Reverse Lemierre's syndrome: a case report

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We present the case of a 60-year-old diabetic who had acute-onset shortness of breath that was preceded by bilateral thigh and hip pain. He was initially admitted for septic arthritis with community-acquired pneumonia. His respiratory complaints resolved, but he continued to have thigh pain. Ultrasound of the lower limbs showed thrombosis of the deep veins of the thigh and MRI showed a collection in the right thigh suggestive of pyomyositis with thrombosis in deep veins abutting the collection. Contrast enhanced CT (CECT) chest showed multiple peripherally located pneumatoceles and cavities in both the lungs suggestive of septic emboli. Here, we present a case of pyomyositis of thigh muscles causing Deep vein thrombosis (DVT) and septic pulmonary emboli (reverse Lemierre's syndrome).

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Introduction

Primary pyomyositis or spontaneous bacterial myositis is characterized by suppuration of single or multiple skeletal muscles [1,2]. The diagnosis of primary pyomyositis requires exclusion of abscesses extending into muscles from bone or subcutaneous tissues, intermuscular abscesses, and those secondary to septicemia. The first case of pyomyositis was described by Scriba and colleagues [3,4]. As it is mostly encountered in the tropics, terms such as tropical pyomyositis (TP) or myositis tropicans are in use, but now, this entity is no longer confined only to tropics. The first case of pyomyositis from a temperate region was reported by Levine in 1971 and in the last three decades, a number of cases have been reported from temperate areas [5–7]. Lemierre's syndrome is thrombophlebitis of the internal jugular vein and bacteremia following a an oropharyngeal infection, caused primarily by anaerobic organisms. When a similar condition is present in the lower limb, it is called reverse Lemierre's syndrome.

Case history

A 60-year-old man, known case of type II diabetes mellitus and hypertension, for 4 years, presented with bilateral thigh and hip pain, with pain being more on the right side for 4 days, which resolved partially with analgesics. However, after 4 days of onset of pain, he developed high-grade fever with cough and shortness of breath. He went to a local hospital and initial investigations showed an elevated total leukocyte count with neutrophilia and high blood sugar with positive urine ketones. He was referred to our center for further management. On reviewing the case, any history of trauma to the limbs or similar history occurring in the past was denied by the patient. He was taking oral hypoglycemic agents and antihypertensives, with poor compliance to therapy. General examination indicated an afebrile patient with a respiratory rate of 22 per minute and a heart rate of 88 per minute, with a blood pressure of 150/90 mmHg. The patient kept his right lower limb in flexion, abduction and external rotation and he had pain in performing the respective opposite movements. Respiratory examination indicated coarse inspiratory crackles in the right infra axillary and infrascapular areas. Examination of cardiovascular, abdomen and nervous system was unremarkable. Fundus examination showed severe nonproliferative diabetic retinopathy with central serous macular edema in the right eye and lasered (photocoagulated) retina in the left eye. Chest radiograph was suggestive of infiltrates in the right lower zone. ECG and bedside echocardiography was normal. His laboratory parameters at presentation are shown in Table 1.

Inflammatory markers – erythrocyte sedimentation rate, C-reactive protein, and ferritin were elevated, suggestive of an inflammatory/infective process.

The initial differential diagnosis included partially treated septic arthritis of the hip, soft tissue infection, muscle hematoma, or pyomyositis. As per the history and initial investigations of the patient, a provisional diagnosis of community-acquired pneumonia with septic arthritis with diabetic ketoacidosis (DKA) and

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prerenal acute kidney injury (AKI) was made. Blood and other cultures were sent and the patient was started on piperacillin–tazobactam and azithromycin empirically along with management of DKA and AKI. Ultrasound of the hip and thigh showed edematous muscles of the thigh and deep venous thrombosis of the right common femoral and proximal saphenofemoral vein with mild synovial effusion in bilateral hip joints. There was no significant lymphadenopathy, intra-abdominal mass, or other vessel thrombosis in the ultrasonography performed. Although we also had a suspicion of pulmonary thromboembolism, computed tomography pulmonary angiography was not performed because of AKI. MRI of the thigh was performed, which showed edematous muscles of the thigh with a collection of around 5×1 cm and thrombosis of the proximal deep veins of the thigh abutting the collection with enlarged obturator lymph nodes. Blood and urine cultures that were sent on day 1 were sterile. He became afebrile and his respiratory symptoms as well as DKA and AKI resolved, but he continued to have pain in the right thigh. CECT chest was performed on day 4 of admission, which showed multiple small thin-walled cavities and pneumatoceles in bilateral lung fields suggestive of partially treated septic emboli, likely to be because of *Staphylococcus aureus* infection arising from septic embolization from the thighs. The patient was shifted to linezolid in view of suspicion of methicillin-resistant S. aureus-associated pyomyositis. In view of the disseminated infection, a positron emission computed tomography was performed, which showed increased uptake in the upper third of the thigh, the extensor compartment of the upper forearm, and disseminated foci in the lungs. However, there was no aspirable collection in any of these locations by then. All the investigations that were performed during the course of hospital stay are shown in Table 2.

Thus, what we initially considered to be septic arthritis turned out to be pyomyositis with thrombosis of the adjacent deep veins, with the thrombus throwing septic emboli to the lung, and thus a rare case of reverse Lemierre's. The patient improved symptomatically over the course of his hospital stay and was able to walk without support within the sixth day of starting linezolid and was discharged later.

Discussion

So what made this case so unique? The simultaneous occurrence of separate septic processes of pneumonia and pyomyositis along with deep venous thrombosis led us to reconsider an alternate etiology that could be explained by a single cause. The other issue that we had initially was the presence of deep vein thrombosis adjacent to the inflammed muscle. Computed tomography of chest indicated septic emboli in the lung parenchyma that we initially believed to be pneumonia. Review of the literature helped us solve the dilemma of the presence of DVT adjacent to the

Table 1 Laboratory parameters at admission

Parameters	Values
Hemoglobin (g%)	9.7
Platelet count (per mm^3)	276 000
Hematocrit (%)	29.8
TLC (per mm^3)	11 900
Urea (mg/dl)	122
Creatinine (mg/dl)	2.2
Uric acid (mg/dl)	5.6
Calcium (mg/dl) (corrected)	9.2
Na (mEq/l)	132
K (mEq/l)	4.7
Bilirubin (total) (mg/dl)	0.7
Total protein (g/dl)	6.7
Albumin (g/dl)	2.5
SGOT (U/l)	35
SGPT (U/l)	33
ALP (U/l)	392
PT/INR	14.9/1.35
Urine routine and microscopy (R/M)	Protein: trace, RBCs: 1–2/hpf, WBCs: nil, Casts: nil

ALP, alkaline phosphatase; INR, international normalized ratio; PT, prothrombin time; RBC, red blood cells; SGOT, serum glutamic oxaloacetic transaminase; SGPT, serum glutamic pyruvic transaminase; TLC, total leukocyte count; WBC, white blood cells.

Table 2 Laboratory parameters

Parameters	Values
ESR (mm/1 h)	63
CRP (mg/l)	102.8
HbA1C (%)	11.6
Vitamin B_{12} (pmol/l)	42.2
Serum folate (ng/ml)	13.3
Serum ferritin	1174.84
T3	0.4 (0.58–1.59)
T4	4.75 (4.87–11.72)
TSH	2.44
24 h urine protein	1 g/day
Serum procalcitonin (ng/ml)	0.24
Serum ProBNP (pg/ml)	333
HIV, HBsAg, anti-HCV	Negative
Lactate dehydrogenase (U/l)	530
Peripheral smear	Normal study, no atypical cells/ toxic granules
Lipid profile	Normal
Blood culture, urine culture	Sterile
2D echo	Normal study, no vegetation or clots

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HbA1C, hemoglobin A1c; HBsAg, hepatitis B antigen; HCV, hepatitis C virus; ProBNP, pro-B-type natriuretic peptide; TSH, thyroid-stimulating hormone.

Table 3 Case reports

Cases	1 (our case)	2	3
Age/sex	60 years/male	17 years/male	24 years/male
Nationality	Indian	Indian	French
Occupation	Shopkeeper	Student	Soccer player
Co-morbidities	T2DM/hypertension	None	None
History of trauma	No	No	Yes
Initial diagnosis	Pneumonia with septic arthritis	Sepsis with acute respiratory distress syndrome and acute kidney injury with source of sepsis UTI cellulitis	ARDS
Muscle involved	Upper thigh muscles	Vastus medialis	Obturator internus
Outcome	Discharged	Discharged	Discharged

AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; T2DM, type 2 diabetes mellitus; UTI, urinary tract infection.

muscle, which was because of inflammation and compression of the vessel by the edematous muscle tissue. Thus, we made a final diagnosis of primary pyomyositis complicated by thrombophlebitis of the saphenofemoral and common femoral vein and septic embolization to the lung, which is also known as reverse Lemierre's syndrome.

Pyomyositis is of two types: primary and secondary. Primary pyomyositis, also known as TP, occurs more frequently in immune-compromised patients (such as T-cell deficiency, chronic granulomatous disease, hyper IgE syndrome, HIV, malignancy, diabetes, use of steroids, and immunosuppressants), as in our patient, who was diabetic with uncontrolled blood sugar levels. Other than immunocompromised states, pyomyositis has also been implicated by factors affecting the muscle itself such as strenuous exercise or muscle trauma, although only a third of patients have evidence of these risk factors [8,9]. Secondary pyomyositis is caused by direct extension from an infectious process, such as Crohn's disease, appendicitis, and neoplasia.

TP is a great mimicker. Diagnosis is often difficult because of lack of specific clinical features and its similarity to common tropical infections. Its natural course usually consists of three stages: invasive (bacterial seeding), suppurative (abscess formation), and septicemic stage (dissemination in the blood with multiple organ dysfunctions). Advances in imaging and microbiological techniques in the last few decades have aided early diagnosis of this clinical entity. Early diagnosis and treatment with drainage of pus and appropriate antibiotics can potentially prevent its complications and fatality. Aspiration of pus from the muscle or muscle biopsy (in case of absent macro abscess as in the early invasive stage) with culture and gram staining is the gold standard for diagnosis.

Lemierre syndrome, also known as human necrobacillosis or postanginal anaerobic septicemia, is septic thrombophlebitis of the internal jugular vein or one of its tributaries that becomes a source of septic emboli in the setting of viral or bacterial throat infection. The most frequently isolated pathogen is *Fusobacterium necrophorum*. When a similar condition presents in the lower limb, it is called reverse Lemierre's syndrome. In our patient, abscess in muscle (i.e. pyomyositis) in the thigh, which was abutting the saphenofemoral vein and the common femoral vein, caused septic thrombophlebitis and subsequently thrombosis and pulmonary septic embolism. The pathophysiology of septic thrombophlebitis is based on the principle of Virchow's triad, i.e. endothelial dysfunction caused by the inflammatory mediators and bacterial toxins, venous stasis because of compression and hypercoagulable state because of the underlying septic process, all of which might have contributed toward thrombus formation in our patient. This also acts as a source of septic embolization and the most common site is the lung, which results in pulmonary abscesses, cavities and empyema (85%), pneumatoceles, pneumothorax, and acute respiratory distress syndrome (10%) [10,11].

Treatment includes antibiotics (covering gram-positive organisms mainly methicillin-resistant S. aureus), surgical drainage, debridement and supportive therapy. The duration of administration of antibiotics should be according to the clinical and radiological response. The use of therapeutic anticoagulation along with intravenous antibiotics remains controversial [12]. There might be spontaneous resolution of thrombus even without anticoagulation.Only two cases of reverse Lemierre's have been reported so far: one in a soccer player in whom right obturator internus pyomyositis with hyper IgE septic iliac thrombophlebitis and pulmonary septic emboli resulted in acute respiratory distress syndrome [13] and the other from the All India Institutes of Medical Sciences, New Delhi, in a 17-year-old male with primary pyomyositis of the vastus medialis complicated by suppurative saphenofemoral thrombophlebitis and secondary thrombosis as described in Table 3 [14].

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Conflicts of interest
There are no conflicts of interest.

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