Varicella pneumonia in patients with HIV/AIDS

Mirjana Popara,(1) Stella Pendle,(1) Leonard Sacks,(1) Raymond A. Smego, Jr.(2) and Mervin Mer(3)

Objective: To determine the potential role of steroid therapy combined with early antiviral and supportive care in patients infected with human immunodeficiency virus (HIV) with varicella pneumonia.

Materials and Methods: A retrospective review was conducted of the incidence, clinical course, and outcome of varicella pneumonia in patients with HIV or acquired immunodeficiency syndrome (AIDS).

Results: Seven of 12 patients (58%) who were hospitalized with chickenpox developed clinically severe varicella pneumonia. All patients had advanced immunosuppression and all developed diffuse reticulonodular radiographic abnormalities, although two patients had normal chest radiographs on admission. All patients received antiviral therapy within 12 hours of hospital admission. The overall mortality rate was 43%. Six patients were treated with systemic corticosteroids in addition to antiviral agents, including all four of the survivors.

Conclusions: Hospitalized patients with HIV or AIDS with chickenpox are at high risk for developing varicella pneumonia. There is a potentially high rate of death despite prompt initiation of appropriate antiviral therapy. Intensive care management and adjunctive use of systemic corticosteroids may improve outcome.

Int J Infect Dis 2002; 6: 6-8

Pneumonia is the most serious complication of primary varicella infection, and the leading cause of death in both immunocompetent and immunosuppressed adults with chickenpox. Varicella is perhaps no more common in patients infected with human immunodeficiency virus (HIV) than in healthy adults, but little is known about the incidence and clinical course of varicella pneumonia in HIV-infected individuals. This report presents seven cases of clinically severe varicella pneumonia that occurred among 12 HIV-infected patients with chickenpox who were ill enough to be admitted to a tropical disease hospital in South Africa. The high incidence of lower respiratory tract involvement (58%) in this patient population, and the poor response to early initiation of acyclovir therapy prompted a review the literature on the subject. In light of previous experience with the adjunctive use of corticosteroids in normal adult patients with life-threatening varicella pneumonia, the potential role of steroid therapy combined with early antiviral and supportive care in HIV infected patients with this complication is discussed.

MATERIALS AND METHODS
This study was conducted at the Sizwe Tropical Diseases Hospital, a 500 bed provincial hospital affiliated with the University of the Witwatersrand in Johannesburg, South Africa. Tuberculosis and HIV infection are the most frequent cases seen at this hospital; arterial blood gas analysis and intensive care (ICU) facilities are not available. A retrospective review was conducted of the inpatient medical records of 20 adult patients admitted between January 1997 and April 1998 who were diagnosed with chickenpox. In all patients, HIV status was determined by seropositivity on enzyme-linked immunosorbent assay (ELISA) and Western blot antibody testing. This study was approved by the Committee for Research on Human Subjects at the University of the Witwatersrand.

RESULTS
Of the 12 patients hospitalized with chickenpox (all with fever and multiple cutaneous lesions), seven (58%) developed clinically severe varicella pneumonia. CD4+ lymphocyte counts ranged from 12 to 250 cell/mm³ (mean, 82 cells/mm³). Mean patient age was 29 years (range, 24–34 y). Clinical and radiographic features and outcomes for all patients are summarized in Table 1. Two patients (patients 1 and 2) had normal chest radiographs upon admission and were started on oral famciclovir and parenteral acyclovir, respectively. Both developed bilateral reticulonodular pulmonary infiltrates within 4 days of starting antiviral therapy. One of these patients died 5 days after admission, and the other developed pneumococcal pneumonia as a superinfec-
tion but survived. Five patients were admitted with diffuse interstitial infiltrates on chest radiographs typical of varicella pneumonia. Two of these patients (patients 3 and 4) died 1 and 2 days, respectively, after initiation of antiviral therapy.

All patients received antiviral therapy within 12 hours of hospital admission. Six patients were also treated with systemic corticosteroids: four received oral prednisone alone (60 mg/d for 2–4 d; mean, 3.5 d) and two were given intravenous hydrocortisone (patient 1, 200 mg as a single dose followed by oral prednisone 60 mg/d for two days; patient 4, 100 mg every 6 hours for two days). Patient 4 subsequently died. The overall mortality rate was 43% (3/7 patients). All four of the survivors (100%) were given corticosteroids in addition to acyclovir, whereas two of three patients (67%) who died had received steroids (difference not statistically significant).

**DISCUSSION**

Although infection with the varicella-zoster virus is a frequent opportunistic occurrence in adults with HIV or AIDS, primary varicella infection is relatively rare. Children with HIV infection seem to have less virulent primary varicella infections, with a lower incidence of pulmonary involvement and a better rate of survival.6

The typical presentation of varicella pneumonia in HIV or AIDS involves fever, cough, dyspnea, chest pain, and a characteristic vesiculopustular skin rash. The chest radiograph invariably shows a diffuse interstitial (typically nodular) or alveolar pattern. Hypoxia may occur more frequently in HIV-infected patients than in immunocompetent persons.4 Although several studies have suggested that smoking is a risk factor for varicella pneumonia,8-10 smoking histories were not available for the patients in this series. Polymerase chain reaction testing of respiratory secretions has been used for diagnostic confirmation of chickenpox pneumonia in HIV and AIDS, and may give a positive result even when respiratory tract viral cultures are negative.4 Recurrent varicella pneumonia requiring acute treatment followed by secondary antiviral prophylaxis has been described, analogous to other AIDS-complicating opportunistic infections.5

Immunocompromised patients with varicella pneumonia frequently do poorly, with mortality as high as 45%.11 In this series, the mortality rate from varicella pneumonia in HIV-infected patients was 43%, despite prompt antiviral treatment; this may, at least in part, relate to the lack of ICU availability. All four patients who survived were treated with steroids, and although this was not significantly different from patients who died (2 of 3 received steroids), it is the authors' clinical impression that corticosteroid therapy may confer some benefit in clinically severe varicella among HIV-infected patients. A 1998 report described six previously well patients with life-threatening varicella pneumonia and respiratory failure who were managed successfully with intravenous acyclovir, systemic steroids, and appropriate supportive care including mechanical ventilation.7 These patients demonstrated a clinically significant therapeutic response compared with control subjects who were treated in the same manner but without adjunctive corticosteroids. Steroid-treated patients had significantly shorter hospital and ICU stays, and there was no mortality despite the fact that they were admitted to the ICU with significantly lower median ratios of PaO2 and fraction of inspired oxygen (PaO2:FiO2) (86.5 versus 129.5; higher PaO2:FiO2 ratios indicate more severe impairment of pulmonary gas exchange) than those patients who did not receive

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (y)</th>
<th>Gender</th>
<th>Appearance*</th>
<th>Oxygen Saturation (%)</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>On Admission</td>
<td>With Deterioration</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>27</td>
<td>M</td>
<td>Bilateral nodular infiltrate</td>
<td>97</td>
<td>49</td>
<td>Famciclovir (po) then acyclovir (iv) plus steroids</td>
</tr>
<tr>
<td>2</td>
<td>34</td>
<td>M</td>
<td>Bilateral reticulo-nodular infiltrate</td>
<td>98</td>
<td>71</td>
<td>Acyclovir (iv) plus steroids</td>
</tr>
<tr>
<td>3</td>
<td>24</td>
<td>M</td>
<td>Bilateral reticulo-nodular infiltrate</td>
<td>82</td>
<td>—</td>
<td>Valaciclovir (po)</td>
</tr>
<tr>
<td>4</td>
<td>34</td>
<td>M</td>
<td>Bilateral reticulo-nodular infiltrate</td>
<td>90</td>
<td>—</td>
<td>Acyclovir (iv) plus steroids</td>
</tr>
<tr>
<td>5</td>
<td>26</td>
<td>M</td>
<td>Bilateral reticulo-nodular infiltrate</td>
<td>90</td>
<td>—</td>
<td>Acyclovir (iv) plus steroids</td>
</tr>
<tr>
<td>6</td>
<td>30</td>
<td>M</td>
<td>Bilateral reticulo-nodular infiltrate</td>
<td>87</td>
<td>68</td>
<td>Acyclovir (iv) plus steroids</td>
</tr>
<tr>
<td>7</td>
<td>29</td>
<td>M</td>
<td>Bilateral reticulo-nodular infiltrate</td>
<td>87</td>
<td>—</td>
<td>Acyclovir (iv) plus steroids</td>
</tr>
</tbody>
</table>

*chest radiograph, po—orally; iv—intravenously.
corticosteroid therapy. These patients also demonstrated more rapid radiologic improvement, and it is believed that this favorable clinical outcome is attributable to the adjunctive use of steroids. Experience suggests that HIV-infected patients with severe life-threatening varicella pneumonia and requiring ICU admission respond to corticosteroid therapy in the same fashion as immunocompetent individuals (Mer M. Personal communication).

CONCLUSION

Patients with HIV or AIDS who are hospitalized with chickenpox are at high risk for developing varicella pneumonia. The 58% incidence seen in the present study is higher than that from previously reported series. There is a potentially high rate of death despite prompt initiation of appropriate antiviral therapy. Intensive care management and adjunctive use of systemic corticosteroids may improve outcomes.

REFERENCES