CASE REPORT

Burkholderia ginsengisoli bacteraemia: emergence of a novel pathogen

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SUMMARY

Burkholderia ginsengisoli is a non-pathogenic Gram-negative bacterium that ordinarily serves as a plant endosymbiont. We report the first case of human infection with *B. ginsengisoli* presenting as bacteraemia in a young man with severe Crohn's disease. Definitive identification of the pathogen could not be accomplished with conventional techniques and required DNA sequencing. The bacteraemia may have been related to ingestion of organic vegetables and compromised gastrointestinal mucosa, coupled with treatment with tumour necrosis factor α inhibitors. Although there are no standard antibiotics to treat this pathogen, we devised a successful treatment regimen.

BACKGROUND

We encountered a patient with severe Crohn's disease, treated with tumour necrosis factor α (TNF-α) inhibitors, who presented with unremitting Gram-negative sepsis. We were intrigued that the blood isolate had unusual growth characteristics for a Gram-negative rod and could not be identified by conventional techniques. Definitive identification by DNA sequencing revealed it to be *Burkholderia ginsengisoli*. Prior to our experience, *B. ginsengisoli* has only been recognised as a plant endosymbiont. We suspect that infection with this novel pathogen was facilitated by ingestion of organic vegetables and gastrointestinal mucosa that had been compromised by Crohn's disease. We further suspect that this may be an emerging pathogen, coupled with increasing use of immunomodulatory agents.

CASE PRESENTATION

We report here the first described case of *B. ginsengisoli* bacteraemia. The patient, a 34-year-old Caucasian man with severe Crohn's disease and short bowel syndrome presented with recurrent fevers. He had no history of drug abuse, congenital or cardiac valvular disease, dental caries or gingivitis. Crohn's disease was diagnosed in 2005 when he had a terminal ileal perforation requiring small bowel resection. Although his bowel was later reanastomosed, recurrent fistulae required further small bowel resections and later colectomy and ileostomy in 2009. Further small bowel resections were performed in 2011 and 2012, followed by cholecystectomy in 2013, ultimately resulting in short bowel syndrome, requiring a peripherally inserted central catheter (PICC) line for hydration.

Initially, this patient's Crohn's disease was treated with 6-mercaptopurine (1 mg/kg) and prednisone (30 mg) daily. In 2012, he was treated with adalimumab, maintained at 40 mg every 2 weeks. In 2014, he was begun on infliximab (5 mg/kg) every 8 weeks.

When the patient first developed fever and chills, he presented to an outside facility where he was hospitalised with blood cultures positive for a fastidious Gram-negative rod. He was treated with 7 days of piperacillin/tazobactam, before being discharged on a 5-day course of oral ciprofloxacin. He initially defervesced, however, when the fever returned a week later he presented to the Buffalo Veterans Administration emergency department. In the emergency department, the PICC line was removed. Physical examination revealed a thin male with a low-pitched grade 2/6 systolic ejection murmur at the apex. He had neither splenomegaly nor peripheral embolic lesions. An ileostomy bag was present in the right lower abdominal quadrant. Laboratory data included: leucocytes 5400 cells/mm^3 (61 neutrophils, 29 lymphocytes, 8 monocytes), haemoglobin 10.6 g/dL and serum creatinine 1.42 mg/dL. Urinalysis was unremarkable.

INVESTIGATIONS

One of two sets of admission blood cultures again grew a fastidious Gram-negative rod. Transoesophageal echocardiography detected a small hypermobile echodensity on the posterior mitral valve leaflet, suggestive of a vegetation. The bacterium was identified as a Gram-negative rod that was indole/oxidase negative. It did not grow on MacConkey agar, but appeared as cream-coloured colonies on chocolate agar. Since recurrent Gram-negative bacteraemia may occur in immunosuppressed states with disseminated strongyloidiasis, stool samples were investigated, which contained neither ova nor parasites. While no immediate investigation of the patient's enteric mucosa was undertaken, it had been inflamed on recent endoscopies.

DIFFERENTIAL DIAGNOSIS

Matrix-assisted laser desorption/ionisation time-of-flight (MALDI-TOF) mass spectrometry analysis, performed at the first institution he visited, identified the bacterium as a member of the *Burkholderia*, *Acinetobacter or Capnocytophagia* genus. For definitive identification, isolates from both hospitalisations were sent to the New York State Department of Health Laboratory, where bacterial DNA sequencing identified both blood culture isolates as *B. ginsengisoli*.

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TREATMENT

Accurate antimicrobial susceptibility testing could not be performed on this isolate because of its poor growth characteristics and absence of established susceptibility parameters. There is no clear guidance in the literature on the antibiotic of choice for treatment of *B. ginsengisoli* infection, however, limited phenotypic characterisation performed on an environmental isolate in 2002 by Kim *et al*[1] had documented sensitivity to streptomycin (5 μg/mL), and resistance to both ampicillin (20 μg/mL) and tetracycline (5 μg/mL), using the disk diffusion method. In our case, initial treatment with piperacillin/tazobactam was based on the preliminary blood culture report of Gram-negative bacilli, and on the patient's symptomatic improvement after initiation of therapy. He was continued on this agent for a total of 6 weeks.

OUTCOME AND FOLLOW-UP

The patient remained afebrile throughout his course. His white cell count ranged from 4400 to 8000 cells/mm^3, with normal differential counts. His erythrocyte sedimentation rate and C reactive protein declined from 48 mm/h to 20 mm/h. His C reactive protein remained <0.3 mg/dL throughout his course of treatment. Follow-up surveillance blood cultures obtained 2 weeks after completion were sterile. He has continued to do well and has had no further bacteraemias during the 6 months post-treatment. He is currently awaiting a small bowel transplantation.

DISCUSSION

To the best of our knowledge, this is the first documented case of human infection attributable to *B. ginsengisoli*. This new agent adds to the list of *Burkholderia* species responsible for bacteraemia in immunocompromised hosts. The genus *Burkholderia* comprises more than 60 species, which occupy a wide range of niches.[2] Phylogenetic analyses divide the genus into two main clusters; the first includes numerous human, animal and plant pathogens such as *B. pseudomallei* and *B. mallei* as well as the 17 defined species of the *Burkholderia cepacia* complex, while the second subgroup is comprised of more than 30 non-pathogenic species primarily associated with plants in what are often potentially beneficial relationships.[2] These typically non-pathogenic species can be isolated from plant material and rhizosphere soil, where they have been described to promote the growth of a range of plants including potatoes, legumes, vegetables and grapevines.[3] *B. ginsengisoli* belongs to this group of endosymbionts; its closest phylogenetic relatives are *B. caledonica* and *B. terricola*. *B. ginsengisoli* was first described in 2006 after isolation from the soil of a ginseng field in South Korea.[1] Its cells are Gram-negative rods, motile by means of unipolar polytrichous flagella. Biochemically it is characterised as catalase positive, oxidase negative and nitrate non-reducing.[1] Optimal growth is on R2A agar, where it appears as circular, convex and cream-coloured colonies. Its optimal growth temperature is 25–30°C, however, it is unique among other Burkholderia endosymbionts in that it can grow at temperatures as high as 42°C, which may explain its ability to persist in the human host.[1]

Since the same organism was isolated from a blood source at two time points in two different institutions, it seems clear that this represents a true blood-borne infection and not a contaminant. In the setting of inflammatory bowel disease, bacteraemia may have multiple aetiologies and, in this case, several questions remain regarding the extent of infection.[4 5] We speculate that exposure occurred through dietary consumption of organic vegetables, both raw and cooked and that the patient's compromised gastrointestinal mucosa facilitated bacterial translocation. In addition, his PICC line might have been infected, although this would not have precluded blood-borne seeding. The absence of culture of his PICC line is one minor limitation of this report.

Whether the pathogenesis may have been augmented by infliximab therapy remains speculative. Infliximab acts by binding and clearing soluble TNF-α, as well as directly binding to cell-associated TNF-α on macrophages and T-cells, inhibiting cell-to-cell interactions and facilitating the dysregulation of matrix metalloproteinases.[6] TNF-α inhibitors have been linked to numerous opportunistic infections including bacterial meningitis, endocarditis, endotoxic shock, mycobacterial infection, hepatitis B infection and HIV infection.[7–10] This case adds to the list of serious infections potentially associated with TNF-α inhibitors.

It is also unclear if the mitral valve echodensity represented endocarditis. While appearance was suggestive, the pathogen was not persistently isolated from blood cultures and it obviously is not a microorganism typical of infective endocarditis. Thus the clinical scenario does not meet strict Duke criteria.[11] Nonetheless, this finding prompted us to treat the patient for a prolonged period.

Why have more infections by this species not been identified or reported? One possibility is that this organism has been misidentified by microbiology laboratories in the past or has been considered a culture contaminant. Bacterial species that are rarely isolated in clinical samples may be difficult to identify, as their phenotypic characteristics are unlikely to be found in commercial automated databases, nor are they described in clinical microbiological textbooks. This highlights the need for pursuing identification that may require genetic sequencing for confirmation.

Learning points

- While this is the first reported case of human infection with *Burkholderia ginsengisoli*, we suspect that this microorganism has appeared in clinical samples previously and might have been overlooked due to failure to readily characterise it.
- We speculate that infection occurred through dietary consumption of organic vegetables and that this patient's compromised gastrointestinal mucosa facilitated bacterial translocation, which may have been further enhanced by tumour necrosis factor α therapy.
- The presence of poorly identified fastidious Gram-negative rods in blood cultures should alert clinicians to the possibility of bacteraemia caused by *B. ginsengisoli*.
- There are no accepted standards for antimicrobial susceptibility testing for *B. ginsengisoli*. However, we did achieve a clinical and microbiological cure with an extended course of piperacillin/tazobactam.
- Our experience highlights the need for pursuing identification of pathogens that may require genetic sequencing for confirmation.

Competing interests None declared.

Patient consent Obtained.

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