Polish Journal of Microbiology
2015, Vol. 64, No 3, 295–298

SHORT COMMUNICATION

Relapsing Bacteraemia due to *Corynebacterium striatum* in a Patient with Peripheral Arterial Disease

ANTEA TOPIĆ[1]*, ROK ČIVLJAK[1,2], IVA BUTIĆ[3], MARIJA GUŽVINEC[3] and ILIJA KUZMAN[1, 2]

[1] Department of Acute Respiratory Diseases, University Hospital for Infectious Diseases "Dr. Fran Mihaljević", Zagreb, Croatia
[2] University of Zagreb School of Medicine, Zagreb, Croatia
[3] Department of Microbiology, University Hospital for Infectious Diseases "Dr. Fran Mihaljević", Zagreb, Croatia

Submitted 28 December 2014, revised 11 April 2015, accepted 13 April 2015

Abstract

We describe the first reported case of *Corynebacterium striatum* (*C. striatum*) relapsing bacteraemia in a patient with peripheral arterial disease and proven *Corynebacterium* species colonization of a chronic foot ulcer, focusing on the difficulties in the management of the patient. We conclude that the optimal duration of the antibiotic treatment for relapsing *C. striatum* bacteraemia from a chronic ulcer should be 6 weeks together with surgical treatment.

Key words: *Corynebacterium striatum*, antibiotic treatment, peripheral arterial disease, relapsing bacteraemia, skin infection

Corynebacterium species other than *Corynebacterium diphteriae* are part of the normal flora of human skin and mucous membranes (Coyle and Lipsky, 1990). *Corynebacterium striatum* (*C. striatum*), a Gram-positive bacillus, was traditionally regarded to be a colonizer or a contaminant (Watkins *et al*., 1993). The first published case of *C. striatum* infection was in 1980 in an immunocompromised patient with pleuropulmonary lesions (Bowstead and Santiago, 1980). Since then, the frequency of *C. striatum* community acquired and nosocomial infections has increased significantly. Reported cases of *C. striatum* infections include a wide variety of different types of infections: bacteraemia (Dall *et al.*, 1989; Martin *et al.*, 2003; Tumbarello *et al*., 1994; Watkins *et al*., 1993), endocarditis (Marull and Casares, 2008; Mashavi *et al.*, 2006; Fernandez Guerrero *et al.*, 2013; Tran *et al*., 2012), central catheter infection (Martinez-Martinez *et al.*, 1997; Chen *et al*., 2012), meningitis (Hoy *et al.*, 1997; Weiss *et al.*, 1996), pleuropneumonia (Cowling and Hall, 1993; Martinez-Martinez *et al*., 1994; Renom *et al*., 2014; Severo *et al.*, 2014), osteomyelitis (Fernandez-Ayala *et al.*, 2001), arthritis (Cone *et al.,* 1998; Scholle, 2007; Westblade *et al*., 2014), and intrauterine infection (Martinez-Martinez *et al.*, 1997). Person to person transmission in intensive care units (Brandenburg *et al.*, 1996; Iaria *et al*., 2007; Leonard *et al*., 1994) and a number of skin infection cases like pyogenic granuloma, infected ischemic ulcer, breast abscess and a skin ulcer in an HIV patient (Bottone *et al*., 2010; Peiris *et al*., 1994; Stone *et al*., 1997; Watkins *et al*., 1993) have also been described. Although *C. striatum* has been linked to chronic ulcer infection and bacteraemia (Martin *et al.*, 2003; Martinez-Martinez *et al*., 1997), to the best of our knowledge, no patient with relapsing bacteraemia after appropriate antibiotic treatment has been reported. We present a case of a 61-y-old man with *C. striatum* relapsing bacteraemia, peripheral arterial disease and proven *Corynebacterium* species colonization of chronic foot ulcer, focusing on the difficulties in the management of the patient.

A 61-y-old man was admitted to the University Hospital for Infectious Diseases, Zagreb, Croatia in November of 2013 because of fever and a painless ulcer of his right foot stump. He had been sick for 14 d with fever and oral clindamycin was prescribed, but without effect. His medical history was remarkable for coronary heart disease (1 y earlier the patient underwent PCA stent insertion and was treated with beta-blocker, ACE-inhibitor, statin and antiplatelet drugs) and 10 y severe peripheral arterial disease with development of gangrene of right foot which resulted in amputation (at the level of the Chopart's joint). During the 6-months

* Corresponding author: A. Topic, Department of Acute Respiratory Diseases, University Hospital for Infectious Diseases "Dr. Fran Mihaljević", Zagreb, Croatia; **e-mail: antea.topic@gmail.com**

prior to the admission of the patient, the ulceration formed with sporadic non-purulent secretion followed by debridement, antibiotic treatment (oral clindamycin) and hyperbaric oxygen treatment with consecutive good healing. The patient was a heavy smoker.

On admission the patient was febrile (38°C), but in good general condition with blood pressure of 130/80 mmHg, pulse 90/min and respirations 18/min. On examination a 1.5 cm ulcer was present above his right foot stump with no surrounding erythema, tenderness or purulent drainage. Right inguinal lymph nodes were enlarged up to 2 cm, painless and elastic. The pulse of his dorsal artery of the foot was faint. Meningeal signs were negative, the patient had no signs of pharyngitis or oral mucosal ulcers, but his oral cavity was in poor condition. His chest and cardiac examination were unremarkable. The abdomen was soft and painless, the liver was palpable 2 cm below the right costal margin, while the spleen was not palpable.

Laboratory tests revealed an increased erythrocyte sedimentation rate (70 mm/h), C-reactive protein was 141.8 mg/l and the total white blood count was 9.0×10^9/l with mature neutrophilia. The red blood cell count was 4.49×10^{12}/l, haemoglobin was 131 g/l and the platelet count 133×10^9/l. The levels of sodium, potassium, chloride, urea nitrogen, creatinin, glucose, total proteins (albumin and globulin), total bilirubin, aminotransferases, lactate dehydrogenase and alkaline phosphatase were normal; only the level of gamma glutamyl transferase was increased at 184 IU/l. Routine coagulation tests were normal with no signs of disseminated intravascular coagulation, but the level of fibrinogen was 8.0 g/l. Urinalysis revealed no abnormalities. The serologic HIV test was negative. Chest X-ray and electrocardiogram were normal. Abdominal ultrasound examination revealed a mild hepatomegaly and small gallstones without inflammation of the gallbladder. Radiographs of the right leg showed no findings of osteomyelitis. Both transthoracic and transesophageal echocardiograms were normal.

Gram-stained smear of scrapings of the ulcerative lesion showed a presence of Gram-positive bacilli without polymorphonuclear leucocytes and the culture revealed *Corynebacterium* species. Four separate sets of blood culture taken at different times on admission grew *C. striatum* susceptible to vancomycin, imipenem, penicillin and amoxicillin-clavulanic acid. The strain was identified using the commercial system of cultivation BacT/ALERT (bioMerieux, France) and identification system VITEK 2 (bioMerieux, France). Upon identification, the strain was confirmed by an in house method of sequence analysis of the internal fragment of the 16S rRNA gene (Savini *et al.*, 2013), using no control, but comparing the final sequence to the one in the PubMed database. Antibiotic susceptibility was determined using E-test (bioMerieux, France) for penicillin, amoxicillin-clavulanic acid, clindamycin, imipenem and vancomycin following the recommendations of the European Committee for Antimicrobial Susceptibility Testing (EUCAST). E-test values revealed that all isolates were resistant only to clindamycin. The MIC_s were as follows: penicillin 0.12 mg/l, amoxicillin-clavulanic acid 0.19 mg/l, vancomycin 0,5 mg/l, imipenem 0.032 mg/l and clindamycin > 256 mg/l.

The initial antibiotic treatment with intravenous amoxicillin-clavulanic acid was continued for 15 d after the diagnosis was established. Defervescence occurred 1 d after the initiation of the treatment and surveillance cultures were negative on day 8. Seven days after the amoxicillin-clavulanic acid treatment ended (during which the patient developed a mild *Clostridium difficile* diarrhoea and was treated with oral metronidazole) recurrence of the fever occurred and two sets of repeated blood culture were positive for *C. striatum* of identical antibiotic susceptibility. Based on the clinical presentation and positive blood culture, intravenous vancomycin was started and after clinical improvement of the patient, was continued for 15 d. The patient fully recovered and was discharged from the hospital with instructions of taking oral amoxicillin-clavulanic acid for another 4 weeks. During these 4 weeks, the patient also underwent surgical treatment (debridement) of the ulcer, which finally resulted in the healing of the ulcer of the right foot. During a 3 month follow up no fever was noted.

C. striatum, a coryneform bacteria usually considered a contaminant, is a non-sporulating, non-acid-fast pleomorphic gram-positive rod that is aerobic and facultatively anaerobic (Coyle and Lipsky, 1990). It was until recently that *C. diphteriae* was considered to be the only pathogen of the coryneform species. Today, besides *C. striatum*, other well known pathogens of the species include *Corynebacterium jeikeium*, *Corynebacterium urealyticum*, and *Corynebacterium amycolatum* (Funke *et al.*, 1997). Most cases of *C. striatum* infection occurred either in immunocompromised patients or patients whose skin barrier integrity was broken, rather than in previously healthy persons, because of *C. striatum*'s low adhesive properties and low pathogenicity. Neither toxin nor other virulence factors explain the transmission from contamination to infection (Watkins *et al.*, 1993). The number of reported cases of diseases generated by *C. striatum* in the past few decades, and especially in the last couple of years, has been on the rise due to the improvement of microbiological techniques and the survival of patients with underlying diseases. *C. striatum* bacteraemia is a rare event and is scarcely documented in literature (Chen *et al.*, 2012; Dall *et al.*, 1989; Martin *et al.*, 2003; Martinez-Martinez *et al.*, 1997; Tumbarello *et al.*, 1994; Watkins *et al.*, 1993). Associated

conditions include diabetes, cirrhosis, chronic renal failure, trauma, surgery and malignancy.

The case we have described is the first reported case of a relapsing bacteraemia in a patient with a proven source of infection (in this instance a chronic foot ulcer) despite appropriate treatment. Several factors promoted the risk of *C. striatum* infection; the presence of a foot ulcer as a result of a compromised peripheral arterial circulation, age, and previous antibiotic treatment. As has previously described (Leonard *et al.*, 1994), we also presume that, in our patient, selective pressure due to a prior antibiotic consumption favoured the overgrowth of *C. striatum*.

Corynebacteria are common skin and culture media contaminants, and discrimination between colonization and infection is, in some cases, difficult. In our case, the presence of four consecutive blood cultures positive only for. *C. striatum* suggests that this microorganism was the likely pathogen. Although the *C. species* cultivated from the foot ulcer was not identified to species level, because it was regarded as a contaminant, the skin-circulation route is most likely. Some authors (Martin *et al.*, 2003) have demonstrated by molecular techniques (PCR) identical strains of *C. striatum* from the skin and the bloodstream in a patient with peripheral arterial disease, confirming the entry of the bacterium trough the skin to the circulation. In our case, as a colonizer of the patient's skin, *C. striatum* established a *de novo* bacteraemia despite antibiotic treatment. Probable causes of the relapsing bacteraemia are a (too) short antibacterial treatment, choice of antibiotics, and vasculopathy.

The optimal duration of antibiotic treatment for. *C. striatum* bacteraemia is not known (Fernandez-Roblas *et al.*, 2009; Martinez-Martinez *et al*., 1996), but the clinical course of the infection in the presented patient (recurrence of fever and bacteraemia) suggests a need for a prolonged antibiotic treatment (we recommend 6 weeks) together with surgical treatment. If aggressive debridement is performed earlier, we presume that much shorter course of antibiotic treatment may be sufficient.

In conclusion, this case highlights the growing importance of *C. striatum* as a serious pathogen and the fact that consecutive positive blood cultures for corynebacteria, and *C. striatum* in particular, should never be overlooked.

Literature

Bottone E.J., M. Fabbri and A. Ashraf. 2010. *Corynebacterium striatum*: Chronic infection of a cutaneous ulcer in a patient with AIDS. *Rev. Infect.* 1: 104–109.

Bowstead T.T. and S.M. Santiago. 1980. Pleuropulmonary infection due to *Corynebacterium striatum*. *Br. J. Dis. Chest.* 74: 198–200.

Brandenburg A.H., A.Van Belkum, C. Van Pelt, H.A. Bruining, J.W. Mouton and H.A. Verbrugh. 1996. Patient-to-patient spread of a single strain of *Corynebacterium striatum* causing infections in a surgical intensive care unit. *J. Clin. Microbiol.* 34: 2089–2094.

Chen F.-L., P.-R. Hsueh, S.-O. Teng, T.-Y. Ou and W.-S. Lee. 2012. *Corynebacterium striatum* bacteremia associated with central venous catheter infection. *J. Microbiol. Immunol. Infect.* 45: 255–258.

Cone L.A., N. Curry, M.A. Wuestoff, S.J. O'Connell and J.F. Feller. 1998. Septic synovitis and arthritis due to *Corynebacterium striatum* following an accidental scalpel injury. *Clin. Infect. Dis.* 27: 1532–1533.

Cowling P. and L. Hall. 1993. Corynebacterium striatum: a clinically significant isolate from sputum in chronic obstructive airways disease. *J. Infect.* 26: 335–336.

Coyle M.B. and B.A. Lipsky. 1990. Coryneform bacteria in infectious diseases: clinical and laboratory aspects. *Clin. Microbiol. Rev.* 3: 227–246.

Dall L., W.G. Barnes and D. Hurford. 1989. Septicaemia in a granulocytopenic patient caused by *Corynebacterium striatum*. *Postgrad. Med. J.* 65: 247–248.

Fernandez-Ayala M., D.N. Nan and M.C. Farinas. 2001. Vertebral osteomyelitis due to *Corynebacterium striatum*. *Am. J. Med.* 111: 167.

Fernandez-Roblas R., H. Adames, N.Z.

Martin-De-Hijas, D.G. Almeida, I. Gadea and J. Esteban. 2009. *In vitro* activity of tigecycline and 10 other antimicrobials against clinical isolates of the genus *Corynebacterium*. *Int. J. Antimicrob. Agents* 33: 453–455.

Fernandez Guerrero M.L., I. Robles, C. Nogales Mdel and D. Nuevo. 2013. *Corynebacterium striatum*: an emerging nosocomial drug-resistant endocardial pathogen. *J. Heart Valve Dis.* 22: 428–430.

Funke G., A. Von Graevenitz, J.E. 3rd Clarridge and K.A. Bernard. 1997. Clinical microbiology of coryneform bacteria. *Clin. Microbiol. Rev.* 10: 125–159.

Hoy C.M., K. Kerr and J.H. Livingston. 1997. Cerebrospinal fluid-shunt infection due to *Corynebacterium striatum*. *Clin. Infect. Dis.* 25: 1486–1487.

Iaria C., G. Stassi, G.B. Costa, C. Biondo, E. Gerace, A. Noto, S.G. Spinella, A. David and A. Cascio. 2007. Outbreak of multiresistant *Corynebacterium striatum* infection in an Italian general intensive care unit. *J. Hosp. Infect.* 67: 102–104.

Leonard R.B., D.J. Nowowiejski, J.J. Warren, D.J. Finn and M.B. Coyle. 1994. Molecular evidence of person-to-person transmission of a pigmented strain of *Corynebacterium striatum* in intensive care units. *J. Clin. Microbiol.* 32: 164–169.

Martin M.C., O. Melon, M.M. Celada, J. Alvarez, F.J. Mendez and F. Vazquez. 2003. Septicaemia due to *Corynebacterium striatum*: molecular confirmation of entry via the skin. *J. Med. Microbiol.* 52: 599–602.

Martinez-Martinez L., A. Pascual, K. Bernard and A.I. Suarez. 1996. Antimicrobial susceptibility pattern of *Corynebacterium striatum*. *Antimicrob. Agents Chemother.* 40: 2671–2672.

Martinez-Martinez L., A.I. Suarez, M.C. Ortega and R. Rodriguez-Jimenez. 1994. Fatal pulmonary infection caused by *Corynebacterium striatum*. *Clin. Infect. Dis.* 19: 806–807.

Martinez-Martinez L., A.I. Suarez, J. Rodriguez-Bano, K. Bernard and M.A. Muniain. 1997. Clinical significance of *Corynebacterium striatum* isolated from human samples. *Clin. Microbiol. Infect.* 3: 634–639.

Marull J. and P.A. Casares. 2008. Nosocomial valve endocarditis due to *Corynebacterium striatum*: a case report. *Cases J.* 1: 388.

Mashavi M., E. Soifer, D. Harpaz and Y. Beigel. 2006. First report of prosthetic mitral valve endocarditis due to *Corynebacterium striatum*: Successful medical treatment. Case report and literature review. *J. Infect.* 52: e139–141.

Peiris V., S. Fraser, C. Knowles, S. Norris and C. Bennett. 1994. Isolation of *Corynebacterium striatum* from three hospital patients. *Eur. J. Clin. Microbiol. Infect. Dis.* 13: 36–38.

Renom F., M. Gomila, M. Garau, M.D.C. Gallegos, D. Guerrero, J. Lalucat and J.B. Soriano. 2014. Respiratory infection by *Corynebacterium striatum*: epidemiological and clinical determinants. *New Microbes New. Infect.* 2: 106–114.

Savini V., G. Gherardi, M. Favaro, C. Fontana, R. Marrollo, A.V. Argentieri, G. Dicuonzo, P. Fazii and D. D'antonio. 2013. About a bloodstream *Corynebacterium striatum* isolate. *Folia Microbiol.* (*Praha*) 58: 451–453.

Scholle D. 2007. A spontaneous joint infection with *Corynebacterium striatum*. *J. Clin. Microbiol.* 45: 656–658.

Severo C.B., L.S. Guazzelli, M.B. Barra, B. Hochhegger and L.C. Severo. 2014. Multiple pulmonary nodules caused by *Corynebacterium striatum* in an immunocompetent patient. *Rev. Inst. Med. Trop São Paulo* 56: 89–91.

Stone N., P. Gillett and S. Burge. 1997. Breast abscess due to *Corynebacterium striatum*. *Br. J. Dermatol.* 137: 623–625.

Tran T.T., S. Jaijakul, C.T. Lewis, L. Diaz, D. Panesso, H.B. Kaplan, B.E. Murray, A. Wanger and C.A. Arias. 2012. Native valve endocarditis caused by *Corynebacterium striatum* with heterogeneous high-level daptomycin resistance: collateral damage from daptomycin therapy? *Antimicrob. Agents Chemother.* 56: 3461–3464.

Tumbarello M., E. Tacconelli, A. Del Forno, S. Caponera and R. Cauda. 1994. *Corynebacterium striatum* bacteremia in a patient with AIDS. *Clin. Infect. Dis.* 18: 1007–1008.

Watkins D.A., A. Chahine, R.J. Creger, M.R. Jacobs and H.M. Lazarus. 1993. *Corynebacterium striatum*: a diphtheroid with pathogenic potential. *Clin. Infect. Dis.* 17: 21–25.

Weiss K., A.C. Labbe and M. Laverdiere. 1996. *Corynebacterium striatum* meningitis: case report and review of an increasingly important *Corynebacterium* species. *Clin. Infect. Dis.* 23: 1246–1248.

Westblade L.F., F. Shams, S. Duong, O. Tariq, A. Bulbin, D. Klirsfeld, W. Zhen, S. Sakaria, B.A. Ford, C.-A.D. Burnham and C.C. Ginocchio. 2014. Septic arthritis of a native knee joint due to *Corynebacterium striatum*. *J. Clin. Microbiol.* 52: 1786–1788.