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Case report

Peptoniphilus asaccharolyticus – Commensal, pathogen or synergist? Two case reports on invasive *Peptoniphilus asaccharolyticus* infection

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ABSTRACT

Peptoniphilus asaccharolyticus are gram-positive anaerobic cocci (GPAC) usually found as commensals of the skin or in the setting of polymicrobial colonisation of chronic wounds and ulcers. However, its pathogenic potential in more severe, invasive infections such as bone, joint or blood stream infections remains unclear, with studies on underlying virulence factors still pending. In this case report we present two cases of *P. asaccharolyticus*-associated infections of the bone and joint as well as a review of the literature. The cases cast a new light on possible synergistic interactions between *P. asaccharolyticus* and more virulent aerobic bacteria as well as on its role as pathogen in severe mono-infection.

1. Introduction

Peptoniphilus asaccharolyticus are gram-positive anaerobic cocci (GPAC) that usually constitute human commensals of the skin, genitourinary system and gut [1]. GPAC represent around 30% of all anaerobic bacteria isolated from clinical specimens [1] and can cause opportunistic infections, with *P. asaccharolyticus* being especially prevalent in chronic wounds and diabetic ulcers, mostly as part of polymicrobial spectra [2]. However, clinical reports or studies on the role of *P. asaccharolyticus* in more severe infections such as skin, soft tissue or bone infection are scarce and in this case report we present two severe cases of *P. asaccharolyticus*-associated infections of the bone and joint as well as a review of the literature. Our findings highlight that both prevalence and pathogenicity of *P. asaccharolyticus* may have been underestimated and that *P. asaccharolyticus* may play a greater role as main pathogen in more severe infections than has been assumed so far.

2. Case reports

A 71-year-old male was admitted to hospital for severe, progressive lower back pain over the past six weeks, following posterior lumbar interbody fusion with instrumentation two months earlier due to upper plate fracture of lumbar vertebra (L5) with involvement of the anterior vertebral margin. Shortly after the operation, the patient displayed a wound healing deficit with concomitant fistulation within the operation site, which was treated with epicutaneous vacuum therapy. Comorbidities included terminal renal insufficiency and arterial hypertension.

Upon admission, the patient's temperature was at 36.2 °C, blood pressure was 120/70 mmHg, pulse rate 68 beats/min. Leucocyte count was normal (8.6/nl), but C-reactive protein and Procalcitonin levels were elevated (32 mg/L and 0.44 ng/ml, respectively). Removal of the vacuum bandages revealed serous, fetid wound secretions, prompting wound examination with epi- and subfascial surgical debridement of the infected tissue. Six deep tissue biopsies were collected for microbiological analyses, all of which yielded *Staphylococcus aureus* and *Peptoniphilus asaccharolyticus*. Anaerobic cultivation was performed on Schaedler anaerobe agar/Schaedler anaerobe KV selective agar (Thermo Fisher) and samples were incubated for 2–5 days in anaerobic jars (Anaerocult, Merck). Species identification was carried out by matrix-assisted laser desorption ionization time of flight (MALDI-TOF) mass spectrometry (Vitek MS, bioMérieux). The patient's antibiotic regimen was switched to Cefazolin for the treatment of *S. aureus* and Penicillin for *P. asaccharolyticus* according to antibiotic susceptibility tests.

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Anaerobic antibiotic susceptibility tests were performed using MIC Test Strips (Liofilchem) to determine minimum inhibitory concentrations (MIC) of antimicrobial agents, which included penicillin, meropenem, clindamycin and metronidazole.

Despite adequate antibiotic therapy and surgical wound management, the patient's condition deteriorated. Extended infectious focus search revealed an endocarditis of the aortic valve. Due to early initiation of antibiotic therapy, blood cultures yielded no bacterial growth, prompting adjustment of the antibiotic regimen to Ampicillin and Flucloxacillin, according to the 2015 ESC guidelines for the empiric management of infective endocarditis [3]. The patient is currently still being treated intravenously for infective endocarditis.

The second case report involves a 62-year-old female patient who presented with wound dehiscence, displaying putrid secretions following an uncomplicated total hip replacement two weeks earlier. Upon admission, the patient's temperature was at 37.0 °C, blood pressure was 130/80 mmHg, pulse rate 72 beats/min. C-reactive protein was elevated (39 mg/L), leucocyte count normal (5.1/nl). The patient had no known co-morbidities and was diagnosed with suspected early prosthetic joint infection and immediate revision surgery ensued with inlay and femoral head replacement. Operation showed a small fistula with underlying adipose tissue showing signs of necrosis. Furthermore, a subcutaneous, fluid-filled cavity became apparent, which was drained. Several intra-operative deep tissue samples yielded *P. asaccharolyticus* in mono-culture and empiric antibiotic treatment with Cefuroxime was continued after having confirmed susceptibility. Cultivation, identification and susceptibility testing methods were the same as for case 1. This patient, too, is currently still being treated intravenously for early prosthetic joint infection.

3. Discussion

Peptoniphilus asaccharolyticus is generally considered a co-occurring obligate anaerobe in chronic wounds or diabetic ulcers, with *P. asaccharolyticus* ranking among the most prevalent anaerobic pathogens, as has been shown in studies analysing the microbiota of chronic wounds [4,5]. However, literature on the prevalence of *P. asaccharolyticus* in more invasive infections is scarce and *P. asaccharolyticus* is generally considered a rare pathogen of severe infections such as bone, joint or blood stream infection, which are usually caused by more virulent aerobic bacteria such as *S. aureus*, *Streptococcus spp.* or Enterobacterales [6]. One reason for this scarcity of information could be that molecular methods used to provide precise identification of difficult-to-culture anaerobic bacteria were not as widely established or used in the past decades as they are nowadays. Furthermore, major taxonomic changes of anaerobic bacteria have occurred, which may hamper the identification of bacterium-disease associations [7].

In the only case report we found on *P. asaccharolyticus*-associated invasive mono-infection, *P. asaccharolyticus* was the causative pathogen in a patient diagnosed with septic arthritis and osteomyelitis. Relevant co-morbidities in this patient included osteoarthritis and diabetes mellitus [8]. In a second case report on olecranon osteomyelitis, *P. asaccharolyticus* was considered a "companion microbe" of a primarily *Actinomyces meyeri*-associated bone infection and its pathogenic role was not further elaborated on [9]. A report on 15 cases of blood stream infections due to *Peptoniphilus ssp*. between 2007 and 2011 showed that half of the infections were polymicrobial, with underlying diseases including septic abortion with choramnionitis, exacerbated COPD/pneumonia, skin and soft tissue infection or bowel/bladder disease [10]. The report concludes that *Peptoniphilus* sp. is a rare but important cause of blood stream infections among patients with underlying septic abortion, soft tissue infection, immunosuppression or pneumonia, either as primary pathogen or within polymicrobial infection [10]. Finally, in an analysis on 61 cases of bone and joint infection due to anaerobic bacteria within a timeframe of four years, *Peptoniphilus* sp. accounted for almost 20% of infections (six cases with *P. asaccharolyticus*; six cases with *P. harei*) [6]. Polymicrobial infections occurred in 50 of 61 cases [6]. These reports illustrate that *P. asaccharolyticus* is a common "fellow player" in polymicrobial infection, but it remains unclear whether this GPAC primarily acts as a commensal, pathogen or synergist.

As for other GPAC, it has been well established that *Finegoldia magna* expresses certain virulence factors that help *F. magna* adhere to the skin and invade deeper tissue layers during the establishment of infection. Virulence factors include *Finegoldia* adhesion factor (FAF), responsible for initial skin adherence, and extracellular subtilase-like serine protease enzyme (SufA), which cleaves collagen IV and V [11]. These virulence factors may pave the way for more virulent bacteria and causative pathogens of skin and soft tissue infection such as *S. aureus* in a synergistic way. However, virulence factors in *P. asaccharolyticus*, which may give hints as to its role as a synergist in invasive, polymicrobial infection, have not been well investigated so far and consequently, we can only speculate on possible virulence factors.

A further synergistic effect between GPAC and more virulent colonisers lies in the ability of certain aerobic bacteria to form biofilms which enhance the pathogenic potential of GPAC. *S. aureus* and *Pseudomonas* sp., for example, are known to form biofilms which are composed of a matrix of bacterial polysaccharides, protein and extracellular DNA, which result in bacterial aggregation [5]. As a result, GPAC are more likely to survive and proliferate when co-aggregating within a polymicrobial biofilm layer [4]. However, the pathogenicity of GPAC may also depend on the individual spectrum of co-occurring bacteria. In a study that analysed synergisms between GPAC and other bacteria in a murine abscess model, GPAC was found to be of equal importance in abscess formation when mixed with group A and D streptococci [12]. When co-infected with *S. aureus* and Enterobacterales, on the other hand, GAPC were classified as less important [12].

P. asaccharolyticus attracted our special attention after we were involved in two parallel cases of severe *P. asaccharolyticus*-associated infections in different hospitals within two weeks. While the first case presented with *S. aureus* co-infection, the second case represented a *P. asaccharolyticus*-associated mono-infection, with both cases showing similar protracted clinical courses of disease. Having ruled out laboratory contamination, we carried out a retrospective analysis and assessed the occurrence of *P. asaccharolyticus* among clinical specimens ever sent to our microbiological laboratory (2016–2019), comparing findings with data in literature.

Within a timeframe of three years, *P. asaccharolyticus* was detected in 19 patients (8 men, 11 women). The mean age was 59 years. Eleven samples showed co-occurrence of other pathogens (see Table 1). Our findings were insofar astonishing as 15 samples derived from invasive material from sterile body sites (e.g. abscess, blood culture, deep tissue) other than superficial wound swabs, with eight cases (42%) showing mono-infection with *P. asaccharolyticus*. While six infections correlated with the natural habitat of *P. asaccharolyticus* (five genitourinary, one abdominal infection), three positive blood cultures and seven bone or joint infections suggest haematogenous spread of *P. asaccharolyticus*. In all cases, species identification was obtained from cultures via MALDI-TOF. Even though our small study number may be a limiting factor, the occurrence of *P. asaccharolyticus*-associated mono-infection may be considered relatively high when comparing our findings with figures from the study by Walter et al. on anaerobic

Table 1
Clinical characteristics of patients with *P. asaccharolyticus*-associated infection from 2016 to 2019.

Case No.	Age/sex	Diagnosis	clinical specimen (quality of material)	Bacteria found	Type of infection
1	27/M	Scrotal abscess	Wound swab (superficial, non-sterile)	*P. asaccharolyticus, Prevotella* sp.	polymicrobial
2	31/M	Abdominal infection	Abdomial swab (superficial, non-sterile)	*P. asaccharolyticus, S. epidermidis*	polymicrobial
3	61/F	Prosthetic join infection	Tissue hip (invasive, sterile)	*P. asaccharolyticus*	monomicrobial
4	51/M	Vertebral osteomyelitis	Tissue back subfascial (invasive, sterile)	*P. asaccharolyticus, S.aureus*	polymicrobial
5	27/F	Spinal abscess	Puncture fluid (invasive, sterile)	*P. asaccharolyticus, Actinotignum schaalii*	polymicrobial
6	83/F	Pneumonia	Blood culture (invasive, sterile)	*P. asaccharolyticus*	Monomicrobial
7	56/M	Diabetic foot ulcer/charcot-foot	Blood cultures (invasive, sterile)	*P. asaccharolyticus*	monomicrobial
8	88/F	Post-operative infection following total hip replacement	Femoral joint swab (invasive, sterile)	*P. asaccharolyticus, Granulicatella* sp., *H. parainfluenzae*	polymicrobial
9	72/M	Gluteal decubitus	Wound swab (superficial, non-sterile)	*P. asaccharolyticus, S. anginosus, Corynebacterium* sp.	polymicrobial
10	72/F	Infection tibial osteosynthesis screw	Tissue tibial (invasive, sterile)	*P. asaccharolyticus, S. aureus*	polymicrobial
11	54/M	Post-operative infection cubital	Tissue cubital (invasive, sterile)	*P. asaccharolyticus, S. aureus*	polymicrobial
12	77/M	Thoracic wound	Wound swab (superficial, non-sterile)	*P. asaccharolyticus*	monomicrobial
13	58/F	Early prosthetic knee joint infection	puncture fluid knee joint (invasive, sterile)	*P. asaccharolyticus, S. aureus*	polymicrobial
14	56/F	Urogenital-Infection	Blood culture (invasive, sterile)	*P. asaccharolyticus*	monomicrobial
15	61/F	Tubo-ovarian abscess	Abscess swab (invasive, sterile)	*P. asaccharolyticus*	monomicrobial
16	59/F	Tubo-ovarian abscess	Abscess puncture fluid (invasive, sterile)	*P. asaccharolyticus*	monomicrobial
17	55/F	Thoracic abscess	Abscess swab (invasive, sterile)	*P. asaccharolyticus*	monomicrobial
18	81/F	Chronic tibial wound	Wound swab (invasive, sterile)	*P. asaccharolyticus, Lactobacillus* sp.	polymicrobial
19	53/M	Scrotal abscess	Abscess puncture (invasive, sterile)	*P. asaccharolyticus, S. aureus*	polymicrobial

bone and joint infections, which only reported six of 61 bone and joint infection due to *P. asaccharolyticus* within a similar study timeframe [6]. Furthermore, anaerobic bacteria are more fastidious and require special media as well as prolonged cultivation times. While most of the quoted studies resorted to nucleic acid amplification techniques (NAT) to complement cultivation-based diagnostics, most microbiological laboratories do not routinely use NAT to detect GPAC and hence, our purely culture-based findings may only represent the tip of the iceberg. This diagnostic gap may have resulted in a general neglect of the clinical significance of *P. asaccharolyticus* and other GPAC [13].

Our case report and epidemiologic findings cast a new light on *P. asaccharolyticus* and prompt three assumptions that require further investigation: firstly, the prevalence of *P. asaccharolyticus* among critical infections such as bloodstream infection, osteomyelitis or prosthetic joint infection may be higher than previously presumed. This is mainly due to cultivation difficulties and predominance of (facultative) aerobic bacteria in the setting of polymicrobial infection, which may suppress cultural growth of anaerobic bacteria. To bridge this diagnostic gap, critical specimens should always be anaerobically cultured and NAT may be used where available. Secondly, the pathogenicity of *P. asaccharolyticus* may have been underestimated in severe, invasive infections with studies on possible virulence factors on *P. asaccharolyticus* still pending. Here, studies on other GPAC such as *F. magna* may serve as a model for further research into *P. asaccharolyticus*-associated virulence factors and into its role as a synergist within polymicrobial colonisation or infection. Thirdly, the role of *P. asaccharolyticus* as causative pathogen in mono-infection should be taken seriously. To this end, the present case report and review of the literature may represent a starting point for clinical and scientific investigation.

4. Conclusion

Returning to our initial question, *P. asaccharolyticus* may be considered an opportunist with the potential to transform from a commensal to pathogen in the presence of certain predisposing factors. These factors can be patient-related and include underlying co-morbidities that compromise the immune system and facilitate haematogenous spread as well as presence of conditions that enhance anaerobic growth such as impaired peripheral perfusion or vacuum therapy. Physiological factors encompass co-occurrence of biofilm-forming bacteria and associated virulence factors. Bacterial synergisms seem to underly nuanced interactions which merit further investigation.

Declarations of interest

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References

[1] D.A. Murdoch, Gram-positive anaerobic cocci, Clin. Microbiol. Rev. 11 (1) (1998) 81–120.
[2] S.E. Dowd, R.D. Wolcott, Y. Sun, T. McKeehan, E. Smith, D. Rhoads, Polymicrobial nature of chronic diabetic foot ulcer biofilm infections determined using bacterial tag encoded FLX amplicon pyrosequencing (bTEFAP), PLoS One 3 (10) (2008), e3326, https://doi.org/10.1371/journal.pone.0003326.
[3] G. Habib, P. Lancellotti, M.J. Antunes, M.G. Bongiorni, J.P. Casalta, F. Del Zotti, et al., 2015 ESC guidelines for the management of infective endocarditis: the task force for the management of infective endocarditis of the European society of cardiology (ESC). Endorsed by: European association for cardio-thoracic surgery (EACTS), the European association of nuclear medicine (EANM), Eur. Heart J. 36 (44) (2015) 3075–3128, https://doi.org/10.1093/eurheartj/ehv319.

[4] K. Smith, A. Collier, E.M. Townsend, L.E. O'Donnell, A.M. Bal, J. Butcher, et al., One step closer to understanding the role of bacteria in diabetic foot ulcers: characterising the microbiome of ulcers, BMC Microbiol. 16 (2016) 54, https://doi.org/10.1186/s12866-016-0665-z.

[5] Y. Choi, A. Banerjee, S. McNish, K.S. Couch, M.G. Torralba, S. Lucas, et al., Co-occurrence of anaerobes in human chronic wounds, Microb. Ecol. (2018), https://doi.org/10.1007/s00248-018-1231-z.

[6] G. Walter, M. Vernier, P.O. Pinelli, M. Million, M. Coulange, P. Seng, et al., Bone and joint infections due to anaerobic bacteria: an analysis of 61 cases and review of the literature, Eur. J. Clin. Microbiol. Infect. Dis. : official publication of the European Society of Clinical Microbiology 33 (8) (2014) 1355–1364, https://doi.org/10.1007/s10096-014-2073-3.

[7] P.A. Shenoy, S. Vishwanath, A. Gawda, S. Shetty, R. Anegundi, M. Varma, et al., Anaerobic bacteria in clinical specimens - frequent, but a neglected lot: a five year Experience at a tertiary care hospital, J. Clin. Diagn. Res. : J. Clin. Diagn. Res. 11 (7) (2017), https://doi.org/10.7860/jcdr/2017/26009.10311. Dc44-dc8.

[8] R. Verma, S. Morrad, J.J. Wirtz, Peptoniphilus asaccharolyticus-associated septic arthritis and osteomyelitis in a woman with osteoarthritis and diabetes mellitus, BMJ Case Rep. 2017 (2017), https://doi.org/10.1136/bcr-2017-219969.

[9] J.Y. Kim, E.K. Kang, S.M. Moon, Y.H. Seo, J. Jeong, H. Cho, et al., Olecranon osteomyelitis due to Actinomyces meyeri: report of a culture-proven case, Infection & chemotherapy 48 (3) (2016) 234–238, https://doi.org/10.3947/ic.2016.48.3.234.

[10] K. Brown, D. Church, T. Lynch, D. Gregson, Bloodstream Infections Due to Peptoniphilus spp.: Report of 15 Cases, vol. 20, Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases, 2014, pp. O857–O860, https://doi.org/10.1111/1469-0691.12657, 11.

[11] E.C. Murphy, M. Morgelin, D.P. Reinhardt, A.I. Olin, L. Bjorck, I.M. Frick, Identification of molecular mechanisms used by Finegoldia magna to penetrate and colonize human skin, Mol. Microbiol. 94 (2) (2014) 403–417, https://doi.org/10.1111/mmi.12773.

[12] I. Brook, R.I. Walker, Pathogenicity of anaerobic gram-positive cocci, Infect. Immun. 45 (2) (1984) 320–324.

[13] E.C. Murphy, I.M. Frick, Gram-positive anaerobic cocci–commensals and opportunistic pathogens, FEMS Microbiol. Rev. 37 (4) (2013) 520–553, https://doi.org/10.1111/1574-6976.12005.