Subdural empyema caused by *Prevotella loescheii* with reduced susceptibility to metronidazole


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Sir,

*Prevotella* spp. are Gram-negative, non-spore-forming anaerobes that are important members of the normal oral, colonic and vaginal flora in humans. These organisms have been isolated from patients with chronic sinusitis, brain abscesses and oral cavity infections often mixed with other anaerobes and streptococci. Metronidazole resistance among *Prevotella* spp. is rare. We report a clinical isolate of *Prevotella loescheii* with reduced susceptibility to metronidazole.

A 62-year-old man presented with a 2 day history of headache, vomiting and confusion. Intermittent sinusitis, but no other history of past illness, was elicited. A computed tomography (CT) brain scan at the time of presentation suggested a left-sided subdural haematoma causing mass effect and midline shift. Following urgent transfer to another hospital, the patient was taken to theatre and burr holes revealed a subdural collection of pus, which was sent for culture and susceptibility testing. Empirical therapy was changed to chloramphenicol 1 g every 6 h. A CT scan 72 h after admission demonstrated reaccumulation of pus, pansinusitis and erosion of the posterior wall of the left frontal sinus. Left frontoparietal craniotomy and frontothemoidectomy were undertaken and a large subdural empyema was evacuated. When an apparently metronidazole-resistant anaerobe was cultured from the specimen, metronidazole was changed to clindamycin 600 mg twice daily and the chloramphenicol continued. The patient’s fever settled after 1 week but he remained in intensive care for 5 weeks because of respiratory failure. Antibiotics were continued for a total of 5 weeks. Neurological recovery was slow and the patient was left with a right-sided hemiparesis and dysphasia.

The initial subdural pus specimen was plated directly on to CLED agar (Oxoid, Basingstoke, UK) incubated at 37°C in air, 7% horse blood agar and chocolate horse blood agar (Oxoid), incubated at 37°C in air supplemented with 5% CO₂. Anaerobic culture was carried out using 7% horse blood agar gentamicin and fastidious anaerobe agar (Lab M, UK) supplemented with nalidixic acid and Tween 80. Enrichment culture was performed in brain heart infusion (BHI) and fastidious anaerobe broth (FAB) (Oxoid). Plates were initially incubated for 48 h with extended incubation for evaluation of colonial morphology.

After 48 h of anaerobic incubation, there was a profuse growth of tiny colonies on the selective and non-selective culture media, some of which were growing up to the metronidazole 5 µg disc. Colonies from within the metronidazole zone, the putative metronidazole-resistant organism and the sensitive organism, were subcultured in air, CO₂ and anaerobically with a metronidazole 5 µg disc on the plate. Both the metronidazole-‘resistant’ and -sensitive isolates were found to be obligate anaerobes that were grey coloured, Gram-negative bacilli, producing β-haemolysis after 48 h incubation and having brick-red fluorescence under long wavelength (366 nm) UV light. Catalase and oxidase production, nitrate reduction and XV dependency reactions were all negative. The API 32A system identified both isolates as *P. loescheii*. Susceptibility testing by the disc diffusion method showed that one of the isolates was resistant to metronidazole but susceptible to penicillin, erythromycin, tetracycline, co-amoxiclav, chloramphenicol and clindamycin; the other isolate was sensitive to all these antibiotics. Results of MIC testing by the Etest (AB Biodisk, Solna, Sweden) method are shown in the Table. The isolate was confirmed as *P. loescheii*, with a MIC of metronidazole of 12 mg/L, by the Public Health Laboratory Service Anaerobe Reference Laboratory.

Resistance to metronidazole develops rarely but may be increasing. Phillips *et al.* have reported occasional low-level resistant isolates of *Bacteroides bivius* (*Prevotella bivius*), *Bacteroides ureolyticus* and perhaps *Bacteroides melaninogenicus* (*Prevotella melanogenica*). Both plasmid-mediated and chromosomally mediated resistance has
been described in *Bacteroides* spp.\(^4\) Several plasmid and chromosomal *nim* genes have been associated with 5-nitroimidazole resistance and the low-copy-number mobilizable plasmid pIP417 (*nimA*) has been transferred *in vitro* by a conjugative process into sensitive strains of *Bacteroides* spp. and *Prevotella* spp.\(^4\) The strain described in this report was examined for the presence of *nim* genes using a previously published method but none were detected.\(^5\) The strain of *P. loescheii* described was isolated from a specimen taken before the patient was taking metronidazole and resistance remained stable through >60 subcultures on metronidazole-free medium. Since microbiology laboratories often use metronidazole sensitivity to detect obligate anaerobes in cultures, the phenomenon of metronidazole resistance in these organisms may, in inexperienced hands, result in failure to report the presence of anaerobes at all. Metronidazole-resistant anaerobes can develop in patients receiving therapy leading to a clinical relapse of infection as previous case reports have suggested.\(^6,7\) This case highlights the possibility that anaerobes may have intrinsically reduced susceptibility to metronidazole and this should be considered in patients who do not respond to metronidazole treatment.

**Table.** MICs (mg/L) of *P. loescheii* clinical isolate and *Bacteroides fragilis* NCTC 9343 as tested by the Etest method

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th><em>P. loescheii</em></th>
<th><em>B. fragilis</em></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>0.75</td>
<td>12</td>
</tr>
<tr>
<td>Penicillin</td>
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<td>0.012</td>
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<tr>
<td>Piperacillin/tazobactam</td>
<td>0.016</td>
<td>0.016</td>
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<tr>
<td>Clindamycin</td>
<td>0.016</td>
<td>0.016</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>0.047</td>
<td>0.064</td>
</tr>
</tbody>
</table>

References


