Abstract

Cellulitis is a commonly presenting acute bacterial infection of dermal and subcutaneous tissue, which typically presents as a warm, erythematous, and poorly demarcated area with tenderness to palpation and associated edema. Cellulitis typically is caused by Streptococcus pyogenes or Staphylococcus aureus, but as seen in this case cellulitis can be due to an underlying Escherichia coli infection. It is vital for clinicians to take a detailed history and perform a thorough physical exam when diagnosing cellulitis, as several inflammatory and neoplastic diseases present similarly. Though the use of blood cultures or needle aspirations in the diagnosis of the underlying bacteria involved in cellulitis is usually inconclusive, it is imperative that clinicians properly assess symptoms necessitating their use. This case also presents possible correlations between COVID-19 and cellulitis, however further research is prompted to determine whether cellulitis is a clinical manifestation of COVID-19, especially in immunocompromised patients.

Introduction

Cellulitis is a commonly presenting acute bacterial infection of dermal and subcutaneous tissue, which falls under the broader category of skin and soft tissue infections (SSTIs) [1]. Cellulitis typically presents as a warm, erythematous, and poorly demarcated area with tenderness to palpation and associated edema [2]. Thorough evaluation of a patient’s history is necessary when differentiating cellulitis from other dermatological disorders, as many inflammatory and neoplastic diagnoses appear clinically similar [4]. Major predisposing factors for developing cellulitis include previous cellulitis, immunosuppression, and pre-existing infections. However, skin barrier disruption as a result of trauma, surgical incisions, intravenous site punctures, or insect bites are direct contributors to the development of cellulitis, as bacteria breaches the protective barrier and infiltrates deep tissue. Diabetes mellitus, venous insufficiency, peripheral arterial disease and obesity are frequently identified comorbidities. Cellulitis most commonly affects middle age and older adults and its incidence is found equally in men and women [2].

While over 14 million cases are reported annually in the United States, the causative organisms remain largely unknown as most cases (85 percent) are not culturable. In the cases where the causative agents have been identified, gram positive bacteria including beta-hemolytic streptococci, most commonly Streptococcus pyogenes, and Staphylococcus aureus are the primary culprits [3]. While still incredibly rare, gram-negative and mixed bacteria (gram-negative with gram-positive) are being identified as more common causes of acute skin infections, as seen in this patient [1].


DOI: 10.55920/JCRMHS.2023.03.001122
Case Report

A 78-year-old male presented to the Emergency Department (ED) with worsening generalized weakness along with a large rash on the lower right extremity which was moderate in pain but worsened upon movement or palpitation. He also presented with a positive COVID-19 infection which began 3-weeks ago and stated that he was experiencing some chest discomfort. The patient’s vital signs were BP 101/56, pulse 81, temperature 99.9 °F (37.9 °C), respiratory rate 14, SpO2 99%, and weight 83.6 kg (184 lb 4.9 oz). He was seen in the ED the day before as well with a mildly painful swelling in the lower right extremity but was subsequently treated and released back home. Past medical history is significant for myelodysplastic syndrome with leukemic transformation prior to a bone marrow transplant done three-years ago. The patient’s recovery was complicated by development of chronic graft-versus-host disease (GVHD) resulting in him becoming immunocompromised. Past medical history is also significant for a malignant neoplasm of the prostate, coronary artery disease (CAD), congestive heart failure (CHF), hyperlipidemia, pancytopenia, renal dysfunction, and osteoarthritis bilaterally in the hips and knees.

On physical examination the patient had erythematous swelling in both lower extremities which was more pronounced on the right side. There was a diffuse darkened erythematous rash measuring roughly 10 x 14 cm along with petechiae on the anteromedial aspect of the right thigh. The erythematous swelling was markedly tender to touch and the tenderness extended medially along the tibia all the way down to the ankle. There was no pain out of proportion which would have suggested consideration of necrotizing fasciitis. The patient presented with a low BP (101/56) and was admitted to the ICU where he repeatedly became hypotensive with a BP of 84/53 at one point, consistent with septic shock. His laboratory tests indicated pancytopenia with a low WBC count (2.6 x 10⁹/L), low hemoglobin level (9.4 g/dL), and a low platelet count (66 x 10³/microliter). Additional lab results revealed elevated BUN (51 mg/dL) and a markedly elevated creatinine (2.74 mg/dL) compared to 1.5 mg/dL a year ago suggesting acute kidney injury superimposed on chronic kidney disease. The patient had been taking immunosuppressive medication (Prograf q48h) to limit the effect of his chronic GVHD. A CT with contrast of the lower right extremity indicated moderate subcutaneous edema with skin thickening but no soft tissue abscess or deep fascia thickening. A venous duplex ultrasound of both lower extremities showed no sign of DVT. These findings suggested a cellulitis infection.

Hypotension due to septic shock was corrected with norepinephrine, fluids (IV 0.9% saline), and hydrocortisone (50 mg q6h); a unit of blood was given to correct the anemia. Blood cultures obtained revealed the causing factor of cellulitis to be Escherichia coli, a gram negative rod-shaped bacteria. The patient was started on antibiotics (Cefepime 1g IV q12h and Vancomycin 20 mg/kg IV Once and Trimethoprim-Sulfamethoxazole) to treat the cellulitis.

Discussion

The most common clinical manifestation of cellulitis is a warm, erythematous, darkened, moderately painful, and poorly demarcated rash which is tender to touch. These symptoms are nonspecific however as there are a handful of other dermatologic conditions such as erysipelas, stasis dermatitis, and necrotizing fasciitis that present similarly. A distinguishing feature of cellulitis is that the tenderness is exaggerated and spreads beyond the regions of the erythematous rash [10]. To further distinguish cellulitis from its mimickers it is essential to take a detailed history to determine whether a patient presents with associated risk factors such as diabetes, chronic kidney disease, immunocompromised, or history of cellulitis [4]. All the clinical manifestations of the patient in this case pointed to cellulitis due to his prototypical rash, immunocompromised state, and renal issues. The typical causal bacteria involved in cellulitis are usually Staphylococcus aureus or Streptococcus pyogenes. It is interesting to note that the patient in this case developed cellulitis with the causing...
bacteria being Escherichia coli, a rather rare presentation. A study of the causing bacteria in cellulitis showed that out of 125 collected positive blood cultures only 6 were due to Escherichia coli, with the majority of them being either the usual Staphylococcus aureus or Streptococcus pyogenes [11]. Furthermore, the development of sepsis is rather uncommon in a cellulitis infection, yet is a rather severe occurrence. A recent study showed that out of 606 cellulitis patients, only 65 (10.7%) of them developed sepsis and of those only 8 were immunosuppressed, a comorbidity also seen in our patient [12]. The six reported cases of cellulitis due to E.coli in immunocompromised adult patients were associated with hematologic malignancies, liver cirrhosis, or renal failure, and out of those six only one other patient presented with sepsis. Additionally, none of the six patients had bacteremia as the E.coli was isolated directly from needle aspirates or skin biopsies [13-15]. Cellulitis in immunocompromised patients due to E.coli present in the blood leading to sepsis is thus a rare finding as observed in this patient; treatment is necessitated in a timely manner.

Cellulitis manifests similarly to many other infections so it is paramount for providers to obtain a detailed history and perform a thorough physical exam as nearly 30% of cellulitis patients are misdiagnosed [7]. Along with similar clinical manifestations to other infections, making a definitive diagnosis of cellulitis can be a challenge as diagnostic testing is often inconclusive, with many blood cultures returning negative for bacteria. In fact, The Infectious Diseases Society of America guidelines state that fluid aspirates or blood cultures are not recommended unless patients present with systemic signs of sepsis, are immunosuppressed or immunocompromised, or present with immersion injuries or animal bites [8]. This patient was not only immunocompromised but also presented with sepsis, justifying the need to obtain a blood culture, which ultimately returned positive for Escherichia coli. It is likely that blood cultures are not needed nor recommended as the typical treatment, which includes a combination of vancomycin and ceftriaxone, is extremely effective and rapidly combats the underlying infection regardless of the causal agent. Rapid treatment of cellulitis with antibiotics rapidly is vital in prevention of further complications including sepsis, osteomyelitis, endocarditis, or lymphangitis [9]. Despite it being uncommon to obtain a blood culture in cellulitis due to the high chance of it being inconclusive, it is imperative that providers be able to determine in a timely manner when obtaining a blood culture becomes necessary so sepsis in a patient does not lead to fatality for example.

COVID-19 typically manifests as a combination of fever, chills, shortness of breath, headache, fatigue, and loss of smell or taste [5]. Two cases have been recorded in which COVID-19 positive patients presented with unilateral orbital cellulitis, however it was concluded that the incidence of SaRS-CoV-2 could not be definitively contributory to the presence of cellulitis and may have been coincidental [6]. It is interesting in our case that while the patient was positive for COVID-19, he developed cellulitis in the proximal region of the right lower limb as opposed to in the orbital area as seen in previous cases. It is unclear whether his relatively long-lasting spell of COVID-19 was contributory to his development of cellulitis, and more likely that his immunocompromised state played a larger role. Further research regarding the association of COVID-19 and cellulitis is prompted.

Conclusion
Cellulitis is typically caused by Streptococcus pyogenes or Staphylococcus aureus and occasionally presents with severe symptoms such as sepsis, so it is crucial for clinicians to accurately diagnose and begin antibiotic treatment quickly regardless of the causal agent [1]. With this case report, the goal is to present an unusual case of cellulitis in which the underlying bacteria was Escherichia coli. Severe cases of cellulitis are more common in patients with predisposing factors such as being immunocompromised in this case, so it is imperative that clinicians take a detailed history to ensure proper and timely management. Furthermore, this case report highlights the need for further research in determining whether cellulitis may manifest as a result of COVID-19, along with the clinical course management of patients with simultaneous COVID-19 and cellulitis infections.

References


