Group C streptococcal cellulitis, looking deeper than the skin

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INTRODUCTION

Group C streptococci (GCS), predominantly *Streptococcus dysgalactiae* subspecies *equisimilis* in humans, are gram-positive, ß-hemolytic bacteria that form part of the normal oral flora and may be seen in cases of pharyngitis and cellulitis. In a review of 88 patients with GCS bacteremia, infections commonly originated from the upper respiratory tract (20.5%), gastrointestinal tract (18.2%), or the skin (17.1%).[1] GCS has also been reported in septic arthritis, endocarditis, meningitis, pneumonia, necrotizing fasciitis, and toxic shock–like syndrome.[2] Rhabdomyolysis is not typically associated with this organism and has been reported in only 2 cases involving GCS pharyngitis and bacteremia.[3,4] Here we report the first case, to our knowledge, of GCS cellulitis associated with rhabdomyolysis.

CASE REPORT

An 85-year-old woman with a medical history of Parkinson disease, gastric esophageal reflux disease, hypothyroidism, breast cancer, and thyroid cancer presented with 2 days of worsening erythema and dull pain of the left lower extremity in the setting of a chronic medial malleolar ulcer. One month prior, the patient had a radiofrequency ablation and stab avulsion followed by wound debridement and split-thickness grafting. The patient denied any pain out of proportion to erythema, dyspnea, fevers, or chills. In the emergency department (ED), the patient was afebrile with an elevated heart rate of 106 and respiratory rate of 28.

Abbreviations used:

AST:	aspartate aminotransferase
ALT:	alanine aminotransferase
CK:	creatine kinase
CRP:	C-reactive protein
ED:	emergency department
GCS:	group C *Streptococcus*

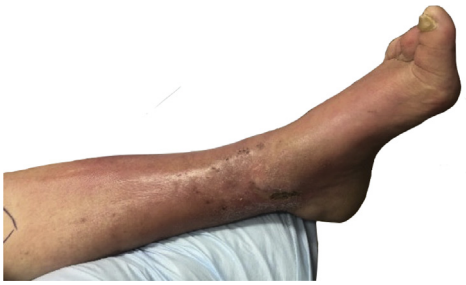

Fig 1. Photograph of the left lower extremity. Moderately erythematous patch extending above the midshin with an impetiginized ulceration on the left medial malleolus. Background scene was deleted using Keynote 08 ver. 4.0, and clinical image remains unaltered.

Her physical examination findings were significant for a new irregular cardiac rhythm and an erythematous patch below the left knee along with impetiginized ulceration of the medial malleolus (Fig 1). Laboratory values are noted in Table I and were significant for a white blood cell count of 24 × 10^9/L, C-reactive protein level of 519 mg/L, and total creatine kinase of 2386 U/L. A metabolic panel

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Table I. Laboratory data

WBC	24 × 10^9/L	Lactate	3.3 mmol/L
Absolute Neutrophil Count	22 × 10^9/L	CRP	518.5 mg/dL
Hemoglobin	13.6 g/dL	ESR	65 mm/h
Hematocrit	41.60%	Total Bilirubin	1.3 mg/dL
Platelet	253 × 10^9/L	Direct Bilirubin	0.7 mg/dL
Potassium	3.2 mmol/L	AST	98 U/L
Bicarbonate	22 mmol/L	ALT	63 U/L
Anion Gap	15	Alkaline Phosphatase	142 U/L
Glucose	151 mg/dL	Lipase	36 U/L
BUN	22 mg/dL	Total CK	2386 U/L
Creatinine	0.8 mg/dL	Corrected Calcium	9.1 mg/dL

BUN, Blood urea nitrogen; *ESR*, erythrocyte sedimentation rate; *WBC*, white blood cell count.

showed a potassium level of 3.2 mmol/L, anion gap of 15 mmol/L, creatinine level of 0.8 mg/dL, and lactate of 3.3 mmol/L. Liver function tests found an aspartate aminotransferase (AST) level of 98 U/L and alanine aminotransferase (ALT) level of 63 U/L. Electrocardiogram showed new atrial fibrillation. Venous ultrasound scan of the left lower extremity showed no evidence of deep venous thrombosis, and radiograph of the left tibia/fibula showed no evidence of osteomyelitis. Imaging of the left ankle showed no osteomyelitis but did show surrounding subcutaneous edema with skin thickening and enhancement consistent with cellulitis (Figs 2 and 3, *A* and *B*).

The patient was subsequently given intravenous vancomycin and ceftriaxone in the ED. She had reported drug allergies to penicillin and cephalosporin; however, given that she tolerated ceftriaxone in the ED without adverse effects, intravenous high-dose ceftriaxone, 2 g/d, and clindamycin, 900 mg 3 times per day were begun for treatment of community-acquired, rapidly evolving cellulitis. Wound swab from the left medial malleolus returned 2 days later with growth of GCS along with moderate skin flora. Admission blood cultures, collected before antibiotic initiation, were negative over 5 days. The left lower extremity was elevated to assist with drainage. The initial elevated C-reactive protein (CRP) decreased slowly, and the patient was hospitalized for 10 days with gradual decrease in erythema and slow regression of the cellulitis.

During the course of her hospitalization, the patient was noted to have further elevation of transaminases (ALT of 146, AST of 192 U/L) and creatinine (1.5 mg/dL) that eventually trended down with intravenous fluids. Right upper quadrant ultrasound scan showed no cholelithiasis but did show echogenic liver consistent with hepatic steatosis. The patient was discharged to short-term rehabilitation with a normal creatine kinase (CK) and CRP and total antibiotic course of 14 days.

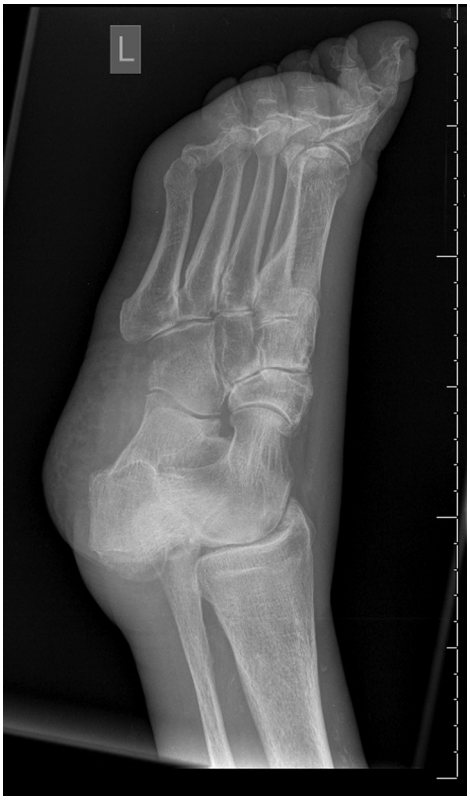

Fig 2. Radiograph of left foot and ankle. Extensive surrounding soft tissue edema without radiographic evidence of osteomyelitis.

DISCUSSION

In this case, we present a patient that had rapidly evolving GCS cellulitis with no signs of necrotizing fasciitis over the course of 2 days. The cellulitis was associated with an elevated CRP and CK, indicating an association with rhabdomyolysis; the patient also had complications of rhabdomyolysis including new

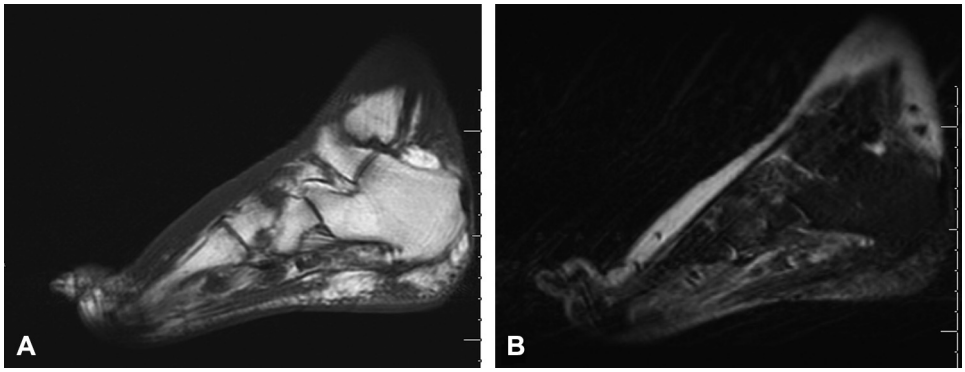

Fig 3. Magnetic resonance imaging of the foot; T1 (**A**) and T2 Short tau inversion recovery (STIR) (**B**). Comparative dorsal soft tissue thickening with subcutaneous edema (**B**) without associated bone marrow edema.

cardiac arrhythmia, lactic acidosis, transient acute kidney injury, and hepatic inflammation seen in 25% of rhabdomyolysis patients.[5] Importantly, the patient did not have any changes in medications, direct muscle injury, electrolyte or endocrine abnormalities, environmental toxin exposure, or childhood myopathy.[6]

Although most cases of purulent, soft tissue abscesses are caused by *Staphylococcus*, most nonpurulent cellulites are caused by *Streptococcus*, which remain sensitive to β-lactam antibiotics.[7] Interestingly, our patient's long recovery and hospitalization course have also been observed in 2 other cases of GCS-associated rhabdomyolysis. One patient with GCS bacteremia required 6 weeks of hospitalization because of a complicated course involving acute respiratory distress syndrome and pyomyositis.[4] The second patient with GCS pharyngitis and rhabdomyolysis was hospitalized for 17 days and able to return to work only 4 weeks after discharge.[3] These prolonged courses are comparable to our 10-day hospitalization course for GCS cellulitis associated with rhabdomyolysis.

In published literature, it is believed that rhabdomyolysis and an exaggerated inflammatory response seen in Lancefield GCS or group G *Streptococcus*, known as *Streptococcus dysgalactiae* subspecies *equisimilis*, may be caused by endotoxins or exotoxins that lead to muscle damage, as seen in the closely related group A *Streptococcus* (GAS) toxic shock syndrome[4,8]; for this reason, the clinical illness is believed to be toxin mediated, which is why clindamycin, a protein synthesis inhibitor, is used in addition to β-lactam antibiotics. Specifically, cysteine protease SPE B and C are produced by group A *Streptococcus* (*Streptococcus pyogenes*) and have been found to enhance local skin and muscle damage in mice models.[9,10] Currently, no endotoxin or exotoxin has been isolated for GCS in lymphocyte proliferation assays[4]; however, future biochemical studies should explore the pathophysiology in order to develop targeted antitoxin therapy.

We hope that this case will expand the range of pathophysiology known to be associated with GCS cellulitis, including rhabdomyolysis; whereas most cases of cellulitis are self-limited streptococcal infections, this case highlights the importance of being alert to toxin-mediated disease, with systemic symptoms out of proportion to visible surface inflammatory signs. This distinction is important because the default therapeutic response is often broader antibiotic coverage, whereas the most appropriate response for virulent yet antibiotic-sensitive pathogens, such as GCS, is more narrowly targeted high-dose antibiotics with vigilant clinical monitoring and supportive care to avoid a poor prognosis and prolonged hospitalization.

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