

# Diagnostic Snapshot



## Lower Extremity Edema: More Than Just the Routine Workup

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Author's disclosure of conflict of interest is found at the end of this article.

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### Abstract

Establishing a differential diagnosis for symptomatic oncology patients can be complex. The challenges for advanced practitioners in diagnosing acute symptoms in this patient population lie in the reality that symptoms exhibited can mimic a variety of diagnoses. It is critical for advanced practitioners to utilize their diagnostic expertise in collaboration with colleagues from other disciplines to optimize patient outcomes.

The patient, NG, is a 51-year-old male diagnosed with widespread recurrent follicular lymphoma after a multitude of prior chemotherapy and immunochemotherapy regimens, including high-dose radioimmunotherapy with autologous stem cell support. He has an extensive past medical and surgical history. NG's history of particular relevance includes congestive heart failure, atrial fibrillation, psoriasis, psoriatic arthropathy, hepatitis, pleural effusion, hypogammaglobinemia, and stroke. Three months prior to presentation he had a shave biopsy performed by a dermatologist for a presumed irritated verruca vs. pyoderma gangrenosum vs. nonmelanoma skin cancer.

NG presented to the Oncology Evaluation Center (OEC) with a 1-day history of significantly increased pain, localized to the lower left leg, and fever of 101.7°F with accompanying rigors. NG's biopsy wound was evaluated by a dermatologist in the outpatient clinic the day prior to his

OEC visit. He was prescribed mupirocin 2% topical ointment to apply to the affected biopsy wound area. At this same visit, he was evaluated by his primary oncology nurse practitioner and was prescribed 80 mg of intravenous furosemide to manage increased ascites and lower extremity edema.

### PHYSICAL EXAM AND DIAGNOSTIC WORKUP

On initial exam, NG was fatigued appearing with dusky coloring and generalized malaise. He had normal heart sounds with no signs of jugular venous distention (JVD). His breath sounds were decreased bilaterally with symmetry chest expansion. Physical exam revealed +3 bilateral pitting edema to lower extremities with diffuse erythema and warmth to the full entirety of both legs, in addition to weak pedal pulses bilaterally. Sensation was intact to both lower extremities, with NG grimacing and voicing worsening pain with light palpation to the left lower leg. There were two open

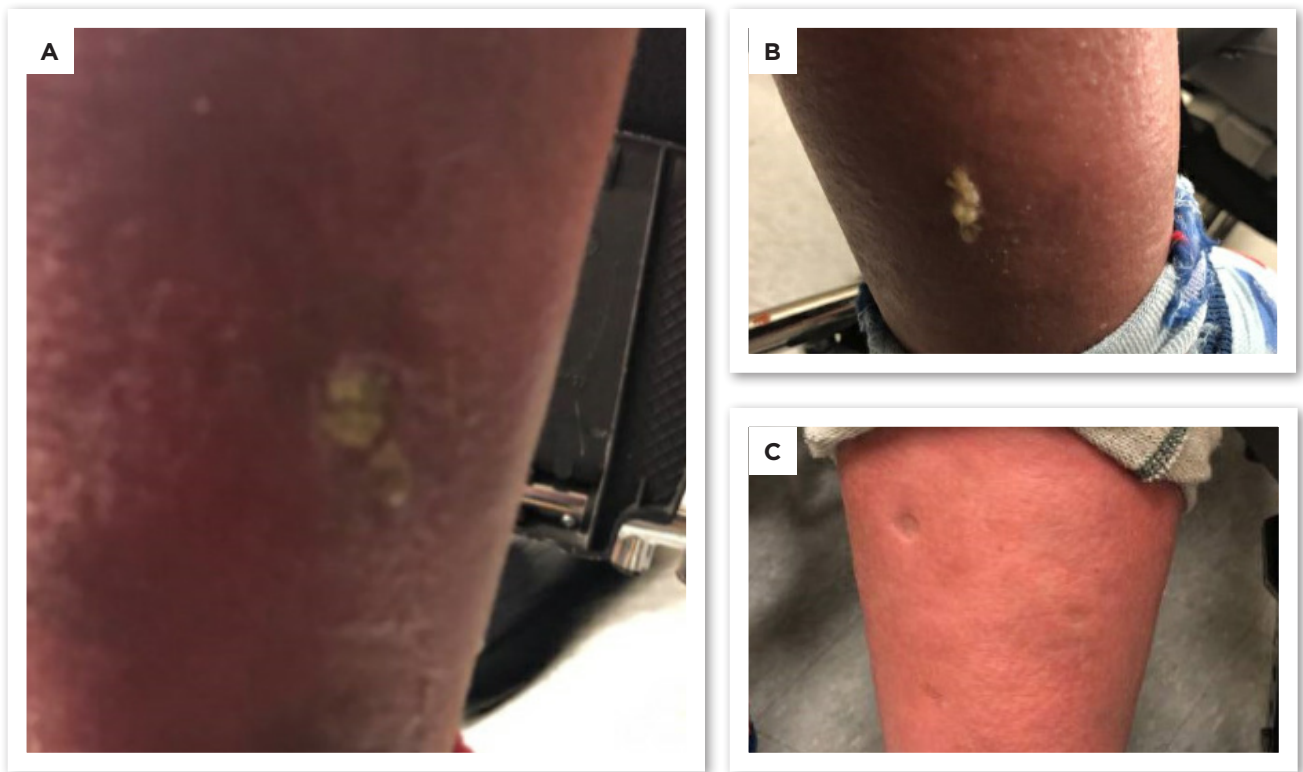


Figure 1. (A) Left posterior leg biopsy site, (B) left posterior leg spontaneous eruption site, and (C) bilateral lower leg.

wounds with fluctuance and pustular drainage on his posterior left lower calf. Wound one was at the site of his previous biopsy, measuring 0.5 cm in diameter without signs of necrosis. Wound two was the result of a spontaneous eruption which occurred the day prior, without signs of necrosis (Figure 1). His vital signs were within normal limits with the exception of bradycardia (heart rate 59 bpm), and he was febrile with a temperature

of 100.8°F. An infectious workup and bilateral vascular ultrasound was ordered. The infectious workup included a complete blood count, comprehensive metabolic panel, lactic acid, two sets of blood cultures, urinalysis, urine culture, and a chest x-ray. His white blood cell count and absolute neutrophil count were normal, creatinine was 3.77 mg/dL elevated from 2.4 mg/dL (4 days prior), hemoglobin 9.8 g/dL, and lactic acid 8.9 mmol/L.

## DIFFERENTIAL DIAGNOSIS



### WHAT IS THE CORRECT DIAGNOSIS?

- A** Cellulitis
- B** Deep vein thrombosis
- C** Necrotizing fasciitis
- D** Congestive heart failure

SEE BACK FOR ANSWER



## WHAT IS THE CORRECT DIAGNOSIS?

- A** Cellulitis
- B** Deep vein thrombosis
- C** Necrotizing fasciitis (correct answer)
- D** Congestive heart failure

**A Cellulitis.** According to Sullivan and de Barra (2018), cellulitis is defined as an acute infection of the skin involving the dermis and subcutaneous tissues. The classic hallmarks of cellulitis are redness, pain, swelling, and heat. The skin becomes red, hot, swollen, and painful with a clear line of demarcation between normal and affected skin. Careful clinical examination may reveal a portal of entry such as an ulcer, trauma, eczema, or cutaneous mycosis. Gram-positive cocci such as *Streptococcus* and *Staphylococcus aureus* are thought to be the predominant cause of cellulitis (Sullivan & de Barra, 2018). Upon inspection of the patient's left lower extremity, there was an absence of demarcation between normal and affected skin, which helped to exclude this diagnosis.

**B Deep Vein Thrombosis.** The risk of venous thromboembolism (VTE) is much higher in patients with active cancer than in the general population (Mahajan et al., 2019). Active cancer accounts for 20% of the overall incidence of VTE. More important than that, cancer is a major cause of death in VTE patients and conversely VTE in the cancer population has a high mortality rate (Fernandes et al., 2019). Clinical signs and symptoms typically associated with a DVT are unilateral or bilateral leg edema, pain, tenderness, local temperature changes, erythema, and a positive Homan's sign. This differential diagnosis was placed lower on the differential list due to the patient's presentation of extreme pain to the left leg and bilateral lower extremity swelling.

**C Necrotizing Fasciitis (Correct Answer).** Necrotizing fasciitis (NF) is a rare but rapidly progressive, life-threatening bacterial infection that can destroy the epidermis, dermis, subcutaneous tissue, fascia, and muscle (Chen et al., 2020). The spectrum of severity ranges from localized

erythema to rapidly spreading erythema and fulminant sepsis seen in necrotizing fasciitis (Sullivan & de Barra, 2018). It is primarily diagnosed based on clinical presentation. Hallmark signs include pain that is out of proportion to the clinical signs. Rapid progression of accompanying symptoms should prompt consideration for necrotizing fasciitis (Jung & Eckmann, 2019). Given NG's presentation of sudden onset of disproportionately increased left lower leg pain in addition to two wounds, one of which was caused by a spontaneous eruption, NF should have been a higher priority when considering his clinical diagnosis.

**D Congestive Heart Failure.** Many effective and life-prolonging chemotherapeutic agents may result in substantial cardiotoxicity leading to symptoms of cardiac dysfunction (Tuzovic et al., 2019). The primary signs and symptoms of acute heart failure are directly related to congestion and elevated filling pressures. Symptoms compatible with congestion include shortness of breath at rest or with activity, orthopnea, paroxysmal nocturnal dyspnea, lower extremity edema, decreased exercise intolerance, and fatigue (Mysliwiec & Bonita, 2017). This diagnosis was suspected due to NG's past medical history and presenting symptoms of bilateral lower extremity edema and bradycardia. On physical exam, he did not exhibit JVD, adventitious breath sounds, or tachypnea, which signaled this differential diagnosis to be the least likely primary culprit.

## DISCUSSION

NG's fragile clinical presentation, acute onset of significant left lower extremity pain, and lactic acid level of 8.9 mmol/L warranted immediate referral to the emergency department (ED) for concern of sepsis. Upon transfer to the ED, NG's chest x-ray was completed revealing mild bibasilar atelectasis

without pleural effusions. While in the ED, NG became hemodynamically unstable, requiring initiation of vasopressors. Emergency surgery services were consulted for concern of necrotizing fasciitis in the left lower extremity. NG was taken to the operating room to undergo incision and debridement of left lower extremity soft tissue within 6 hours of initial presentation to the OEC. Unfortunately, NG succumbed to complications of sepsis 2 days following his surgery. Necrotizing fasciitis and other necrotizing soft tissue infections have a mortality rate of 25% to 35% (Chen et al., 2020).

Initial pharmacotherapy should include empiric broad-spectrum antibiotics until soft-tissue gram stain, culture, and sensitivity results return (Chen et al., 2020). The most recent Infectious Diseases Society of America guideline recommends either vancomycin or linezolid in combination with piperacillin-tazobactam, a carbapenem, or ceftriaxone-metronidazole (Chen et al., 2020). Clindamycin should also be included in empiric therapy due to its effect on toxins released by certain organisms, including *Staphylococcus aureus* and group A *Streptococcus* (Chen et al., 2020). NG's case was complex given his past medical history and disease comorbidities. In assessing his acute symptoms during this visit, it was extremely challenging to tease out the succession of symptoms

that led him to the OEC for evaluation. Nonetheless, his constellation of symptoms and elevated lactic acid warranted prompt transfer to the ED. ●

## Disclosure

The author has no conflicts of interest to disclose.

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