Case Report

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Lethal soft-tissue necrosis early after organ transplantation: a case report

Pieter R. C. de Jong, MD[a,*], Mathieu M. E. Wijffels, MD, PhD[a], Bart J. A. Rijnders, MD, PhD[b], Nicole Juffermans, MD, PhD[c]

Introduction and importance: Necrotizing soft tissue infection (NSTI) is a rapidly spreading infection which affects subcutaneous tissue, extending to a muscular level. Early and aggressive surgical exploration is frequently necessary, especially in patients with significant comorbidities or advanced age. NSTIs are commonly caused by *Streptococcus pyogenes* or methicillin resistant *Staphylococcus aureus*, though monomicrobial infections with *Candida species* have been reported.

Case presentation: A 64-year-old developed an NSTI of the upper left leg following bilateral lung transplantation. The patient presented with atypical clinical and radiographical symptoms, leading to initial management with antimicrobial therapy. Cultures taken preoperatively and intraoperatively were positive for *Candida albicans* without the presence of other microorganisms. Surgical exploration revealed extensive necrosis of the upper left leg and groin, resulting in deep sepsis which ultimately led to the patient's death.

Clinical discussion: NSTI should be monitored with extra vigilance in immunocompromised or otherwise at risk patients, especially when exhibiting atypical symptoms or disease course. Extensive surgical exploration remains the cornerstone of adequate treatment.

Conclusion: NSTIs caused by monomicrobial infections with *C. albicans* are rare and typically progress rapidly. We report a case of monomicrobial NSTI in an immunocompromised patient following bilateral lung transplantation characterized by atypical presentation and course, with *C. albicans* as the main pathogen.

Keywords: necrotizing soft tissue infection, lung transplantation, *Candida albicans*

Introduction and importance

Necrotizing soft tissue infection (NSTI) is a rapidly spreading, deep-seated infection which typically affects subcutaneous tissue, often extending to a muscular level[1]. It is associated with a mortality rate of 15%–29% and loss of limb in 20%–26% of cases. As such, it should be treated promptly and aggressively with antibiotics, surgical debridement or amputation[1,2]. Early surgical exploration can facilitate an early diagnosis and should be considered, especially in patients with comorbidities such as diabetes mellitus or liver disease[2,3]. Hallmarks of NSTI include fascial frailty and grey inflammatory fluid ("dishwater") with the absence of pus. Although not present in all cases, subcutaneous emphysema can frequently be found in radiographical imaging[4]. NSTI can be categorized into type I (polymicrobial) and type II (monomicrobial) based on the pathogens identified in tissue cultures[1]. The typical pathogens are *Streptococcus pyogenes*, methicillin resistant *Staphylococcus aureus* (MRSA), and *Escherichia coli*[1,2]. In rare cases NSTI can be caused by *Candida* species, usually in immunocompromised patients. Due to the rarity of these cases, they have been scarcely reported[5-10]. Here we present a case of an immunocompromised patient following bilateral lung transplantation (LUTX) who developed an NSTI with a sudden and fulminant course 2 months post-surgery, absent most classic symptoms and radiographical findings associated with NSTI. This case report was written in line with the SCARE 2023 criteria[11].

HIGHLIGHTS

- Monomicrobial necrotizing soft tissue infection caused by atypical pathogen.
- Critical care for immunocompromised patient following lung transplantation.
- Insidious disease course causing challenges in diagnostics and treatment.
- Challenges in medical ethics due to treatment causing debilitating surgical interventions.
- Pitfalls and challenges in atypical disease presentation.

Case presentation

A 64-year-old patient with a history of Chronic Obstructive Pulmonary Disease and pulmonary hypertension based on an

[a]Department of General Surgery, Erasmus Medical Center, Rotterdam, the Netherlands, [b]Department of Microbiology, Erasmus Medical Center, Rotterdam, the Netherlands and [c]Intensive Care Unit, Erasmus Medical Center, Rotterdam, the Netherlands

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*Corresponding author. Address: Department of General Surgery, Erasmus Medical Center, the Netherlands. E-mail: (prcdejong@outlook.com) (P. R. C. de Jong).

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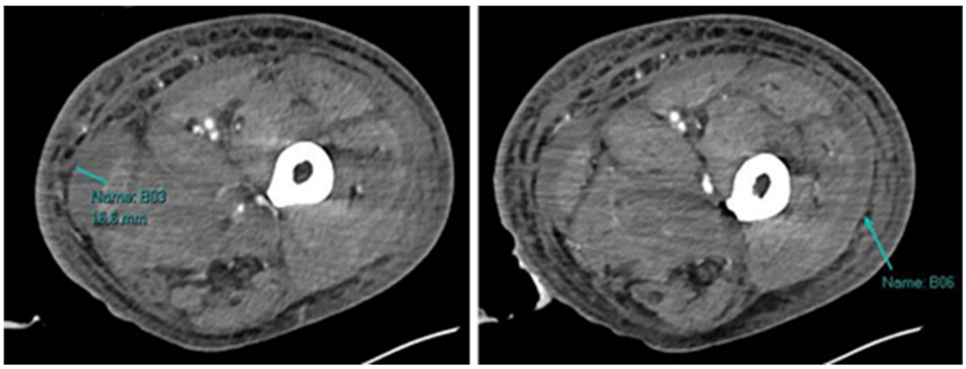

Figure 1. CT image of fluid surrounding the medial (left) and lateral (right) muscular fascia.

alfa-1-antitrypsine deficiency, was admitted for LUTX. There were no intraoperative complications. Following the procedure, the patient was admitted to the intensive care unit (ICU) due to hemodynamic instability and was ventilated using extracorporeal membrane oxygenation (ECMO). The patient received antibiotics based on donor characteristics, and immunosuppressants based on the local LUTX protocol. Selective bowel decontamination was given throughout the admission.

On postoperative day 1 (POD 1) edema of the upper right leg was observed, interpreted as an out flow issue due to the ECMO treatment. Dialysis was initiated due to kidney failure. The ECMO was removed the following day without complications. On POD 7, metabolic encephalopathy was diagnosed and treated expectantly. Due to increasing infection parameters (IP) after stopping antibiotic treatment on, meropenem was started on POD 10. After clinical improvement, meropenem was discontinued after three days. On POD 26 the patient developed transplant rejection for which additional methylprednisolone was started, and a pleural puncture was performed. Antibiotics were administered after the patient developed pneumonia on POD 37, and treatment was stopped after three days. A central venous catheter (CVC) was removed from the subclavian artery after faulty placement via endovascular procedure with access through the brachial artery

On POD 42 the patient developed erythema and swelling of the left leg, for which an ultrasound was performed, showing no deep venous thrombosis. A subsequent CT revealed extensive fluid surrounding the fascia of the adductor- and lateral compartment of the upper left leg without subcutaneous emphysema (Fig. 1). An incision was made medially and laterally up to the fascia. Medially a substantial amount of muddy fluid was relieved, but no necrosis was seen. A *Candida albicans* was cultured from the fluid, and micafungin was initiated in addition to ceftriaxone and clindamycin.

On POD 49 micafungin was switched to fluconazole, and the antibiotics were stopped the following day after 7 days of treatment. A CT scan was performed on POD 52 due to clinical deterioration, increased IP, and hypotension, showing unaltered fluid surrounding the medial and lateral muscular fascia of the upper left leg, without the presence of abscesses or subcutaneous emphysema. Fluconazole was switched back to micafungin in addition to starting ceftriaxone and clindamycin. A vacuum-assisted closure device (VAC) was applied to the medial wound. Due to increasing pain and swelling, an additional CT scan was made, revealing a hematoma underneath the VAC system, which was incised (Fig. 2).

The patient's clinical condition deteriorated in the following days, with increasing IP, deteriorating vital signs, and vasopressin exigency. CT imaging showed a decrease of the subcutaneous hematoma previously incised and a new intramuscular abscess in the adductor compartment. The abscess was drained in the operating theatre, whereupon inspection of the muscle compartments no

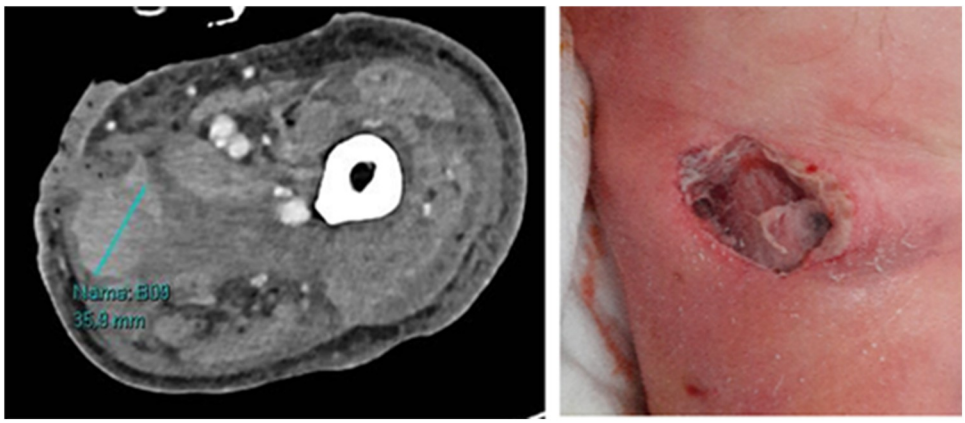

Figure 2. CT scan showing subcutaneous hematoma (left) and incision showing no necrosis of fascia or muscle tissue (right).

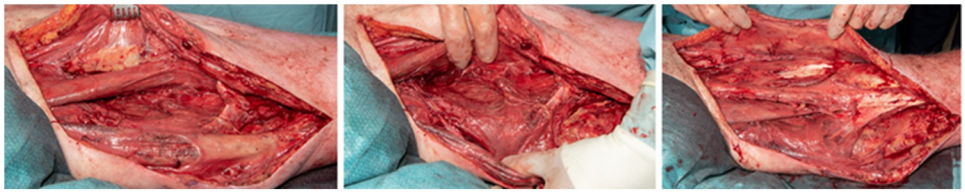

Figure 3. Intraoperative pictures taken during exploration of the left groin showing extensive necrosis of the medial (left), intermediate (middle) and lateral (right) compartment.

necrosis was observed. The CVC in situ was changed and cultured, showing *Enterococcus faecium*. Surgical exploration of the groin was performed twice the same day due to further deterioration; intraoperative pictures are shown in Fig. 3. Necrosis of all adductors, flexors, and m. Vastus lateralis was observed, leading to the decision to perform an exarticulation of the hip. Necrosis of the gluteus maximus was suspected, however due to hemodynamic deterioration the surgery was not extended for further exploration.

A second look to assess progressive necrosis was performed the following day. Necrosis of the gluteus musculature with progression toward the perineum and left abdominal wall was observed (Fig. 4), and the procedure was ceased. The progression of disease was deemed too severe for further treatment without extensive tissue excision, and in accordance with the patient and family's wishes, all treatments were stopped. Shortly after discontinuing supportive treatment the patient deceased 63 days after receiving a LUTX. Cultures taken intraoperatively from necrotizing tissue showed growth of *C. albicans* and *E. faecium* and were negative for *S. aureus* and *S. pyogenes*. An obduction was performed, which revealed no other abnormalities suspected as a cause of death. A full overview of the course of events is depicted in Fig. 5. All surgical interventions were performed by or under supervision of an experienced trauma surgeon in an academic hospital, with patient in supine position and under general anesthesia. The patient was admitted to the ICU for the entire duration of admission and was under direct care of a multidisciplinary team of experienced ICU physicians, pulmonary medicine physicians, trauma surgeons, and medical microbiologists. There were no changes in planned interventions.

Clinical discussion

Due to the rapidly spreading nature and subsequent high mortality of NSTI, timely diagnosis and treatment are crucial. Diagnosis can often be made based on clinical presentation, as extreme tenderness to palpitation, crepitus, bullae, and erythema are traditionally present. As the disease progresses, a deep sepsis which requires aggressive resuscitation and ICU admission can be expected[12]. Surgical exploration with (extensive) necrosectomy or amputation is a key component in the treatment of these infections, often requiring multiple surgeries.

Type II (monomicrobial) NSTI is typically caused by a group A *streptococcus* followed by MRSA, and can occur in any patient, regardless of comorbidities or use of medication[13]. Type I (polymicrobial) NSTI is generally seen in those who are immunocompromised, have significant comorbidities or advanced age. These infections often present with subcutaneous emphysema and can be difficult to distinguish from gas gangrene. Ludwig's angina (submandibular), Lemierre's syndrome (jugular vein) and Fournier's gangrene (scrotal or perineal) are specifically located infections that can be discerned[14]. Some reported cases of NSTI have been caused by a monomicrobial infestation with yeasts, specifically C*andida species*[5-10,15-19] often presenting as surgical site infections[6-8,16] following trauma[5,9], or as Fournier's gangrene.[10,17-19] These infections are highly progressive and develop over a matter of days.

C. albicans is a commensal yeast fungus inhabiting the mucosal surface of the skin, and gastrointestinal and genital tracts, which has the ability to turn pathogenic in immunocompromised or dysbiotic individuals[20]. Infections caused by

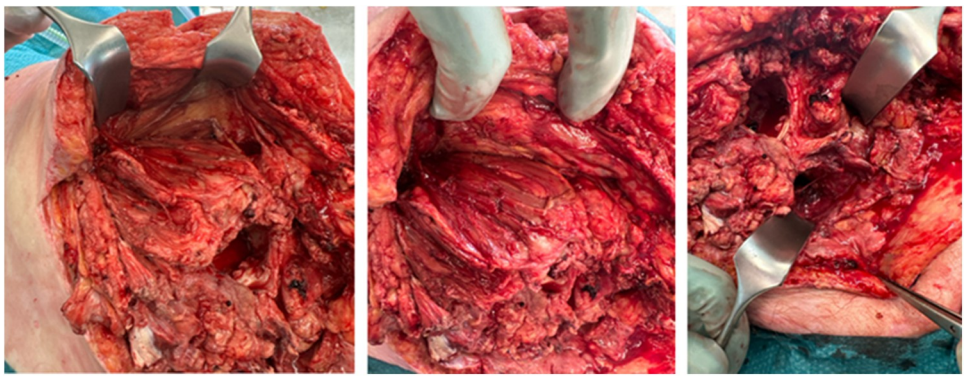

Figure 4. Intraoperative view of gluteal muscles (left, middle), extending in the perineal area (right).

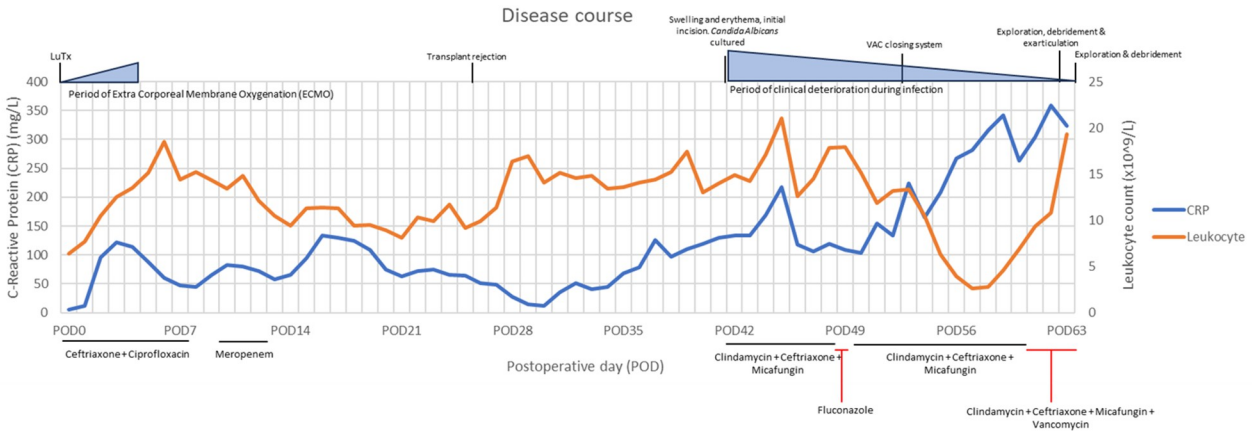

Figure 5. Disease course starting from day of surgery. LUTX, lung transplantation; CRP, C-reactive protein; POD, postoperative day.

C. albicans are usually superficial, however invasive fungal infections resulting in systemic candidiasis may occur, leading to septic shock in almost one-third of those affected[21,22]. Advanced age, increased Charlson comorbidity index and septic shock during the onset of infection are poor prognostic factors, resulting in a mortality of 34%–60%[23]. Although prior antimicrobial therapy is a risk factor for invasive candidiasis, the underlying mechanisms are poorly understood. Drummond *et al* reported that antibiotic treatment enhanced the susceptibility for invasive candidiasis due to impaired lymphocyte-dependent interleukin-17A and Granulocyte-macrophage colony-stimulation factorantifungal immunity[24].

Here we present a case of an immunocompromised patient following bilateral LUTx who developed an NSTI caused by *C. albicans* as the main pathogen. The infection was characterized by atypical presentation and progression. Initially, the patient presented with swelling and erythema of the left upper leg, upon which an incision was made revealing "dishwater" fluid. Notably absent were the extreme pain, crepitations, and sepsis typically associated with NSTI, as well as subcutaneous gas on radiographical examination. At this point, no necrosis was observed and only *C. albicans* was cultured. After a week of treatment with ceftriaxone, clindamycin and micafungin during which time IP remained high, the patient began to clinically deteriorate, three days following the end of the antibiotic treatment. A similar treatment regimen proved unsuccessful, and further deterioration requiring multiple surgeries, ultimately leading to death over the next 10 days, resulting in a disease duration of 3 weeks.

Notably the initial incision showed little to no necrosis, whereas a second look performed only 9 hours later showed extensive necrosis of all muscle compartments of the upper left leg. It should be considered that the increase in vasopressin between the surgeries could have contributed to the extent of the necrosis. Cultures taken 1 day presurgery and intraoperatively showed *E. faecium* culturalization as well as *C. albicans*, however in lieu of its presence in earlier cultures and the extent of the disease present at inspection lead us to believe that *C. albicans* is the main pathogen in this case. Due to the clinical symptoms and radiographical signs at first presentation, there was a delay in the surgical exploration leading to the definitive diagnosis, which could have contributed to the extent of the infection and the outcome of this case, although appropriate microbial therapy was given.

As a case report, there is limited possibility to generalize the validity of this study and due to the rarity of this disease, it is difficult to extradite its findings to the broader population. In addition, we were unable to establish a cause-effect relationship. However, due to the severity of the outcome, we believe it is important to publish any experience with this form of NSTI, as it can be critical information for anyone caring for the critically ill or immunocompromised. In lieu of an alternative diagnosis for the deterioration, more extensive surgical exploration should have been considered sooner, especially considering there were radiological signs suspect for NSTI. To strengthen suspicions of invasive candidiasis, biomarkers (beta-delta glucan or *C. albicans* germ tube antibodies) could be determined, as blood cultures offer suboptimal sensitivity[25]. Furthermore, heightened vigilance should be applied in the daily care of immunocompromised and critically ill patients to identify possible portals of entry.

We present this case to demonstrate the necessity for vigilance in immunocompromised patients who contract NSTIs. As physicians, we must constantly weigh the potential benefit of a treatment against the risks of implementing debilitating therapies such as extensive exploration or amputation. The decision to perform explorative surgery in a patient without discerning symptoms of NSTIs remains challenging; however, considering the comorbidities of the patient in this case and the lack of clinical improvement during conservative therapy, perhaps the decision to surgically explore should have been made sooner.

Conclusion

We presented a case of NSTI in an immunocompromised patient following bilateral LUTx characterized by *C. albicans* as the main pathogen, characterized by atypical course and presentation leading to the patient's death.

Ethical approval

This is not a research study and is therefore exempt from ethical approval by the local ethics committee.

Consent

Written consent was acquired and is available for review by the Editor-in-Chief of this journal.

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The authors received no funding for the study.

Author's contribution

Pieter de Jong: study concept, data collection, writing the paper, tables and figures; Mathieu M. E. Wijffels: data analysis and revisions; Bart Rijnders: revisions; Nicole Juffermans: revisions.

Conflicts of interest disclosure

There are no conflicts of interest to state.

Guarantor

Mathieu M. E. Wijffels and Nicole Juffermans.

Research registration unique identifying number (UIN)

Not applicable to this case report.

Provenance and peer review

This paper was not invated.

Data availability statement

Data sharing is not applicable to this article.

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