Infection (2019) 47:479–482
https://doi.org/10.1007/s15010-018-1246-x

CASE REPORT

# *Actinomyces* spp. bloodstream and deep vein thrombus infections in people who inject drugs

**Emma Tippett[1] · Nupur Goyal[2] · Stephen Guy[1,3] · Jenny Wong[4]**

Received: 15 July 2018 / Accepted: 31 October 2018 / Published online: 8 November 2018


## Abstract

**Introduction** *Actinomyces* spp. cause several well-described syndromes including cervicofacial and pelvic infections. *Actinomyces* spp. infection as an opportunistic infection among people who inject drugs has rarely been described with few case reports published.

**Methods and results** Here we describe four people who inject drugs admitted with *Actinomyces* spp. infections, all with an overlapping syndrome and who presented a challenge to both diagnose and to manage.

**Discussion** This case series highlights the potential to overlook *Actinomyces* spp. infection in people who inject drugs and aims to increase clinician awareness of diagnosis, empirical and directed treatment, and potential complications of this infection.

**Keywords** Actinomyces · Actinomycosis · Anaerobe · Injecting drug use · Intravenous drug use

**Abbreviations**

| | |
|---|---|
| DVT | Deep vein thrombosis |
| Spp | Species |
| PWID | People who inject drugs |

## Introduction

*Actinomyces* spp. are non-motile, filamentous, anaerobic Gram-positive bacilli distantly related to *Corynebacterium, Propionibacterium* and *Mycobacteria* [1]. There are in excess of 30 species currently described, some of which are colonising flora of the oropharynx, gastrointestinal tract and urogenital tract. A large number are potentially pathogenic to humans, with *A. israelii* and *A. odontolyticus* being the most commonly reported [1]. *Actinomyces* spp. are often described as a 'companion' organism and are frequently isolated in combination with other species of *Actinomyces* as well as other aerobic or anaerobic bacteria with the complex being termed 'actinomycoses' [2].

The clinical presentations of *Actinomyces* spp. infection varies but is characteristically a subacute to chronic infection that demonstrates the ability to cross tissue planes with a well-documented predilection for cervicofacial infection originating from orodental source [1], or pelvic infections associated with intra-uterine devices [3]. Infection may be associated with tissue fibrosis, development of a draining sinus or fistula, or expression of characteristic macroscopic or microscopic 'sulphur granules': a consolidation of propagating *Actinomyces* with associated inflammatory infiltrate. *Actinomyces* spp. may also produce a range of other clinical infections including pulmonary empyema, soft tissue infections of the breast [4], central nervous system infections or osteomyelitis.

We isolated *Actinomyces* spp. from the bloodstream and/or endovascular tissue of several people who inject drugs (PWID); all of whom were injecting through an 'injecting sinus' into the deep veins of the groin and had associated infected deep vein thrombosis (DVT). Treatment was notably challenging with complications of both infection and treatment. A review of the literature uncovered few descriptions of *Actinomyces* spp. being an opportunistic infection

✉ Emma Tippett
emmadtippett@gmail.com

1 Western Health, Gordon St, Footscray, Melbourne 3011, Australia

2 Eastern Health, 5 Arnold St, Box Hill, Melbourne 3128, Australia

3 Department of Medicine, Melbourne Medical School, Western Precinct, The University of Melbourne, St. Albans, VIC 3021, Australia

4 Dorevitch Pathology, 18 Banksia St, Heidelberg, Melbourne 3084, Australia

associated with injecting drug use. The aim of this report is to describe and discuss the diagnosis and treatment of patients with *Actinomyces* spp. infection, and review the literature regarding *Actinomyces* spp. in PWID.

## Methods and results

This case series was conducted in concordance with Western Health ethics study number CS2018.01. We noted several cases of *Actinomyces* spp. isolated from blood cultures in our diagnostic microbiology laboratory. Subsequently, a search was conducted of the microbiology department database of blood culture results and four patients were identified from whom *Actinomyces* spp. were isolated at Western Health from 1st Jan 2017 to 31st Dec 2017.

The electronic records of all four cases were then reviewed and information regarding risk factors, presenting complaint, investigation findings, clinical course, and treatment plans and outcomes were collected and collated. The factors all patients had in common were the injection of drugs into the groin in the presence of a sinus tract from previous heavy intravenous drug use, localised pain and erythema, raised inflammatory markers (Table 1) and a relatively long duration until control of infection (Table 2).

Radiological imaging findings were abnormal in all patients with either an extravascular soft tissue collection in the groin evident or an occlusive deep vein thrombosis of the femoral deep veins. In three patients, *Actinomyces* spp. was isolated from blood culture, one on two separate occasions, and in the remaining patient *Actinomyces* spp. was isolated from soft tissue and endovascular specimens collected during surgical debridement. Complications of infection included one patient with life-threatening vascular rupture and haemorrhage, and two patients with evidence of septic pulmonary emboli developing during treatment. Therapeutic anticoagulation was initiated upon identification of the DVT in three patients and following Doppler ultrasound confirmed propagation of the deep vein thrombus and chest imaging suggested a new pulmonary infarct in the final patient. As *Actinomyces* spp. was not recurrently isolated, the possibility of infective endocarditis was not investigated with transthoracic echocardiogram.

Empirical antibiotics for all patients primarily targeted *Staphylococcus aureus* with flucloxacillin and vancomycin being prescribed. Failure to improve on these antibiotics resulted in initial broadening of antibiotic spectrum until the causative organisms were identified. Isolation of companion bacteria was common with *Micrococcus* spp, *Peptoniphilus* spp, and *Enterobacter cloacae* complex also being identified (Table 2). Time from specimen collection to identification of *Actinomyces* spp. ranged from 3 to 9 days.

All patients were treated with prolonged courses of antibiotics in association with anticoagulation for DVT. Intravenous penicillin was prescribed as initial treatment for at least 2 weeks followed by a prescribed 3-month course of either clindamycin or amoxicillin, with a planned review prior to cessation of antibiotics. In one case, oral ciprofloxacin was used instead of intravenous penicillin as intravenous access was unable to be secured. Drug side effects occurred with one episode of acute tubular necrosis and one of drug-induced hepatitis, both requiring modification of the antibiotic regimen. None of the four patients attended for review at the end of therapy and so the degree of compliance with the oral antibiotic therapy post-discharge is not known. However, all have had subsequent contact with the health care system for unrelated issues and are documented to have survived.

## Discussion

*Actinomyces* spp. can cause severe infections that are well recognised in cervicofacial and pelvic syndromes, but have not commonly been described as an opportunistic pathogen in PWID. A study published in 1995 comparing bacteriology of soft tissue abscesses in PWID reported isolation of *Actinomyces* spp. in 16% of cases with *Actinomyces odontolyticus* being the predominant pathogen [5]. Interestingly, there has been very little published work exploring *Actinomyces* spp. infection in PWID since then. A literature review of infections with *Actinomyces* spp. due to intravenous drug use identified eight case reports; two cases of septic emboli

**Table 1** Patient demographic and clinical information of presentation

| Patient | Age | Gender | Presenting complaint | Symptomatic prior to presentation (days) | Presence of sinus tract | Temperature > 38 °C | C-reactive protein (mg/L) | White blood cell count |
|---|---|---|---|---|---|---|---|---|
| 1 | 44 | Male | Groin pain and erythema | 7 | Yes | No | 80 | 12.8 × 109 |
| 2 | 36 | Female | Groin pain, erythema and chills | 6 | Yes | Yes | 208 | 6.5 × 109 |
| 3 | 39 | Female | Groin pain, erythema and lethargy | 3 | Yes | Yes | 243 | 11.7 × 109 |
| 4 | 35 | Female | Whole leg swelling and erythema | 6 | Yes | Yes | 79 | 5.7 × 109 |

**Table 2** Investigations, complications and management

| Patient | Duration of admission | Complication of infection | Specimen | Species | Time to identification | Co-isolate from same specimen | Empirical antibiotics | Targeted intravenous antibiotics | Discharge antibiotics |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 14 days (plus 23 days with hospital in the home) | Required surgical debridement<br>Acute interstitial nephritis from β-lactam | Endovascular tissue | *A. turicensis* | 5 days | Micrococcus spp | Piperacillin/tazobactam<br>Vancomycin | Benzyl penicillin | Clindamycin |
| 2 | 11 days | Pulmonary septic emboli<br>Pulmonary wedge infarct<br>Drug-induced hepatitis | 1 of 3 blood cultures | *A. turicensis* | 9 days | Unidentified Gram-positive cocci<br>*Peptoniphilus asaccharolyticus* | Flucloxacillin<br>Gentamycin changed to ceftriaxone<br>Metronidazole<br>Vancomycin | Benzyl penicillin | Amoxicillin/clavulanic changed to clindamycin |
| 3 | 8 days | Life-threatening haemorrhage from common femoral vein<br>Septic pulmonary emboli | 2 of 3 blood cultures | *A. odontolyticus* | 3 days | *Enterobacter cloacae* complex | Flucloxacillin changed to piperacillin/tazobactam<br>Vancomycin changed to piperacillin/tazobactam | Ciprofloxacin | Amoxicillin |
| 4 | 10 days (plus 10 days with hospital in the home) | Persistent leg swelling | 1 of 2 blood cultures | *A. turicensis* | 5 days | Nil | Flucloxacillin | Benzyl penicillin | Amoxicillin |

secondary to DVT [6, 7]; three cases of infective endocarditis [8–10]; two cases of soft tissue abscesses [11, 12] and an isolated case of a prosthetic joint infection [13]. The difficulty in isolating *Actinomyces* spp. is highlighted in several case series reporting upwards of 40% of cases being culture negative but *Actinomyces* spp. being identified on histological examination based on characteristic morphology [3]. Furthermore, as *Actinomyces* spp. is a fastidious relatively slow-growing organism, culture techniques may require specific culture conditions, and so clinical suspicion and communication to the laboratory must be present to isolate *Actinomyces* spp. from tissue specimens [14, 15].

In this case series, we describe four PWID in whom *Actinomyces* spp. was isolated from sterile site specimens. Of note, despite *Actinomyces israelii* being the most commonly described *Actinomyces* pathogen reported in the literature, we isolated *Actinomyces turicensis* in three of four patients. This discrepancy may reflect anatomical distribution with *Actinomyces israelii* being more dominant in the oropharynx and *Actinomyces turicensis* more prominent in the urogenital region [15]. Whilst *Actinomyces* spp. from skin may contaminate blood culture specimens, it was very likely to be the primary pathogen in at least three of the four of our cohort as it was isolated from tissue in Patient 1, isolated on two occasions in Patient 3 and was the only organism isolated in Patient 4.

Treatment was challenging due to initial empirical antibiotics focussing on *Staphylococcus* spp., delay in microbiological identification of *Actinomyces* spp., and potentially life-threatening complications of both infection and treatment. There were a number of common features uniting these patients that may be clinically useful in predicting patients in whom *Actinomyces* spp. should be considered. (1) All patients predominantly inject through a sinus into the groin. Given the relative risk of anaerobic and Gram-negative infection in the anatomical location close to the perineal region, as well as the moist environment of the sinus, consideration should be given to empirical antibiotic selection with spectrum beyond *Staphylococcus aureus*. (2) All patients had a relatively subacute presentation with localised pain and general lethargy symptoms occurring for 3–7 days prior to presentation but with definitive signs of infection on examination and on biochemical

parameters. No patients were describing severe rigors and were all haemodynamically stable.

Routine antimicrobial susceptibility testing on these isolates was not undertaken as *Actinomyces* spp. are reliably sensitive to penicillins. Alternative options in penicillin allergy are clindamycin, except in the case of *Actinomyces urogenitalis*, or tetracyclines [16]. Ciprofloxacin has performed poorly against *Actinomyces* spp. in in vitro studies [17]; however, there is documented evidence of clinical use of ciprofloxacin in refractory cases with good effect [18, 19]. Recommended duration of treatment is unclear; successful outcomes have been reported in early or mild infection with 3-month courses [20]. In our cohort, all patients were prescribed 3 months of antibiotics. All four patients were lost to follow-up; however, none presented with relapse suggesting successful treatment with 3 months or less of antibiotics.

Complications to monitor for include septic emboli in the presence of DVT, invasive infection with local vessel rupture, drug side effects and issues with adherence and completion of prescribed medical care. Furthermore, case reports have described Actinomyces-infective endocarditis in PWID [8–10].

In summary, *Actinomyces* spp. infections are uncommon and often prove difficult to diagnose and manage. Evidence of infection associated with an injecting sinus tract into the femoral vessels, in combination with a relatively subacute course should raise concern for severe *Actinomyces* spp. infection characterised by bloodstream infection, DVT, septic pulmonary embolus and vascular rupture. Given the relative difficulty in isolating and identifying *Actinomyces* spp., empirical treatment may be warranted in this cohort.

## Compliance with ethical standards

**Conflict of interest** The authors have no conflict of interest to declare.

## References


1. Wong VK, Turmezei TD, Weston VC. Actinomycosis. BMJ. 2011;343:d6099.
2. Holm P. Studies on the aetiology of human actinomycosis. Acta Pathol Microbiol Scand Suppl. 1951;91:172–3.
3. Bonnefond S, Catroux M, Melenotte C, Karkowski L, Rolland L, Trouillier S, et al. Clinical features of actinomycosis: a retrospective, multicenter study of 28 cases of miscellaneous presentations. Medicine (Baltimore). 2016;95(24):e3923.
4. Bing AU, Loh SF, Morris T, Hughes H, Dixon JM, Helgason KO. *Actinomyces* species isolated from breast infections. J Clin Microbiol. 2015;53 10:3247–55.
5. Summanen PH, Talan DA, Strong C, McTeague M, Bennion R, Thompson JE Jr, et al. Bacteriology of skin and soft-tissue infections: comparison of infections in intravenous drug users and individuals with no history of intravenous drug use. Clin Infect Dis. 1995;20(Suppl 2):279–82.
6. Weiand D, Barlow G. The rising tide of bloodstream infections with *Actinomyces* species: bimicrobial infection with *Actinomyces odontolyticus* and *Escherichia coli* in an intravenous drug user. Oxf Med Case Rep. 2014;2014 9:156–8.
7. Hoye S, Tolan D, Brownjohn A. Septic pulmonary embolism in an intravenous drug user. Acute Med. 2010;9(1):15–9.
8. Mehrzad R, Sublette M, Barza M. Polymicrobial endocarditis in intravenous heroin and fentanyl abuse. J Clin Diagn Res. 2013;7 12:2981–5.
9. Oh S, Havlen PR, Hussain N. A case of polymicrobial endocarditis due to anaerobic organisms in an injection drug user. J Gen Intern Med. 2005;20 10:958-.
10. Westling K, Lidman C, Thalme A. Tricuspid valve endocarditis caused by a new species of actinomyces: *Actinomyces funkei*. Scand J Infect Dis. 2002;34(3):206–7.
11. Sofianou D, Avgoustinakis E, Dilopoulou A, Pournaras S, Tsirakidis G, Tsakris A. Soft-tissue abscess involving *Actinomyces odontolyticus* and two *Prevotella* species in an intravenous drug abuser. Comp Immunol Microbiol Infect Dis. 2004;27(2):75–9.
12. Webb D, Thadepalli H. Skin and soft tissue polymicrobial infections from intravenous abuse of drugs. West J Med. 1979;130 3:200–4.
13. Zaman R, Abbas M, Burd E. Late prosthetic hip joint infection with *Actinomyces israelii* in an intravenous drug user: case report and literature review. J Clin Microbiol. 2002;40 11:4391–2.
14. Bennhoff DF. Actinomycosis: diagnostic and therapeutic considerations and a review of 32 cases. Laryngoscope. 1984;94(9):1198–217.
15. Clarridge JE III, Zhang Q. Genotypic diversity of clinical *Actinomyces* species: phenotype, source, and disease correlation among genospecies. J Clin Microbiol. 2002;40(9):3442–8.
16. Lerner PI. The lumpy jaw. Cervicofacial actinomycosis. Infect Dis Clin North Am. 1988;2(1):203–20.
17. Smith AJ, Hall V, Thakker B, Gemmell CG. Antimicrobial susceptibility testing of *Actinomyces* species with 12 antimicrobial agents. J Antimicrob Chemother. 2005;56(2):407–9.
18. Macfarlane DJ, Tucker LG, Kemp RJ. Treatment of recalcitrant actinomycosis with ciprofloxacin. J Infect. 1993;27(2):177–80.
19. Prashant N, Azuhairy A. Actinomycosis of distal phalanx twenty years after flap reconstruction of index finger: a case report. Malays Orthop J. 2018;12(1):48–50.
20. Atad J, Hallak M, Sharon A, Kitzes R, Kelner Y, Abramovici H. Pelvic actinomycosis. Is long-term antibiotic therapy necessary? J Reprod Med. 1999;44(11):939–44.