Sepsis in neonates due to imipenem-resistant Klebsiella pneumoniae producing NDM-1 in India

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Keywords: neonatal sepsis, neonatal intensive care unit, carbapenem resistance, New Delhi metallo-β-lactamase

Sir,

Treatment of neonatal infections is becoming increasingly difficult due to multidrug-resistant organisms. Carbapenems are the last resort for the treatment of severe infections, however, the emergence of carbapenemases in Enterobacteriaceae has left the clinician cornered with very few options. Recently a new carbapenemase designated New Delhi metallo-β-lactamase (NDM-1) was identified in Klebsiella pneumoniae.2,3 Most reported cases of infection with NDM-1 producers have involved adult patients. This communication reports the presence of blaNDM-1 in two isolates of K. pneumoniae from neonates admitted to a neonatal intensive care unit (NICU) at a tertiary care centre in India.

The first neonate was clinically septic. Imipenem-resistant K. pneumoniae (Kp-1) was isolated from an endotracheal aspirate, but blood culture was negative. The patient was started on colistin, however, the parents removed the child from the hospital against medical advice and the patient was lost to follow-up. The other neonate was born at a different hospital and was admitted to the NICU with suspected sepsis. Blood culture yielded imipenem-resistant K. pneumoniae (Kp-2). A combination of colistin and minocycline was given for a period of 10 days, after which the patient recovered and was discharged.

The identity of the isolates was confirmed by an ID 32 E test (bioMérieux, Marcy l’Etoile, France). A disc diffusion test using antibiotics (BD Diagnostics, Franklin Lakes, NJ, USA) was performed according to CLSI guidelines.4 MICs were determined with 40 mg/L phenylalanine arginine β-naphthylamide (PAβN) (Sigma-Aldrich, St Louis, MO, USA). Testing with the cephalosporin/clavulanic acid combination disc test, modified Hodge test and imipenem/EDTA double-disc combination tests was also undertaken.

Both isolates were resistant to a range of antibiotics, including β-lactams, quinolones and aminoglycosides. Kp-1 was susceptible only to colistin and tigecycline, but Kp-2 was susceptible to colistin, tigecycline, tetracycline, minocycline and doxycycline (Table 1). Both isolates showed phenotypic evidence of carbapenemase, metallo-β-lactamase (MBL) and extended-spectrum β-lactamase (ESBL) production. Augmentation of the zone was noted in both isolates with ceftazidime, but not cefotaxime. Investigations of production of AmpC using cefoxitin, cefotixin with 3-aminocephalosphoronic acid (APB) (Sigma) and cefotixin plus APB containing EDTA (Sigma) were negative. PFGE performed following PulseNet standardized procedures with XbaI demonstrated that the two isolates were clonally distinct (Figure S1, available online).

The MICs of imipenem were >32 mg/L and not affected by the presence of PAβN, indicating that efflux did not contribute to carbapenem resistance. To elucidate the mechanism of carbapenem resistance, PCR for blaOXA-23, blaVIM-IMP-SPM-1, blaKPC, blaVIM-IMP-SPM-1-NDM-1 and blaOXA-24 was carried out as previously described. Detection of NDM-1 was performed by PCR with

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References


<table>
<thead>
<tr>
<th>Isolate no.</th>
<th>Source of isolate</th>
<th>Antibiotic resistance [MIC (mg/L)]</th>
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<tbody>
<tr>
<td>Kp-1</td>
<td>endotracheal aspirate</td>
<td>AMP (&gt;256), AMK (&gt;256), GEN (&gt;1024), CIP (&gt;32), CPD (&gt;256), CRO (&gt;256), CTX (&gt;256), CAZ (&gt;256), FEP (&gt;256), IPM (&gt;32), PIP (&gt;256), ATM (&gt;256), SXT (&gt;32), TZP (&gt;256), NET (&gt;256), SAM (32), MIN (12), DOX (48), TGC (2), TET (96), CST (1)</td>
</tr>
<tr>
<td>Kp-2</td>
<td>blood</td>
<td>AMP (&gt;256), AMK (&gt;256), GEN (&gt;1024), CIP (&gt;32), CPD (&gt;256), CRO (&gt;256), CTX (&gt;256), CTX (&gt;256), CAZ (&gt;256), FEP (&gt;256), IPM (&gt;32), PIP (&gt;256), ATM (&gt;256), SXT (&gt;32), TZP (&gt;256), NET (&gt;256), SAM (256), MIN (4), DOX (6), TGC (0.5), TET (2), CST (1)</td>
</tr>
</tbody>
</table>

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<tr>
<th>ESBL phenotypic test</th>
<th>Modified Hodge test</th>
<th>MBL detection, IPM+EDTA</th>
<th>AmpC detection with APB</th>
<th>PCR of bla genes</th>
<th>Presence of porins (OmpC and OmpF) and outer membrane protein OmpA</th>
</tr>
</thead>
<tbody>
<tr>
<td>positive</td>
<td>positive</td>
<td>positive</td>
<td>negative</td>
<td>bla&lt;sub&gt;TEM-1&lt;/sub&gt;, bla&lt;sub&gt;SHV-11&lt;/sub&gt;, bla&lt;sub&gt;NDM-1&lt;/sub&gt;, bla&lt;sub&gt;OXA-1&lt;/sub&gt;</td>
<td>OmpC, OmpA</td>
</tr>
</tbody>
</table>

AMP, ampicillin; AMK, amikacin; GEN, gentamicin; CIP, ciprofloxacin; CPD, cefpodoxime; CRO, ceftriaxone; CTX, cefotaxime; CAZ, ceftazidime; FEP, cepfelime; IPM, imipenem; PIP, piperacillin; ATM, aztreonam; SXT, trimethoprim/sulfamethoxazole; TZP, piperacillin/tazobactam; NET, netilmicin; SAM, ampicillin/sulbactam; MIN, minocycline; DOX, doxycycline; TGC, tigecycline; TET, tetracycline; CST, colistin.

Acknowledgements

We thank Dr. Guillaume Arlet (Service de Bacteriologie, Hospital Tenon, Paris, France) for the control DNA of CTX-M major groups, George A. Jacoby (Link, Massachusetts) for providing E. coli J53 and Heinz Schwarz (Max-Planck-Institute of Tubingen, Germany) for the antibodies.

Funding

The study was supported by institutional funding of the Women Scientist Scholarship Scheme for Societal Programmes of the Women Scientist Scholarship Centre of Okayama University for Infectious Diseases in India and a fellowship from A. R. and R. V. was a recipient of the Women Scientist Scholarship Scheme for Societal Programme of the Women Scientist Scholarship Centre of Okayama University for Infectious Diseases in India. A S. R. has received a fellowship from the Women Scientist Scholarship Centre of Okayama University for Infectious Diseases in India. We thank Dr. Guillaume Arlet (Service de Bacteriologie, Hospital Tenon, Paris, France) for the control DNA of CTX-M major groups, George A. Jacoby (Link, Massachusetts) for providing E. coli J53 and Heinz Schwarz (Max-Planck-Institute of Tubingen, Germany) for the antibodies. The Collaborative Research Centre of Okayama University for Infectious Diseases in India gave a fellowship to S. R., and R. V. was a recipient of the Women Scientist Scholarship Scheme for Societal Programmes of the Women Scientist Scholarship Centre of Okayama University for Infectious Diseases in India. A S. R. has received a fellowship from the Women Scientist Scholarship Centre of Okayama University for Infectious Diseases in India.
Transparency declarations

None to declare.

Supplementary data

Figure S1 is available as Supplementary data at JAC Online (http://jac.oxfordjournals.org/).

References


