Necrotizing Fasciitis Due to *Kocuria rosea* With Progression to Severe Sepsis, Septic Shock and Death: A Reason for Concern About Proper Treatment of Emerging Opportunistic Pathogens

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Citation: Danner OK, Turner A, Williams M, Matthews LR, Nguyen J, et al. (2017) Necrotizing Fasciitis Due to *Kocuria rosea* With Progression to Severe Sepsis, Septic Shock and Death: A Reason for Concern About Proper Treatment of Emerging Opportunistic Pathogens. J Surg: JSUR-169. DOI: 10.29011/JSUR-169.000069

Received Date: 11 September, 2017; Accepted Date: 03 October, 2017; Published Date: 10 October, 2017

Abstract

Necrotizing Soft Tissue Infections (NSTI) are serious infections of the soft tissue compartment with resultant underlying tissue necrosis. When NSTIs invade deeply into the fascia, it is commonly referred to as necrotizing fasciitis, which is an aggressive infection associated with significant morbidity, including multisystem organ failure and the need for extensive tissue debridement, and a high risk of mortality. *Kocuria* is a typically indolent species of bacteria, which is ubiquitous in nature and frequently found as normal skin flora in humans and other mammals. However, in immunocompromised patients, normally non-virulent bacteria such as *Kocuria* species can become opportunistic pathogens and cause life-threatening emergencies. This case report highlights the potential consequence of an under-treated *Kocuria rosea* soft tissue infection with progression to necrotizing fasciitis associated with severe sepsis and septic shock in an immunocompromised, obese diabetic host. The patient also had a gluteal hematoma, which ultimately became infected and grew out *Kocuria rosea*. It is our goal to increase awareness and understanding that normally innocuous microorganisms, such as *Kocuria rosea* and potentially *Staphylococcus simulans*, may become virulent and be associated with significant morbidity and mortality under the right clinical circumstance. Particularly, in an immunocompromised host, these microorganisms can become opportunistic pathogens if left untreated or not treated in an efficient and proper clinical manner with early incision and drainage of skin abscesses and appropriately directed empiric antibiotics.

Introduction

Necrotizing Soft Tissue Infections (NSTI) are infections of any of the layers within the soft tissue compartment with severe changes related to dying tissue [1,2]. When the soft tissue infection invades deeply, also referred to as necrotizing fasciitis if it involves the fascia, NSTIs can cause aggressive infections associated with significant morbidity, including organ failure and the potential need for amputation, and high risk of mortality. The rapid progression and significant threat of morbidity and mortality associated with NSTIs make the need for rapid diagnosis and treatment critical. Diabetes mellitus, immune-compromised states, vascular disease, and obesity are common comorbidities associated with the development of NSTIs. Survival tends to be higher among patients who receive surgical treatment, when it is performed in a timely manner [3].

The causative agent for NSTIs may be a single microbial or polymicrobial infection. The most commonly isolated bacteria are Group a Streptococcus, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Clostridium perfringens*, *Aeromonas hydrophilia*, *Pseudomonas aeruginosa*, and other virulent microorganisms. Although, according to a recent study the majority of patients with necrotizing fasciitis have a polymicrobial infection with isolation of more than one type of bacteria [4]. However, in immunocompromised patients, historically indolent bacteria such as *Kocuria* species can become opportunistic pathogens and cause life-threatening emergencies.
Although not previously known to cause human infections, *Kocuria* species have emerged as opportunistic human pathogens, mostly in immune compromised hosts with severe underlying disease. Recently, there has been an increasing incidence of different types of *Kocuria* infections being reported, which is most likely due to the adoption of better identification methods [1]. This case report highlights the potential consequence of under treated *Kocuria* infection with progression to necrotizing fasciitis and septic shock in an immunocompromised diabetic host in response secondary to a *Kocuria rosea* gluteal soft tissue infection.

**Case Presentation**

JS was a 62-year-old woman with a past medical history significant for type II diabetes mellitus, stage 4 chronic kidney disease, congestive heart failure with an ejection fraction of 50%, chronic obstructive pulmonary disease, pulmonary hypertension, obstructive sleep apnea, and mechanical aortic valve replacement on Coumadin who was found down at home by a family member. Of note, on a visit to her PCP a week prior to presentation, she complained of “Boils” on her buttock that were painful and draining for 2 days. She had a history of these in the past which spontaneously drained. Furthermore, she was wheelchair bound and was thus given a course of clindamycin antibiotics by her PCP as an outpatient. According to emergency medical services personnel, she was found face-down in her room for an unknown period of time. The patient presented to the ED as a sepsis alert due to being febrile with altered mental status. She was found to be nonresponsive and unable to follow commands or participate in her care upon on arrival. Her ED course was notable for hypoxia on high flow oxygen supplementation via a non-rebreather mask requiring intubation and full ventilator support for acute hypoxic respiratory failure. She subsequently became hypotensive with a drop in her systolic blood pressure to the 90’s post intubation with MAPs in low 70’s. A 2-liter bolus of lactated Ringer’s solution was administered due to presumed septic shock. Therefore, a right internal jugular central venous line was placed and a norepinephrine infusion was initiated for relative hypotension. Her post intubation chest x-ray revealed a right sided pulmonary consolidation and pleural effusion. Cultures and labs were drawn. Vancomycin and piperacillin-tazobactam empiric antibiotics were infused for likely sepsis. A few hours later her CT of head was read as negative. Her CT scan for pulmonary embolism was not able to be completed due to an elevation in her Blood Urea Nitrogen (BUN) level of 139 and elevated serum creatinine (Cr.) of 3 mg/dL. Upon return from the CT scanner, the patient was noted to have a bloody bowel movement consisting of stool mixed with blood. Given her elevated INR, she underwent emergent reversal of her coagulopathy with Prothrombin Complex Concentrate (PCC) prior to transport up to the MICU.

While in ICU, the patient had a seizure which resolved with a 2-mg lorazepam intravenous bolus. Given her multiple comorbidities and the concern for necrotizing fasciitis versus superinfected bilateral buttock hematomas, a surgical consultation was obtained and the patient was scheduled to be taken to the OR.
for emergent incision, drainage and debridement of the bilateral gluteal region lesions. The patient nevertheless remained in septic shock, but her blood pressure was initially able to be maintained at adequate levels using the norepinephrine infusion. However, her mean arterial pressure continued to drop with intermittent periods of ventricular fibrillation upon return to the ICU. Therefore, vasopressin and epinephrine were added for hemodynamic support due to refractory hypotension. The patient also required electrical cardioversion for ventricular fibrillation/ventricular tachycardia, which was suspected to be contributing to her hemodynamic instability. She was administered magnesium sulfate 2 grams i.v., 3 boluses of sodium bicarbonate and was subsequently started on a lidocaine and amiodarone drip.

The patient was transported to the OR on assist control mechanical ventilation with a rate of 30, PEEP +14 and 100% oxygen. She was placed under general inhalational anesthesia during procedure with no issues. All pre-operative vasopressors were continued throughout the procedure and during her transport back to the ICU. Intraoperatively, the right and left buttck tissues were sharply incised in a large elliptical fashion along the affected area of skin. Bilateral large hematomas were encountered with large amounts of necrotic fat. The necrotic fat was extensively and deeply debrided. However, given concerns for possible rectal involvement and the continued hemodynamic instability of the patient, the decision was made to limit the extent of the dissection to removal of obviously necrotic and devitalized tissue. All area of contained fluid were opened and drained bilaterally. The wound was irrigated with copious amounts of sterile saline solution and betadine-soaked Kerlex gauze was packed into the wound. The dressing was secured with stapled mesh panties. Intraoperative findings include a large infected hematoma with necrotic fat of bilateral gluteal regions extending down to anus and most likely to rectum. Wound cultures were sent in the OR and were positive for Kocuria rosea in addition to Staphylococcus simulans. Blood cultures were taken in the ICU which were positive for Trueperella bernardiae. At the conclusion of the case, the patient was transferred to the surgical ICU in critical condition. The patient became hypotensive postoperatively despite being on the maximum dose of the vasopressors: norepinephrine, vasopressin, and epinephrine. The patient’s family members were immediately contacted to discuss her disposition and the goal of care. The family decided that they would like to uphold her DNR wishes that the patient would like to uphold her DNR wishes. While the discussion took place, the patient went into asystole. The family clearly expressed that they did not want the team to resuscitate her. The patient was thus pronounced deceased shortly after midnight and within 24 hours of presentation to the ED for severe sepsis and septic shock due to necrotizing fasciitis secondary to a Kocuria rosea soft tissue infection of her buttocks.

Discussion

Necrotizing fasciitis is a serious soft tissue infection associated with significant morbidity and risk of mortality. They are typically caused by virulent polymicrobial bacterial infections but can be caused by a single pathogenic bacterial species. NSTIs due to indolent microbial organisms, such as Kocuria and Staphylococcus simulans, are uncommon causes of significant infections. However, in immunocompromised hosts due to conditions such as poorly controlled diabetes mellitus, Acquired ImmunoDeficiency Syndrome (AIDS), and diseases requiring steroid therapy, normally indolent microorganisms acquire a higher pathogenic potential. When they result in infections under uncommon situations or circumstances in hosts which do not normally result in infectious conditions, they are referred to as opportunistic pathogens.

Microorganisms of the genus Kocuria (family Micrococccaceae, order Actinomycetales, class Actinobacteria) are gram-positive coccoid bacteria often found as tetrads and irregular clusters that are catalase-positive and coagulase-negative. These bacteria are responsible for different types of infection, mostly in immunocompromised hosts with serious underlying conditions [5,6]. However, the prevalence of human infections caused by Kocuria species is underestimated, as commonly used phenotypic assays are known to misidentify Kocuria isolates as Staphylococci. Kocuria classification is now typically confirmed by 16S rRNA gene sequencing, and one study even used matrix-assisted laser desorption/ionization time-of-flight mass spectrometry for species identification, which appears to be an efficient method [7].

Kocuria is ubiquitous in nature and is frequently found as normal skin flora in humans and other mammals. Only five of the 18 species in this genus are known to be opportunistic pathogens [6]. Therefore, virulence of this bacteria is unlikely in an immunocompetent host. However, there has been a recent rise in the incidence of infections caused by Kocuria species causing both superficial infections and deep-seated/invasive infections1. A number of studies have been published establishing Kocuria species in infections associated with urinary tract infections, cholecystitis, catheter-associated bacteremia, dacryocystitis, canaliculitis, keratitis, native valve endocarditis, peritonitis, descending necrotizing mediastinitis, brain abscess and meningitis [8-10]. Infectious diseases are more frequent and serious in patients with diabetes mellitus, which potentially increases their morbidity and mortality. The greater frequency of infections in diabetic patients is caused by the hyperglycemic environment that favors immune dysfunction (e.g., damage to the neutrophil function, depression of the antioxidant system, and humoral immunity), micro- and macroangiopathies, neuropathy, decrease in the antibacterial activity of urine, gastrointestinal and urinary dysmotility, and greater number...
of medical interventions in these patients [8]. Besides the classical complications of the disease, DM has been associated with reduced response of T cells, neutrophil function, and disorders of humoral immunity. Consequently, DM increases the susceptibility to infections, both the most common ones as well as those that almost always affect only the immunocompromised [11-13].

The case summary described above involves the presentation of skin boils on the buttocks of a woman suspected to be colonized with *Kocuria rosea* and *Staphylococcus simulans*. In the setting of poorly-controlled diabetes, the patient became an immunocompromised host with increased risk of susceptibility to generally non-virulent pathogens, such as *Kocuria* species. The pathogenesis of her severe sepsis with septic shock was likely due to hematogenous dissemination of the polymicrobial necrotizing fasciitis infection, which originated from her soft-tissue skin infection.

**Conclusion**

*Kocuria* species is thought to be non-virulent in the immunocompetent host. However, in patients with co-morbidities leading to an immunocompromised state, this bacterium can potentially have life-threatening effects, especially if not treated appropriately and early. Recent findings have implicated *Kocuria* in infections associated with urinary tract infections, cholecystitis, catheter-associated bacteremia, descending mediastinitis, brain abscess formation and meningitis. In this report, the *Kocuria* spp. bacterium was responsible for a necrotizing soft-tissue infection leading to severe sepsis with septic shock, multiple system organ failure and ultimately death. The purpose of this report is to increase awareness and understanding that normally innocuous microorganisms, such as *Kocuria rosea* and potentially *Staphylococcus simulans* may be associated with significant morbidity and mortality under the right clinical circumstance, particularly in an immunocompromised host.

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