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【 CASE REPORT 】

Clinically Infrequent *Arcanobacterium haemolyticum* Bacteremia Complicated by Foot Decubitus Ulcer: An Educational Reminder for Primary Care Physicians

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Abstract:
An 81-year-old Japanese man with no history of diabetes mellitus was admitted to our hospital for a fever with a new ulcerative lesion on the left heel. Blood cultures on admission grew *Arcanobacterium haemolyticum* in aerobic bottles. He was therefore diagnosed with *A. haemolyticum* bacteremia and osteomyelitis complicated with foot decubitus ulcer. He was successfully treated with intravenous antibiotic therapy and debridement of the left heel. Our case and literature review show that it is important to recognize that *A. haemolyticum* is a systemic causative pathogen in immunocompetent patients in primary care practice.

Key words: *Arcanobacterium haemolyticum*, bacteremia, decubitus ulcer, osteomyelitis

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Introduction

Arcanobacterium haemolyticum, a Gram-positive-to-variable rod, is a well-known cause of pharyngitis for young adults and is usually thought to be a non-systemic pathogen (1). This pathogen has been implicated as a cause of skin and soft tissue infections in patients with underlying predisposing diseases, such as diabetes mellitus (2), and is rarely reported to cause systemic deep infections in immunocompetent patients. In order to emphasize the importance of recognizing this organism as a causative pathogen, we herein report an immunocompetent adult patient with *A. haemolyticum* blood stream infection complicated with skin and soft tissue infections and osteomyelitis and review the relevant literature.

Case Report

An 81-year-old Japanese man who had a history of hypertension and left leg deep vein thrombosis, had been taken to a dermatology outpatient care clinic regularly for treatment of his sacral decubitus. He had no history of diabetes mellitus and was confined to a bed due to severe lumber spinal stenosis and osteoarthritis of the knees.

One month prior to admission, a new lesion of left heel decubitus ulcer was noticed during the regular outpatient follow-up with swelling and redness. He was given a prescription for cefaclor 250 mg three times a day for 2 weeks by the dermatologist, and the ulcer of the left heel improved. However, 18 days after finishing oral antimicrobial agents, he was admitted to our hospital because the ulcerative lesion on the left heel had turned swollen and reddish, accompanied by a fever and shaking chills. On admission, he was alert and oriented. His general appearance was sick, with a blood pressure of 132/75 mmHg, heart rate of 56 beats/min, respiratory rate of 22 breaths/min, and body temperature of 38.8℃. A physical examination revealed that the base of the left heel ulcer had reached the calcaneus.

Blood cultures on admission grew *Streptococcus dysgalactiae* in two sets of anaerobic bottles and gram positive and catalase negative bacilli in aerobic bottles. This Gram-positive bacilli was later identified as *Arcanobacterium haemolyticum* by an automated identification test (Walkerway®, PC3.1J; Brea, USA). The identification was confirmed using the API Coryne Panel® (BioMérieux, Lyon,

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Table 1. Susceptibility testing results of *Arcanobacterium haemolyticum*.

Antimicrobial agents	Susceptibility Results	MIC (μg/mL)
penicillin G	Susceptible	0.12
ampicillin	Susceptible	0.25
cefazolin	Susceptible	≤8
cefotiam	Susceptible	≤8
flomoxef	Susceptible	≤4
imipenem/cilastatin	Susceptible	≤1
ampicillin/sulbactam	Susceptible	≤8
gentamicin	Susceptible	2
erythromycin	Susceptible	≤0.25
clindamycin	Susceptible	≤0.5
minocycline	Susceptible	≤2
levofloxacin	Susceptible	≤0.5
vancomycin	Susceptible	≤0.5
fosfomycin	Intermediate	16

France), which gave a 98.1% probability for *A. haemolyticum*. The susceptibility testing results showed that the strain was susceptible to all antimicrobial agents evaluated using the Clinical Laboratory Standards breakpoints for *Staphylococcus* minimum inhibitory concentrations, since there were no interpretive guidelines for Coryneforms (Table 1). The diagnosis was finally confirmed as polymicrobial bacteremia with *Streptococcus dysgalactiae* and *A. haemolyticum* complicated with left heel ulcer and osteomyelitis.

The patient underwent debridement of the left heel immediately. After receiving the blood culture results, a culture from the left heel was obtained to investigate the source of the infection. However, the culture from his left heel was negative, as he had already been treated with antimicrobial therapy on hospital day 8. He had been intravenously treated with ampicillin/sulbactam 3 g every 6 hours for 6 weeks and did well. Repeated blood cultures turned negative on hospital day 3. No further complications, sequelae, or recurrence occurred. He was transferred to a rehabilitation hospital on hospital day 51.

Discussion

A. haemolyticum has been mainly isolated from non-streptococcal pharyngitis in young adults. It has also been recognized and isolated from immunocompromised patients, particularly those with diabetes mellitus and malignant neoplasms presenting with skin and soft tissue infection (1, 2). On rare occasions, it has been reported to cause systemic deep infection, such as meningitis (3), Lemierre's syndrome (4), and endocarditis and bacteremia (5).

We conducted a literature review using PubMed for case reports and case series published in English. The query used was "[*Arcanobacterium haemolyticum*] AND [bacteremia OR sepsis OR systemic infection]". Skov, et al. reported 16 patients with bacteremia previously (1966-1997) and suggested that those patients could be classified into two main groups: those who were immunocompromised or had known risk factors for infectious diseases, and those who were immunocompetent (3). Our literature review yielded 13 patients with bacteremia over the past 20 years, and the main outcomes are presented in Table 2 (1, 2, 4-10). In cases 1-3, the patients were classified as having an immunocompromised condition, while in cases 4-8, the patients did not have any immunocompromised conditions but had known risk factors for infectious diseases. In our case *A. haemolyticum* and *S. dysgalactiae* could not be isolated from the ulcer after debridement; however, the decubitus ulcer seemed most likely to be the origin of the infection. Our patient is similar to those described in cases 4, 5, and 8 in terms of the entry site (2, 6, 7). These cases were remarkable in that even without the presence of immunocompromising diseases, wounds or scars could still be the entry sites of this organism and cause systemic infection. Another notable finding in our literature review was that patients without an immunocompromised condition were relatively young, and the focus of the infection was generally the upper respiratory system. In case 12, the entry site of infection was reported to be pharyngotonsillitis (4), and in cases 9, 10, and 13, the patient presented with a sore throat for a couple of days (8-10). This feature may be associated with *A. haemolyticum* pharyngitis.

A. haemolyticum is a facultative anaerobic, β-hemolytic Gram-positive to Gram-variable and catalase-negative bacilli. It can be distinguished by its ability in Christie, Arkins and Munch-Petersen (CAMP) test for differentiating from β-hemolytic streptococci (11). In clinical microbiology laboratories, laboratory technicians may encounter them as part of the normal oral flora or as contaminants due to its innocuous and Coryneform appearance (12). It is important to consider that *A. haemolyticum* can function as a sole pathogen or as a component of a polymicrobial infection causing systemic infection and bacteremia (5).

A. haemolyticum is usually susceptible to all classes of antimicrobial agents, except for trimethoprim-sulfamethoxazole (13). The isolate in our patient was susceptible to all antimicrobial agents tested, and the patient was successfully treated by β-lactams. However, it is important to follow the clinical course carefully, since treatment failure can occur. Indeed, a few isolates of *A. haemolyticum* have been shown to be penicillin-tolerant despite *in vitro* studies showing penicillin susceptibility (14). Vancomycin-resistant strains of *A. haemolyticum* due to the expression of the *vanA* gene have also been reported (15).

In conclusion, our patient is an educational remider that uncommon pathogens, such as *A. haemoliticum*, that are ususally considered non-systemic organisms can cause deep-seated infection with bacteremia complicated with osteomyelitis. The early recognition of the organism and appropriate antimicrobial therapy are essential for the management of this infection in primary care settings.

The authors state that they have no Conflict of Interest (COI).

Table 2. Characteristics of 13 Reported Cases of *Arcanobacterium haemolyticum* Bacteremia.

Case no./ Immuno-compromised conditions	Ref. no.	Age	Sex	Underlying conditions	Complications	Entry site of infection
1/Yes	2	63	male	diabetes mellitus	Osteomyelitis	foot ulcer
2/Yes	2	64	male	diabetes mellitus, toe ulcer	Soft tissue infection	toe abscess
3/Yes	2	52	male	diabetes mellitus	Soft tissue infection	foot ulcer
4/No	2	91	female	bed bounded, decubitus	Soft tissue infection	sacral sore
5/No	2	58	male	bed bounded, multiple infarct cerebral disease	Soft tissue infection	decubitus ulcer
6/No	5	21	female	congenital heart disease	Endocarditis	unknown
7/No	6	62	male	after surgery for pes planus	Soft tissue infection	wound
8/No	7	74	male	foot ulcer after debridement	Osteomyelitis, Sepsis	wound
9/No	8	20	male	none	Mycoplasma pneumonia, Empyma	unknown
10/No	9	21	male	none	Lemierre's syndrome	unknown
11/No	1	18	male	asthma	Pneumonia, Sepsis, Pyomyositis	unknown
12/No	4	23	male	none	Lemierre's syndrome	pharyngotonsillitis
13/No	10	20	female	none	Lemierre's syndrome	unknown

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