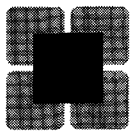

Rapid progression of HIV-1 infection to AIDS

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■ Homosexually acquired human immunodeficiency virus type 1 infection is usually slowly progressive, and reports of its rapid progression to acquired immunodeficiency syndrome are rare. We present a case of acute human immunodeficiency virus type 1 and cytomegalovirus coinfection that progressed to acquired immunodeficiency syndrome and death in 7 months. The factors that determine the clinical outcome of human immunodeficiency virus type 1 infection are poorly defined; however, coinfection with other agents, such as cytomegalovirus, may influence its natural history.

□ INDEX TERMS: HIV INFECTIONS; HIV-1; ACQUIRED IMMUNODEFICIENCY SYNDROME; CYTOMEGALIC INCLUSION DISEASE
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THE NATURAL HISTORY of human immunodeficiency virus type 1 (HIV-1) infection acquired homosexually in adult men is that of a slowly progressing illness. Only occasionally do patients progress rapidly from primary infection to acquired immunodeficiency syndrome (AIDS). We report a patient with acute HIV-1 illness and documented seroconversion whose condition progressed to AIDS and death in 7 months. This case includes the uncommonly reported feature of acute HIV-1 and cytomegalovirus (CMV) coinfection which may shed additional light on this phenomenon.

CASE REPORT

A 22-year-old male college student was admitted to the hospital with a 5-day history of fever, myalgias, headache, sore throat, and abdominal pain. His medical and surgical history were unremarkable. There was no history of significant travel, blood transfusion, or intravenous drug abuse. He denied any homosexual experiences. On exam, he appeared ill and was febrile. He had exudative pharyngitis, small posterior cervical and axillary lymph nodes, and mild periumbilical abdominal tenderness. The rest of the exam was unremarkable.

Initial laboratory studies revealed a white blood cell count of 2.42 $\times 10^3/\mu L$ with 82% neutrophils, 13% lymphocytes, and 5% monocytes. Hemoglobin was 15.5 g/dL, and the platelet count was 101 $\times$ $10^3/\mu L$. Serum studies for hepatitis A and B, heterophile antibody, and cytomegalovirus (CMV) IgG antibodies were negative. The CD4 count was 320 cells/μL (37.7%), and the CD8 count was 171 cells/μL (20.1%). An initial HIV-1 antibody test by enzyme-linked immunosorbent assay was negative (*Table*).

The patient improved over the next several days with supportive care only. Ten weeks after the initial illness he had lost 15 pounds, had oral thrush, hairy leukoplakia, and multiple small, nontender lymph nodes in the cervical, axillary, and inguinal areas. Serologic studies for CMV and Epstein-Barr virus and T-cell subsets were obtained (*Table*). A repeat HIV-1 antibody test by enzyme-linked immunoabsorbent assay was positive and confirmed by Western blot. At that time, stored serum from the initial hospitalization was analyzed (*Table*). The patient reported a single anal-receptive homosexual experience 4 weeks before the initial hospitalization. He was put on a regimen of zidovudine and monthly aerosolized pentamidine.

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TABLE
PATIENT'S SEROLOGIC DATA

Test	Initial presentation	+10 Weeks	+14 Weeks	+20 Weeks	+25 Weeks
Human immunodeficiency virus*	0.033 CO = 0.266	0.719 CO = 0.274	0.710 CO = 0.274	0.505 CO = 0.269	NA
Western blot	ND	p24,p51 p66,qp 120/160	p24,p66 qp 120/160	p24,p51 p66 qp 120/160	NA
P-24 antigen	413.7 pg/ml	ND	57.6 pg/ml	101.3 pg/ml	NA
CD4, cells/μL(%)	320 (37.7%)	166 (7.3%)	151 (11.7%)	101 (13.5%)	50 (11.4%)
CD8, cells/μL (%)	171 (20.1%)	136 (59.7%)	646 (50.0%)	381 (51.0%)	307 (70.0%)
CD4/CD8	1.87	1.22	0.23	0.27	0.16
Cytomegalovirus*					
IgM	NA	≥1:10	NA	<1:10	NA
IgG	Negative	Positive	NA	Positive	NA
Epstein-Barr virus†					
Early antigen	NA	1:10	NA	NA	NA
IgM VCA	NA	≤1:10	NA	≥1:10	NA
IgG VCA	NA	1:1280	NA	1:1280	NA
Heterophile antibody	Negative	NA	NA	NA	NA

CO, cutoff (optical density) NA, not available ND, none detected
* by enzyme-linked immunoabsorbent assay
†by indirect immunofluorescence

Fourteen weeks after his initial presentation, the patient was admitted with generalized seizure activity. A magnetic resonance imaging scan revealed four intracerebral ring-enhancing lesions. The CD4 count was 151 cells/μL and the CD8 count was 646 cells/μL. Serum cryptococcal antigen and toxoplasma antibodies were negative. A needle biopsy of one of the brain lesions revealed large-cell immunoblastic non-Hodgkin's B-cell lymphoma. Central nervous system irradiation was started, and the patient slowly improved while receiving outpatient radiation therapy.

Between weeks 20 and 25 after presentation, he was diagnosed clinically to have both CMV and toxoplasma retinitis. Despite aggressive treatment with ganciclovir, pyrimethamine, and clindamycin, the retinitis progressed, resulting in blindness.

At 28 weeks, he was hospitalized with poorly controlled seizures. Computed tomography revealed encephalomalacia corresponding anatomically with the previously visualized masses. No new lesions were noted. He died 4 days later, secondary to uncontrolled seizures.

DISCUSSION

Fifty percent of HIV-1-infected patients are free of AIDS at 10 years, and fewer than 1% of patients develop AIDS in less than 2 years.[1,2] This patient's clinical course progressed from normal health to opportunistic neoplasm and infection in less than 5 months, and to death in 7 months. Such rapid progression to AIDS has only rarely been documented,[3–5] and the factors responsible for rapid progression are poorly understood.

This patient had both epidemiologic and serologic evidence of acute coinfection with HIV-1 and CMV. Acute coinfection with HIV-1 and CMV has been reported in two cases of intravenous drug abuse with unusually severe clinical syndromes.[6] Webster and colleagues reported a more rapid progression to AIDS in 108 hemophiliac patients coinfected with HIV-1 and CMV.[7]

In vitro studies suggest a bidirectional interaction between CMV and HIV-1 in coinfected cells that increases the replication of both viruses.[8] CMV can also induce the expression of Fc receptors on cell surfaces, permitting HIV-1 infection of CD4-negative cells.[9] There is skepticism about the in vivo significance of these interactions,[10] but our case and those of Bonetti and colleagues[6] clearly document acute infections with both viruses.

The biologic properties of HIV-1 variants may also play a role in determining clinical outcome. In a study of 49 patients, Tersmette and colleagues showed that individuals with high-replicating syncytium-inducing variants of HIV-1 progressed more quickly to AIDS. Information about the in vitro characteristics of the HIV-1 isolates in our case and the others mentioned in this report[3–5] are not available.[11]

In cases such as ours, which demonstrate rapid

progression of HIV-1 illness, the possibility of preexisting disease with coincidental HIV-1 seroconversion must be recognized. This seems unlikely in our case since primary central nervous system lymphoma is rare in otherwise healthy adults, and most frequently involves patients 40 to 60 years old. In contrast, non-Hodgkin's lymphoma in the HIV-1 infected population is increasingly recognized and frequently presents with primary central nervous system involvement.

In summary, the factors that determine clinical outcome in HIV-1-infected adults are poorly defined but may include the size of the inoculum, the route of infection, host genetic factors, and variations in HIV-1 strains. Also intriguing is the possibility that coinfection with other agents such as CMV may influence the natural history of HIV-1 infection.

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