Spondylodiscitis Due to *Clostridium ramosum* Infection in an Immunocompetent Elderly Patient

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The first ever case of spondylodiscitis caused by *Clostridium ramosum* in an elderly immunocompetent patient has been reported. *C. ramosum* is usually an intestinal bacterium but may occasionally be isolated in clinical specimens as an opportunistic pathogen. This report shows that this anaerobic organism can cause bone tropism without there having been any contamination due to spinal surgery. The infection cleared after empirical therapy using intravenous amoxicillin and oral metronidazole.

CASE REPORT

A 74-year-old man came for consultation complaining of increasingly severe low lumbar pain from which he had been suffering for the preceding 6 weeks. While still at home, a major functional incapacity had developed and he was admitted to the university hospital. He was apyretic and had lost 9 kg. He had no particular antecedent except for a prostatic adenoma. A physical examination upon admission revealed a major rachidane syndrome with tenderness to percussion on the thoracic and lumbar vertebral column, bilateral tenderness over the lumbar region, and low back sensitivity. He had no sensorimotor deficit or neurological complications. Respiratory, cardiovascular, gastrointestinal, and neurological examinations were normal. A rectal examination indicated a moderate prostatic adenoma. Laboratory investigations revealed an erythrocyte sedimentation rate of 87 mm/h, a C-reactive protein value at 166 mg/liter, and a white blood cell count of $11.6 \times 10^9$ cells/liter with 75% neutrophils. Prostatic specific antigen was at 166 mg/liter, and a white blood cell count of $11.6 \times 10^9$ cells/liter with 75% neutrophils. Prostatic specific antigen was normal. Normal thoracolumbar spinal X rays revealed collapse of the anterior superior part of body of the 12th thoracic (T-12) and first lumbar (L-1) vertebrae with loss of disk space. Bone scintigraphy revealed an elevated fixation in T-12 and L-1. Results of magnetic resonance imaging (MRI) were consistent with an advanced spondylodiscitis situated on the T-12 and L-1 vertebrae with a paravertebral abscess and extra-osseous soft tissue impinging on the epidural space (Fig. 1). Urine and blood cultures were negative. Diskal puncture aspiration fluid was sent to the laboratory by means of a blood culture transport medium. A Gram stain of the substance obtained from the aspiration revealed abundant leukocytes with a few gram-variable rods. After 48 h at 37°C, anaerobic cultures performed on blood agar (Biomérieux, Marcy l’Etoile, France) in an anaerobic jar with a GENbox anaerobic system (Biomérieux) yielded a pure culture of smooth gray, nonhemolytic colonies with irregular borders. The aerobic cultures remained negative after 5 days. Gram staining of the anaerobic culture demonstrated thin, long gram-negative or gram-variable rods without spores (Fig. 2). The isolate was nonmotile, did not produce catalase or indole, but was able to ferment maltose, glucose, saccharose, cellobiose, mannose, raffinose, salicin, lactose, sucrose, and mannitol. The API 20A identification strip (Biomérieux) profile obtained (5735722) did not identify the isolate as *Clostridium ramosum* for certain. Due to variability of the biochemical reactions, two possibilities were suggested by our identification kit: *C. ramosum* and *Actinomyces israelii*. The identity of the isolate was subsequently confirmed by the sequence of the 16S rRNA gene. A PCR using universal 16S ribosomal DNA primers 27f (5' - GTGCTCCAGAGATTTGATCCTGCTGATG-3') and 1492r (5' - TACGGATCTACGGTGACGCAAG-3') was performed. PCR products were automatically sequenced (Genome Express, Meylan, France). The completed sequence was compared to sequences deposited in the GenBank using the BLAST (Basic Local Alignment Search Tool) server (http://www.ncbi.nlm.nih.gov/BLAST/) (3). Analysis of the sequence gave the maximum identity (99%) with the 16S ribosomal DNA sequence of *C. ramosum* (12). Before confirmation of bacteriological results, empirical antibiotic therapy had already been started using 1 g of intravenous amoxicillin three times daily and 500 mg of oral ciprofloxacin twice daily. Then, after isolation of *C. ramosum*, antibiotic susceptibility tests were determined with the E-test (AB Biodisk, Solna, Sweden) (10). The MICs of most antimicrobial agents tested, except for that of ciprofloxacin, were low for the organism. Values (in milligrams/liter) were as follows: penicillin, 0.0125; amoxicillin, 0.032; amoxicillin-clavulanic acid, 0.032; cefotaxime, 0.19; metronidazole, 0.25; ciprofloxacin, >32; clindamycin, 8. The therapy was therefore changed to intravenous amoxicillin (2 g three times daily for 4 weeks) and oral metronidazole (500 mg three times daily for 4 weeks). The back pain was relieved within 1 week, and after 2 weeks of treatment, hematological and biochemical parameters returned to normal levels. After 1 month of total immobilization, the patient was transferred to a rehabilitation unit. He was discharged with an oral therapy of amoxicillin (2 g three times...
daily) and metronidazole (500 mg three times daily) for 4 weeks. The follow-up MRI 2 months after discharge showed destruction of the T-12 vertebral body and disappearance of the T-12–L-1 inter somatic space consistent with cicatrization of the vertebrae. Inflammatory markers were normal. The patient was back home 2 months after his admission to the hospital. The resolution of the disease was complete. He had no severe functional sequelae or neurological deficit. He was autonomous and independent. No further investigation was undertaken to determine the origin of the disease as unfortunately the patient died in an accident a few days later.

Bacteria of the genus *Clostridium* are ubiquitous in nature and can be found in soil, decaying vegetation, and marine sediment or in the intestinal commensal flora of humans, other vertebrates, or insects (2). Clostridia represent an important part of the anaerobic microflora of humans (2, 29). They have the potential of causing both endogenous and exogenous infections. They are also commonly recovered from infected sites but usually as a component of polymicrobial flora. They may act synergistically with other pathogens, making their role in pathogenesis difficult to establish (2, 29). Apart from the diseases caused by toxins produced by *Clostridium tetani, Clostridium botulinum, Clostridium perfringens,* or *Clostridium difficile,* the main diseases caused by *Clostridium* spp. are bacteremia, intra-abdominal infections, female genital tract infections, pleuropulmonary infections, and soft tissue infections (2). *C. perfringens* is the *Clostridium* species most frequently isolated from blood culture, and *Clostridium septicum* is the *Clostridium* species most frequently isolated from intra-abdominal specimens (2, 4, 5, 16). Bone infection is uncommon: to the best of our knowledge, *C. difficile* is the bacterium most frequently isolated from bone specimens (4, 5, 14, 16, 26). However, no more than six cases of clearly established osteomyelitis due to *Clostridium* spp. have been reported (14). As is true for other endogenous infections due to anaerobes, the development of clostridial disease is usually associated with common predisposing factors, including underlying illness such as cancer, leukemia, and diabetes mellitus (2).

*Clostridia* are gram-positive, spore-forming anaerobic rods, but many strains appear to be gram negative or gram variable. Three clostridial species (*C. ramosum, Clostridium innocuum,* and *Clostridium clostridioforme*), i.e., the so-called RIC group may pose a problem for the routine diagnostic laboratory. This group can be easily be misidentified as belonging to other genera because of factors such as Gram stain variability, lack of spores, and atypical clostridial colonial morphology. Loss of gram-positive appearance occurs most frequently in direct stains of clinical material, or in cultures after inoculation for extended periods, or in species showing terminal spores (1). In our case, the Gram stain of the substance obtained from the aspiration revealed leukocytes and a few gram-variable rods. The typical terminally located spores are hard to detect. This direct examination led to diagnosis problems and hindered the bacteriologist. In the same way, the clostridial species of the RIC group present a similar aspect on blood agar. Furthermore, a publication had evaluated different identification kits (Biomérieux and Innovative Diagnostic Systems) for their ability to identify these clostridial species. Only 70% of *C. ramosum* isolates were identified by our kit (1). The anaerobe iden-
C. ramosum is one of the Clostridium species that is often isolated from children's stool samples. This microorganism resides in the lower intestinal tracts of humans as part of the flora (2, 24). It has also been cultured from gastrointestinal abscesses and ear infections. It has rarely been associated with severe infections or bacteremia (7, 27, 29). Since many other Clostridium species and nonclostridial bacteria are often present in such infections, it is difficult to assess its pathogenic role. The number of positive cultures for C. ramosum is probably underestimated. The organism may easily be missed in anaerobic cultures, because it usually stains as gram negative rather than gram positive, and the typical terminally located spores are often difficult to detect. However, there have been a few reports of unusual infections with C. ramosum as the sole microorganism isolated (Table 1) (8, 18, 20, 21, 29). These infections occur mainly in immunocompromised hosts (29). To the best of our knowledge, this report describes the first ever case of an infection caused by Clostridium spp. situated on the spine without preexisting factors. Spondylitis and spondylodiscitis due to anaerobic bacteria are rarely reported. In the literature, cases of infective discitis have been published on 12 previous occasions, each one associated with an immunocompromised status (6, 9, 11, 13, 15, 19, 23, 25, 28; I. Z. Abolnik, J. V. Eaton, D. J. Sexton, Letter, Clin. Infect. Dis. 21:694–695, 1995; J. Esteban, R. Calvo, M. Pardeiro, F. Soriano, Letter, J. Hosp. Infect. 39:77–78, 1998; F. Retornaz, P. H. Roche, V. Seux, C. Caperan, A. Touta, and J. Soubeyrand, Letter, Rev. Med. Int. 22:199–200, 2001). The source of the isolate is not known. The patient described here was elderly but was not immunocompromised and did not have any skin or ear infections. The origin of infection was probably the patient’s own digestive tract. C. ramosum is able to produce immunoglobulin A1 and A2 proteases, which may facilitate mucosal penetration (17, 24). Mucositis (oral ulceration, atrophy, or edema) is a common portal of entry, and the bacterium may invade the epithelium, reaching the vascular subcutaneous tissue. This may enhance intravascular invasion with C. ramosum and favor secondary infections (29). However, the diagnosis could not be confirmed because the patient died before gastrointestinal investigation could be carried out.

The results of the E-test contributed moderately to differentiate the C. ramosum infection from other clostridia. Penicillin shows excellent activity against clostridia. However, resistance to penicillin is common with C. ramosum (20% of cases); this species produces β-lactamases (penicillinases) that are induced by β-lactam antibiotics (1, 2, 22). C. ramosum was susceptible to penicillin in the present study. A number of clostridial species are frequently resistant to clindamycin, especially C. ramosum and C. innocuum (1). In this report C. ramosum was resistant to clindamycin. Chloramphenicol, pipercillin, metronidazole, imipenem, and combinations of β-lactam drugs with β-lactam inhibitors are active against all strains of clostridia with only a few exceptions. Clostridia show variable resistance to cephalosporins and tetracyclines. Anaerobes are usually considered to be resistant to quinolone agents (2).

To summarize, C. ramosum is an intestinal bacterium which is only occasionally isolated in clinical specimens, and this is the first ever clinical report of a case of spondylodiscitis due to C. ramosum in an immunocompetent patient. It reveals the pathogenic potential of this bacterium to cause bone infection.

### REFERENCES


