Correspondence

Bacteraeumia due to Bacteroides fragilis with reduced susceptibility to metronidazole

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Sir,

Surveys of antimicrobial susceptibilities of isolates of the Bacteroides fragilis group showed that isolates were usually susceptible to metronidazole.1 Metronidazole-resistant phenotypes have rarely been reported. Here we report B. fragilis bacteraemia with reduced susceptibility to metronidazole developing during treatment.

A 70-year-old man was admitted for excision of rectal adenoma. Prophylaxis with intravenous cefuroxime (750 mg/8 h) and intravenous metronidazole (500 mg/8 h) was started. Three days after surgery, the patient developed lower abdominal pain with signs suggestive of peritonitis. Emergency laparotomy revealed a perforated rectum and an offensive pelvic collection. Specimens from theatre grew mixed coliforms susceptible to cefuroxime, B. fragilis susceptible to a 5 µg metronidazole disc and Enterococcus faecalis. The patient was continued on cefuroxime and metronidazole. Four days later, the patient developed a fever of 38.6°C and a raised white blood cell (WBC) count (25 × 10^3 cells/mm^3). Gentamicin 7 mg/kg once daily was added to the therapy. A CT scan revealed no collection. In spite of the above therapy he remained pyrexial with a WBC count of 24 × 10^3 cells/mm^3. An anaerobic blood culture bottle grew anaerobic Gram-negative bacilli identified as B. fragilis by rapid ID 32 A (bioMérieux). This isolate was resistant to a 5 µg metronidazole disc, penicillin, erythromycin and tetracycline but susceptible to augmentin, clindamycin and meropenem by disc diffusion. Cefuroxime and metronidazole were stopped and treatment was changed to meropenem (1 g/8 h). The patient became apyrexial and was discharged home 12 days later.

Using 16S rDNA restriction fragment length polymorphism (RFLP) analysis as described by Stubbs et al.,2 the Anaerobe Reference Unit (PHLS, Cardiff) found that the blood culture isolate showed an RFLP pattern consistent with B. fragilis and confirmed resistance to a 5 µg metronidazole disc. The MIC of metronidazole was 6.0 mg/L by the Etest method. PCR for nim genes associated with metronidazole resistance detected the nimA gene. Unfortunately, the original metronidazole-susceptible strain was not saved for comparison.

The nimA gene, one of five nim genes (A, B, C, D and E) associated with moderate- to high-level resistance to 5-nitroimidazole, is located on a low-copy-number mobilized plasmid.3 The reactive molecules generated during the intracellular reduction of metronidazole are responsible for nucleotide transversion in nimA gene-associated B. fragilis.4 Thus, this resistant isolate may have acquired its resistance trait either through mobilization of the nimA gene from another Gram-negative anaerobic bacterial species or as a result of the mutagenic potential of the metronidazole on an already existing B. fragilis with the nimA gene. As the patient in this report was receiving optimal doses of metronidazole, we believe the risk of inducing metronidazole-resistant strains was minimal and the resistant strain was selected out as a result of an undefined factor.

The resistant isolate in this report showed complete resistance to a 5 µg metronidazole disc and the MIC value was 6 mg/L, below the breakpoint (32 mg/L) set by the NCCLS. Fang et al.5 reported that among six metronidazole-resistant B. fragilis group strains detected by a modified disc diffusion method, only one strain had an MIC value reaching the breakpoint (32 mg/L) for metronidazole. The nim gene was absent in that strain but was present in the other resistant strains that recorded MIC values between 0.5 and 8.0 mg/L. Further studies are needed to determine MIC values for strains that are associated with nim genes. Laboratories should assess their methods of anaerobic culture to optimize recovery of these pathogens and monitor resistance. We found a correlation between in vitro susceptibility testing and clinical response to therapy for Bacteroides bacteraemia that reflects the importance of antimicrobial susceptibility testing for patients whose blood specimens yield Bacteroides species.

References

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