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Case Report

An Unusual Case of Advanced Spontaneous Clostridial Myonecrosis with Multiple Distant Sites

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Abstract

We present an unusual and severe case of spontaneous Clostridial myonecrosis in an elderly patient. Diagnosis was confirmed with the combination of imaging and postmortem blood cultures. In literature many questions remain unanswered. The specific form of spontaneous Clostridial myonecrosis has been reported several times in the literature, none however had the severe skipping characteristics of our patient and we hypothesize that this condition is underdiagnosed in elderly patients. By reporting this case we hope to raise awareness for this spontaneous form of the disease. As well as to provide a treatment guideline, especially since in these cases time is life.

Keywords: *Spontaneous Clostridial Myonecrosis; Gas Gangrene; Clostridial Myonecrosis; Clostridium septicum*

Abbreviations

ED: Emergency Department; SCM: Spontaneous Clostridial Myonecrosis; CT scan: Computed Tomography Scan; ABG: Arterial Blood Gas

Introduction

We present an unusual and severe case of spontaneous Clostridial myonecrosis, documented by combined radiography and CT scan imaging and confirmed by post-mortem blood cultures. Following a literature review in PubMed over the last decade, we found that case reports for clostridial myonecrosis are under-represented in the cohort of elderly patients (> 75 years). Therefore, we hypothesize that this condition is underdiagnosed in elderly patients.

Case Presentation

An 84-year-old woman who lived alone and independent was brought to our emergency department (ED) after her neighbor was worried when seeing no sign of life in the morning and alarmed her family. Several hours passed and eventually the family arrived at her premises together with an emergency ambulance to find her lying on the floor of her bedroom. She had no previous medical history, no known allergies and no changes in her medication for years (she took an anti-arytmica, SOTALEX®). Arriving at the emergency department at 2 pm the patient was conscious, complained of mild pain all over her body (VAS score of 3/10) but could not specify this any further.

Vital signs were stable: blood pressure (BP) of 149/61 mm Hg, pulse 60 beats per minute, oxygen level of 98%, and body temperature 35,4°C. Heart, lung and abdominal examination were without any particularities. Neurologic examination on arrival showed a normal level of consciousness and no paralysis. She had a normal speech, although communication was difficult because of hearing loss. She seemed orientated without any confusion although she couldn't explain or remember why she was found lying on the floor.

Further observations at physical examination were:

1) A cold right foot and lower leg with delayed capillary refill and absence of peripheral pulses.

2) Light reddish coloring of her left lower leg, without blisters or crepitation's palpable, peripheral pulses were palpable and the limb had a normal temperature.

3) Painful mobilization of both hips.

4) At the back there were no signs of infections on the skin and the spine was not painful at palpation.

Lab results of the arterial blood sample were available within the hour after her arrival. This showed a pH of 7,36 (reference range, [RR] 7,35 - 7,45), pO_2 of 63,7 mmHg (RR 83 - 108 mmHg), Hemoglobin of 10,5 g/dL (RR 12 - 16 g/dL), Sodium of 140 mmol/L (RR 136 - 146 mmol/L), Potassium of 3,9 mmol/L (RR 3,4 - 4,5 mmol/L), lactate of 2,3 mmol/L (RR 0,5 - 1,6 mmol/L), ureum of 80,6 mg/dL (RR < 71 mg/dL), creatinine 2,2 mg/dL (RR 0,5 - 0,9 mg/dL). The working diagnosis was an arterial thrombosis of the right leg and fluid resuscitation was started, following a contrast nephropathy scheme (glucose 5% with Sodium bicarbonate 150 mEQ at 210 ml/hour) in order to perform a contrast CT scan of the lower limb. The vascular trainee was informed of the presence of the patient at the ED. In the meantime further blood results were available and showed elevated troponin T levels (0.037 ng/mL, RR < 0.030 ng/mL), high NT-proBNP (34600 pg/mL RR < 125 pg/mL), high level of D-dimer (> 8000 ng/mLfib.eq RR < 500 ng/mLfib.eq) and a high C-reactive Protein (CRP) level of 205 mg/L(RR < 5 mg/L), CL level of 1757 U/L (RR < 167 U/L), LDH level of 365 U/L (RR < 250 U/L), SGOT level of 55 U/L (RR < 32 U/L). The range of the CT scan was extended in search of a focus of an infection and at 17.15 pm a cat scan of the thorax, abdomen and the limbs was performed.

A clinical re-evaluation was performed by the vascular trainee the moment the patient returned from the radiology department. By then almost four hours passed since her arrival. A progression of skin discoloration to purple and bullae formation on the left leg was now prominent, still without any signs of crepitation and the area was delineated (Figure 1 and 2).

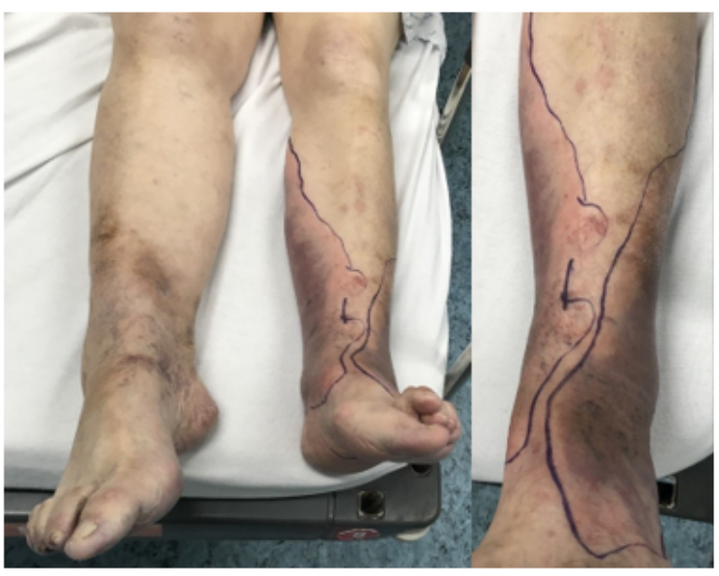


Figure 1 and 2: *Purple discoloration and bullae formation of the left leg.*

The patient received a shot of amoxicillin clavulanic acid 1g intravenously at this point. Neurological reexamination showed less and delayed response. The images of the CT scan became available the moment the vascular surgeon arrived at the emergency department, only 30 minutes later.

The CT scan showed several abnormalities illustrated in the figures below, respective descriptions are listed below.

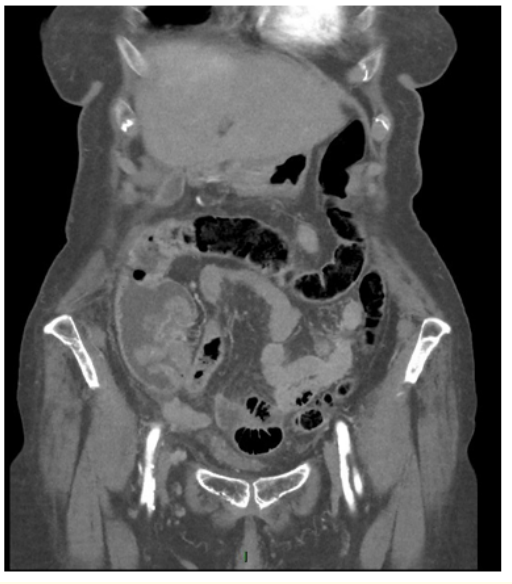


Figure 3: *A suspicious big polypus mass in the colon at the valve of Bauhin, possibly cT2NOMO, diverticulosis, without signs of diverticulitis.*

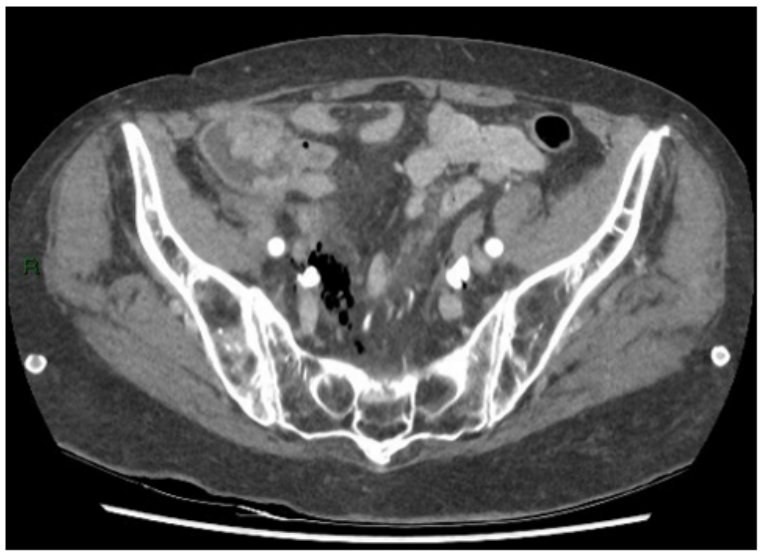


Figure 4: *Gas surrounding the iliac vessels on the right side.*

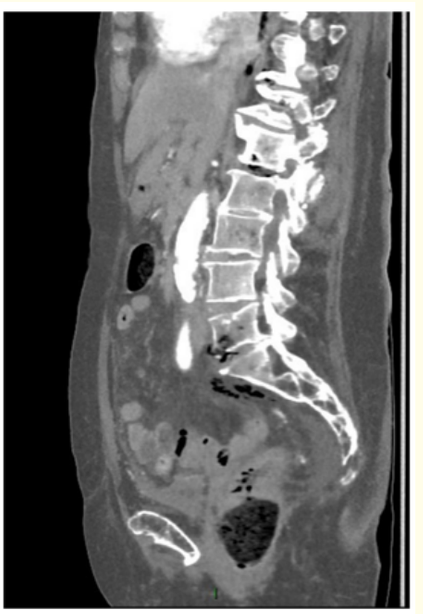


Figure 5: *Gas in the retroperitoneal space most profound at the intervertebral space of L5-S1 with spreading along the iliac veins, most remarkable on the right side. Suspicion of localized osteonecrosis in L5-S1.*

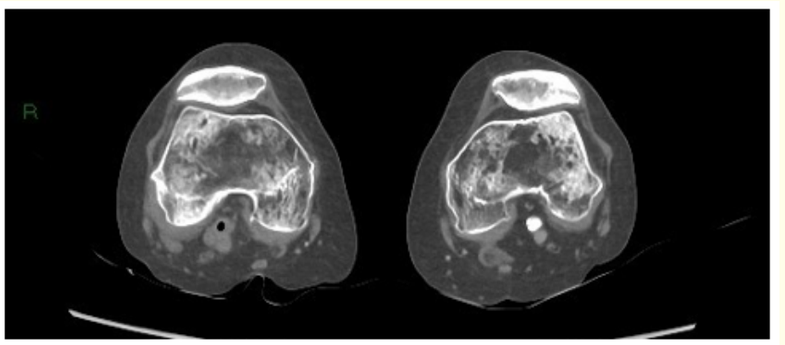


Figure 6: *Gas bubble in the popliteal artery on the right side.*

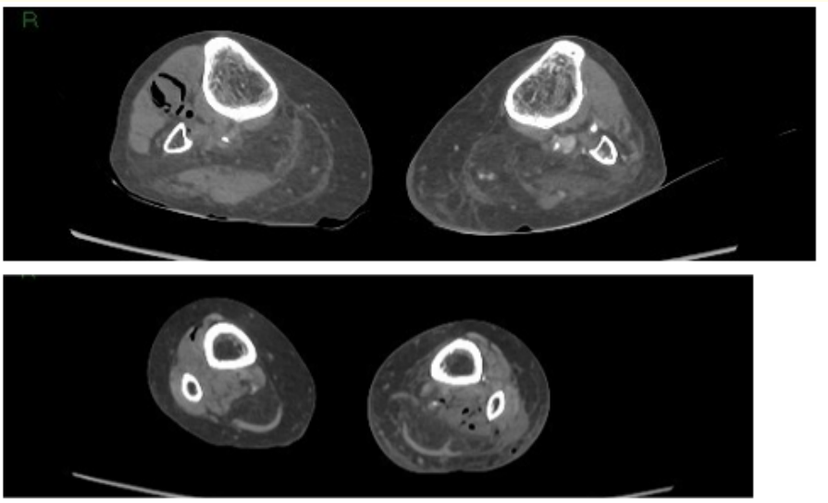


Figure 7 and 8: *Gas in both lower leg muscle compartments.*

Given the rapid evolution of the skin on the left lower calf in combination with gas in the muscle compartments and retroperitoneal space an anaerobic infection was undoubtedly responsible for her clinical situation. Infection with a *Clostridium* strain became our first diagnosis although the focus of entry was unclear, no external wounds were visible. The spread of gas inside the distal superficial femoral artery on the right side and retroperitoneal space made us broaden our differential diagnosis. Possible necrotizing fasciitis due to group A streptococcus pathogen or a retroperitoneal perforation of the *de novo* found colon tumor, a complicated spondylodiscitis with hematogenous spreading of emboli were considered. Other less likely options were a pyomyositis which causes muscle abscesses mostly by *S. aureus* or viral myositis and rhabdomyolysis.

While discussing possible differential diagnosis and if there were any therapeutic options the patient deteriorated further with deviation of the eyes to the right side, anisocoria and Cheyne stokes breathing. Glasgow coma scale dropped rapidly, her blood pressure stayed stable initially and eventually started to drop to 90/50 mmHg with a heart rate of 70 beats' minute. Still there was no fever. Arterial blood sample showed elevating lactate level to 3,6 mmol/L, pH level of 7,25 and dropped oxygen level (pO_2 level of 58,8 mmHg).

A multidisciplinary team consisting of the emergency physician, the vascular surgeon and the neurosurgeon on call decided that there was an inability to intervene with surgical debridement because of the multiple distant spread gas seen on CT scan. Because of her rapid declining state and lack of therapeutic options; additional investigation such as a skin biopsy of the left leg and a CT scan of the brain to visualize air were not executed. In consensus with the family a palliative comfort treatment was decided upon and the patient died 10 hours after her initial arrival in the hospital.

The blood culture results, available postmortem, confirmed our diagnosis of spontaneous myonecrosis due to *Clostridium septicum*.

Review

Pathogenesis and diagnosis

Historically, during war gas gangrene (synonymous with myonecrosis) was a common wound infection, with an incidence as high as 5%. With improved circumstances the incidence is now estimated to be 0.1%.

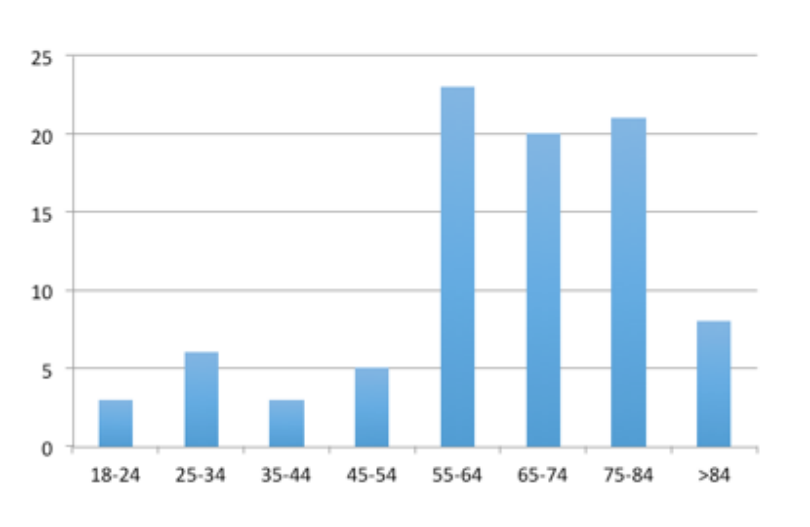
In the current literature two types of *Clostridial* myonecrosis are described, one in traumatized tissue and is associated with *Clostridium perfringens* and *Clostridium histolyticum,* the other arising spontaneously, caused by *Clostridium septicum* with hematogenous seeding from the gastrointestinal tract to the muscles. The incidence of spontaneous *Clostridium* Myonecrosis (SCM) is not known, possibly due to difficult differential diagnosis before blood culture results. *C. Septicum* is estimated to cause 20% of all (traumatic and spontaneous) cases [1]. *Clostridium* species are anaerobic, large, gram-positive gas producing rods with the ability to produce environmentally resistant endospores that are widespread in nature and can be found in soil and the intestinal tracts of human and animals [2]. Still, *Clostridium Septicum* is considered a rare component of the gastro-intestinal flora, only found in 2% of the population, preferably localized in the cecum and ileocecal junction [3]. Its capacity to cause disease likely reflects the coincidental occurrence of transient carriage and an enhanced host susceptibility [4].

C. septicum produces multiple toxins, of which the alpha toxin, a necrotizing pore-forming cytolysin, is the most lethal and an essential virulence factor causing the extensive myonecrosis that is associated with fulminant SCM [5].

The capability of infecting normal healthy tissue due to its aerotolerant characteristics distinguishes SCM from other *Clostridium* strains such as *C. perfringens* and *difficile* that are strictly anaerobic [6].

Although the pathogenesis of SCM is still unclear, three possible patterns for SCM are described. First through a visceral anaerobic cellulitis, second by visceral anaerobic cellulitis with contiguous spread to adjacent muscle and third a myonecrosis arising at a site distant from the initial visceral lesion, with is less common [7]. Our case presents itself as a myonecrosis in multiple distant sites.

It is suspected that the infection or dormant spores descend along the ilio-psoas sheath from, most often a gastrointestinal mucosal origin lesion, with following hematogenous spreading [8]. What is well describe in literature is that frequently these gastrointestinal lesions are undiagnosed adenocarcinoma of the colon, as so in our casus [9]. Other described predisposing factors such as leukemia, inflammatory bowel disease, diverticulitis, gastrointestinal surgery, leukemia, lymphoproliferative disorders, chemotherapy, neutropenia, radiation therapy, advanced AIDS, diabetes, necrotizing enterocolitis, cecitis or distal ileitis and the use of NSAID we could not withhold in our patient [10]. As *C. difficile* infection disproportionately affects older patients with dramatic differences observed in those ≥ 65 year of age, we do not know if age is also related with higher prevalence of SCM. We performed a retrospective PubMed literature search of *C. septicum* case reports over the last 10 years to have an idea of the prevalence in elderly people. 160 case reports were gone through to find 89 described adult patients with *C. septicum* infection, see graph 1 below. We see a remarkably higher prevalence starting from the age group of 55 till 64 year and this remains stable over each decade of age, to drop to a much lower percentage over the age of 85.



Graph 1: *PubMed reported number of SCM case reports related to age at diagnosis.*

In contrast to the fact that rapid recognition and treatment are vital to better outcome stands the fact that diagnosis is often difficult and delayed [11].

Clinical presentation often begins with a sudden onset of severe localized muscle pain in the absence of manifest injury and with no other causes to explain muscle pain. Keeping in mind differential diagnosis such as viral myositis, where absence of injury is also present, but pain is mostly diffuse, rather than localized and rhabdomyolysis where pain can be explained by causes such as trauma, drugs intake, toxins or metabolic disorders. Sometimes heaviness or numbness are mentioned as early sign [12]. The skin over the affected area may appear pale at first and then rapidly discolouring to bronze appearance progressing to purple or red hue [13]. Typically combined with development of edema and bullae filled with cloudy haemorrhagic or purplish fluid. Most often crepitations are present and can make the differential diagnosis with streptococcal myositis [1,14].

Initial systemic manifestations vary from the presence of fever and tachycardia to the development of signs of systemic shock as illness progresses with thrombocytopenia, anaemia, diffuse intravascular coagulation, kidney failure, acute respiratory distress syndrome and all ultimately leading to multiple organ failure [13]. Sometimes the disease can be obscure and only present with tachycardia initially. In those cases, severe pain, hypotension and fever are often late findings [9].

Routine laboratory analyses should be performed. Levels of creatine phosphokinase, myoglobin and potassium can be elevated after release from tissue and muscle breakdown.

Additionally, an ABG, lactate and pre-calcitonin can be useful when evaluating sepsis. Imaging such as radiography, (echography), CT scan or MRI, air may be visible in the soft tissue [1]. Contributing to differential diagnosis such as pyomyositis, where there is usually no systemic toxicity or air on imaging. A definitive diagnosis is proven by a large gram variable rod at the disease site. Particularly a gram stain of the bullous fluid may be useful [14]. Blood cultures are vital, since the bacteraemia usually precedes the (cutaneous) manifestations by several hours.

If muscle necrosis is present, with spreading of the necrosis to skin, fat, subcutaneous tissue and fascia, large gram-positive bacilli can be microscopically visible in between the degenerating muscle bundles without characteristically a lack of inflammatory cells(leukocytes) [12].

Treatment and prognosis

The treatment has two main pillars: early and aggressive, often multiple, surgical debridement and antibiotic therapy [15]. Awaiting the definitive causative, broad spectrum empiric antibiotic treatment should be started as soon as possible covering group A *streptococcus, Clostridium* species and mixed aerobes and anaerobes. The most recommended antibiotics are piperacillin-tazobactam 4,5g plus clindamycin 900 mg intravenously every eight hours [16].

Thorough surgical debridement is believed to be the single best predictor of outcome [13]. In case of a surgical exploration the muscle typically does not bleed or contract on stimulation. The muscle aspect is grossly oedematous and reddish blue to black discoloration [12]. Localized and focused surgical debridement is often not feasible without imaging, since external markers may be absent [11]. In case of elevated compartment pressures, a fasciotomy may be necessary [1].

Once the definitive causative species *C. septicum* is known the antibiotic therapy can be switched to penicillin 3 - 4 million units plus clindamycin 900 mg both intravenously every eight hours or tetracycline 500 mg intravenously every six hours. Of course, adaptations need to be made in regard to the antibiogram.

All the available evidence was extrapolated from the treatment of traumatic gas gangrene with *C. perfringens* and animal studies. In one animal study vancomycin led to increased mortality, compared to other antibiotics. It is suggested that *C. septicum* could have an intrinsic resistance to vancomycin. [16] In case of penicillin allergy only clindamycin can be used.

One controversial aspect of the treatment, in combination with the above mentioned, is hyperbaric chambre especially since there is lack of randomized controlled trials and the fact that *C. septicum* is aerotolerant [16]. One study did show promising results with a decrease in mortality from 70 to 25% [9]. However, it should never delay or hamper antibiotics admission or surgical debridement's.

Theoretically since a *C. septicum* is a component of the gut flora, a colectomy or lesion resection could provide source control eliminating the systemic access point. In combination with antibiotics, this showed promising results in some studies [9]. Every patient that survives the initial disease should have a colonoscopy planned to rule out gastrointestinal tract lesions [16].

Needless to state that the prognosis is poor and mortality rates go up to 67-100%. In most of the cases death occurs within 24 hours [17]. More specifically risk factors for fatal outcome are underlying malignancy and an immunocompromised state. The prognosis of the spontaneous type is worse compared to the traumatic type. Survival is reported as low as 19% [14].

Discussion and Ethical Dilemma

Luckily spontaneous myonecrosis due to *C. septicum* is a rare diagnosis since correct treatment is often too late and its insidious clinical manifestation. Our patient did not present as a textbook clinical image. She had no fever, even at rapid progression of the disease she showed barely any systemic toxicity but mostly neurological symptoms and progressing colour discoloration at the left lower leg. At arrival she complained of pain everywhere in her body. The pain in both lower legs and back, suffering at flexion of hips can be explained due to the bilateral iliopsoas spread of air. She stayed hemodynamically stable for a long time, remarkable at her advanced age, but eventually deteriorated rapidly. The left lower leg was not suspicious at the initial admission time but changed fast with formation of bullae and discoloration. However, there was no crepitus, which might be explained by the lack of gas subcutaneously. Previous described cases in literature have shown gas in the iliac vein, which may be compared to the gas found in the distal superficial femoral artery on the right side. In our patient the gas was also present retroperitoneal, as well as in between vertebral discs, bone, around and in the vessels of both legs. We believe that this spread of gas to multiple skipping or distant intra-arterial and retroperitoneal sites makes our case unique and contributes to a clear ethical dilemma. Because of this diffuse spread no surgical life sparing treatment was possible. This would have been different if the air would have solely been localized in the leg(s). In which case a surgical debridement or amputation could have helped the patient. Given the patients rapid neurological decline it is highly likely that the central nervous system was also implicated. Sadly, we did not perform a CT scan of the brain.

On the other hand, are you medically privileged to decide on a bilateral or unilateral amputation or disfiguring debridement in patients who are no longer able to decide whether they want that life changing treatment, especially at advanced age?

Looking at our patient she had a 100% mortality rate even if at presentation we knew the exact causative, she could not receive a thorough debridement. We believe that an admission at the ICU with intravenous antibiotics would not have changed the outcome given the advanced disease progression.

Although it is a rare condition, it is vital to consider the differential diagnosis in time and start appropriate treatment. This in all age groups, as we hypothesize that SCM is an underestimated diagnosis in elderly. Therefore, we hope to strive for faster and better care in comparable and less dispersed cases.

Conclusion

Everyday geriatric patients report to an emergency department after a fall without major consequences. It's imperative that a rare diagnosis as spontaneous myonecrosis receives recognition. It is vital to consider the differential diagnosis in time and start appropriate treatment. This in all age groups, as we hypothesize that SCM is an underestimated diagnosis in elderly. The spread of gas intramuscular, subcutaneous, skin and to multiple distant intra-arterial and retroperitoneal sites makes the present case unique and substantiates the decision to cease treatment, since no surgical life-sparing treatment was possible. It's our hope that improved recognition of this disease can contribute to better care and outcome in comparable and less dispersed cases.

Conflict of Interest

None of the authors have any conflict of interest.

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