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Case Report

Monomicrobial Necrotizing Fasciitis and Emphysematous Cystitis: Autopsy Report and Literature Review

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Abstract

Necrotizing fasciitis (NF) and emphysematous cystitis (EC) are life-threatening conditions even with appropriate and rapid medical and surgical treatment. Herein, we report a case of a 65-year-old male patient who presented with concomitant EC and NF of the left thigh. The patient was managed with an emergency debridement of the left thigh shortly after arrival along with broad-spectrum antibiotic and fluid resuscitation. Tissue culture was positive for Clostridium perfringens. Despite the prompt management, the subcutaneous emphysema extended to gluteal, scrotal regions and to posterior abdominal wall muscles. The evolution was complicated by distributive shock and subsequently by multiple organ failure leading to death within 24 hours after the emergency room admission. To the best of our knowledge, this is the first case of concomitant EC and NF caused by Clostridium perfringens leading to death despite intensive treatment. Moreover, it is the first case providing clinical, radiologic, microbiologic and postmortem pathologic results.

Keywords: Autopsy; Necrotizing fasciitis; Emphysematous cystitis

Abbreviations

NF- Necrotizing fasciitis.

EC- Emphysematous cystitis.

ER- Emergency room (ER)

MDCT- Multidetector computed tomography

CT- Computed tomography

MRI- Magnetic resonance imaging

PICC line-Peripherally inserted central catheter

Introduction

Necrotizing fasciitis (NF) is a fulminant infection of the deep soft tissues, characterized by high risk of sepsis and mortality [1]. The classification based on the underlying causing bacteria divides NF in two groups: polymicrobial (type I) NF caused by both aerobic and anaerobic bacteria, more prevalent in older adults with chronic disease and monomicrobial (type II) NF mainly associated with Gram-positive organisms such as group A Streptococcus or methicillin- resistant Staphylococcus Aureus [1]. A type III NF classification has been proposed caused by organisms such as Klebsiella, Clostridium, Pseudomonas producing more severe clinical manifestations but no consensus has been reached yet [2].

Emphysematous cystitis (EC) is a rare form of complicated urinary tract infection characterized by gas within the bladder wall and lumen [3], more frequently seen in older females with diabetes mellitus but other risk factors such as neurogenic bladder, chemotherapy, immunosuppressed state (transplant recipient) or post-surgery were described. [4] Its association with NF is uncommon. Herein, we report clinical, radiological and postmortem findings of a patient with severe comorbidities who developed a fatal NF despite prompt surgical intervention and antibiotic treatment.

Case Report

We report a case of a 65-year-old male patient who presented to the emergency room (ER) for rapid deterioration of general condition, asthenia and with left leg above-knee erythema. He reported abdominal pain for 24 hours, ileostomy bleeding and confusion. He had a history of right hepatectomy for hepatocellular carcinoma complicated by subphrenic abscess and right calyceal fistula treated by drainage, biliary-colonic fistula treated by ileostomy, right nephrectomy for clear cell renal cell carcinoma, severe malnutrition (under parenteral nutrition), chronic pancreatitis and type II diabetes. Clinical examination revealed jaundice, drowsiness, hypotension (90/55 mm/Hg), no fever (36.5 °C), left thigh subcutaneous crepitus and blister formation. Blood tests revealed metabolic acidosis, electrolyte imbalance, and leukocytosis with neutrophilia, inflammatory syndrome, anemia, liver and kidney function alteration. The results are summed up in Table 1. Clinical diagnosis of NF was made based on rapid progression of tissue lesions and the presence of cutaneous emphysema. Broad-spectrum antibiotic including Clindamycin, Meropenem and Amikacin were immediately given shortly after arrival and an emergency debridement of the left thigh was performed.

Despite the prompt management, the subcutaneous emphysema extended to gluteal, scrotal regions and to posterior abdominal wall muscles. Multidetector computed tomography (MDCT) confirmed the presence of subcutaneous emphysema but also revealed bladder pneumatosis (Figure 1). Cultures of tissue samples were positive for Clostridium perfringens. The evolution was complicated by septic and distributive shock, hemolytic anemia and subsequently by multiple organ failure (acute liver failure, acute kidney failure) leading to death within 24 hours after ER admission.

Autopsy findings included swollen, edematous and discolored areas around the debrided site, « cobblestone » appearance of bladder mucosal surface, nodular liver cut-surface and splenomegaly. Microscopic examination confirmed the persistence of NF (Figure 2), the presence of cirrhosis and EC (Figure 3). NF was characterized by important suppuration and extensive tissue necrosis with bacterial colonization and gas-inclusions in the subcutaneous fat with extent to deep fascia and skeletal muscles on high power view. EC was histologically characterized by cystic dilatations in bladder mucosa, submucosa and muscularis layer. In the mucosal and submucosal connective tissue there were signs of chronic inflammation and, focally, small hemorrhages.

Analysis	Description	Results	Reference range (units)
Arterial blood gas results	pH	**7.23**	7.35-7.45
	pO2	**124**	75-100 mmHg
	pCO2	**22**	35-45 mmHg
	CO2 total	**9.9**	22-28 mmHg
	Bicarbonate	**9.2**	22-26 mmol/l
	Sodium	**129**	135-145 mmol/l
	Potassium	**6.1**	3.5-4.8 mmol/l
	Glucose	**215**	70-100 mg/dl
	Lactate	**4.7**	<2 mmol/l
Complete blood cell count	WBC	**58.29**	3.5-11 x 10^3/mm^3
	Neutrophils (%)	**93.9**	40-75%
	Lymphocytes (%)	**2.5**	20-40%
	Monocytes (%)	3.1	2-8%
	Eosinophils (%)	**0**	1-4%
	Basophils (%)	0	0-1%
	RBC	**1.76**	3.5-11 x 10^3/mm^3
	Hb	**6.4**	13-18 g/dl
	Hct	**20.3**	40-53%
	Platelets	214	150-440 x 10^3/mm^3
Clinical chemistry tests	Urea	**163.8**	16.6-48.5 mg/dl
	Creatinine	**1.64**	0.7-1.2 mg/dl
	Glomerular filtration rate	**43**	>60 ml/min/1.73 m^2
	Total bilirubin	**24**	<1.2 mg/dl
	Direct bilirubin	**16**	<0.2 mg/dl
	AST	**639**	<40 U/l
	ALT	**179**	<41 U/l
	Total protein	**42**	64-83 g/l
	Albumin	**18**	40-49 g/l
Inflammatory test results	CRP	**130**	<5 mg/l

Table abbreviations: WBC: White blood cells; RBC: red blood cells; Hb: hemoglobin; Hct: hematocrit; AST: aspartate aminotransferase; ALT: alanine transaminase; CRP: Reactive C Protein.

Table 1: Blood test results at admission.

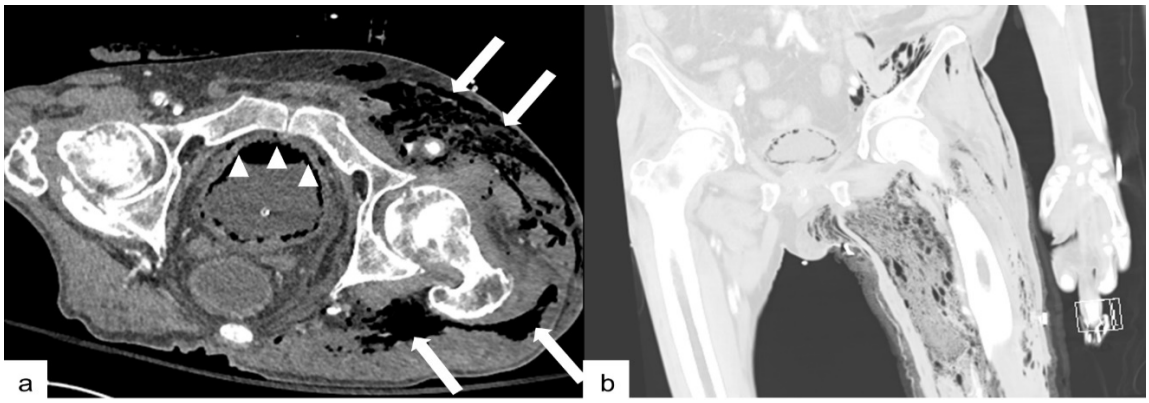

Figure 1: Bladder pneumatosis and subcutaneous emphysema (**a)** MDCT in venous phase, axial plane at the level of the pubis revealing moderately distended bladder displaying mural pneumatosis (arrowheads); Subcutaneous emphysema dissecting the muscular and the fascial planes of the left pelvic region (arrows) (**b)** MDCT in coronal plane and lung window setting showing the extent of the free gas within the muscular planes of the medial compartment of the left thigh, reaching superficially the peri trochanteric muscles and the scrotal pouch and deeply the left iliopsoas muscle. Bladder pneumatosis is also well shown.

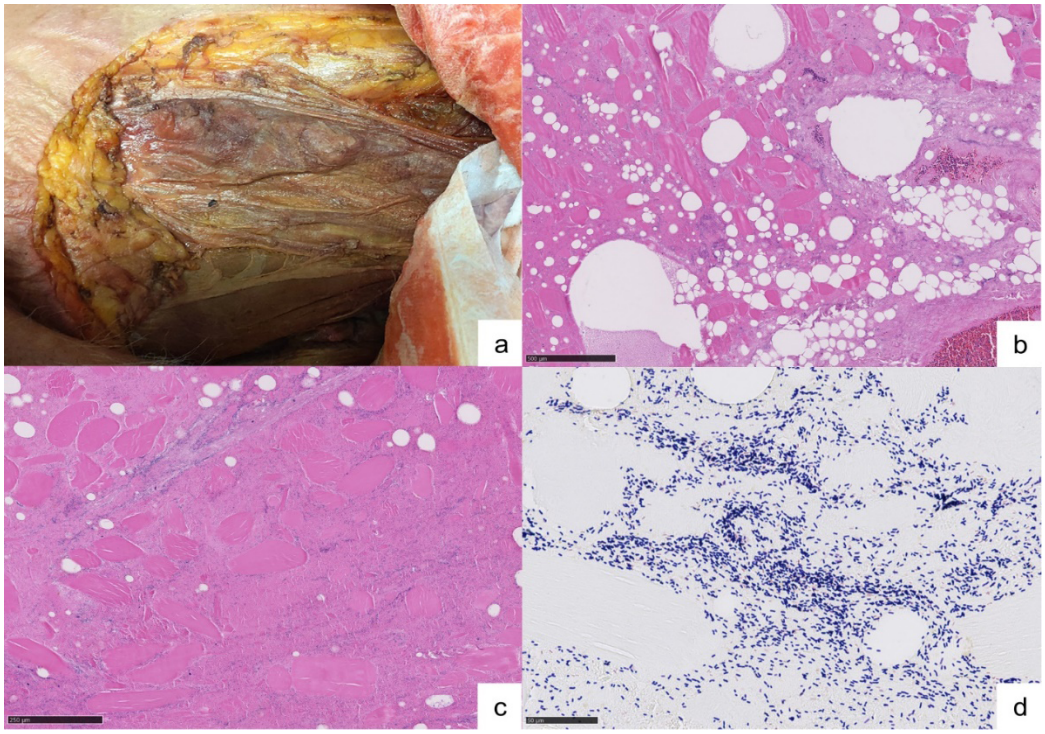

Figure 2: Necrotizing fasciitis (**a)** Macroscopic view of debridement site; (**b, c)** Overview of hematoxylin & eosin (HE x50 and HE x100): extensive tissue necrosis with bacterial colonization and gas-inclusions in the subcutaneous fat with extent to deep fascia and skeletal muscles; (**d**) GRAM Staining (x400) Rod-shaped, Gram Positive (blue) and Gram negative (red) bacteria.

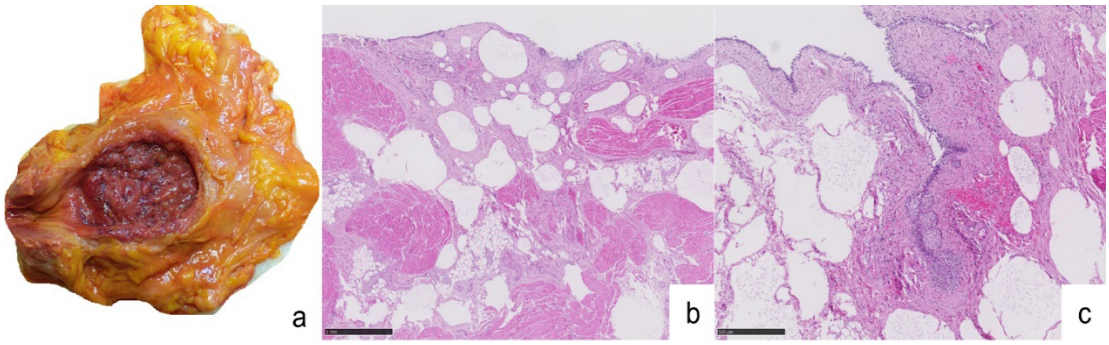

Figure 3: Emphysematous cystitis (**a)** « cobblestone » and hemorrhagic macroscopic appearance of bladder mucosal surface; (**b, c)** Overview of hematoxylin & eosin (HE x25 and HE x50): cystic dilatation in bladder mucosa, submucosa and muscularis layer; signs of chronic inflammation and, focally, small hemorrhages.

Discussion

Both NF and EC are critical conditions that require prompt and intensive treatment. NF causes progressive destruction of the muscle fascia and overlying subcutaneous fat, leading to death in 25% to 35% of patients, despite increased awareness and treatment advances [1]. The main reasons of aggressivity in NF are the rapid progression of disease and the subtlety of early signs and symptoms, which may delay diagnosis and intervention [2]. EC is considered a complicated urinary tract infection with an overall mortality rate of 3-12%, typically observed in elderly women (6^{th} -7^{th} decade) with diabetes mellitus [5]. The most frequent microbes involved are Escherichia coli (60%) and Klebsiella pneumoniae (10-20%) while other germs are infrequent. [5] Clostridium perfringens is a Gram-positive, rod-shaped, anaerobic, spore-forming pathogenic bacteria and infrequently associated with EC or NF, most commonly associated with post-traumatic infection [6]. It is responsible for gas production in the tissue that can be identified on X-rays or computed tomography scan (CT). With the best of care, the mortality varies between 5-30%, while host factors such as an immunocompromised state, diabetes mellitus, and spontaneous infections can have higher mortality rates of 67% or higher and, if untreated, the disease has 100% fatality [6]. The entry points for bacteria are mainly puncture wounds and surgical wounds, especially gastrointestinal surgeries. In the present case, the entry point is unclear, because multiple entry sites were suspected including the ileostomy or the PICC line (Peripherally inserted central catheter) used for parenteral nutrition.

Diagnosis of both NF and EC is usually clinical and radiological, with bacteriological test confirmation, but in selected cases, pathology analysis may help understanding the extent and the mechanisms of the disease spread. NF diagnosis is primarily based on clinical findings that include poorly defined and indistinct margins and tenderness beyond the involved area, warmth, swelling, and induration, followed by blisters or bullae formation and skin discoloration, duskiness and necrosis in advanced stage. [7] Imaging is also helpful. Ultrasound [8], CT [9] or magnetic resonance imaging (MRI) [10] can be used to diagnose NF, with a sensitivity of 80% and 100% for CT scan and for MRI scan, respectively. Asymmetric fascial thickening, fat stranding, and gas tracking along fascial planes are important imaging findings on CT and MRI scans [7]. EC can be diagnosed using a plain radiography of the abdomen showing a curvilinear radiolucency outlining the bladder wall. The bladder mucosal surface may also have a "*cobblestone*" or "*beaded necklace*" appearance. Ultrasound usually reveals diffuse bladder wall thickening with increased echogenicity. CT scan is highly sensitive for analyzing the extension of the disease and the presence of intraluminal and intramural gas [3, 11].

CT scan performed in our case also revealed fat stranding, and gas tracking along fascial planes, extending from the thigh to the gluteal, scrotal regions and to posterior abdominal wall muscle, along with intraluminal and intramural bladder gas accumulation.

The gold standard treatment for NF is prompt surgical debridement with subsequent daily debridement until the surgical team determines that all necrotic tissue has been removed along with empiric broad-spectrum antibiotics until soft tissue Gram stain, culture, and sensitivity results are available with subsequent tailored therapy when the pathogen is identified. Aggressive I.V. fluid resuscitation and vasopressor support for septic shock should also be considered [1]. Hyperbaric oxygen therapy and I.V. immunoglobulin G may also be taken into account but data in literature remains controversial [12]. Treatment for EC is usually conservative, implying adequate bladder drainage, broad-spectrum antibiotics and tight glycemic control (most of the patient's present diabetes) [5].

While association between bowel and bladder pneumatosis [13, 14] have been described, few reports describing histological alterations encompassing both NF and EC are available. Wang et

al [11] reported a concomitant NF and EC case of a 62 years-old male with positive tissue cultures, treated with emergent right hip disarticulation for NF and subsequent cystoprostatectomy with ileal conduit due to the failure of conservative management and lack of clinical improvement. Chen et al. [15] reported a case of 74 years-old man presenting NF and concomitant EC treated by intravenous antibiotics, and surgical debridement of his left hip was performed. Both patients presented diabetes. The responsible pathogen was Klebsiella pneumoniae in both cases and the postoperative course was uneventful for both patients. Our case presented a fulminant evolution despite prompt surgical and medical intervention.

In conclusion, the association between NF and EC is rare. Both diseases show high mortality if untreated. Monomicrobial infection with Clostridium perfringens as causative agent is exceptional.

The diagnosis is usually clinical and radiological but in atypical cases like the one reported here, microscopic analyses might help understanding the pathophysiology and the extent of this nowadays uncommon disease.

Two other cases with concomitant NF and EC are described in literature and the present case is the first one reporting clinical, radiologic, microbiologic and pathologic findings to the best of our knowledge.

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Conflicts of Interest

The authors declare that there is no conflict of interest. No funding was received.

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