Actinobacillus ureae septic arthritis in a returning traveler from Gambia: A case report and a review of literature

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Abstract
We present, to our knowledge, the second case of a Actinobacillus ureae septic arthritis in a returning traveller from The Gambia with a past medical history of monoclonal gammopathy of undetermined significance complicated by a severe polyneuropathy of the lower extremities.

Background
Actinobacillus ureae, formerly known as Pasteurella ureae [1], is a non-motile and non-sporing Gram-negative rod [2]. Together with the genera Haemophilus it constitutes the family of Pasteurellaceae [3]. It is rarely reported as a causative infectious micro-organism in humans [4-6]. A. ureae was first isolated in human sputum in three patients with chronic rhinosinusitis [4]. Later, it was also detected in routine sputum testing in patients without any respiratory symptoms and was therefore believed to be a commensal of the respiratory tract [5].

Symptoms may occur in the presence of damage of the upper respiratory tract or bronchial tree or a compromised immune system [5]. Arthritis caused by A. ureae is even more rare, as only one single case has been described in the literature [7]. Here, we report the second published case of septic arthritis due to A. ureae, with a possibly tropical origin.

Case report
A 67-year-old man presented at the emergency department, twenty-four hours after returning from a fourteen-day holiday to The Gambia. He suffered from a swollen, red and painful left foot, which had started three days before admission. The day before admission the patient also had developed fever up to 39 degrees Celsius. In The Gambia, he mentioned to have walked barefoot almost constantly. At the Gambia, he had resided in several hotels and resorts. He had received adequate travelling immunization and had used atovaquone/proguanil as malaria prophylaxis. His past medical history revealed a polyneuropathy caused by a monoclonal gammopathy of undetermined significance (MGUS), with a possibly tropical origin.

Due to the severity of infection, he was hospitalized to be treated with fluvoxacillin 1000 mg four times a day intravenously under the suspicion of a cellulitis. The next day, he had increasing loss of motion of the affected ankle with worsening pain and swelling. Arthritis was confirmed after aspiration of purulent fluid by an ultrasound guided diagnostic synovial puncture. Furthermore, the blood cultures revealed growth of gram-negative rods. At this point the antibiotics were switched to ceftriaxone 2000 mg once a day intravenously.

Both the cultures of blood and synovial aspirate eventually revealed the presence of A. ureae, determined by matrix-assisted laser desorption/ionization time-of-flight analyzer (MALDI-TOF, Bruker). An overview of antibiotics susceptibility testing is given in table 1.

Antibiotic regimen was narrowed to benzylpenicillin 1x10^6 IE four times a day intravenously. The infection parameters declined and the body temperature normalized. The pain and loss of motion improved gradually. An arthroscopic irrigation with saline was performed to potentiate bacterial eradication and to restrict intra-articular damage. Repeated scupulous investigation revealed a wood splinter deep under the skin of the heel of the affected foot, which may potentially have functioned as a portal of entry, although the extracted nail seems to be an alternative legitimate explanation.

The intravenous benzylpenicillin regimen was continued for two weeks. After two weeks, he was discharged from the hospital. Antibiotic treatment was switched to levofloxacin (500mg twice daily) orally for another four weeks. Our patient fully recovered without any sequelae, including normal ankle joint function.

Discussion
To the best of our knowledge, we reported, the second known case of septic arthritis due to Actinobacillus ureae in a traveler returning from The Gambia. A Medline search was performed using the terms

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Actinobacillus ureae', 'Pasteurella ureae' and 'infection', as this microorganism is uncommonly recognized as a causative infectious agent in humans [4-6]. Twenty-nine cases of infections caused by A. ureae were identified [6-32]. The most frequently reported infection was meningitis. Only one case concerned arthritis [7]. An overview is given in table 2. Interestingly, the case of arthritis of Kaur et al. and our patient both concern A. ureae arthritis possibly acquired in Africa. However, no specific associations with the tropics are currently known from literature. Besides, both cases originate from varying demographic locations.

Infections with A. ureae seem to be associated with several comorbidities. A substantial part of the meningitis cases was associated with skull fractures or intracranial surgery. Both the current case and the case of arthritis of Kaur et al. concern patients with skin damage. Several patients had a hampered immune system, due to Waldenström’s macroglobulinaemia, HIV-positivity and use of immunosuppressive agents. Whether this suggests that disruption of immunity not only predisposes to infection in general, but also to infection with A. ureae specifically remains unclear.

The laboratory tests used in this case were CRP, an acute phase protein, and WBC. Both were elevated and in combination with the clinical signs this raised the suspicion of an infection. This was confirmed with bacterial growth in the blood and synovial aspirate cultures.

Routine incubation of the blood and synovial fluid led to rapid identification of the A. ureae. Three blood culture sets (two on the day of admission and one on the second day) were incubated and the aerobic bottles became positive within 14 hours (BACTEC, BD). The synovial fluid grew in the blood culture media and not on the directly inoculated agar, but this could be due to the fact that the synovial fluid was collected after antibiotics were started. In conclusion, the A. ureae grew within 24 hours on blood agar plates and was identified by the MALDI-TOF.

A. ureae can be adequately treated with beta-lactam antibiotics. Alternative options include tetracyclins, sulfonamids/trimethoprim, macrolids and aminoglycosides, which was confirmed from our antibiotic susceptibility tests.

Additionally, in treating septic arthritis it must be considered to perform joint irrigation as to potentiate bacterial eradication and limit intra-articular damage [33]. In both our and the formerly described case of A. ureae, residual damage was not reported.

A. ureae seldom is a causative infectious agent of septic arthritis. Currently available literature might suggest an association with disruption of immunity. We recommend to routinely perform blood or synovial cultures in patient with arthritis, which may sometimes detect uncommon pathogens, for which antibiotic susceptibility guided treatment can be initiated.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.
Table 2. An overview of literature

| Case | Year | Gender | Age | Localisation | Relevant history | Antibiotics (AB) | Duration | AB | Additional therapy | Outcome |
|------|------|--------|-----|--------------|-----------------|-----------------|----------|----|-------------------|---------|
| 1[7] | 2004 | F, 59  | Arthritis, multifocal | Rheumatoid arthritis treated with anti-TNF-alfa and methotrexate Trip to Kenya Several skin abrasions | IV piperacillin/ tazobactam and ciprofloxacin Oral ciprofloxacin | 6 weeks | Wound debridement Articular irrigation Subtotal synovectomy | | Survived |
| 2[8] | 1968 | M, 2 Malaria | Bacteremia Malnutrition | N/A | N/A | Died |
| 3[9] | 1996 | M, 65 Bone marrow | Rheumatoid arthritis | IV bentyl/penicillin Oral tetracyclin | 2 weeks | 2 weeks | - | Survived |
| 4[10] | 1995 | N/A Bronchitis, chronic | N/A | N/A | N/A | N/A | N/A | - | |
| 5[11] | 1981 | N/A Bronchopneumonia | Bacteremia Liver cirrhosis | N/A | N/A | N/A | N/A | N/A | |
| 6[12] | 1981 | M, 19 Bronchopneumonia | | | | | | | |
| 7[13] | 1979 | F, 2 days Conjunctivitis Premature newborn | | | | | | | |
| 8[14] | 2007 | F, 4 Conjunctivitis | | IV amoxicillin/ clavulanate | 5 days | - | Full recovery |
| 9[15] | 1993 | M, 59 Endocarditis Previous S. aureus endocarditis Periodontal surgery without AB prophylaxis | | IV gentamicin IV piperacillin Oral cefotiam | 5 weeks 6 weeks | 5/8 | - | Survived |
| 10[16] | 1988 | M, 27 months Otitis media | | Oral amoxicillin/ clavulanate | 10 days | - | Full recovery |
| 11[17,18] | 1961 | M, 39 Meningitis | Alcohol abuse Skull fracture | N/A | N/A | N/A | Survived |
| 12[19] | 1966 | M, 48 Meningitis | | N/A | N/A | N/A | Survived |
| 13[20] | 1967 | M, 16 Meningitis | | N/A | N/A | N/A | Died |
| 14[21] | 1978 | F, 53 Meningitis Bacteremia Intracraniary surgery | | N/A | N/A | N/A | Survived |
| 15[22] | 1983 | M, 40 Meningitis Endocarditis Schizophrenia Alcohol abuse Odontal infection | | N/A | N/A | N/A | Coma |
| 16[23] | 1983 | M, 55 Meningitis Bacteremia Insulin-dependent diabetes | | Ampicillin | N/A | - | Survived Hearing loss |
| 17[24] | 1983 | M, 54 Meningitis Previous skull fracture Alcohol abuse | | Penicillin | N/A | N/A | Survived |
| 18[25] | 1985 | M, 6 Meningitis Previous skull fracture | | IV ampicillin and chloramphenicol | N/A | - | Survived |
| 19[26] | 1989 | M, 52 Meningitis Previous skull fracture Chronic sinusitis | | ampicillin | 2 weeks | N/A | Survived |
| 20[18] | 1987 | M, 26 Meningitis Bacteremia Alcohol abuse Two pneumococcal meningitis in history Previous skull fracture | | IV cefotaxime and penicillin | 8 days | Neurosurgical repair of fistula from lamina cribrosa and nasal cavity | | Survived |
| 21[27] | 1994 | M, 25 Meningitis HIV-positive Head trauma | | IV ceftriaxone switched to IV penicillin | N/A | - | Survived |
| 22[28] | 1995 | M, 17 Meningitis Skull fracture Dural tears | | IV penicillin and cefazidime | N/A | Frontal craniotomy with partial debridement left frontal lobe Repair dural tears | | Survived Complete neurological recovery |
| 23[29] | 2002 | M, 22 Meningitis Previous neurosurgery Skull fracture | | IV ceftriaxone | 10 days | - | survived |
| 24[17] | 2009 | M, 75 Meningitis Waldenström’s macroglobulinaemia | | IV cefotaxime Oral amoxicillin | 15 days 1 week | - | Survived |
| 25[30] | 1978 | M, 14 Meningo-encephalitis Previous basal skull fracture Dural tear | | IV ampicillin | N/A | - | Survived |
| 26[6] | 1989 | M, 44 Peritonitis Alcohol abuse Liver cirrhosis Denver shunt | | IV clindamycin IV ampicillin and gentamicin | 5 days | 10 days | - | Survived |
| 27[31] | 1976 | M, 47 Pneumonia Previous alcohol abuse Emphysema Multiple rib fractures | | N/A | N/A | - | Died |
| 28[32] | 2000 | M, 28 Pneumonia AIDS Hepatitis type C | | IV ceftriaxone | 10 days | - | Survived |
| 29[17,18] | 1984 | M, 47 Septicaemia Alcohol abuse Liver cirrhosis | | N/A | N/A | N/A | Died |
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