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CASE REPORT

Lemierre's syndrome: forgotten, but not absent

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SUMMARY

Lemierre's syndrome is rare, with no known reported cases in the Caribbean thus far. We highlight a case of a young woman who presented with diabetic ketoacidosis precipitated by oral pharyngeal sepsis, whose condition rapidly deteriorated within 24 hours requiring ventilation and administration of antibiotics. Her sepsis was accompanied by internal jugular vein thrombosis in keeping with a diagnosis of Lemierre's syndrome, which was treated aggressively with antibiotics, intensive care and mechanical ventilatory support in the intensive care unit. She made a full recovery. Though this is the first reported case in the Caribbean of this 'forgotten disease', it must not be forgotten because prognosis and outcome are markedly improved with prompt and aggressive treatment.

BACKGROUND

Lemierre's syndrome as a complication of oropharyngeal sepsis has rarely been diagnosed and has never been reported in West Indian literature. It was first described by Courmont and Cade in 1900, but was finally named by Dr Andre Lemierre, a French microbiologist, in 1936.¹ Lemierre's syndrome is characterised by bacteraemia following a recent oropharyngeal infection and thrombophlebitis of the internal jugular vein.² It is more common in men,³ and generally occurs in the second decade of life.⁴ Its approximate incidence is 0.8 per million persons per year⁵ and mortality, compared with the preantibiotic era, is much improved at 0%–18%.^{6–8} Although it is viewed as a 'forgotten disease',^{9 10} it must be explored as a differential diagnosis for oropharyngeal sepsis. Lemierre's syndrome can be life threatening if it is not promptly recognised and treated adequately. Bacteraemia in Lemierre's can be polymicrobial,¹¹ with *Fusobacterium necrophorum* reported in 90% of the cases.¹² Septic thrombophlebitis of the jugular vein, one of the key characteristics of this syndrome, leads to thrombosis and septic emboli via haematological spread to other organs.^{6 13} We describe a case of a previously healthy young woman who presented with diabetic ketoacidosis precipitated by an infection. She rapidly deteriorated within 24 hours, requiring ventilation and intravenous administration of antibiotics. She made a complete recovery and was discharged after 20 days.

CASE PRESENTATION

A 25-year-old woman with diabetes presented to the emergency department with a 1-week history of headache, right-side neck and shoulder pain and

a 2-day history of intermittent fever, dry cough and odynophagia. Examination revealed a young woman, oriented in time, place and person. She was ill looking, afebrile (temperature 37°C), with a pulse of 115 bpm and blood pressure of 95/60 mm Hg. Respiratory, cardiovascular, neurological and abdominal examinations were normal. Kernig's and Brudzinski's signs were negative. She had right-side neck tenderness and exudative tonsillitis.

INVESTIGATIONS

Investigations revealed a white blood cell (WBC) count of 7.7 (4.1–11.2×10³/uL), haemoglobin of 10.9 (11.7–15.5 g/dL), thrombocytopenia with a platelet count of 22 (159–399×10³/uL) and elevated C reactive protein level of 33.9 (0–0.5 mg/dL). She had toxic granulation on blood film. Initial electrolytes, blood urea nitrogen (BUN) and creatinine levels were normal: Na 136 (138–146 mmol/L), K 4.6 (3.5–5.0 mmol/L), BUN 14 (8–26 mg/dL) and creatinine 0.4 (0.6–0.9 mg/dL). Liver function tests were within normal ranges: aspartate aminotransferase (AST) 27 (16–40 IU/L) and alanine aminotransferase (ALT) 3 (10–55 IU/L), with a mild direct hyperbilirubinaemia: direct bilirubin 2.0 (0.1–0.4 mg/dL) and total bilirubin 2.4 (0.4–1.4 mg/dL). An ECG showed a sinus tachycardia and chest X-ray showed bilateral infiltrates without pleural effusions. However, a right pleural effusion was noted on a repeat chest X-ray 2 days later. CT imaging of the neck and chest revealed acute thrombosis of the right internal jugular vein and septic emboli throughout the lung parenchyma bilaterally. Duplex of the right upper limb and neck showed thrombosis of the right internal jugular vein. The prothrombin, partial thromboplastin and international normalised ratio were: 12.7 s, 35.6 s and 1.18 (normal range: 9.5–13.5, 27.0–35.0, 0.8–1.2), respectively. HIV, Monospot and Mantoux tests were all negative. Immunology screening revealed an antinuclear antibody 1+ finespeckled pattern and anti-DNA negative. An extractable nuclear antigen panel showed MI2A++, RP11+, and RP155+. Complement levels (C3 and C4) were within normal ranges at 157 mg/dL (90–180) and 26 mg/dL (10–40), respectively, and she was negative for cytoplasmic antineutrophil cytoplasmic antibodies. An echocardiogram was normal with no vegetation or thrombus. Urine and blood cultures both revealed no bacterial growth after 5 days. Antiphospholipid and thrombophilia screening, erythrocyte sedimentation rate and perinuclear antineutrophil cytoplasmic antibodies were unavailable.



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TREATMENT

Following basic investigations, the patient commenced ceftriaxone treatment. On day 2 post hospitalisation, she became markedly distressed, acidotic (pH 7.159) and was transferred to the intensive care unit for ventilatory support and continuation of meropenem and vancomycin antibiotics as well as vasopressors. She was also anticoagulated with rivaroxaban for the treatment of the internal jugular vein thrombosis.

OUTCOME AND FOLLOW-UP

Acute kidney injury developed within 2 days with a rise in creatinine to 1.9 mg/dL. This resolved during the course of treatment.

Her course was otherwise unremarkable and uneventful, with full recovery. She was discharged on day 20 with oral anticoagulants, oral antibiotics and insulin therapy with scheduled follow-up at the outpatient medical and diabetes clinics.

DISCUSSION

We highlight a very common presentation of acute tonsillitis that was complicated by thrombophlebitis, internal jugular vein thrombosis and multiple septic emboli to the lungs known as Lemierre's syndrome. Our patient presented with neck pain, fever, dry cough and odynophagia. Similar symptoms were noted in other studies. The frequencies of common features included a sore throat (82.5%), which usually preceded all other symptoms; fever (82.5%–100%); swollen and/or tender neck (52.2%); jaundice (33%) with deranged liver enzymes and hyperbilirubinaemia.⁷ As found in this case, many patients demonstrate classical symptoms in keeping with less sinister conditions such as acute viral pharyngitis.¹⁴ A high index of suspicion is therefore needed as the diagnosis is mainly a clinical one.¹⁵ A bacterial pathogen may be identified from blood cultures. It is not surprising to obtain a negative blood culture as was found in our case, as many studies also failed to identify a causative organism.¹⁶ The absence of positive blood cultures should not negate this clinical diagnosis as antibiotics may have commenced before taking blood cultures. Furthermore, it is not a major criterion for Lemierre's, as cultures are often negative.¹⁷ It is also important to note that *F. necrophorum*, the most commonly identified organism, may take up to 7 days to grow in blood culture and may be mistaken for *Bacteroides* sp.⁶ *F. necrophorum* are gram-negative bacilli, obligate anaerobes whose existence in normal oral flora is debatable.¹⁸ Infection is precipitated by mucosal damage that facilitates entry and extension into the parapharyngeal spaces and is further propagated by the organism's multiple virulence factors. Lemierre's syndrome was also known as postanginal sepsis due to its association with disease of the nasopharynx³ and necrobacillosis as a result of the necrotic abscesses produced by *F. necrophorum*.¹⁹ Other pathogens such as *Bacteroides* sp, *Prevotella*, *Peptostreptococcus*, *Eikenella corrodens* and *Streptococcus* among others have been identified.⁸ Severe thrombocytopenia without bleeding is consistent with *F. necrophorum* subspecies *necrophorum*, the only organism that aggregates platelets.⁶ Both severe thrombocytopenia and the presence of necrotic abscesses support *F. necrophorum* as the aetiological agent even though the cultures were negative. CT scans at presentation revealed thrombosis of the internal jugular vein, which is found in 30%–70% of cases,²⁰ and septic emboli to the lungs, which is the most common site for metastatic septic foci.⁷

The diagnosis of classical Lemierre's syndrome is based on fulfilling three criteria; namely, oropharyngeal sepsis, internal jugular vein thrombophlebitis and metastatic infection,²¹ as was

Learning points

- ▶ Lemierre's syndrome is rare.
- ▶ It may be a re-emerging disease.
- ▶ Its rather mundane presentation demands that healthcare providers be vigilant for Lemierre's syndrome.

found in our case. Differential diagnoses besides viral pharyngitis include pneumonia, infective endocarditis, acute retroviral illness, infectious mononucleosis and leptospirosis.¹⁴

Treatment was initiated with ceftriaxone, which was subsequently switched to meropenem and vancomycin 24 hours after admission when our patient developed acute respiratory distress and required ventilation. According to various authors as cited by Lu *et al*,¹³ and Riordan *et al*,⁶ antibiotics directed at anaerobes are most effective, especially clindamycin, cefoxitin, imipenem and combination therapy with metronidazole and penicillin. The microbes are generally resistant to macrolides and even more so to gentamicin and quinolones. The development of acute respiratory distress syndrome is rare.¹⁴ However, our case demonstrated a marked improvement after just 5 days in the intensive care unit, after which she was managed in the medical ward where she was anticoagulated for internal jugular vein thrombosis. Anticoagulation therapy in Lemierre's is controversial.⁶ Studies have suggested the potential for haematogenous spread of infection with this therapy.¹⁷ Features supporting anticoagulation initiation in a case series by Lu *et al*¹³ include the retrograde extension of the thrombus to involve the cavernous sinus, failure to improve after adequate antimicrobial therapy for 2–3 days or coexisting thrombophilia. This case had neither of the first two indications. However, in light of the unavailability of anti-phospholipid antibody testing and thrombophilia screening, she was started on oral anticoagulation and will continue receiving this treatment for at least 3 months, as recommended.²⁰ Surgical management in the form of ligation or resection of the internal jugular vein is rarely indicated. This may follow in the case of persistent septic embolisation despite appropriate medical therapy.⁷ The acute renal failure in this patient resolved with fluids and antibiotics. Such complications of this syndrome are relatively uncommon and, according to Eykyn and Leugers as cited by Riordan *et al*,⁶ fewer than 5% of cases require renal replacement therapy. Other complications of Lemierre's syndrome include bone and joint manifestations in the form of septic arthritis (13%–27%), osteomyelitis (<3%), skin and soft tissue lesions (0%–16%), purulent meningitis (rare in classical Lemierre's) and though unusual, cardiovascular complications such as endocarditis and pericarditis.⁶

Although rare, Lemierre's syndrome is still present. Its rather mundane presentation demands healthcare providers be vigilant for Lemierre's, a not-to-be-forgotten and re-emerging disease.²²

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