Table 1. Gram-negative bacilli isolated from MDACC patients during survey periods between 1985 and 1996.

<table>
<thead>
<tr>
<th>Organism</th>
<th>1985 Number (%)</th>
<th>1986 Number (%)</th>
<th>1993 Number (%)</th>
<th>1996 Number (%)</th>
<th>Cumulative Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter species</td>
<td>18 (2)</td>
<td>15 (2)</td>
<td>18 (3)</td>
<td>25 (3)</td>
<td>76 (2)</td>
</tr>
<tr>
<td>Citrobacter species</td>
<td>30 (3)</td>
<td>40 (5)</td>
<td>20 (3)</td>
<td>17 (2)</td>
<td>107 (3)</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>294 (31)</td>
<td>248 (29)</td>
<td>194 (29)</td>
<td>203 (27)</td>
<td>939 (29)</td>
</tr>
<tr>
<td>Enterobacter species</td>
<td>78 (8)</td>
<td>94 (11)</td>
<td>75 (11)</td>
<td>101 (13)</td>
<td>348 (11)</td>
</tr>
<tr>
<td>Klebsiella species</td>
<td>144 (15)</td>
<td>129 (15)</td>
<td>111 (16)</td>
<td>115 (15)</td>
<td>499 (16)</td>
</tr>
<tr>
<td>Morganella species</td>
<td>12 (1)</td>
<td>11 (1)</td>
<td>10 (1)</td>
<td>7 (1)</td>
<td>40 (1)</td>
</tr>
<tr>
<td>Proteus species</td>
<td>100 (11)</td>
<td>59 (7)</td>
<td>63 (9)</td>
<td>42 (6)</td>
<td>264 (8)</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>169 (18)</td>
<td>171 (20)</td>
<td>92 (14)</td>
<td>143 (19)</td>
<td>575 (18)</td>
</tr>
<tr>
<td>Pseudomonas species</td>
<td>25 (3)</td>
<td>12 (1)</td>
<td>26 (4)</td>
<td>12 (2)</td>
<td>75 (2)</td>
</tr>
<tr>
<td>Stenotrophomonas maltophilia</td>
<td>33 (4)</td>
<td>22 (2)</td>
<td>23 (3)</td>
<td>45 (6)</td>
<td>123 (4)</td>
</tr>
<tr>
<td>Serratia species</td>
<td>28 (3)</td>
<td>24 (3)</td>
<td>21 (3)</td>
<td>23 (3)</td>
<td>96 (3)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>10 (1)</td>
<td>26 (3)</td>
<td>26 (4)</td>
<td>25 (3)</td>
<td>87 (3)</td>
</tr>
<tr>
<td>Total</td>
<td>941</td>
<td>851</td>
<td>679</td>
<td>758</td>
<td>3,229</td>
</tr>
</tbody>
</table>

NOTE. MDACC = The University of Texas M. D. Anderson Cancer Center. These organisms were isolated over four different 3-month collection periods during the years indicated.

epidemiology of infections at their individual sites and to devise antimicrobial regimens based on local information rather than on reports from other institutions.

Potent antipseudomonal coverage should be strongly considered in such situations, particularly in view of the fact that two large surveys of *P. aeruginosa* bacteremia in cancer patients at our institution have clearly demonstrated that inadequate initial antipseudomonal coverage and/or a delay in the administration of appropriate antibiotic therapy has an adverse effect on the outcome of such infections [5, 10].

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References

Central Nervous System Disturbances Following Clarithromycin Ingestion

CNS and psychiatric symptoms have been reported in association with administration of a wide variety of drugs but have rarely been reported after clarithromycin ingestion [1]. Herein, three cases of CNS stimulation, two in middle-aged adults and one in a child, following the initiation of clarithromycin therapy are reported. In each case, symptoms abated promptly after discontinuation of therapy.

A 46-year-old male physician complained of cough productive of yellow sputum and was prescribed clarithromycin (500 mg b.i.d.) by a colleague. He was afebrile. That evening, after taking two doses, the man reported mild euphoria, a heightened sense of energy, and mild insomnia. The next morning, he again took clarithromycin and later told a co-worker that he felt “aggressive.” The second night, after taking a fourth dose of

clarithromycin, he had more pronounced euphoria and insomnia as well as giddiness.

Therapy was discontinued, and all symptoms resolved. The only other reported side effect was a bitter taste in the saliva. The man denied ingesting other drugs or caffeine-containing products. A few days later, he voluntarily took clarithromycin (one dose) and became mildly symptomatic again. Administration of the drug was then discontinued. These symptoms did not recur in the 15 months following this event.

A 4-year-old boy started therapy with clarithromycin (125 mg b.i.d.) that was prescribed by his pediatrician for a “chest infection.” Several hours after receiving the first dose, the patient was noted by his parents to be hyperactive (“running around and jumping on the bed,” behavior that was highly unusual for him). His father detected tachycardia and brought the child to the emergency department for evaluation.

In the emergency department, his vital signs were normal except for a mild tachycardia (heart rate, 114); he was happy and playful but overactive, agitated, and difficult to confine to the bed for physical examination. An electrocardiogram revealed sinus tachycardia. The only other medication that had been administered was acetaminophen. Clarithromycin therapy was discontinued. A telephone interview later revealed that the symptoms abated after clarithromycin treatment was discontinued and did not recur in the ensuing 10 months.

A 39-year-old woman was prescribed clarithromycin (500 mg b.i.d.) for treatment of a sinus infection. After two doses, she developed severe insomnia and agitation and became emotionally labile. She stopped treatment, and her symptoms promptly subsided. Upon reintroduction of therapy at the advice of her physician, the symptoms recurred. She then discontinued administration of the medication and reported no recurrences in the following 3 months.

Two reports previously described CNS symptoms following clarithromycin ingestion, but neither report included young healthy individuals receiving a normal therapeutic dose of the drug. Nightingale et al. [2] described two patients with AIDS who developed altered mental status shortly after they began treatment with clarithromycin (1,000 mg b.i.d.). One patient became hyperactive and had anxiety and delusions of grandeur; these symptoms abated after discontinuation of therapy, but the patient became agitated and psychotic when treatment was reintroduced. The second patient developed agitation, insomnia, and paranoid delusions 3 days after starting clarithromycin therapy; this patient’s symptoms resolved 24 hours after administration of several medications was discontinued and resumed shortly after treatment with clarithromycin alone was reintroduced. Wallace et al. [3] grouped together the symptoms of dizziness, light-headedness, confusion, and insomnia and reported that these occurred in seven of 13 elderly (mean age, 70.1 years) patients who were being treated with clarithromycin (1,000 mg b.i.d.).

The Physicians’ Desk Reference [4] reports that sleep disorder occurs in “less than 1%” of 120 patients taking clarithromycin therapy, and CNS symptoms were not specifically described in phase 3 clinical trials of the drug [5].

To my knowledge, this is the first report describing agitation, euphoria, and insomnia in otherwise healthy young patients receiving therapeutic doses of clarithromycin who lacked confounding variables. It is also the first report, whatsoever, of CNS disturbances occurring in a pediatric patient. The only other medication taken by any one of the patients was acetaminophen, which the pediatric patient took. This child tolerated acetaminophen alone both before and after the incident.

In all three patients, the symptoms promptly abated after discontinuation of clarithromycin treatment. In the two adult patients, the symptoms began to recur after treatment was reintroduced. Long-term follow-up revealed that none of the patients had these symptoms ever again. Therefore, it is nearly certain that clarithromycin was the cause of these CNS disturbances.

Patients being treated with clarithromycin are often taking other medications. For a patient who develops mania, euphoria, agitation, or insomnia while taking clarithromycin therapy, it would be reasonable to first discontinue treatment unless a more obvious culprit is present. (In some cases, CNS infections related to the underlying condition may need to be ruled out.) Signs of CNS stimulation in such patients may rapidly reverse upon discontinuation of administration of clarithromycin.

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References