ABSTRACT

Despite the many significant advances in HIV therapy that have been introduced during the past decade, no single treatment approach is best for all HIV-infected patients, and individualization of therapy is essential. Some patient populations continue to present special challenges in HIV care. A series of case vignettes is used to illustrate some of the important treatment decisions involved in the management of the initial presentation with severe AIDS, treatment of patients with substance abuse and poor treatment adherence, deciding whether to switch from a well-tolerated twice-daily treatment regimen to a once-daily treatment, and the management of HIV infection and anemia. A recent case report describing an apparently rapidly progressing HIV variant with multidrug resistance also is reviewed.

shows moderate anemia, neutropenia, and low total lymphocyte count. The patient has moderate hypoxemia and an elevated alveolar-arterial oxygen gradient of 43 mm Hg. The patient’s HIV test is positive. He has cryptomeningitis and Pneumocystis carinii pneumonia. His CD4 cell count is 21 cells per mm$^3$ and his viral load is 234 000 copies per mL.

An important issue in HIV management is identifying people in the community who are infected with HIV but who are not receiving medical care. Unfortunately, many people still present to hospitals with advanced HIV disease. This failure of the healthcare system to identify HIV-positive people at earlier stages of infection is reflected in screening guidelines that have been developed by the US Centers for Disease Control and Prevention$^3$, and in data from Saag et al, who have reported that the average CD4 cell count of newly presenting patients is 100 cells per mm$^3$ (Saag, Personal communication). As a result, the presentation illustrated in this case, which is characterized by advanced disease and with multiple opportunistic infections, is not unusual and is increasingly encountered in settings in which HIV is managed.

For this patient, an important management question is whether he should begin ART now to help manage his advanced disease, or whether he should be medically stabilized first. There are good arguments for both points of view. As shown in many of the clinical trials of ART, there can be a very rapid CD4 cell response to initiation of ART in a patient with such a low pretreatment CD4 cell count. Rapidly increasing his CD4 cell population may be very helpful for this patient, especially because of his cryptomeningitis infection. On the other hand, many clinicians would argue that the best place to initiate ART is in the primary care setting once the patient is stabilized. This issue is the subject of an AIDS Clinical Trials Group trial, which is now accruing patients in the United States.

**CASE 2: SUBSTANCE ABUSE AND HISTORY OF POOR TREATMENT ADHERENCE**

A 39-year-old woman with a history of unprotected intercourse and injection drug use presents with a CD4 cell count of 101 cells per mm$^3$ and a viral load of 88 000 copies per mL. She has previously received ART but stopped treatment for social reasons. She has now resolved these personal issues that caused her to discontinue treatment; she is on buprenorphine therapy and wishes to restart ART as soon as possible.

In general, there are 3 broad categories of treatment that would generally be considered for this patient. The first is a fixed-dose nucleoside reverse transcriptase inhibitor combination (ie, abacavir/lamivudine or tenofovir/emtricitabine) and efavirenz after pregnancy prevention counseling. The second option is zidovudine/lamivudine and lopinavir/ritonavir or atazanavir/ritonavir. The third option is zidovudine/lamivudine and tenofovir or, alternatively, tenofovir/emtricitabine and zidovudine. She has ongoing substance use issues, which may complicate her ability to tolerate the side effects of efavirenz. A protease inhibitor (PI) may be well suited for this patient for several reasons. The PI may be preferable to efavirenz because it has no central nervous system toxicity. With her history of poor adherence to treatment, the PI may theoretically provide a broader genetic barrier to resistance. She also has advanced disease, a setting in which a boosted PI often is used. However, there is no compelling reason to use one of these treatment options in preference to the others. Other factors also may be important in selecting treatment, including possible coinfection with hepatitis B or hepatitis C, a history of lamivudine treatment, and pregnancy. These factors also may affect her ability to tolerate drug toxicity and to adhere to her treatment regimen, in addition to the likelihood of important drug interactions. This case vignette illustrates the importance of considering the patient’s medical and social characteristics before beginning ART.

**CASE 3: POSTPARTUM TREATMENT ON A TWICE-DAILY REGIMEN**

The patient has recently delivered her first child, and she does not intend to breastfeed. She has been treated with zidovudine/lamivudine/nevirapine during pregnancy, which she tolerated very well. Her CD4 cell count after 3 months of ART has risen to 320 cells per mm$^3$, and her viral load is undetectable.

In general, treatment options for this patient include maintaining her on her current regimen, switching her to a once-daily efavirenz-based regimen (assuming pregnancy prevention counseling), and once-daily nucleoside combination with a boosted PI. Research suggests that efavirenz is generally a better choice than nevirapine$^7$, which is reflected in treat-
ment guidelines. Although physicians often try to use a once-daily regimen for a patient who is starting treatment for the first time, it may be desirable to maintain this patient on her current regimen. The patient’s preference also is an important consideration. With respect to the viral load and CD4 cell counts, there is no clear evidence that a boosted PI is superior to a nonnucleoside reverse transcriptase inhibitor for initial response rate or durability of response. This question is being examined in ongoing clinical trials.

**CASE 4: THE “NEW YORK” CASE: TRANSMISSION OF MULTIDRUG-RESISTANT HIV**

A recent case report, known as the “New York Case,” has generated considerable controversy since it was reported by the New York Health Department and The Aaron Diamond AIDS Research Center at Rockefeller University in 2005. The authors described a case of infection with multidrug-resistant HIV and rapid progression to AIDS. The viral variant was unusual in that it employed the CCR5 and CXCR4 entry cofactors to infect lymphocytes. The patient was a homosexual man who was in his late 40s; he developed febrile illness in early November 2004 and was found to be HIV positive in December 2004. He had a history of multiple sexual contacts and methamphetamine use, which often is associated with HIV infection because of disinhibition of sexual behavior. Previous HIV tests conducted as recently as May 2003 had been negative. Based on his testing history, he was thought to have had HIV infection for only 4 to 20 months before the appearance of AIDS symptoms. His viral load and CD4 and CD8 T cell history are shown in Figure 1. As shown in the Figure, his lymphocyte count fell rapidly after his positive HIV test. By December 2004, his CD4 cell count was approximately 80 cells per mm$^3$. Importantly, although he was thought to be only recently infected, his HIV was highly resistant to many antiretroviral agents, which
the authors describe as transmission of a multidrug-resistant HIV variant (Figure 2).<sup>2</sup> Although transmission of drug-resistant HIV has been described previously, the transmission of HIV variants that are resistant to a broad range of drugs is relatively rare.<sup>2</sup> The rapid progression to AIDS in this patient is a subject of controversy. It is not clear whether this represents an HIV variant that is associated with unusually fast progression or a genetic susceptibility to infection in this particular patient. Identification of the source of the virus may help to clarify this.

**CASE 5: HIV AND ANEMIA**

The patient is a 49-year-old man who was infected with HIV approximately 10 years previously as a result of sexual contact. He has never received ART. His CD4 cell count is 250 cells per mm<sup>3</sup>, and his viral load is 38 000 copies per mL. He is asymptomatic and hesitant to begin treatment of his HIV infection because of concern about drug side effects. His hemoglobin level is 10.5 g, and workup suggests that he has anemia of chronic disease. On direct questioning, he states that he feels somewhat less energetic and more easily fatigued with physical exertion than in the past.

Several studies have shown that even mild-to-moderate anemia can have a significant impact on patient quality of life.<sup>3,4</sup> In addition, anemia is an independent marker of HIV disease progression, although the underlying cause of this relationship is not well understood.<sup>5</sup> Anemia tends to be milder among patients who are receiving ART.<sup>6,7</sup> When initiating HIV therapy in a patient with anemia, it is reasonable to avoid antiretroviral agents that are known to cause anemia, such as zidovudine.<sup>8</sup>

**Figure 2. Drug Susceptibility Phenotype to Selected Agents**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Fold change in IC&lt;sub&gt;50&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nevirapine</td>
<td>&gt;700</td>
</tr>
<tr>
<td>Control</td>
<td></td>
</tr>
<tr>
<td>Efavirenz</td>
<td>0.6</td>
</tr>
<tr>
<td>Lopinavir</td>
<td>&gt;300</td>
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<td>Control</td>
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<tr>
<td>Enfuvirtide</td>
<td>0.3</td>
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IC<sub>50</sub> = inhibitory concentration.
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**CONCLUSIONS**

The case studies presented here illustrate a range of challenging treatment issues in HIV care. There are now a large number of antiretroviral medications in clinical practice, and randomized clinical trials have examined many of the combinations of these agents. No single treatment strategy is preferred in every case, and optimal HIV care requires that treatment be individualized on the basis of factors, such as duration and severity of illness, history of treatment and adherence to treatment, likelihood of pregnancy, and the presence of other severe medical conditions, such as anemia.
REFERENCES


