Gram-negative bacteremia and asplenia in a well 15-year-old girl

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A 15-year-old girl who had undergone a splenectomy at seven years of age for idiopathic thrombocytopenic purpura presented with a two-day history of fever, myalgia and headache. On examination, she was afebrile, did not appear toxic and no focus of infection was found. Her complete blood cell count showed a white blood cell count of $14 \times 10^9/\text{L}$ with 91% neutrophils, 4% monocytes and 5% lymphocytes; hemoglobin level of 145 g/L and platelet count of $372 \times 10^9/\text{L}$. Her serum electrolyte and creatinine levels were normal. Urine and blood cultures were obtained, and she was sent home without antibiotic therapy.

The urine culture grew mixed organisms suggestive of contamination, but Gram-negative bacilli grew in the aerobic blood culture vial (BACTEC 9240 Peds plus blood culture bottle, BD Diagnostics Inc, USA) after 45 h of incubation (Figure 1). The girl was, therefore, referred to the pediatric emergency department. Her fever, headache and myalgia had resolved. Physical examination again revealed a nontoxic female in no distress. Her temperature was 36.3°C, heart rate was 70 beats/min, respiratory rate was 16 breaths/min, blood pressure was 90/60 mmHg and oxygen saturation was 98% in room air. Aside from an abdominal scar, the physical examination was normal. Laboratory studies revealed a white blood cell count of $10.5 \times 10^9/\text{L}$ with 51% neutrophils, 4% band forms, 7% monocytes and 38% lymphocytes; hemoglobin level of 133 g/L and platelet count of $167 \times 10^9/\text{L}$. Red blood cell morphology was notable for 1+ Howell-Jolly bodies. C-reactive protein level was 1.1 g/L and erythrocyte sedimentation rate was 1 mm/h. Blood cultures were repeated. Because no obvious focus of infection was found and the patient appeared well, she was given a dose of intravenous ceftriaxone and was discharged to be reassessed in 24 h.

On the day the original blood culture vial grew Gram-negative bacilli, it was subcultured onto 5% sheep blood agar in CO₂, chocolate agar in CO₂, MacConkey agar in ambient air and CDC anaerobic blood agar under anaerobic conditions. Within 24 h, all agar incubated aerobically showed growth of Gram-negative bacilli, but the anaerobic media displayed no growth. The organism was not identified using the Gram-negative identification card on the VITEK 2 (bioMérieux

Figure 1) Gram-negative bacilli on Gram stain from the blood culture. Note single organisms throughout and chains in the centre and bottom left. Photo courtesy of Dr Nigrin

Canada Inc). A presumptive identification of *Acinetobacter* species was made two days later because of the biochemical characteristics (negative oxidase, indole and urease tests, positive catalase test and asaccharolytic profile) (1). Due to the atypical Gram stain appearance (smaller coccobacilli rather than larger coccobacilli and/or diplococci, typical of *Acinetobacter* species), the isolate was referred to the Alberta Provincial Laboratory for Public Health for further identification. The antimicrobial susceptibility was performed using an AST-GN10 card on the VITEK 2. The antimicrobial susceptibility results showed the following minimum inhibitory concentrations – ceftazidime 2 mg/L or lower, imipenem 4 mg/L or lower, piperacillin 8 mg/L or lower, trimethoprim/sulfamethoxazole 2/38 mg/L or lower, tobramycin 1 mg/L or lower and ciprofloxacin 1 mg/L or lower.

The patient was treated with a 14-day course of ciprofloxacin following the single dose of ceftriaxone; she remained asymptomatic. Two sets of blood cultures drawn before, and on day 4 of antibiotic therapy were negative. What organism was ultimately identified?

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The bacterial isolate was a small Gram-negative coccobacillus that could not be definitively identified by biochemical analysis at the Provincial Laboratory for Public Health. As per their current algorithm for identifying unusual, small Gram-negative coccobacilli, they performed cellular fatty acid analysis. The organism was identified as *Bordetella holmesii* using the results from both the cellular fatty acid profile and the biochemical analysis.

DISCUSSION

To our knowledge, this is the first case of *B holmesii* bacteremia in northern Alberta. This organism was first isolated in 1983 and formally named in 1995 (2). Although the epidemiology is not well defined, *B holmesii* has been described as a cause of bacteremia, endocarditis and respiratory illness. Bacteremia has been described in immunocompromised patients with diabetes, lymphoma, long-term steroid therapy, solid organ transplant or AIDS (2-8). In the largest case series (3) of 30 patients with *B holmesii* bacteremia, 85% were functionally or anatomically asplenic. Contamination of blood cultures with *B holmesii* is yet to be described, and seems unlikely in our case because asplenia is a well-recognized risk factor for *B holmesii* bacteremia. There have been two case reports (3,9) of *B holmesii* endocarditis complicating bacteremia. With regard to respiratory illness, *B holmesii* has been described as a cause of a pertussis-like syndrome with cough (100%), whoop (9%), post-tussive vomiting (26%) and coughing paroxysms (61%), noted in a case series (4,5) of 33 patients.

As in our case, the illness associated with *B holmesii* bacteremia is usually mild and nonspecific, with symptoms including headache (50%), chills (38%), vomiting (38%), cough (27%), a median temperature of 38.3°C at presentation and a median white blood cell count of $13.7 \times 10^9/L$ (10). However, hospital admission is common in the face of Gram-negative bacteremia in an immunocompromised host. To date, there have been no reports of death associated with *B holmesii* infection (3,9).

Laboratory identification of the organism may pose some difficulty. *B holmesii* is a slow-growing, Gram-negative, oxidase-negative, urease-negative and asaccharolytic organism (3,10). Unlike other *Bordetella* species, *B holmesii* has no oxidase activity, and unlike *Acinetobacter* species, it produces a brown soluble pigment (2,10,11). Our patient's bacteremia had resolved before administration of antimicrobials, and it seemed likely that she would have made an uneventful recovery even

without antibiotics. It is, therefore, possible that many cases of *B holmesii* bacteremia are not recognized. In theory, the treatment of *B holmesii* should be challenging given the potential for misidentification, the lack of established susceptibility breakpoints and the limited data on the efficacy of antimicrobials, but treatment failures are yet to be described despite the use of a wide variety of antimicrobials including aminoglycosides, macrolides and cephalosporins.

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