CASE REPORT

Bilateral thigh methicillin-resistant *Staphylococcus aureus* necrotising fasciitis in a man with newly diagnosed Human Immunodeficiency Virus (HIV)

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SUMMARY

Methicillin-resistant *Staphylococcus aureus* (MRSA) necrotising fasciitis (NF) is rare and constitutes a medical and surgical emergency. We report a case of a 53-year-old man with type-2 diabetes mellitus and newly diagnosed HIV infection who presented with 1 week of progressively worsening bilateral sharp thigh pain. On presentation, he was febrile, tachycardic and had bilateral thigh erythema and mild tenderness without open wounds. He had leucocytosis, lactic acidosis and acute kidney injury. Urgent incision and drainage (I&D) was performed for suspected NF. Blood cultures and I&D were positive for MRSA. Biopsy of bilateral thighs showed NF. He was treated with wound washout and 6 weeks of intravenous antibiotics. After undergoing skin graft for wounds, he was discharged to physical rehabilitation. Here we report severe sepsis from bilateral thigh MRSA NF in a patient with newly diagnosed HIV.

BACKGROUND

Necrotising soft tissue infections (NSTIs) are defined by infection and necrosis of any layer within the soft tissue compartment most commonly affecting adipose tissue, fascia or muscle.¹ NSTIs are highly lethal, with median mortality rates estimated to be 32%.^{1–3} Owing to the severe nature of the disease and rapidly progressing course, early diagnosis and treatment are crucial to patient survival.

The cornerstone of treatment for NSTIs is early surgical debridement of necrotic tissue and empiric antibiotics.^{1–4} Since infection generally involves deeper subcutaneous tissues, the true extent of involvement cannot be known until it is visualised intraoperatively. Amputation may be required in up to 20% of cases.⁵ Empiric antibiotics should be de-escalated once the causative agent is isolated.

Although NSTI is a well-documented occurrence, we report a case of a man with community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) necrotising fasciitis (NF) involving his bilateral anterior thighs. An examination of the available literature shows that NF due to CA-MRSA is exceedingly rare.⁶ This rarity is further compounded by multifocal involvement of the patient's bilateral anterior thighs, which, to the best of our knowledge, has never been previously reported.

CASE PRESENTATION

A 53-year-old African-American man with hypertension and diabetes mellitus type 2 (T2DM)

presented to the hospital with symptoms of progressively worsening bilateral thigh pain for 1 week. He described the pain as sharp, diffuse in both thighs, 10/10 in severity, worse with movement or pressure on his thighs and associated with subjective fevers and chills. He denied any history of trauma, bug bites, rash or surgery to the affected areas. He stated that the onset of pain began gradually while driving his truck. Initially, the pain was not bothersome, but it became progressively worse, particularly in the 24 hours prior to his presentation. He reported self-discontinuing all of his prescribed medications 1 year ago and had not seen his primary care doctor over the same time period.

The patient's medical history was notable for hypertension and T2DM on oral hypoglycaemics. He denied any history of previous surgery. Both his parents had T2DM and he lived with his second wife and daughter. He endorsed alcohol use one to two times per week with no more than three drinks in a day, current tobacco use of one pack per day and denied use of illicit drugs including intravenous drugs. He reported high-risk sexual behaviour with female partners only. He works as a semitrailer truck driver and drives primarily in the Southeastern USA.

At presentation, the patient's temperature was 97.6° Fahrenheit, heart rate 113 beats per minute, blood pressure 110/68 mm Hg, respiratory rate 16 breaths per minute and an oxygen saturation of 100% on room air. He appeared in pain, but not in any respiratory distress. He had good insight and was alert and oriented to person, place and time. His oral mucosa was dry and a thick layer of thrush was noted on the tongue. His lungs were clear to auscultation bilaterally. On cardiac examination, patient was tachycardic without any murmurs. Bilateral thighs were mildly erythematous, warm and tender to palpation without crepitus. Tenderness to palpation was more pronounced over the left thigh in comparison to the right. The patient had no focal neurological deficits.

INVESTIGATIONS

The patient's white cell count (WCC) was 15 700 cells/mm³ with 87.5% neutrophils and 25.7% bands. The haematocrit was 38.2%, haemoglobin (Hb) 12.6 g/dL, and platelet 179 000 cells/mm³. The sodium level was 117 mmol/L, potassium 5.3 mmol/L, chloride 82 mmol/L, bicarbonate 21 mmol/L, creatinine 2.4 mg/dL, glucose 741 mg/dL, lactate 4.7 mmol/L, procalcitonin 199.9 ng/mL

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and C reactive protein >270 mg/L. Culture from incision and drainage (I&D) of bilateral thighs and two out of two blood culture bottles were positive for MRSA. The patient was found to be HIV genotype-1 (HIV-1) positive with viral load 310 000 copies/mL and CD4 312 cells/mL.

Lower extremity (LE) ultrasound duplex was negative for deep venous thrombosis. A CT scan of bilateral LE showed extensive inflammatory fat stranding with fluid along the superficial fascial planes, left greater than right, with swelling/oedema of the anterior musculature. There was no evidence of soft tissue gas, abscess or osteomyelitis. Transesophageal echocardiogram (TEE) was significant for mild global left ventricular hypokinesis with ejection fraction of 42% with no valvular vegetation.

Surgical fascial biopsy from bilateral thighs showed fibroconnective tissues with focal necrosis, compatible with NF (figures 1 and 2). Left knee arthrocentesis: cloudy synovial fluid, WCC 35 160 cells/mm³ with 95% neutrophils and no crystals. Bacterial cultures from both biopsy and arthrocentesis grew MRSA within 24 hours.

DIFFERENTIAL DIAGNOSIS

- ▶ Necrotising fasciitis
- ▶ Cellulitis
- ▶ Myositis
- ▶ Septic arthritis

TREATMENT

We treated the patient's septic shock due to MRSA NF with empiric antibiotics: vancomycin, piperacillin-tazobactam and clindamycin, volume resuscitation and vasopressors. An urgent I&D and wound washout was performed by surgery within 6 hours of admission. Antibiotics were de-escalated to vancomycin monotherapy on MRSA isolation from wound and blood

cultures. HIV infection was treated with emtricitabine, tenofovir and raltegravir.

OUTCOME AND FOLLOW-UP

The patient was taken urgently to the operating room after presentation. His bilateral quadriceps were mildly oedematous, pink and viable without presence of gross necrosis (figures 3 and 4). However, serous per fascial fluid was noted. The wound was kept open and packed with gauze with a plan for a second look at a later time. The patient was intubated for the procedure and became hypotensive after the procedure. He remained in the intensive care unit postsurgically and required volume resuscitation with lactated Ringer's solution and a norepinephrine drip for refractory hypotension secondary to septic shock. He was extubated on day 5 and transferred to the general medicine floor on day 9.

On day 3, the patient was found to be HIV-1 positive, a diagnosis previously unknown to him. As per consultation with our infectious disease specialists, the patient was initiated on emtricitabine, tenofovir and raltegravir. A TEE on day 11 was negative for valvular vegetation.

During his hospital course, the patient continued to have intermittent fevers, but negative blood cultures. On hospital day 20, he reported worsening left knee pain, with swelling, erythema and tenderness. Arthrocentesis of his left knee was performed and cultures grew MRSA which was treated with intravenous vancomycin. He was taken to the operating room on hospital day 22 for knee washout and re-exploration of his thigh wounds. The left thigh wound was extended caudally through the fascia. Normal fascia and muscle were noted; however, non-foul smelling, turbid fluid was noted which grew

Figure 1 Fibroconnective tissue with focal necrosis (arrow) (H&E, ×50).

Figure 2 Skeletal muscle and fascia with necrosis (arrows) (H&E, ×400).

Figure 3 Gross image of right thigh showing surgically debrided tissue.

Figure 4 Gross image of left thigh showing surgically debrided tissue.

MRSA. On hospital day 32, he underwent wound closure with skin grafts. He is planned to receive vancomycin for a total of 6 weeks.

DISCUSSION

NF is a life-threatening, invasive infection of the skin and soft tissue that carries a median mortality of 32.2% for with treatment and 100% without treatment.^{1–3} NSTIs are commonly classified by causative microbial organism(s), anatomic location and depth of tissue necrosis. NF is classified into two universally accepted types: type I (mixed aerobic and anaerobic), type II (monomicrobial, typically group A streptococci and/or staphylococcal species).^{1–7} The majority of the cases, ~70–90%, are due to a type I which primarily affects the trunk and perineum.¹ Type II primarily affects the lower extremities of young and healthy individuals. It is rarely due to CA-MRSA, with one retrospective study reporting only 14 CA-MRSA NF cases of 843 total wound culture positive MRSA cases.⁶

Predisposing risk factors for CA-MRSA NF include a history of intravenous drug use, MRSA infection, chronic hepatitis C or diabetes mellitus.^{6–7} HIV, penetrating trauma, obesity and gastrointestinal tract malignancy have been reported to be risk factors for type I NF.⁷ HIV has not been associated with a higher rate of MRSA NF; however, patients with CD4<200 have a higher risk of overall MRSA skin and soft tissue infection.^{6–8–9} Our patient's risk factors included uncontrolled T2DM and HIV infection but interestingly had CD4>200 cells/mL.

The classic triad for NF includes severe local pain that is out of proportion to skin findings, erythema and swelling.¹⁰ Unlike other soft tissue infections, patients with NF are more likely to have vital sign abnormalities such as tachycardia, fever, tachypnoea and hypotension.¹¹ However, in early stages of NF, systemic signs may not be present. Hence, clinical suspicion based on risk factors and physical examination becomes vital for early diagnosis. Initially, our patient had the classic triad, along with tachycardia, but lacked other systemic signs of shock. Nevertheless, the patient developed septic shock rather quickly.

There are no specific laboratory results for the diagnosis of NF, but leucocytosis with WCC more than 20 000 cells/mm³ along with clinical signs should definitely raise suspicion.¹² To aid in clinical decision, the scoring system Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) was developed by Wong *et al.*^{12–13} The scoring system includes C reactive protein, WCC, Hb, sodium, creatinine and glucose levels. The cut-off score of 6 points carries a 92% positive predictive value and 96% negative predictive value for diagnosis of NF.^{12–13} Our patient had an LRINEC score of 11, placing him at high risk for NF.

Plain radiographs and CT scans have low sensitivity and specificity, but may be helpful in establishing a diagnosis in equivocal cases by showing soft tissue swelling and gas formation.^{3–10–14} MRI remains the imaging modality of choice for soft tissue infections, particularly because it can define the anatomic extent of infection. However, MRI is rarely used to diagnose NF because it is time consuming and may delay surgical intervention.^{1–15} We performed a CT scan on our patient, which showed fluid collection and fat stranding along the superficial fascial planes in the bilateral anterolateral thighs concerning for NF.

NF is a surgical and medical emergency requiring urgent surgical debridement and broad spectrum antibiotics. Patients who do not get primary debridement of the affected area within 24 hours after the onset of symptoms carry nine times higher mortality.¹⁶ Furthermore, the relative risk of death is 7.5 times greater in patients with restricted primary debridement.^{1–17}

Infectious Disease Society of America recommends prompt surgical consultation and empiric broad spectrum antibiotics, covering Gram-positive, Gram-negative and anaerobic organisms, for the treatment of NF. A suggested regimen includes vancomycin, piperacillin-tazobactam and clindamycin/metronidazole.⁴ Other treatment options include hyperbaric oxygen therapy. However, there is a paucity of data supporting their efficacy.^{18–20} Our patient received surgical intervention and appropriate broad spectrum antibiotics within 6 hours of presentation, which may have prevented his mortality.

Most reported cases of NF typically involve a single soft tissue site, but can rarely involve two or more areas of necrosis that are non-contiguous. Our patient had biopsy proven bilateral thigh NF without perineal involvement (Fournier gangrene), which makes this case even more intriguing. A recent review of cases showed the rarity of multifocal NF (MNF), just 33 reported cases from 1966–2011.²¹ Interestingly, a vast majority (86%) of the MNF were attributed to type II NF, unlike overall incidence of <20% among all cases of NF.^{1–21} To the best of our knowledge, MNF due to CA-MRSA has not yet been reported.

In summary, early diagnosis of NSTIs is of the essence. Rapid and aggressive surgical debridement combined with broad-spectrum empiric antibiotic therapy and volume resuscitation remain the pillars of treatment. Delays in surgery of >24 hours have been linked to higher rates of mortality.^{1–16–17}

Learning points

- ▶ Necrotising fasciitis (NF) is a medical and surgical emergency requiring high clinical suspicion for early diagnosis.
- ▶ Methicillin-resistant *Staphylococcus aureus* is an uncommon cause of NF but should be suspected in patients with diabetes and immunocompromised patients.
- ▶ Emergent surgical debridement and empiric broad spectrum antibiotics remain the cornerstone of NF treatment.

Contributors DC collected most of the background information, obtained patient consent, collected and analysed data, drafted and critically revised the manuscript. DC approved the final version of the manuscript for publication. AS assisted in the collection of background information, data and its analysis. AS also drafted and critically revised the manuscript. AS approved the final version of the manuscript for publication. Juan Galvis assisted in the collection of background information, data and its analysis. As also drafted and critically revised the manuscript for its medical and ethical accuracy. Approved the final version of the manuscript for publication. Juan Guardiola assisted in the collection of background information, data and its analysis. Juan Guardiola also drafted and critically revised the manuscript for its medical and ethical accuracy. Juan Guardiola approved the final version of the manuscript for publication.

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