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A unique autopsy case of spontaneous necrotizing soft tissue infection of the chest-wall in a healthy adult without major risk factors

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ABSTRACT

NSTI (Necrotizing Soft Tissue Infection) is an infection of any layer within the soft tissue compartment that is rapidly progressive and often fatal. The authors describe a case of a 67-year-old man who developed a spontaneous NSTI and died of septic shock approximately 36 h after he was first admitted to the emergency room. The infection started from the chest as a result of a minimum muscle strain, in the absence of any cutaneous lesions or important risk factors such as immunosuppression. The infection was caused by *Streptococcus pyogenes*.
The described case has many peculiarities that make it almost unique.

Introduction

The infection of the soft tissue compartment with necrotic changes is called necrotizing soft tissue infection (NSTI) [1,2]. In recent years international mass media has defined this pathology with alarming titles such as "microbes eating meat" or "meat devours' disease" generating alarm in the population. Actually, this is not a pathology of recent onset, as evidenced by Hippocrates's third book of Epidemics (IV century BC), reporting the first definition of the necrotizing fasciitis [3]. In adults, NSTI is most described in the extremities, perineum, abdomen, neck and head [5,6]. In neonates or in children in general NSTI is most described in the trunk as omphalitis [4]. The most cases of necrotizing infections are polymicrobial; monomicrobial NSTI is common in immunosuppressed patients [7]. The infection may also occur spontaneously, but this is incredibly rare [8,9]. Causative organisms in NSTI are: *Bacteroides*,*Streptococcus, Enterococcus*, *Peptostreptococcus*, and *Staphylococcus* spp., *Escherichia coli*, *Proteus* spp., or other Gram negative rods, *Clostridium* spp. [10] or other anaerobes and fungi. The pathogenesis is hypothesized to be related with reduced immune response and inadequate blood flow to the fascia, creating an environment suitable for pathogens proliferation [5].

For NSTI several risk factors have been described, such as immunodeficiency, advanced age, smoking, diabetes mellitus, obesity, intravenous drug use, peripheral vascular disease, chronic renal failure, trauma, recent surgery, burns, dermal abscess, perforated bowel, and insects bites [11,12]. Adverse prognostic factors include advanced age, female gender, delay in diagnosis or debridement, extensive tissue involvement, degree of organ system dysfunction, and other medical comorbidities (such as bacteremia and diabetes mellitus).

In the early stages, this kind of infection is hard to be separated from other superficial infections such as cellulitis, leading to high morbidity and mortality [13,14].

As the infection progresses, systemic signs occur, with high fever, tachycardia, skin blistering, and wound discharge [1]. Rapid diagnostic procedure including CT scan, plain radiographs, MRI and ultrasonography may be helpful for the diagnosis of NSTI [15], but the tissue biopsy, tissue and blood culture may be required to confirm the diagnosis and isolate the pathogens.

Because NSTI can rapidly lead to death in affected patients who are otherwise apparently healthy, and because of the rising number of medicolegal cases that are related to health care, cases of death associated with NSTI are increasingly entering the realm of forensic medicine and pathology. The described case presents some particular aspects of NSTI that will help to remind forensic pathologists of this disease entity, whether they are managing cases related to potential medical malpractice or simply have to determine the cause of an unexpected death in a patient [16,17].

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This type of infection is rarely described in the general forensic literature, therefore forensic pathologists should consider this type of infection when they perform autopsies in similar cases.

Whether they encounter NSTIs in the course of caseworks, forensic pathologists need to be aware of pathogenesis, gross autopsy findings, and appropriate culturing techniques of these infections.

Case report

A 67-year-old man without any known comorbidity except diabetes mellitus, was admitted to the emergency room (ER) for a moderate back pain radiating from ribs 3–4 on the right side. The pain had first begun after only a simple movement of the chest when the patient stretched. The patient was not febrile and he had normal vital signs. Clinical examination revealed a back hematoma between the 3rd and 4th ribs. He underwent a radiographic examination of the chest, that revealed the presence of a compound fracture of rib 3 on the right side. The patient was discharged.

The next day, the patient was hospitalized again for persisting pain of the right hemithorax. Clinical examination found edema of the right chest and of the right abdominal wall. High-resolution computerized tomography (CT) scan showed numerous enlarged lymph nodes in the right axillary chain. There was also imbibition of the soft tissue compartment of the right hemithorax, but without evidence of accumulation of fluid, such as in the form of hematoma or abscess, and without lung or pleural involvement (Fig. 1). Moreover, the CT scan excluded the presence of the rib fracture. Laboratory investigation revealed increased levels of glucose (308 mg/dl; normal reference ranges 60−110 mg/dl) and creatinine (2.24 mg/dl; normal reference ranges 0.81–1.43 mg/dl). At the end of the ER investigations, he was admitted to the medical ward for therapy-resistant-pain.

During the evaluation the patient's clinical condition deteriorated with worsening of the state of consciousness, dyspnea and marbling to the lower limbs. He also developed a new onset atrial fibrillation. A cardiologic assessment was performed and discovered a collapsed inferior vena cava and an ejection fraction strongly reduced (35 %; normal reference ranges 55–70 %). Therapy with amiodarone and saline solution/glucose was started. The patient had a Glasgow Coma Scale (GCS) of 12. He also had tachypnea 22 beats per minute (normal reference ranges 60–100 bpm) and metabolic acidosis, so he was moved to the intensive care unit (ICU). Physical examination showed a decrease of the blood pressure (90/50 mmHg; normal reference ranges 80/120 mmHg). Blood tests showed a normal white blood cell count and there was no evidence of acute kidney injury. However, the levels of other indices were consistent with non-specific inflammation. A diagnosis of septic shock was reached. Blood cultures were collected and broad spectrum antibiotic therapy was initiated with intravenous vancomycin (2 g in saline solution 250/mL/h) and piperacilline/tazobactam 4.5 g every 6 h). Fluid resuscitation therapy was also initiated, with norepinephrine infusion due to the fluid-resuscitation resistant hypovolemia. Within a few hours, the clinical condition of the patient had further deteriorated, and he died of septic shock and multi-organ failure only 36 h after being first admitted to the ER. Blood cultures were negative for aerobic and anaerobic pathogenic organisms.

The forensic autopsy

A forensic autopsy was performed 48 h later, to rule out medical malpractice. The autopsy revealed the presence of large and multiple reddish areas on the skin of the right hemithorax that extended to the right side and to the right gluteus, with 4 de-epithelialized areas (Fig. 2). At the internal examination, the muscles underlying these areas of skin were soft and blackish-brown in color.

Organ and body fluid samples were taken for further analysis. For post-mortem microbiological analyses, blood samples were collected from aorta and inoculated onto various agar plates (chocolate, blood supplemented with colistin and nalidixic acid (CAN); McConkey, mannitol salt; Sabouraud; Schaedler; and Schaedler kanamycin-

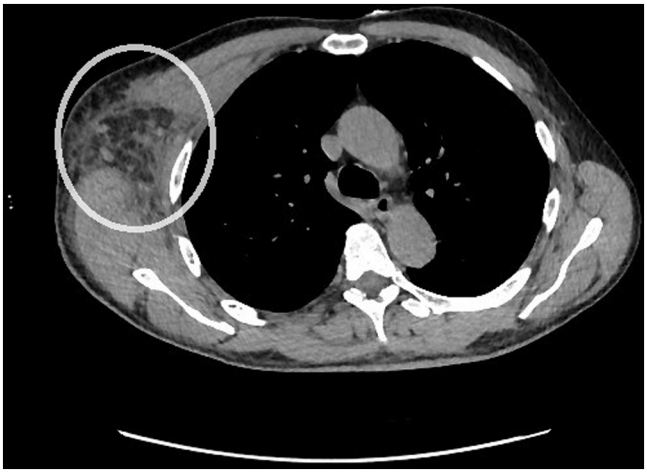

Fig. 1. High-resolution computed tomography showing imbibition of the soft tissue compartment of the right hemithorax (indicated by white dotted circle) without evidence of accumulation of fluid, such as hematoma or abscess, and without lung or pleural involvement.

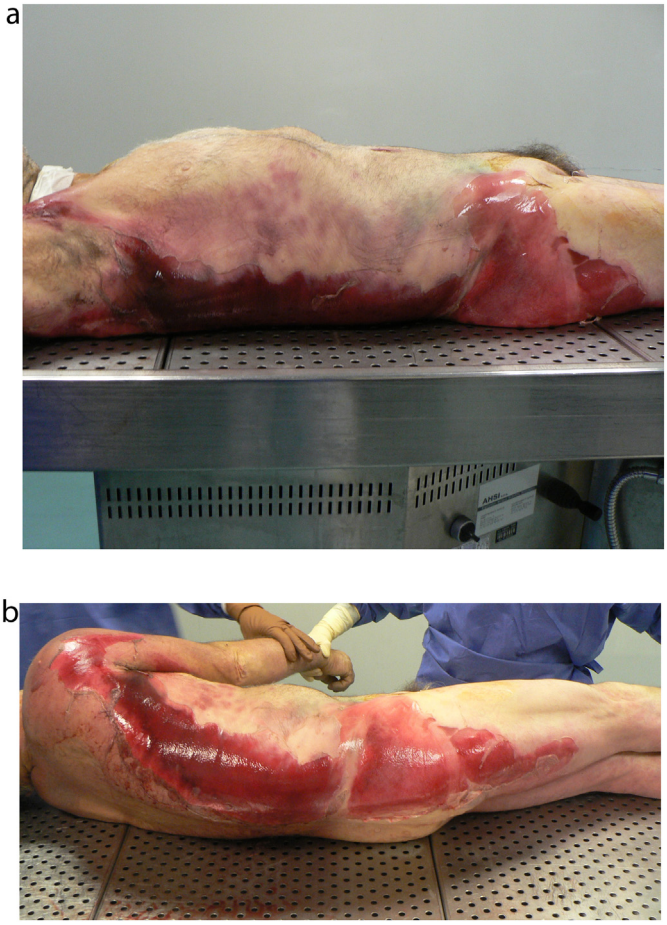

Fig. 2. External analysis showing the presence of large and multiple reddish areas on the right hemithorax that extend to the right side and to the right gluteus with de-epithelialized areas.

vancomycin (all media from Becton Dickinson). Plates were incubated at 35 ± 2 °C in ambient air, 5% carbon dioxide, or anaerobic conditions, as previously described [18]. Blood samples were also inoculated in BACTEC Plus aerobic and anaerobic bottles (Becton-Dickinson, Erem- bodegem, Belgium). After over-night incubation, a *Streptococcus pyogenes* isolate was isolated in pure culture from both solid media and broths. The organism was identified using the Bruker MALDI Biotyper instrument (Bruker Daltonik GmbH, Bremen, Germany), as described elsewhere [19]. Antimicrobial susceptibility testing showed that the isolate was sensitive to β-lactam antibiotics including penicillin, amoxicillin, and cephalosporins, and to glycopeptides and tetracycline, while it was resistant to macrolides. Blood was also tested using the multiplex PCR-based FilmArray blood culture ID (BCID) panel (bioMérieux, Marcy l'Etoile, France), and was positive for *S. pyogenes* DNA.

Histological analysis of the organs was also performed, revealing widespread necrosis of the soft tissues and muscle fibers of the right hemithorax, the buttocks, the right flank and the pectoral region, with an associated inflammatory infiltrate comprising. Other histologic findings included: lymphocyte infiltration with rare neutrophils in the left epicardium; pulmonary interstitial hemorrhage; mild cerebellar lymphocyte infiltration; pancreatic steatonecrosis; rare lymphocyte infiltrates in the kidneys.

The cause of death in this patient was determined to be septic shock due to *S. pyogenes*-associated NSTI. The infection had originated in the right chest wall and extended to the right abdomen.

Discussion

The case under discussion has many peculiarities that make it almost unique. In fact, in adults, NSTI is usually described in the extremities, perineum (*Fournier gangrene*), abdomen, and head/neck [4–6]. Occurrence in the chest wall is rare and primary chest wall NSTI, as the one described, is incredibly rare [9]: the few cases reported in the literature are subsequent to lung surgery, the presence of a thoracic chest-tube or esophageal resection [20].

Moreover, in this case under discussion, the infection started in association with only a minor trauma of the chest due to a simple movement (stretching). No cutaneous lesion was identified, despite the causative organism being S. pyogenes, a bacterium that more usually colonizes skin or mucous membranes.

NSTI can be classified in four categories based on the type of organism involved:

- NSTI type I (polymicrobial/synergistic, 70–80 %);
- NSTI type II (monomicrobial, 20 %);
- NSTI type III (Gram - monomicrobial);
- NSTI type IV (fungal) [18,19].

Most cases of necrotizing infections are polymicrobial (Type I), while monomicrobial NSTIs (Type II) are common in immunosuppressed patients [21].

In the present case the patient had a monomicrobial NSTI, but he was not immunosuppressed: he only had type 2 diabetes mellitus as a risk factor. This particular case can thus be categorized as type II NSTI. Infections in this category, especially in the presence of group A beta-haemolitic streptococci, show an extremely rapid evolution to septic shock and death (almost 70 %), despite undergoing any medical/surgical treatment or intensive supportive care [22].

In conclusion the case described is almost unique because the infection developed in a man without major risk factors, after a minor trauma (stretching) of the chest during a simple movement; furthermore, the infection was monomicrobial, another rare finding in a non-immunosuppressed patient, and was caused without any cutaneous lesion by a bacterium usually colonizing the skin or mucous membranes (*S. pyogenes*).

This type of infection is rarely described in the general forensic literature, therefore forensic pathologists should nevertheless be open minded and consider this type of infection when they perform autopsies in similar cases.

Whether they encounter NSTIs in the course of medical malpractice cases or in sudden unexpected deaths, forensic pathologists especially need to be aware of key points of these infections, such as their pathogenesis, gross autopsy findings, and appropriate culturing techniques. It is especially important for forensic pathologists to be able to recognize the gross lesions associated with NSTIs, because they can often mimic postmortem changes such as livor mortis. Overall, this increased awareness will improve the forensic pathologist's ability to promptly and accurately diagnose NSTIs, provide a comprehensive and accurate evaluation to best assist in potential malpractice cases, and promptly inform at-risk people who may have been in close contact with the patient before death.

Declaration of Competing Interest

All authors deny any financial and personal relationships with other people or organizations that could inappropriately influence their work. In particular they deny employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding.

CRediT authorship contribution statement

Fabio Suadoni: Conceptualization. **Sara Gioia:** Writing - original draft. **Beatrice Tiri:** Data curation. **Antonella Mencacci:** Supervision. **Simona Vento:** Investigation. **Massimo Lancia:** Writing - review & editing.

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