Journal of Medical Microbiology (2008), **57**, 236–239 DOI 10.1099/jmm.0.47578-0

Case Report

Clostridium butyricum sepsis in an injection drug user with an indwelling central venous catheter

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Received 17 August 2007
Accepted 9 October 2007

Clostridium novyi has been associated with a large outbreak of severe infections in injection drug users. A case of bacteraemia with *Clostridium butyricum* in an injection drug user is reported. During treatment for *Staphylococcus aureus* osteomyelitis, the patient used an indwelling central venous catheter to inject cocaine. He was admitted with *C. butyricum* sepsis that responded to broad spectrum antibiotics, including vancomycin. Local investigation for other cases was unrevealing; however, growth of an unusual pathogen in clinical specimens should be investigated as it may represent a sentinel event with public health implications.

Introduction

The incidence of bacterial infections is higher in persons who inject illicit drugs intravenously (Cherubin & Sapira, 1993). Typical organisms include *Staphylococcus aureus*, various streptococci, aerobic Gram-negative rods and various anaerobic bacteria (Cherubin & Sapira, 1993). In 2000, a large outbreak of severe skin and soft-tissue infections with systemic symptoms in injection drug users was investigated in Scotland, England and Ireland (Jones *et al.*, 2002; McGuigan *et al.*, 2002). The suspected aetiological agent was *Clostridium novyi* type A and it was believed to have arisen from contaminated street heroin. The extent and severity of this outbreak led to recommendations for vigilance in order to recognize clustered or severe infections in injection drug users that might alert public health officials to potential outbreaks. In July of 2006 we recognized an unusual clostridial pathogen in an injection drug user at our hospital.

Case report

In June of 2006, a 47-year-old man with a history of rheumatoid arthritis and injection drug use was hospitalized 2 weeks after stepping on a piece of glass that penetrated his right foot. Computed tomography revealed a right foot abscess with probable osteomyelitis of the first metatarsal head. The abscess was surgically drained and cultures grew meticillin-susceptible *S. aureus* (MSSA). He was treated with continuous intravenous infusion of 12 g nafcillin per day during hospitalization and was discharged to complete a 6 week course of this antibiotic at home. One week after discharge he developed a diffuse, confluent, erythematous rash consistent with a drug eruption. His central venous catheter site was without signs of infection. He was switched to 1 g intravenous vancomycin twice daily and sent home.

Three days later the patient injected cocaine through his central venous catheter and reported immediately feeling 'hot and dizzy'. He proceeded to infuse his regularly scheduled vancomycin dose. Throughout the afternoon he continued to have episodes of dizziness and disorientation. In a moment of confusion he pulled out his central venous catheter. When symptoms worsened that night he called a friend who brought him to the emergency department.

His past medical history was significant for hepatitis C virus infection and rheumatoid arthritis, for which he was treated with 100 mg azathioprine twice daily. In 2004 he had septic arthritis of the left sternoclavicular joint with associated osteomyelitis secondary to MSSA. He denied alcohol use, had a 30 pack per year history of smoking, and admitted to a history of sporadic injection drug use with cocaine. He used a commercially available nutritional supplement containing creatine phosphate but denied probiotic use. A review of systems was positive for the presenting symptoms and, in addition, he complained of bilateral lower back pain that was chronic.

On presentation, he appeared moderately ill but was afebrile (35.7 °C). The remainder of his vital signs were as

Abbreviations: CDC, Centers for Disease Control and Prevention; MSSA, meticillin-susceptible *Staphylococcus aureus*; UCH, University of Colorado Hospital.

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follows: heart rate 111 beats min^{-1}, blood pressure 85/43 mmHg (his discharge blood pressure 1 week prior to this was 123/81 mmHg), respiratory rate 17 breaths min^{-1} and room air oxygen saturation by pulse oximetry 95 %. His lungs were clear, heart tachycardic but regular and without murmurs, and his abdominal exam benign. His back exam was normal without lumbar redness, warmth, swelling or tenderness. His right foot had a clean-appearing open post-surgical wound with minimal surrounding erythema. Skin was without rashes or lesions and there were no signs of infection at his recent central venous catheter insertion site. His initial white blood cell count was 15 300 cells μl^{-1} (up from 5700 cells μl^{-1} 2 days prior to this) with 14 g haemoglobin dl^{-1} and 301 000 platelets μl^{-1}. His blood urea nitrogen and creatinine were newly elevated at 24 mg dl^{-1} and 1.6 mg dl^{-1}, respectively, and he had a mild non-anion gap metabolic acidosis with 19 mmol HCO_3 l^{-1} and an anion gap of 12. Venous lactate was 3.9 mmol l^{-1}. An EKG showed sinus tachycardia and a chest roentgenogram was normal.

He was treated aggressively with intravenous hydration and admitted to the medical intensive care unit. He required blood pressure support with intravenous noradrenaline and vasopressin, and was started empirically on 2 g cefepime every 12 hours, 1 g vancomycin every 12 hours and 500 mg levofloxacin once daily. He responded favourably to these measures and was weaned off vasopressors within 24 h. He remained afebrile and was transferred to a medical floor continuing the same antibiotics. His white blood cell count increased to 29 300 cells μl^{-1} during the first 72 h of hospitalization. Two blood cultures drawn on admission grew anaerobic Gram-positive rods, later identified as *Clostridium butyricum* using Electronic RapID Compendium software, RapID ANA II positive rods (Remel), with a probability of greater than 99.9 %. Two follow-up blood cultures obtained on the third hospital day grew *C. butyricum*. On the sixth hospital day blood cultures were sterile.

The patient remained clinically stable, and cefepime and levofloxacin were discontinued on the fifth hospital day. A test for antibodies against the human immunodeficiency virus was negative. Evaluation of the right foot by surgical consultants and using radiographs suggested improvement in the right foot infection without residual abscess. Transoesophageal echocardiography revealed no signs of infective endocarditis. Computed tomography of the abdomen and pelvis after the administration of oral and intravenous contrast showed no evidence of a gastrointestinal source of infection or lymphadenopathy but was suspicious for a prostatic abscess. Further evaluation, including prostate biopsy and culture, revealed no evidence of infection, and suggested that the reported abnormality represented a bladder diverticulum. Computed tomography of the lumbar spine showed no evidence of infection.

The patient continued to do well and was discharged to complete a 6 week course of vancomycin for his MSSA osteomyelitis. He was switched to oral levofloxacin for the last 2 weeks of therapy when his central venous catheter was removed secondary to continued injection drug use. This switch occurred 12 days after his last positive blood culture for *C. butyricum*. Outpatient colonoscopy was scheduled to rule out colonic malignancy as a source of his clostridial bacteraemia but the patient did not keep his appointment with gastroenterology. One year after the initial admission he is without evidence of recurrent infection.

In order to investigate the possibility of a local outbreak of clostridial infections in injection drug users secondary to contaminated drug we took the following steps. First we reviewed blood and abscess culture results at our institution from the prior 2 months. Second, we contacted the microbiology lab at the major teaching hospital in Denver, Colorado, the University of Colorado Hospital (UCH), to review recent culture results. Our institution, Denver Health and UCH provide the majority of care for the underserved population in the city of Denver. Third, we contacted our state health department, the Colorado Department of Public Health and Environment, to report our case and ask whether or not they had received other reports of severe infections in injection drug users in the state of Colorado. No other cases were identified in this manner. One month after our initial inquiry we reviewed culture results at our institution and spoke again with UCH and Colorado Department of Public Health and Environment. No other cases were identified.

Discussion

C. butyricum is a strictly anaerobic endospore-forming Gram-positive rod that is uncommonly reported as a human pathogen. It is a soil inhabitant in various parts of the world, has been cultured from the stool of healthy children and adults, and is common in soured milk and cheeses (Meng *et al.*, 1999; Schechter & Arnon, 1999). At least two prior cases of bacteraemia with *C. butyricum* have been reported in case series of clostridial bacteraemia (Haddy *et al.*, 2000; Rechner *et al.*, 2001). Two cases of polymicrobial peritonitis, including *C. butyricum* in paediatric patients, have been reported, and it is has been cultured from blood in the setting of neonatal necrotizing enterocolitis (Howard *et al.*, 1977; Gothefors & Blenkharn, 1978; Sturm *et al.*, 1980; Brook, 1995). Finally, *C. butyricum* appears to be one of the aetiological agents of type E infantile botulism and has been implicated in outbreaks of foodborne botulism (Aureli *et al.*, 1986; McCroskey *et al.*, 1986; Meng *et al.*, 1997; Chaudhry *et al.*, 1998; Fenicia *et al.*, 1999, 2002).

To the best of our knowledge *C. butyricum* has not been described as a pathogen in injection drug users. However, as a genus, *Clostridia* are known to cause infectious complications in injection drug users and have been cultured frequently from both street heroin and injection paraphernalia (Tuazon *et al.*, 1974). In the case presented

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here, the acute onset of symptoms and the persistence of the bacteraemia suggest the possibility of injection of contaminated drug or contaminated injection paraphernalia. An alternative source of *C. butyricum* bacteraemia seems unlikely in this case for at least two reasons. First, extensive evaluation for another source of infection was not revealing. Second, the patient was receiving intravenous infusions of vancomycin at home, an effective antibiotic for treatment of this infection. It is possible that the organism was misidentified by our anaerobic identification system, but this appears very unlikely based on the identification report (Table 1).

Chemical and infectious contamination of street drugs is known to occur (Hamilton *et al.*, 2000; Jones *et al.*, 2002; McGuigan *et al.*, 2002; CDC, 2005). It is interesting that *C. butyricum* spores are commercially available in Japan where they are used as a probiotic (Seki *et al.*, 2003; Shimbo *et al.*, 2005). We considered this a possible source in our case but felt it was very unlikely as the patient denied probiotic use. We believe it is more likely that our patient's syringe was heavily contaminated by spores of this bacterium from an environmental source, but we also considered the possibility of cocaine contaminated by *C. butyricum* spores. Unfortunately, the cocaine and injection paraphernalia were not available for evaluation.

Table 1. Results of the RapID II positive rods identification report for the organism cultured from blood identified as *C. butyricum*

Test	Result
URE	−
BLTS	−
aARA	+
ONPG	+
aGLU	+
bGLU	−
aGAL	+
aFUC	−
NAG	−
PO_4	−
LGY	−
GLY	−
PRO	−
PAL	−
ARG	−
SER	−
PYR	−
IND	−

aARA, α-L-Arabinoside; aFUC, α-L-fucoside; aGAL, α-D-galactoside; aGLU, α-D-glucoside; ARG, arginine-β-naphthylamide; bGLU, β-D-glucoside; BLTS, β-D-disaccharide; GLY, glycine-β-naphthylamide; IND, tryptophan; LGY, leucyl-glycine-β-naphthylamide; NAG, *N*-acetyl-β-D-glucosaminide; ONPG, β-D-galactoside; PAL, phenylalanine-β-naphthylamide; PO_4, phosphate; PRO, proline-β-naphthylamide; PYR, pyrrolidonyl-β-naphthylamide; SER, serine-β-naphthylamide; URE, urea.

In summary, we have presented a case of *C. butyricum* bacteraemia and sepsis in an injection drug user. To the best of our knowledge, this is the first such report. We suspect contamination of injection paraphernalia as the source, although this was unproven. Growth of unusual human pathogens in clinical specimens should be investigated thoroughly as it can represent a sentinel event with public health implications. Suspected illicit substance contamination, both infectious and non-infectious, should be considered a public health threat and surveillance for this possibility is warranted in the appropriate setting.

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