control of influenza virus infection in animal models [2] and humans [3].

Persistent infection with influenza A (H1N1) virus of 10 months’ duration has been described in a child with severe combined immunodeficiency syndrome [4]. In contrast to the case reported herein, the child did not develop a humoral immune response to the infection, and virus isolates did not undergo antigenic drift [5].

In conclusion, this is the first demonstration of humoral immunity–driven antigenic drift during persistent influenza virus infection in a single host. Furthermore, antigenic change in the viral hemagglutinin was similar to that occurring within the community. We suggest that immunocompromised children who develop influenza should be screened for persistent infection, as these cases may provide valuable insight into antigenic drift of influenza virus within the community.

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References


Takayasu’s Arteritis in a Human Immunodeficiency Virus–Infected Adolescent

Although arteritis and aneurysmal dilatation of the aorta have been described in HIV-infected adults, to our knowledge, Takayasu’s arteritis (TA) has not been reported concurrently with HIV infection. We describe an adolescent with presumed transfusion-acquired HIV infection who had TA that was successfully treated with steroids.

A 16-year-old Indian male presented with high-grade fever and malaise. Six years earlier, he had received fresh frozen plasma in India for presumed viral hepatitis. Serology for HIV type 1 was positive by western blotting with a plasma viral load of 3,730 copies/mL and a CD4+ lymphocyte count of 343/mm3 (18%). Therapy with isoniazid, pyrazinamide, and ethambutol was commenced for persistent fever after which defervescence occurred. On arrival in the United States 4 months later, treatment with stavudine and lamivudine was initiated, and antituberculous therapy was stopped because of the lack of evidence for tuberculous infection. One month later, antituberculous therapy was restarted for a recurrence of fever.

An extensive evaluation revealed only an elevated erythrocyte sedimentation rate of 55 mm/h and a chest CT showing circumferential mural thickening of the aortic arch and the descending thoracoabdominal aorta consistent with aortitis. An aortogram demonstrated focal dilatation of the aortic arch and the thoracoabdominal aorta between the diaphragm and celiac trunk. Blood pressures measured on all four limbs were normal; however, left brachial and radial pulses were absent. No bruits or murmurs were audible. An infectious etiology (i.e., cytomegalovirus, Mycobacterium avium complex, or Treponema pallidum) or a site for tuberculous infection was not established. Immunologic testing revealed antineutrophil cytoplasmic antibody (by indirect fluorescent antibody assay), elevated levels of C1q immune complexes (5.387 μEq/mL), elevated IgG levels (1,550 mg/dL), and mildly elevated Raji levels (24.86 μEq/mL). von Willebrand’s factor antigen, C3/C4, and neopterin levels were all normal.

Treatment with prednisolone (1 mg/[kg·d]) was commenced. Over the next 6 weeks, defervescence occurred with normalization of the erythrocyte sedimentation rate and C1q immune complex, IgG, and Raji levels. The prednisolone dosage was gradually tapered over 12 months to 5 mg/d. Antituberculous therapy was continued for 12 months. His plasma HIV type 1 viral load has remained undetectable during antiretroviral therapy with CD4+ lymphocyte counts of 135–238/mm3. Clinically, the patient remains asymptomatic with normal cardiovascular function including pulses.

Vasculitis involving medium-sized vessels has been described in HIV-infected adults and children [1]. The etiology is thought to be related to either circulating immune complexes or direct endothelial involvement by HIV. Asymptomatic nonmycotic aneurysms of medium-sized and, less commonly, large-sized vessels (aorta) have also been reported [2]. To our knowledge, the only pediatric case of aortic disease occurred in a 7-year-old girl who died of respiratory failure following measles pneumonia and at autopsy had coincidental macroscopic irregular longitudinal stria tions of the ascending aorta [3]. No cases of aortic aneurysms in HIV-infected children could be found during a thorough literature review.

TA is a chronic inflammatory disease primarily affecting large vessels, such as the aorta and its main branches; it is
commonly seen in young patients (32%–77% of patients were younger than 20 years of age in a large series [4]) and is more commonly described in individuals of Asian ethnicity. Aneurysm formation occurs in 15%–30% of patients with TA, particularly children [4]. The cause of TA is unknown, although an autoimmune process has been postulated. There were early reports of Mycobacterium tuberculosis infection in association with TA in areas where tuberculosis is highly endemic, but a direct causal relationship has not been demonstrated [5]. No cases of concurrent TA and HIV infection were found in a review of the world literature despite these diseases having similar geographic distributions and age incidences in Asia. No direct causal relationship could be demonstrated between HIV infection, suspected tuberculous infection, and large vessel arteritis in this case, and the patient’s ethnicity and geographic location may make this a chance occurrence. However, the possible autoimmune nature of TA and the observed frequency of autoimmune phenomena in HIV infection should make this combination more likely, especially in children.

We propose that large vessel arteritides such as TA should be considered in HIV-infected individuals, including children, who present with persistent fever when an initial workup has been nondiagnostic.

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References


Stavudine-Induced Macrocytosis During Therapy for Human Immunodeficiency Virus Infection

Nucleoside analogue reverse transcriptase inhibitors are important components of most treatment regimens for HIV infection. Three of these agents (zidovudine, zalcitabine, and didanosine) have been known to cause leukopenia, anemia, and/or thrombocytopenia. Zidovudine has been associated most frequently with dose-related bone marrow toxicity manifested as macrocytic anemia. Stavudine and lamivudine have not been reported to cause hematologic toxicity at currently recommended doses [1, 2].

We noted that as patients’ treatments were switched from zidovudine- to stavudine-containing regimens, there was minimal or no decrease in macrocytosis, while there was a rapid return to baseline mean corpuscular volumes (MCVs) in patients receiving non-stavudine-containing regimens. Zidovudine-naïve patients who began stavudine treatment were noted to have increases in MCVs similar to those in patients taking zidovudine therapy. Some of the MCVs were remarkable enough (>110 fL) to prompt investigation of vitamin B12 and folate levels (which were normal in all seven patients tested). Although phase 1 studies revealed that anemia and macrocytosis occurred in patients receiving dosages higher than those currently used, stavudine at currently recommended dosages has not been reported in the literature (or the package insert) to cause hematologic abnormalities [3].

We retrospectively reviewed the charts of 122 patients whose treatment regimens included stavudine. Thirty-one patients (10, 110 fL) to prompt investigation of vitamin B12 and folate levels (which were normal in all seven patients tested). Although phase 1 studies revealed that anemia and macrocytosis occurred in patients receiving dosages higher than those currently used, stavudine at currently recommended dosages has not been reported in the literature (or the package insert) to cause hematologic abnormalities [3].

We retrospectively reviewed the charts of 122 patients whose treatment regimens included stavudine. Thirty-one patients (10, 3 months; 10, poorly documented or changing treatment regimens; 7, documented noncompliance; and 4, lost to follow-up) were excluded from the study. Of the 91 remaining patients, none had a known history of alcohol abuse or malabsorption syndromes.

The results of the chart review are shown in figure 1. Macrocytosis was observed in 89% of patients as defined by an MCV of >95.0 fL and in 73% as defined by an MCV of >100.0 fL. The mean MCV at initiation of stavudine treatment was 96.3 fL (range, 78.9–118.8 fL). The mean MCV at least 3 months after initiation of stavudine treatment was 104.6 fL (range, 79.0–122.1 fL). The mean increase in MCV was 9.3 fL (range, −10.3 to 29.3 fL; P < .05).

Fifty-three percent of patients were zidovudine naïve before initiation of stavudine treatment. These patients had a mean MCV of 89.5 fL (range, 78.9–99.5 fL) at initiation of therapy and a mean increase in MCV of 13.9 fL (range, 0.1–29.4 fL; P < .05) at least 3 months after initiation of stavudine treatment.

Figure 1. Initial mean mean corpuscular volumes (MCVs) before initiation of stavudine treatment for HIV-infected patients (including zidovudine [AZT]–naïve patients and those who had previously been treated with AZT) (□) and final mean MCVs after at least 3 months of stavudine therapy (■).

The views expressed herein are those of the authors and do not reflect the official policy or positions of the U.S. Navy or the U.S. Department of Defense.

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