Lemierre's Syndrome in a Patient with Severe Lupus Nephritis

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ABSTRACT

Lemierre's syndrome is a rare septic thrombophlebitis of the internal jugular vein with frequent metastatic complications following an acute oropharyngeal infection. Immunocompromised patients are at higher risk of developing this syndrome owing to the decreased host response and increased risk of oropharyngeal sepsis. We herein report a 24-year-old woman with severe lupus nephritis on immunosuppressive therapy, who developed Lemierre's syndrome following a pharyngeal infection despite an adequate and timely antibiotic therapy. We hereby draw an attention to the importance of accurate and timely diagnosis and appropriate management of Lemierre's syndrome in immunocompromised patients so as to achieve a successful prognosis for this deadly infection.

Keywords: *Lemierre's syndrome, lupus nephritis, immunocompromised state*

INTRODUCTION

Lemierre's syndrome is a septic thrombophlebitis of the internal jugular vein that develops as an important complication of an oropharyngeal infection.[1] In the pre-antibiotic era, the disease was encountered with a fatal outcome. However, with the advent of effective antibiotic therapy, this disease has become more uncommon, or frequently overlooked.[2] Most cases of this syndrome have been reported in healthy adults. However, it has also been reported in immunocompromised patients with autoimmune diseases and who are on immunosuppressive therapy.[3,4] Neutropenia and defective immune function owing to the use of immunosuppressive drugs may make these patients more vulnerable to Lemierre's syndrome as oropharyngeal infection, a common occurrence in immunocompromised patients, may easily spread into the lateral pharyngeal space when the host response is decreased. We report a case of this deadly infection in a patient with severe systemic lupus erythematosus (SLE) with nephritis, a case on which there are very few reports in the medical literature.

CASE REPORT

A 24-years-old woman with recently-diagnosed SLE and severe lupus nephritis (diffuse proliferative glomerulonephritis, [Class IV G (A) ISN/RPS classification system], was treated with methylprednisolone pulses followed by high doses of oral steroid in another center. Two weeks following this, she presented to the Emergency Department of our hospital with irrelevant talks, unusual behaviour, and a staring look that promptly improved when the prednisolone dose was lowered to 20 mg per day. Her investigations at the time of admission were normal hemogram, Creatinine

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2.8 mg/dL, Routine urine examination was positive for bood and protein, 24-hour urine protein 4.4 gm/day, positive ANA, anti-double-stranded DNA antibody > 300 (negative < 30), negative anticardiolipin antibody, normal activated partial thromboplastin time (APTT), and grossly low C3 and C4. The cerebrospinal fluid analysis and the CT scan of the head were normal. The patient was treated with intravenous cyclophosphamide pulse of 800 mg for her lupus nephritis. Over the days, she showed a steady improvement and was discharged from the hospital.

After three weeks of the first pulse of intravenous cyclophosphamide, the patient developed a sore throat that was treated with Amoxycillin and later with Azithromycin as she developed allergic rashes with the former. Five days following the onset of the sore throat, she came to the clinic again with progressive sore throat, a cord-like swelling in the left side of the neck, and puffiness of the face, chest wall, and upper extremity of the left side (Figure 1). Examination revealed a minimally-inflamed, left-sided tonsil and a thick cord-like mass down the whole left side of the neck . The left-sided cervical and axillary lymph nodes were enlarged and tender.

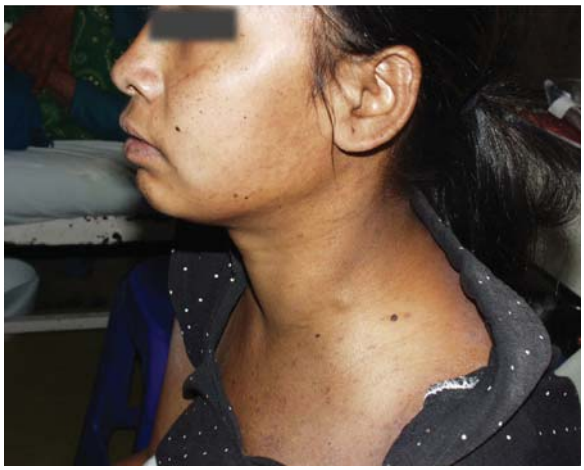

Figure 1. Cord-like swelling over the left side of the neck; the left side of face also looks puffy.

Laboratory investigations showed normal hemogram and blood culture failed to grow any organisms. The chest x-ray film showed a left lower zone consolidation. A doppler ultrasound of the neck revealed a non-compressible and grossly-dilated left internal jugular vein (IJV) with an echogenic wall and a thick lumen containing a heterogenous thrombus extending to a length of 5 cm (Figure 2).

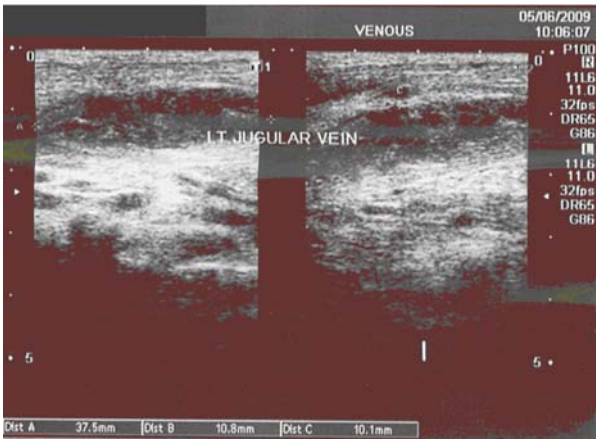

Figure 2. Doppler ultrasound showing dilated left IJV containing a thrombus.

With the diagnosis of septic thrombophlebitis of the left IJV following an oropharyngeal sepsis (Lemierrre's syndrome), the patient was admitted and started on a course of broad spectrum antibiotics with intravenous ceftriaxone, cloxacillin and metronidazole. Anticoagulation therapy was started with intravenous heparin and later maintained on warfarin. The patient improved rapidly without any complications and was discharged in two weeks to complete a three-week course of antibiotics. The anticoagulation was maintained for three months. Following this incident, the patient received five more pulses of cyclophosphamide on a monthly basis. The further plan is to replace cyclophosphamide with azathioprine for the maintenance therapy of her lupus nephritis.

DISCUSSION

The patient had presented with a prodrome of upper respiratory tract infection followed by neck pain, neck mass, and pulmonary consolidation — symptoms suggestive of Lemierre's syndrome, otherwise known as necrobacillosis or postanginal sepsis.[5] This syndrome was first well characterized by Lemierre in 1936, who reported 20 cases from his personal experience, 18 of whom died.[1] It was then a relatively common disease with a high mortality (more than 50% of affected patients) in the preantibiotic era; however, with the advent of antibiotics, there has been a substantial decrease in the occurrence as well as mortality of postanginal septicaemia.

The most frequent causative organism responsible for Lemierrre's syndrome is *Fusobacterium necrophorum*.[6] In a recent report, Chirinos et al [7] reported *F. necrophorum*-positive cultures in 82 % of 109 cases of Lemierre syndrome, whereas in 13 % of cases, cultures remained sterile, as in our case. The most likely cause

for a sterile culture could be the prior use of antibiotics as, in our case, as this often occurs during the treatment of upper respiratory tract infection.

Most of the cases of Lemierre's syndrome have been reported in healthy adolescents and adults, more often in males[5]. However, it has also been reported in immunocompromised patients with systemic lupus erythematosus[3] and autoimmune hepatitis[4], both treated with azathioprine. Neutropenia and defective immune function owing to the use of immunosuppressive drugs may make these patients more vulnerable to this syndrome as oropharyngeal infections, a common occurrence in immunocompromised patients, may easily spread into the lateral pharyngeal space. Though our patient had a normal neutrophil count, she had a significant immune dysfunction owing to her underlying disease and its treatment with a high dose steroids and cyclophosphamide.

Lemierre's syndrome appears to progress in several steps. The first stage is the primary infection, which is usually pharyngotonsillitis, but other infections like odontogenic infections and sinusitis have also been reported as predisposing infections[7]. It is proposed that from here the infection spreads to the lateral pharyngeal space, mainly via lymphatic vessels. Infection of this compartment may lead to thrombophlebitis of the IJV. Organisms of the Bacteroidaceae family and many Gram-negative bacteria contain a lipopolysaccharide component with a Lipid A moiety in their cell wall which could be responsible for the intravascular coagulation.[8] In particular, hemaglutinin production augments the fulminant nature of the disease, causing septic thrombus formation.[9] Finally, metastatic complications occur resulting from the haematogenous spread from the IJV nidus. The lungs are the most common sites of metastatic spread (80% of cases) followed by joints (17% of cases).[7] Our patient had a metastatic infection in the left lung, probably as a result of septic embolization with pulmonary infarction as evidenced by the left lower zone consolidation on chest x-ray.

A temporal pattern of pathogenesis is usually seen in this disease as these three stages occur in an orderly fashion. (Figure 3) The time interval between the oropharyngeal infection and the onset of the second stage is usually less than one week, as in our case. In the future, as the syndrome becomes more familiar to clinicians, the incidence of both of these complications (septic IJV thrombosis and metastatic infections) should decrease.[7]

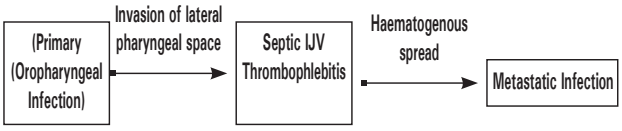

Figure 3. Stages in the evolution of Lemierre's syndrome[7]

The approach to a patient with pharyngitis and/or a tender, swollen neck in any immunocompromised patient should be aggressive. Apart from routine investigations and blood culture, diagnostic methods to detect IJV thrombosis include contrast-enhanced CT scan, MRI and ultrasound.[10] Doppler ultrasound, the least expensive and most easily available modality, is a sensitive tool to detect an echogenic thrombus in the jugular vein lumen. Contrast-enhanced CT scan may clearly demonstrate the IJV thrombosis; however, its use may exacerbate renal insufficiency due to the use of contrast agents particularly in patients with preexisting renal disease. MRI demonstrates venous thrombosis clearly, but is expensive and may not be available in many centres particularly in resource-poor settings like ours. In our case, the IJV thrombosis was well delineated by Doppler ultrasound, and moreover, the patient was not a candidate for contrast-enhanced CT scan owing to her nephritis and impaired renal function.

Treatment of Lemierre's syndrome primarily consists of prolonged antibiotic therapy and, if necessary, surgical drainage of purulent collections from the site of infection. Antibiotics are given intravenously for one to two weeks and then prescribed orally for an additional two to four weeks. Prolonged antibiotic use is necessary for the eradication of the endovascular nature of the infection.[11] The use of heparin in patients with Lemierre's syndrome is controversial owing to the risk of spreading the septic focus; moreover, there are no prospective studies of its use in septic thrombophlebitis.[12] In some cases, intravenous heparin has shortened the course of Lemierre's syndrome and avoided the need for surgery. In our case too, heparin seemed to be of benefit in this regard.

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