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A subcutaneous infection mimicking necrotising fasciitis due to Butyricimonas virosa

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Keywords:	Butyricimonas; anaerobes; necrotizing fasciitis; negative pressure wound therapy (NPWT); LRINEC
Abstract:	Introduction: B. virosa is a gram-negative rod who was first identified in rat faeces in 2009. Since then only six human infections have been described in literature. We report a clinical case of a subcutaneous infection mimicking necrotizing fasciitis due to B. virosa. Patient and methods: A 78-year-old man was referred to our hospital because of a wound infection with suspicion of necrotizing fasciitis. Treatment consisted of immediate surgical exploration with obtainment of intra-operative specimens for microbiologic examination, 15 days of negative pressure wound therapy (NPWT) and antibiotic treatment with piperacillin-tazobactam (12 days) plus vancomycin (9 days). Results: Surgical exploration did not show necrotising fasciitis but a subcutaneous infection mimicking necrotising fasciitis. The intra-operative specimens revealed the presence of Butyricimonas virosa and Finegoldia magna. Cultures taken during the NPWT replacements became negative and the patient was able to leave the hospital after 18 days. Conclusions: Considering there was no necrotizing infection present it may have been possible to safely close the wound sooner. However it is difficult to differentiate between an actual necrotizing fasciitis and a subcutaneous infection mimicking necrotizing fasciitis. Therefore further studies on effective assessment tools to diagnose necrotizing fasciitis could be helpful.
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A subcutaneous infection mimicking necrotising fasciitis due to Butyricimonas virosa

Abstract

Introduction: *B. virosa* is a gram-negative rod who was first identified in rat faeces in 2009. Since then only six human infections have been described in literature of which five bactereamias and one bone abscess. We report a clinical case of a subcutaneous infection mimicking necrotizing fasciitis due to *B. virosa.*

Patient and methods: A 78-year-old man was referred to our hospital because of a wound infection at the surgical site with suspicion of necrotizing fasciitis. Treatment consisted of immediate surgical exploration with obtainment of intra-operative specimens for microbiologic examination, 15 days of negative pressure wound therapy (NPWT) and antibiotic treatment with piperacillin-tazobactam (12 days) plus vancomycin (9 days).

Results: Surgical exploration did not show necrotising fasciitis but a subcutaneous infection mimicking necrotising fasciitis. The results of the intra-operative specimens revealed the presence of *Butyricimonas virosa* and *Finegoldia magna.* Cultures taken during the NPWT replacements became negative and the patient was able to leave the hospital after 18 days.

Conclusions: Considering there was no necrotizing infection present it may have been possible to safely close the wound sooner. However it is difficult to differentiate between an actual necrotizing fasciitis and a subcutaneous infection mimicking necrotizing fasciitis. Therefore further studies on effective assessment tools to diagnose necrotizing fasciitis, such as the (modified) LRINEC score and enhanced CT, could be helpful.

Keywords: *Butyricimonas,* anaerobes, necrotizing fasciitis, negative pressure wound therapy, LRINEC

Introduction

The *Butyricimonas* genus was first discovered in rat faeces in 2009 [1] . It is a gram negative, anaerobic species that is a normal inhabitant of the intestine in humans and animals. The novel genus is a member of the *Porphyromonadaceae* family. Currently there are six different species part of the *Butyricimonas* genus: *B. virosa, B. synergistica, B. paravirosa, B. faecihominis, B. phoceensis* and *B. faecalis* [1-4]. *B. virosa* is the only species within the genus known to cause infection. There have been six reported cases of infection of which five bacteraemias, all correlated to peritonitis due to abdominal disease, and one bone abscess due to contamination of an open wound after fasciotomy [5-10]. We report a case of subcutaneous infection with *B. virosa* mimicking necrotizing fasciitis.

Patient and methods

A 78-year-old man, who underwent a pelvic lymph node removal 16 days earlier for staging of a prostate cancer, was referred to our hospital because of a wound infection at the surgical site with suspicion of necrotizing fasciitis.

The patient has a medical history of a herpes zoster infection (dermatome L3) in 2014, a rectosigmoid colon cancer in 2015 (pT3N0M0) and a colonoscopy in 2016 that showed 9 polyps.

At presentation in the emergency room the patient mentions progressive abdominal erythema, swelling and pain since 3 days, for which immediate treatment with flucloxacillin was initiated, but without improvement.

Physical examination showed an erythematous, hard, swollen and caloric zone with central necrosis and no capillary refill of approximately 2 cm in the left lumbar and iliac region (Fig. 1).

Figure 1. Clinical evaluation of local inflammation.

The laparotomy wound seemed well healed.

There was no fever present and the patient was in a stable hemodynamic condition.

Blood results showed a C-reactive protein of 222.6 mg/L (<5.0) and a white blood cell count of 12.01 x 10^3 cells/µL (3.65-9.30). Blood cultures were obtained.

An abdominal CT scan was performed and showed gas at the subcutaneous level with a fluid collection along the fascial plane. Also a small defect of the rectus fascia (12.69 mm) was identified (Fig. 2).

Figure 2. Abdominal computed tomography showing the subcutaneous infection and a small defect in the rectus fascia of 12.69 mm.

Since imaging suggested a necrotizing fasciitis, an immediate surgical exploration was indicated to evaluate the extent of involvement and to debride devitalized tissue. Intra-operative specimens were obtained for microbiologic examination. The patient remained stable during the course of the procedure.

Subcutaneous negative pressure wound therapy (NPWT) was used immediately after the surgical debridement to drain toxic metabolites. The NPWT was replaced every two days. New intra-operative specimens were obtained during every replacement.

Empiric intravenous antibiotic therapy with piperacillin-tazobactam plus vancomycin was started. In addition, the local redness was observed during the complete admission period.

Results

The patient's status remained stable without fever. Blood culture results came back negative.

Gram staining of the intra-operative specimens revealed the presence of Gram-negative rods. Six days after initial surgery *Butyricimonas virosa* and *Finegoldia Magna* were identified in the first intra-operative specimens by using matrix-assisted laser desorption/ionization–
time-of-flight mass spectrometry (MALDI-TOF MS). The specimens from the first NPWT replacement still showed a small amount of *B. virosa*, but every culture thereafter returned negative. There was no antibiogram available, but the eradication of bacterias in the specimens indicated the given antibiotic therapy was adequate. Vancomycin was administered for 9 and piperacillin-tazobactam for 12 days.

The patient's condition evolved favourably and the wound was finally closed 15 days after initial surgery. He was discharged 3 days later. During ambulatory follow-up a good wound healing was observed 5 days later and no further follow-up was indicated.

Discussion

The *Butyricimonas* genus was first described by Sakamoto et al. in 2009 and to date six different species are discovered [1-4]. *Butyricimonas virosa*, being the only known pathogenic species, has previously caused six infections reported in literature, making this the seventh [5-10]. Both first and second cases described a bacteraemia 24 and 18 days after surgery in a patient with a diagnosis of colonic and duodenal adenocarcinoma [8, 10]. The third case reported a bone abscess due to a contaminated open wound after fasciotomy for post-traumatic acute compartment syndrome [6]. The other three bacteraemias were all associated with secondary

peritonitis due to abdominal diseases, which were diverticulitis and intestinal perforation [5, 7, 9].

In conclusion five out of six reported infections are associated with abdominal disease, as is our case. This case however is the first subcutaneous infection with *Butyricimonas virosa* reported in literature.

The *Butyricimonas* genus is known to be a part of the human intestinal flora [1-4]. All the previous suggests that abdominal disease increases the risk of an infection with *B. virosa.*

Finegoldia magna is a bacteria that is often found in polymicrobial infections. It is a Gram-positive anaerobic coccus that is a known inhabitant of the mouth, gastrointestinal and genitourinary tract and skin, as well as a highly successful opportunistic pathogen in humans [11].

This patient presented with a necrotizing fasciitis-like clinical image for which immediate surgical intervention was performed, NPWT was applied and empiric antibiotic treatment was initiated.

Perioperative evaluation did not show a necrotizing fasciitis. This was confirmed with an intra-operative frozen section of the fascia. We applied the NPWT for a total duration of 15 days. Considering there was no necrotizing infection present it may have been possible to safely close the wound sooner.

Early differentiation between actual necrotizing fasciitis and a subcutaneous infection mimicking necrotizing fasciitis, as in our case, is the only possibility to prevent over-treatment in the future.

Necrotizing fasciitis is a primarily clinical diagnosis and when there is a strong clinical suspicion immediate surgical treatment and empiric antibiotics should be initiated without wasting time. However when the patient is stable it is a possibility

to use the LRINEC or modified LRINEC score to assess a potential necrotizing fasciitis, but both scores need further development and prospective studies before they can be reliable to differentiate between necrotizing fasciitis and cellulitis [12]. Imaging tests can also be used for diagnosis. A study on enhanced CT suggested that absence of fascial enhancement was specific for necrotizing fasciitis [13].
The empiric antibiotic treatment that is currently recommended for necrotizing fasciitis consists of vancomycin or linezolid plus piperacillin-tazobactam or ceftriaxone with metronidazole [13]. This is why our patient received an initial treatment of piperacillin/tazobactam and vancomycin. In absence of an antibiogram and a favourable clinical evolution we continued this antibiotic therapy for respectively 12 and 9 days. The previous cases describing infections with *B. virosa* report a sensitivity to ampicillin, ampicillin-sulbactam, amoxicillin-clavulanic acid, piperacillin-tazobactam, metronidazole, clindamycin and meropenem [5, 7, 10]. *F. magna* usually shows resistance to penicillin, clindamycin, metronidazole, erythromycin and tetracycline. Thus in this case antibiotic treatment with ampicillin, ampicillin-sulbactam, amoxicillin-clavulanic acid, piperacillin-tazobactam and meropenem should have been possible.

Conclusion

To our knowledge, this is the first case of a subcutaneous infection due to *Butyricimonas virosa*, mimicking a necrotizing fasciitis. It is difficult to differentiate between an actual necrotizing fasciitis and a subcutaneous infection mimicking necrotizing fasciitis. Therefore further studies on effective assessment tools to diagnose necrotizing fasciitis, such as the (modified) LRINEC score and enhanced CT, could be helpful.

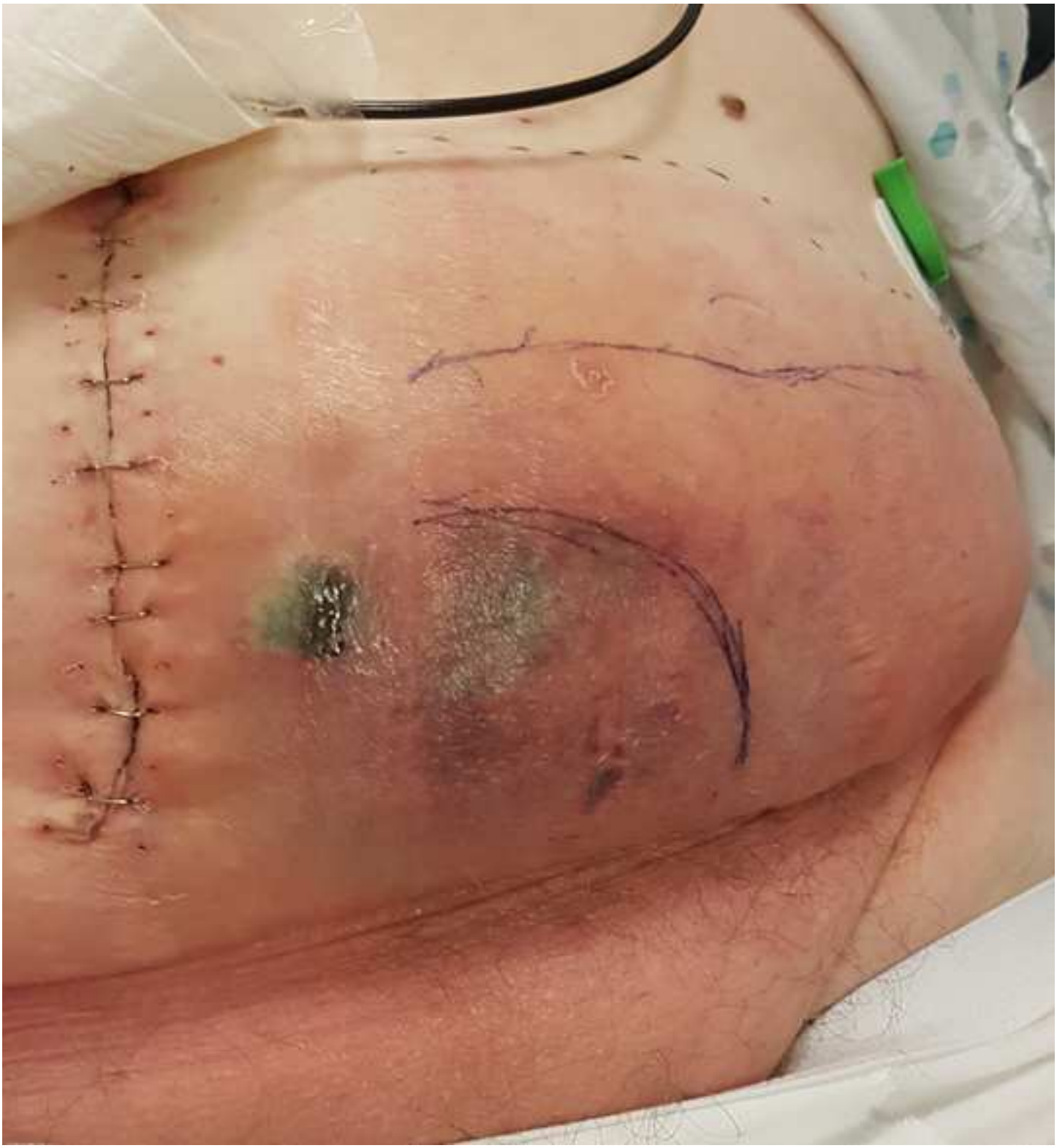
This is the seventh case of *Butyricimonas virosa* infection reported in literature to this date.

References

1. Sakamoto M, Takagaki A, Matsumoto K, Kato Y, Goto K, Benno Y. Butyricimonas synergistica gen. nov., sp. nov. and Butyricimonas virosa sp. nov., butyric acid-producing bacteria in the family 'Porphyromonadaceae' isolated from rat faeces. Int J Syst Evol Microbiol. 2009;59(Pt 7):1748-53.
2. Sakamoto M, Tanaka Y, Benno Y, Ohkuma M. Butyricimonas faecihominis sp. nov. and Butyricimonas paravirosa sp. nov., isolated from human faeces, and emended description of the genus Butyricimonas. Int J Syst Evol Microbiol. 2014;64(Pt 9):2992-7.
3. Togo AH, Diop A, Dubourg G, Nguyen TT, Andrieu C, Caputo A, et al. Butyricimonas phoceensis sp. nov., a new anaerobic species isolated from the human gut microbiota of a French morbidly obese patient. New Microbes New Infect. 2016;14:38-48.
4. Le Roy T, Van der Smissen P, Paquot A, Delzenne N, Muccioli GG, Collet JF, et al. Butyricimonas faecalis sp. nov., isolated from human faeces and emended description of the genus Butyricimonas. Int J Syst Evol Microbiol. 2019.
5. Enemchukwu CU, Ben-Faras H, Gialanella P, Szymczak WA, Nosanchuk JD, Madaline TF. Butyricimonas virosa bacteraemia and bowel disease: case report and review. New Microbes New Infect. 2016;13:34-6.
6. Ferry T, Laurent F, Ragois P, Chidiac C. Post-traumatic chronic bone and joint infection caused by Butyricimonas spp, and treated with high doses of ertapenem administered subcutaneously in a 30-year-old obese man. BMJ Case Rep. 2015;2015.

7. Garcia-Agudo L, Nilsen E. Butyricimonas virosa: A rare cause of bacteremia. Anaerobe. 2018;54:121-3.
8. Mehta SR, Estrada J, Basallo C, Farala A, Fierer J. Butyricimonas virosa bacteraemia identified by MALDI-TOF. New Microbes New Infect. 2015;8:127.
9. Ogawa Y, Sato M, Yamashita T, Nakano R, Mochizuki S, Kasahara K, et al. Polymicrobial Anaerobic Bacteremia Caused by Butyricimonas virosa and Brachyspira pilosicoli in a Patient with Peritonitis following Intestinal Perforation. Ann Lab Med. 2018;38(1):71-3.
10. Ulger Toprak N, Bozan T, Birkan Y, Isbir S, Soyletir G. Butyricimonas virosa: the first clinical case of bacteraemia. New Microbes New Infect. 2015;4:7-8.
11. Boyanova L, Markovska R, Mitov I. Virulence arsenal of the most pathogenic species among the Gram-positive anaerobic cocci, Finegoldia magna. Anaerobe. 2016;42:145-51.
12. Bechar J, Sepehripour S, Hardwicke J, Filobbos G. Laboratory risk indicator for necrotising fasciitis (LRINEC) score for the assessment of early necrotising fasciitis: a systematic review of the literature. Ann R Coll Surg Engl. 2017;99(5):341-6.
13. Stevens DL, Bryant AE. Necrotizing Soft-Tissue Infections. N Engl J Med. 2017;377(23):2253-65.

Clinical evaluation of local inflammation



Abdominal computed tomography showing the subcutaneous infection and a small defect in the rectus fascia of 12.69 mm