New Delhi Metallo 1: Have Carbapenems Met Their Doom?

To the Editor—Carbapenems are the most potent antibiotics used to treat sepsis. High-level resistance to carbapenems is mediated by hydrolysis of the drugs by carbapenemases. Carbapenem-resistant Pseudomonas and Acinetobacter species have been described extensively [1,2]. The recent emergence of a new carbapenemase, the New Delhi metallo 1 (NDM1) enzyme, has been linked to the Indian subcontinent and is accumulating among organisms, possibly because of efficient plasmid transfer. From September 2009 through May 2010, 310 carbapenem-resistant gram-negative bacilli were isolated from clinical samples at our tertiary care center. These consisted of Enterobacteriaceae (57), Pseudomonas species (173), and Acinetobacter species (71). The incidence of carbapenem resistance among Enterobacteriaceae was 5.3% in blood isolates, 7.81% in respiratory tract isolates, and 5.27% in urine isolates.

We phenotypically identified carbapenem-resistant organisms by the modified Hodge test and molecularly identified NDM1 in 49 of 57 Enterobacteriaceae isolates, comprising Klebsiella species (28), Escherichia coli (13), Enterobacter species (5), Morganella morganii (2), and Citrobacter species (1) [3]. All patients had received treatment with carbapenem in the past month. Other associated risk factors were indwelling invasive devices, such as urinary catheters (67% of patients) and central venous catheters (54%), and severe illness (63%). There were 8 carbapenem-resistant isolates that were nonproducers of NDM1 (they may have been producers of Klebsiella pneumoniae carbapenemases or other metallo-β-lactamases).

Processing of stool samples from the patients with identification of NDM1 was performed because Enterobacteriaceae are gut commensal organisms, and their carriage may pose a risk of dissemination in the community. A total of 10 patients were available for stool screening for NDM1 at 1 month after completion of treatment. None of the Enterobacteriaceae isolates from the stool samples were carbapenem resistant.

The development pipeline for antibiotics against gram-negative bacteria is dry, and no new drugs are available. Colistin and tigecycline are the only available agents for treatment of patients infected with gram-negative organisms, and both agents have limitations. Rational use of carbapenems with rapid de-escalation is urgently required. Stringent infection control in hospitals is needed to limit the spread of these organisms.

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Photodynamic Therapy for the Treatment of Endoanal Condylomata Acuminata

To the Editor—Common treatments for anogenital condylomata acuminata, which is caused by human papillomavirus (HPV) types 6 and 11 and is among the most common sexually transmitted diseases, involve topical drugs (podophylo-
toxin and imiquimod) or invasive methods (electrocautery, cryosurgery, surgery, and laser CO₂) and are frequently limited by intraoperative and postoperative pain, bacterial superinfection, prolonged healing time, and recurrent infection. Photodynamic therapy (PDT) with topical 5-aminolevulinic acid (ALA) is an emerging technique for the treatment of genital HPV-induced benign and premalignant lesions, including mucosal ones (those on the vagina [1, 2], urethral meatus [2], and tongue [3]).

In accordance with the ethical standards of the institutional and regional responsible committees on human experimentation and with the Helsinki Declaration of 1975 (as revised in 1983), we enrolled consecutive patients affected by endoanal condylomata acuminata in a pilot case-control study. After written informed consent was obtained, subjects were allocated in a 1:1 ratio to receive 1 of the following 2 treatments: PDT alone (group 1) or PDT followed by laser CO₂ vaporization (group 2). ALA 16% in polyethylenglycole gel was applied to lesions by means of anoscopy. After 3 h, patients were irradiated via an endoanal probe with red light (PDT; CLD100; EPEM; peak emission, 630 nm; fluence at skin level, 1 V/cm²) for a duration of 1:1500 s. Patients belonging to group 2 underwent laser CO₂ vaporization (SmartXide; DEKA) of lesions 60 min after PDT under spinal anesthesia. Paracetamol was then prescribed (at a dosage of 100 mg as needed, up to 3 times/day). Anoscopic follow-ups were scheduled for up to 12 months. Patients belonging to group 1 underwent additional sessions of PDT at weeks 2, 4, and 6 if lesions persisted. Further persistences and recurrences in either group were treated by means of laser CO₂.

A total of 22 patients were enrolled, and 21 successfully completed the study. As summarized in Table 1 and in accordance with previous reports [1, 2], PDT with ALA yielded high cure rates (>90%) and low recurrence rates (<10%) of anogenital condylomata acuminata. Intense burning during light application did not have a significant effect on patient compliance, since it regressed immediately and spontaneously via the transitory interruption of the light spot, thus exploiting the additive capacity of PDT. Patients who underwented PDT alone experienced quicker healing of treated areas and less need of pharmacological control of postoperative pain, compared with patients treated with adjuvant laser CO₂. It also should be pointed out that, different from surgical procedures used for the removal of endoanal condylomata acuminata, PDT does not require anesthesia and is not known to cause scarring, which, in turn, may determine severe functional complications (eg, anal stenosis).

To sum up, this represents the first report of PDT with ALA as treatment for condylomata acuminata affecting the anal canal, and, despite several limitations, our study supports this procedure as an effective, safe, and well-tolerated treatment option for HPV-induced lesions affecting the skin and mucous membranes [1–3].

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Table 1. Characteristics of Patients with Condyloma Acuminatum and Main Results of Treatment and Follow-Up

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean age (range), years</th>
<th>Male:female ratio</th>
<th>No. of patients with complete remission/total no. of patients (%)</th>
<th>Mean no. of treatment sessions needed</th>
<th>No. of patients with postoperative paracetamol intake/total no. of patients (%)</th>
<th>No. of patients with recurrences in 12 months/total no. of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDT</td>
<td>36.7 (25–55)</td>
<td>9:2</td>
<td>10/11 (91)</td>
<td>1.36</td>
<td>1/11 (9)</td>
<td>0/11 (0)</td>
</tr>
<tr>
<td>PDT and laser CO₂</td>
<td>33.0 (20–52)</td>
<td>9:1</td>
<td>9/10 (90)</td>
<td>1.0</td>
<td>7/10 (70)</td>
<td>2/10 (20)</td>
</tr>
</tbody>
</table>

NOTE. PDT, photodynamic therapy.

References


Serological Response to H1N1 Influenza Virus Infections in Adults Treated with Oseltamivir

To the Editor—We read the article by Hung et al [1] with great interest. Our findings are consistent with their points of views that a significant proportion of pa-