics which had led instead to issues of antibiotics resistance and antimicrobial stewardship. Nevertheless, our patient was from a rural area which is roughly 143 km away from the hospital and in fact, dismissed his initial symptom of pus discharge from his ear for almost a week due to likely lack of awareness and education.

Our case is unique in that although patient met the crucial diagnostic criteria for LS which include positive cultures and radiological evidence of internal jugular venous thrombophlebitis, the causative organism is very unusual and the source of infection being otitis media instead of the oropharyngeal infection is not commonly reported [2,3]. *Fusobacterium necrophorum* and *Fusobacterium nucleatum* are the two bacterial species most often associated with this condition although other bacteria have also been implicated, including *Streptococcus, Bacteroides, Peptostreptococcus*, and *Eikenella* [4]. So far, there is no reported LS caused by *Achromobacter Xylosoxidans*.

We also considered whether this organism could be a contaminant as it is only mostly seen in reported cases and not known to cause LS. However, the *Achromobacter* sp. being ubiquitous in the environment has been an emerging opportunistic pathogen [5] and can cause infections in wide range of organs (pneumonia, urinary tract infections, and meningitis) as noted by Abbott and Peleg [6]. Historically, it was also first isolated from ear discharges in patients with chronic otitis media [7]. Therefore, correlating with the patient's progression of disease and his response to the streamlined antibiotic, it was decided that the bacteria cultured was the likely culprit organism. The culture also purely grew this organism with no mixed growth detected.

In our patient's clinical scenario, the untreated otitis media led to septic thrombophlebitis of the peritonsillar veins at the lateral pharyngeal space extending to the IJV [8]. Although not fully understood, the pathophysiology of septic or also called as suppurative thrombophleblitis initially begins with disruption of the endovascular wall formation which causes thrombus formation and then the organism in close proximity invades the vein, proliferates and further add onto the thrombus formation and inflammation. Subsequently, it potentially causes septic embolization to the lungs as evidently shown in this case [9].

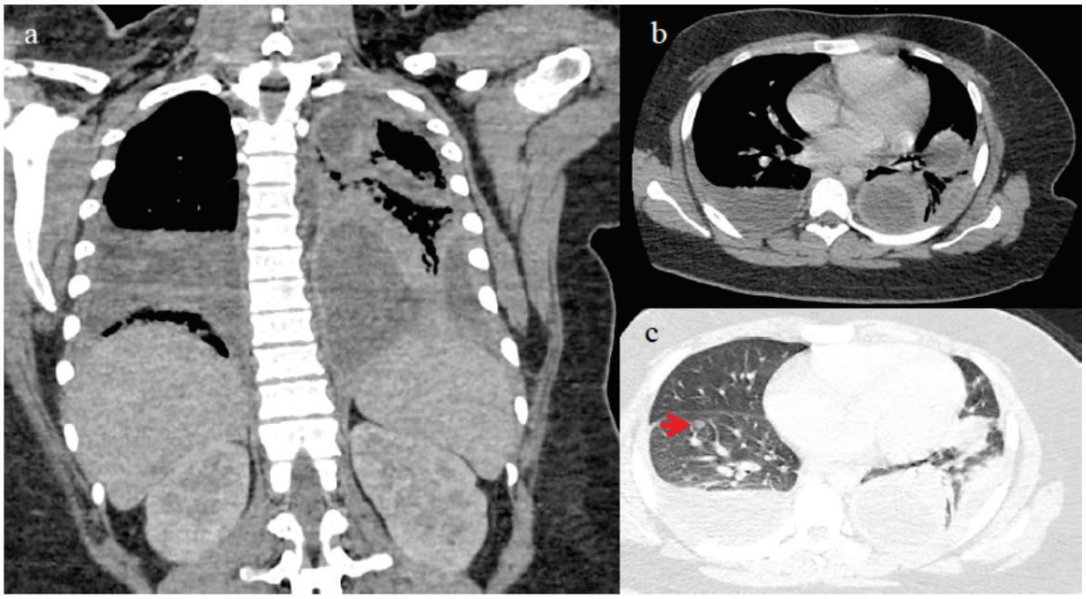

Figure 3. *(a) Coronal and (b) axial contrast-enhanced CT Thorax 2 weeks after the first radiograph demonstrate disease progression as evidenced by bilateral rim enhancing pleural effusions with loculations on the left, suggestive of empyemas. (c) Transverse lung reconstruction CT image shows cavitating nodule (arrow).*

In our case, the pus culture was positive despite having negative blood cultures which can be explained by the length of time needed for cultures to grow and suppression of growth because of prior appropriate antibiotic use [10]. The precise diagnosis initially eluded the physician in view of the clinical features which included diarrhea and the biochemical investigations of thrombocytopenia, raised creatine kinase, and elevated transaminitis. These features prompted the treatment for leptospirosis, an endemic tropical disease in our region.

There is a wide array of non-invasive imaging modalities for diagnosis of LS, such as ultrasound Doppler, CT, and MRI. The modality selected depends on hospital resources and urgency of patient's clinical condition [11]. With regards to this case, CECT brain was initially done to look for signs of meningitis and abscess but incidentally revealed IJV thrombosis with thrombophlebitis as evidenced by rim enhancing hypoattenuating filling defect causing jugular venous distension [12]. Thrombosis may propagate inferiorly into the subclavian vein or even superiorly into the cavernous, transverse or sigmoid sinus, such as in this case, which is not uncommon [3,10,13,14].

Patient also had evidence of severe sepsis evidenced by initial presenting SVT, severe pneumonia requiring non-invasive ventilation and septic encephalopathy. Despite adequate antibiotics, timely surgical intervention was required for adequate control of sepsis [14,15]. Surgery such as debridement or drainage is crucial in ensuring swift recovery, especially in settings where patient is not responding well to antibiotics or there is evidence of continued septic embolization [14].

Anticoagulation in LS is controversial due to lack of controlled studies [15]. It has been debated that thrombosis associated with LS will resolve spontaneously, but it is also unclear if anticoagulation will actually expedite the resolution of thrombosis [4]. Therefore, it is also justified to not provide anticoagulation in LS as it may not have any effect in the thrombosis outcomes especially in uncomplicated cases. [15] Despite this, anticoagulation is given in selected cases such as when thrombus extends into the cerebral sinuses, for large or bilateral clot burden, or when a patient fails to improve in the first 72 hours with the appropriate antibiotics with or without surgical therapy [15]. In view of low bleeding risk in our young patient, thrombosis that extended to the sigmoid sinus and septic embolization to the lungs, anticoagulation was commenced as recommended in the American College of Chest Physicians 2012 guidelines [15].

Conclusion

This case highlights the importance of high clinical suspicion of LS in the presence of infections involving the ear, nose, or throat with pulmonary and CNS symptoms. Therefore, clinicians has to be more vigilant and updated in terms of the common organisms coupled with the most appropriate antibiotics used in tackling LS and complications of LS particularly in leading to metastatic infections. Timely administration of antibiotics along with surgery for sepsis control will improve the prognosis of patients.

Radiological imaging plays an integral role in securing the diagnosis of LS, assessing the extent of the disease, and monitoring progress. In regards to anticoagulation, more research is needed in this field therefore such treatment should be individualized based on risk-benefit assessment.

Lastly, there is a need for awareness and education amongst the people in the rural areas about seeking early medical attention as proper and timely use of antibiotics will be able to save lives.

What is new?

Lemierre's Syndrome is rare but serious complication of head and neck infections can occur if not treated early or adequately with antibiotics. This case report illustrates the unusual organism (first ever reported) associated with Lemierre's Syndrome diagnostic challenge in this patient who was treated initially as Leptospirosis, a very common tropical disease in Sarawak and usually managed with surgery and anticoagulation.

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Consent for publication

Written informed consent was obtained from the father of the patient for publication of this case report and any accompanying images.

Ethical Approval

Ethical approval is not required at our institution to publish an anonymous case report.

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Summary of the case

1	**Patient (gender, age)**	Male, 15 years old
2	**Final diagnosis**	LS secondary to left acute otitis media complicated with lung empyema
3	**Symptoms**	High grade fever, non speficic gastrointestinal symptoms and unilateral purulent otorrhea.
4	**Medications**	Broad Spectrum Antibiotics streamlined to IV Ceftazidime for 6 weeks with LMWH and then Warfarin for 3 months
5	**Clinical procedure**	Left Cortical Mastoidectomy, Ultrasound Guided Pigtail Insertion for Pleural Drainage
6	**Specialty**	Internal Medicine