Immunoglobulin G(κ) [IgG(κ)] and IgG(λ) Paraproteinemia in a Child with AIDS and Response to Highly Active Antiretroviral Therapy

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We report an 8-year-old boy with AIDS, extremely elevated serum immunoglobulin G (IgG) concentration and IgG kappa [IgG(κ)] and IgG lambda [IgG(λ)] paraproteinemia. This paraproteinemia partially responded to highly active antiretroviral therapy. This case emphasizes the importance of controlling B-cell activation.

B-cell activation during human immunodeficiency virus type 1 (HIV-1) infection is a specific response to HIV-1 determinants (1, 2, 3). This activation, which can be either monoclonal or oligoclonal, can result in hypergammaglobulinemia, a common finding in AIDS (12). Moreover, oligoclonal immunoglobulin (Ig) bands can be observed in asymptomatic HIV-1-seropositive individuals (14).

We report an 8-year-old HIV-1-seropositive boy with AIDS and an extremely elevated serum IgG level (nephelometry) (University of Mississippi, Jackson, MS). Two months prior to his birth, his mother was diagnosed with HIV-1 infection. Despite maternal treatment and patient prophylaxis with zidovudine (ZDV), the patient’s HIV-1 DNA PCR test (Amplicor HIV-1 Monitor Test; Roche Diagnostic Systems, Branchburg, NJ) was positive at 4 and 6 weeks of age. His initial CD4 cell count remained well until developing Streptococcus pneumoniae sepsis at 7 months of age. Despite CD4 counts above 1,000/mm3, his serum IgG levels were extremely elevated at 380,000 copies/ml. After counseling about the possibility of malignancy developing in their child, his parents agreed to initiate the highly active antiretroviral therapy (HAART) program of ZDV, lamivudine, and lopinavir. Over the next 6 months, the child’s HIV-1 RNA levels, serum Ig, and total protein levels (data not shown) decreased, and the CD4 cell percentage and count improved (Table 1). Serum protein electrophoresis (SPE) and immunofixation were performed prior to and after the HAART.

The initial (prior to HAART treatment at age 7.5 years old) SPE (Hydrasys LC; Sebia, Norcross, GA) demonstrated diffusely increased gammaglobulins with three discrete bands that immunofixed as two monoclonal IgG(κ) bands and a single monoclonal IgG(λ) band (Fig. 1). These findings were consistent with an oligoclonal Ig immune response. The cerebrospinal fluid protein level was normal, and oligoclonal IgG bands were not present. Urine protein (130 mg/24 h) electrophoresis showed three monoclonal IgG(κ) bands and one monoclonal IgG(λ) band (data not shown). The follow-up (after HAART at 8 years of age) SPE demonstrated a striking reduction in the intensity of the oligoclonal bands, and one IgG(κ) band had disappeared (Fig. 1).

We present the clinical and laboratory findings of an HIV-1-seropositive child with paraproteinemia consisting of oligoclonal IgG bands. Oligoclonal Ig in HIV-seropositive patients has been previously described as mixed κ and λ light chains (8, 11), single heavy chains (7, 11), and single κ chains (13), although IgA(κ) and IgM(κ) bands have also been identified (15, 16). Hypergammaglobulinemia, a well-known consequence of HIV-1 infection resulting from B-cell activation, is often associated with paraproteins and may be observed at any stage of the disease (6, 8, 11, 14). IgG bands in the serum of HIV-1-seropositive subjects are known to be specific for viral determinants (9). Although hypergammaglobulinemia frequently occurs in HIV-1 infection, a striking feature of this case was the magnitude of the IgG paraproteinemia and the appearance of IgG chains in the urine. The child’s serum oligoclonal IgG

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band pattern was similar to that of previously reported adult patients (2, 6, 13). HIV-1-seropositive patients with monoclonal or oligoclonal bands are more likely to develop non-Hodgkin lymphoma than those without paraproteinemia (4). Moreover, atypical plasma cells, plasma cell aggregates, and plasma cell hyperplasia of the bone marrow may develop even in the absence of plasma cell neoplasia in HIV-1-seropositive patients (16). Some HIV-1-seropositive patients present with transient paraproteinemias, while others have persistent paraproteins with or without true plasma cell malignancies (5). Furthermore, Epstein-Barr virus has been associated with the development of non-Hodgkin’s lymphoma in patients with AIDS (1). The bone marrow examination of our patient did not, however, reveal any abnormalities as to the percentage, number, or morphology of plasma cells.

Potent antiretroviral therapy in HIV-1-seropositive patients with paraproteinemia decreases the hyperactivation of B cells, which normalizes total IgG concentrations. In addition, the viral suppression by antiretroviral therapy results in a diminished HIV-1-virus-specific antibody response (10). When HAART treatment was successfully maintained for 6 months in our patient, the paraproteinemia decreased, and one of the IgG(\text{H9260}) oligoclonal bands became undetectable (Fig. 1). Although we did not measure the serum IgG level just prior to the adherent antiretroviral therapy, the greatly reduced gamma region on the SPE supports our claim that the serum IgG level declined secondary to the antiretroviral therapy. Currently, the patient has been adherent to his antiretroviral therapy. His most recent CD4% is up to 32%, and viral load is undetectable.

In conclusion, this case report adds new information that sustained activation of B lymphocytes plays a crucial role in the immune dysfunction in pediatric HIV-1 infection. Although this patient and some reported adult patients (9) did not develop lymphoma over a 3-year period, we believe that long-term follow-up protocols should be developed to determine the outcome of children with this condition and to determine if lymphoma develops as an ultimate pathogenetic event.

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**TABLE 1. Comparison of serum immunoglobulin levels, peripheral blood CD4 cells, and plasma HIV-RNA levels in a child with paraproteinemia**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value of parameter for age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4 mo</td>
</tr>
<tr>
<td>Serum Ig (mg/dl)</td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>1,200</td>
</tr>
<tr>
<td>IgA</td>
<td>85</td>
</tr>
<tr>
<td>IgM</td>
<td>112</td>
</tr>
<tr>
<td>PBMC</td>
<td></td>
</tr>
<tr>
<td>CD4 (%)</td>
<td>49</td>
</tr>
<tr>
<td>CD4 (cells per µl)</td>
<td>4,416</td>
</tr>
<tr>
<td>Plasma RNA (copies/ml)</td>
<td>ND</td>
</tr>
</tbody>
</table>

ND, not done; PBMC, peripheral blood mononuclear cells.

b Previously nonadherent to therapy, the patient was restarted on highly active retroviral therapy and continued taking his medications for the next 6 months as documented on four separate occasions.

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![FIG. 1. Immunofixation of (A) the patient’s serum prior to treatment (age, 7.5 years old) and (B) the patient’s serum after treatment (age, 8 years old). Prior to treatment, the serum contained three IgG monoclonal bands: two monoclonal IgG(κ) bands and one monoclonal IgG(λ) band. After treatment, one of the previously identified monoclonal IgG(κ) bands is no longer identifiable. The letters at the top of the figure represent the following: ELP, electrophoresis; G, IgG; A, IgA; M, IgM; K, kappa light chain; L, lambda light chain.](http://cvi.asm.org/on/10.1128/CLID.0058-00)
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REFERENCES