Low-Dose Dexamethasone as Adjunctive Therapy for Disseminated Mycobacterium avium Complex Infections in AIDS Patients

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Five human immunodeficiency virus-infected patients with disseminated Mycobacterium avium complex infection had progressive weight loss and persistent fever despite multidrug antimycobacterial therapy. These patients were given daily low-dose oral dexamethasone (typically 2 mg/day) as adjunctive therapy. All had substantial and sustained weight gain (12 to 50% of pre-steroid treatment body weight [P < 0.03]), reduction in fever, and an improved sense of well-being. The serum albumin level increased during dexamethasone therapy (from 3.06 ± 0.59 g/dl [mean ± standard deviation] to 3.9 ± 0.22 g/dl [P < 0.01]), while the serum alkaline phosphatase level fell (from 368 ± 247 U/liter to 128 ± 43.6 U/liter [P < 0.04]). Further studies of the potential role for corticosteroids in the management of disseminated M. avium complex infections in human immunodeficiency virus-infected patients are warranted.

Disseminated Mycobacterium avium complex (MAC) infections occur in 15 to 24% of human immunodeficiency virus (HIV)-infected patients with advanced immunodeficiency and are characterized by fevers, progressive weight loss, and failure to thrive (10, 17). Although specific antimycobacterial therapy may benefit certain of these patients (5, 6, 10–12), the reported median survival after diagnosis is only 6 to 8 months (10, 12). Long-term low-dose dexamethasone therapy yielded strikingly beneficial results in several deteriorating HIV-infected patients on multidrug antimycobacterial regimens. Experience with five of these patients is described.

Results. Table 1 describes clinical features of five HIV-infected patients who had disseminated MAC infection, determined on the basis of recovery of this organism from blood. Each had advanced immunodeficiency, with a CD4+ lymphocyte count of ≤10 cells per mm³. All five had progressive weight loss and fever while on multidrug antimycobacterial regimens which included clarithromycin. Patient 3 was also receiving total parenteral nutrition because of a complete inability to eat.

While continuing on the same (or a slightly modified) multidrug antimycobacterial regimen, the five patients began low-dose dexamethasone therapy (typically 2 mg once daily [range, 1 to 4 mg/day]). Coincident with the addition of the corticosteroid, there was a remarkable and abrupt change in course. All five had marked weight gain without evidence of fluid retention, averaging 31 pounds (14.1 kg; range, 14.5 to 64 lb [6.6 to 29 kg, respectively]), representing a mean increase in body weight of 25% (12 to 50%). In comparison with the predexamethasone weight, this change was significant (P < 0.03 by Student’s one-tailed t test). Weight gain of ≥10% was maintained for a mean of 5 months (4 to 11.5 months). In addition, all had a reduction in fever and all reported an increased sense of well-being. Improved laboratory parameters were also observed. The mean t (± standard deviation) albumin level of 3.06 ± 0.59 g/dl at onset of dexamethasone therapy increased to 3.9 ± 0.22 g/dl (P < 0.01 by Student’s one-tailed t test), and the mean alkaline phosphatase level of 368 ± 247 U/liter fell to 128 ± 43.6 U/liter (P < 0.04 by Student’s one-tailed t test). Total parenteral nutrition was able to be completely discontinued in patient 3; in this patient, the serum albumin level had risen from 2.1 g/dl to 4.2 g/dl. In addition, for patients 2 and 3, hematocrit values of 21 and 28% increased to 35 and 40%, respectively.

Dexamethasone therapy was continued until death for four patients (mean duration of therapy, 9.8 months). Dexamethasone therapy was discontinued after 5 months of therapy for patient 5 because of the development of cytomegalovirus retinitis. This patient remains alive 19 months after diagnosis of disseminated MAC. Besides cytomegalovirus retinitis, other possible complications of steroid therapy included an episode of presumed candida esophagitis in patient 4, who also developed chronic pancreatitis associated with hyperglycemia. In addition, acute pancreatitis developed during the terminal hospitalization of patient 3.

Four patients have died. Two patients underwent necropsy, which showed lymphoma, MAC, and interstitial pneumonia for patient 1 and cytomegalovirus and pyogenic pneumonia for patient 3. Patient 2 died of an undetermined type of pneumonia. The cause of death for patient 4 is not known.

DISCUSSION

There is an appropriate reluctance to immunosuppress HIV-infected patients further through the introduction of corticosteroids. Nonetheless, these agents may be useful in the management of a variety of complications of HIV infection, such as thrombocytopenia, cerebral edema caused by toxoplasmosis, and pneumonia due to Pneumocystis carinii infection (3, 4). Despite some reports of presumed steroid-induced adverse outcomes (3, 9), these agents have been generally well tolerated. In this report, possible adverse effects of dexamethasone therapy included the development of candida esophagitis, cytomegalovirus retinitis, and acute and chronic pancreatitis, the last associated with hyperglycemia. All of these events, however, are known to occur in HIV-infected patients not receiving corticosteroids (7, 15).

Steroids were given to the five patients in this report to improve their sense of well-being, control fevers, and stimulate...
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Opportunistic infections</th>
<th>Antimycobacterial agents</th>
<th>Duration of anti-MAC therapy (mo)</th>
<th>Wt loss (% of body wt)</th>
<th>New opportunistic infections</th>
<th>Maximum wt gain in lb (kg [% of body wt])</th>
<th>Duration of ≥10% wt gain (mo)</th>
<th>Duration of steroid therapy (mo)</th>
<th>Concomitant medications*</th>
<th>Total length of survival after diagnosis of MAC (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23</td>
<td>Male</td>
<td>P. carinii pneumonia</td>
<td>Clarithromycin plus 2 others</td>
<td>1</td>
<td>9</td>
<td>None</td>
<td>31 (14.1 [24])</td>
<td>7</td>
<td>12.5</td>
<td>Didanosine, fluconazole, acyclovir, diphenylhydantoin, famotidine, diazepam, aerosol pentamidine</td>
<td>13.5</td>
</tr>
<tr>
<td>2</td>
<td>38</td>
<td>Female</td>
<td>Thrush, microsporidial ocular infection</td>
<td>Clarithromycin plus 7 others</td>
<td>2.5</td>
<td>22</td>
<td>None</td>
<td>24 (10.9 [24])</td>
<td>11.5</td>
<td>11.5</td>
<td>Zidovudine, acyclovir, didanosine, famotidine, trimethoprim-sulfamethoxazole, diazepam, fluconazole</td>
<td>14</td>
</tr>
<tr>
<td>3</td>
<td>27</td>
<td>Female</td>
<td>None</td>
<td>Clarithromycin plus 6 others</td>
<td>10</td>
<td>24</td>
<td>None</td>
<td>64 (29.0 [50])</td>
<td>5</td>
<td>5</td>
<td>Zidovudine, acyclovir, trimethoprim-sulfamethoxazole, metoclopramide, fluconazole, amitriptyline, famotidine</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>45</td>
<td>Male</td>
<td>Thrush</td>
<td>Clarithromycin plus 2 others</td>
<td>1</td>
<td>14</td>
<td>Esophageal candidiasis (presumed)</td>
<td>20.5 (9.3 [14])</td>
<td>8</td>
<td>10</td>
<td>Trimethoprim-sulfamethoxazole, fluconazole, acyclovir, famotidine, gemfibrozil, omeprazole, nystatin, metoclopramide, epoetin alfa, glipizide, norotiptyline, hyoscyamine sulfate</td>
<td>20</td>
</tr>
<tr>
<td>5</td>
<td>40</td>
<td>Male</td>
<td>Cryptococcal meningitis</td>
<td>Clarithromycin plus 2 others</td>
<td>5.5</td>
<td>12</td>
<td>Cytomegalovirus retinitis</td>
<td>14.5 (6.6 [12])</td>
<td>5</td>
<td>5</td>
<td>Trimethoprim-sulfamethoxazole, fluconazole, phenobarbital, diphenylhydantoin, epoetin alfa</td>
<td>≥19</td>
</tr>
</tbody>
</table>

* Dexamethasone therapy was continued until death for four of the five patients.
* Excluding antimycobacterial therapy.
* Patient 5 was alive as of 1 July 1994.
appetite. Surprisingly excellent results occurred, with objective weight gains of 12 to 50% of pre-steroid treatment body weight. These weight gains were long lasting and were accompanied by a marked and sustained improvement in sense of well-being, fever reduction, and, in certain instances, normalization of abnormal liver function tests, serum albumin levels, and hematologic parameters.

The mechanism by which administration of low-dose dexamethasone may account for these favorable results is unknown. Our limited experience has suggested that a 2-mg dose may be less effective if rifamycin derivatives are given concomitantly, presumably because of the enhanced hepatic metabolism of the steroid (1).

In patients with advanced cancer, dexamethasone can temporarily stimulate appetite but, in contrast to these findings, does not increase body weight (13). Anti-inflammatory actions, including inhibition of transcription of certain cytokines presumably released during MAC infection, may explain the favorable results we observed (16). This hypothesis is consistent with the beneficial results observed anecdotally in other AIDS patients with disseminated MAC who were treated adjunctively with either prednisolone (16) or thalidomide (2). Whether or not corticosteroids may also have actions which result in slowing of HIV replication in vivo is an open question (8).

Occult adrenal insufficiency was unlikely to have been present in the patients in this study because of the absence of postural hypotension, hyponatremia, or hyperkalemia and the relative preservation of the adrenal cortex found at necropsy (done for patients 1 and 3). Clinically significant adrenal insufficiency is uncommon among HIV-infected patients (14).

The findings of this study, while preliminary in nature, should provide an impetus for additional investigations of the role of corticosteroids as an adjunct to specific antimicrobial therapy in the management of disseminated MAC infection in AIDS patients.

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REFERENCES