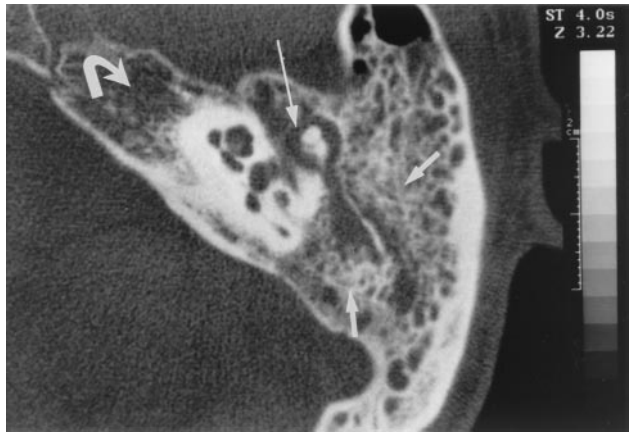

Figure. Horizontal computerized tomographic scan through the attic, with diffuse inflammation in the tympanic cavity (**long arrow**) and the squamous bone (**short arrows**). Note the slight modification of the bony pattern of the apex (**curved arrow**).

dle-ear cavities and skin were filled with soft tissue, and there was erosion of the cortical bone of the apex. A blood count showed 3.5×10^9/L leukocytes with 82% myeloblasts. Bone marrow examination confirmed acute myeloid leukemia (type 1 FAB). Cerebrospinal fluid was positive for blast cells. The patient underwent combination chemotherapy with idarubicin and cytosine arabinoside, along with intrathecal chemotherapy. Complete remission was obtained, and his hearing returned. Control MRI was performed with no evidence of tumor burden. The patient received two cycles of consolidation chemotherapy and 18-Gy of cranial radiation; complete remission persisted 6 months after diagnosis.

Several cases of leukemic infiltration of the ear have been described in patients with chronic or acute myeloblastic or lymphoblastic leukemia (1,2). Involvement of the cochlea and vestibule have also been reported (2,3). Free-floating cells are found in the perilymphatic spaces of the inner ear with or without hemorrhage (3). Hyperleukocytosis or acute myeloid leukemia subtypes 4 and 5 predispose patients to develop chloromas, which may occur in the ear, sometimes overlying the VIIth or VIIIth nerve, and lead to facial palsy and hearing loss, as in our patients (2,4). Chloromas sometimes precede the onset or relapse of leukemia by a few months (5,6). Because of the possibility of infection (eg, herpes zoster), examination of biopsy specimens is important for the diagnosis but may be difficult (especially in the middle ear) because of thrombocytopenia or an acquired coagulopathy (6,7). However, CT scans and MR images are likely to discriminate between infection and tumor involvement of the middle and inner ear. In our patients, treatment quickly led to resolution of the otologic manifestations and complete hematologic remission.

Jean-Emmanuel Kurtz, MD
Emmanuel Andrès, MD
Francis Veillon, MD
Frédéric Maloisel, MD
André Gentine, MD
Raoul Herbrecht, MD
Bruno Lioure, MD
Patrick Dufour, MD
Departments of Onco-Hematology, Internal Medicine, Radiology, and Otorhinolaryngology
Hôpitaux Universitaires de Strasbourg, Strasbourg, France

1. Gotay V. Unusual otological manifestations of chronic lymphocytic leukemia. *Laryngoscope*. 1976;86:1856–1863.
2. Paparella MM, Berlinger NT, Oda M, El Fiky F. Otological manifestations of leukemia. *Laryngoscope*. 1973;83:1510–1526.
3. Schuknecht HF. Neoplastic growth. In: Schuknecht HF, ed. *Pathology of the Ear*. Cambridge, Mass: Harvard University Press; 1976:446.
4. Zappia JJ, Bunge FA, Koopman CF Jr, McClatchey KD. Facial nerve paresis as the presenting symptom of acute leukemia. *Int J pediatric Otorhinolaryngol*. 1990;19:259–264.
5. Nieman RS, Barcos M, Berard C, et al. Granulocytic sarcoma: a clinicopathologic study of 61 biopsied cases. *Cancer*. 1981; 48:1426–1437.
6. Kurtz JE, Maloisel F, Andrès E, et al. Syndrome abdominal aigu d'allure chirurgicale et leucémie aiguë. *Ann Chirug*. 1998; 52:434–438.
7. Lechner K, Geissler K, Jager U, et al. Treatment of acute leukemia. *Ann Oncol*. 1999; 10(suppl 6):45–51.

HUMAN IMMUNODEFICIENCY VIRUS-ASSOCIATED POLYMYOSITIS DURING IMMUNE RESTORATION WITH COMBINATION ANTIRETROVIRAL THERAPY

To the Editor:

A 24-year-old asymptomatic woman was referred in June 1997 after testing positive for the human immunodeficiency virus type 1 (HIV-1). Her CD4+ T-cell count was 10/μL, and her plasma level of HIV RNA was 143,900/mL. Therapy with trimethoprim-sulfamethoxazole was initiated in combination with zidovudine (250 mg twice daily), lamivudine (150 mg twice daily), and indinavir (800 mg three times per day). Tests for syphilis, hepatitis B and C viruses, toxoplasmosis, cytomegalovirus (viremia), and human T-cell lymphoma virus 1/2 were negative. There was no cytomegalovirus retinitis.

After initiation of combination antiretroviral therapy, there was a prompt increase in her CD4+ T-cell count to above 100/μL. Memory CD4+ T cells (CD45RA-) contributed to the initial increase. After 6 months, the number of CD45RA+ 62L-selectin+ cells (true naive cells) increased substantially. The initial defective CD4+ T-cell prolifera-

tion to recall antigen was progressively corrected. Surprisingly, after 18 months, a T-cell proliferative response to HIV-1 antigen was detected, a finding that is seldom observed in patients treated at a chronic stage.

In September 1997, her serum creatine kinase level increased to 2442 IU/L and her lactate dehydrogenase level increased to 608 IU/L, without symptoms. Although zidovudine was replaced with stavudine (30 mg twice daily), the creatine kinase level remained elevated (2234 IU/L), and she developed muscular complaints (Table 1). An electromyogram revealed mildly increased insertional activity (muscle irritability). Motor unit action potentials were polyphasic but of normal amplitude, and there was no early recruitment. A biopsy specimen showed necrotic and nonnecrotic muscle fibers infiltrated by macrophages (CD68+) and T cells, mainly CD4+. Tests for anti-HIV gp41 and gp120, anticytomegalovirus, and anti–Epstein-Barr virus antibodies were negative. The patient's white blood cells expressed the human leukocyte antigens A3374, B5370, and DRB1 1303. Complement components were normal. There were no cryoglobulinemia nor circulating immune complexes. Tests for antinuclear antibodies and rheumatoid factor were negative.

HIV-associated polymyositis was diagnosed, and treatment with prednisone (0.5 mg/kg daily) was begun in October 1997. Combination antiretroviral therapy was continued. One month later, the dose of prednisone was decreased to 5 mg every 10 days; at each dose, the patient complained of recurrent myalgias. A second electromyogram, 6 months after the first, was normal. Treatment with prednisone was continued until January 1999, then decreased, and discontinued in June, without clinical or biologic relapse.

Clinical and pathologic findings in HIV-associated polymyositis and in polymyositis occurring in HIV-negative patients are similar, with the exception of skin changes, which are uncommon in the former (1). HIV-associated polymyositis is often difficult to distinguish from zidovudine-induced myopathy; however, ragged-red fibers (due to the proliferation of abnormal mitochondria), abnormal mitochondrial levels, and the reversibility of the disease after discontinuation of the drug may indicate a diagnosis of zidovudine-induced myopathy (2). As these criteria were not met, we assumed that HIV-polymyositis occurred in our patient, whose clinical status improved only after treatment with corticosteroids was begun.

The pathophysiology of HIV-polymyositis is not known. Neither viral replication nor HIV-RNA transcripts detected by in situ hybridization have been documented within muscle fibers. In addition, both polymerase chain reaction (PCR) and hybridization using PCR products of gag and pol genes failed to demonstrate integration of HIV proviral genome in the myonuclei (3). However, autoimmune manifestations have been seen in HIV-infected patients, including miscellaneous antinuclear antibodies, rheumatoid factor, antiphospholipid antibodies, anti–smooth muscle antibodies, antibodies directed against platelets, erythrocytes, erythropoietin, and mixed cryoglobulinemia (4). Thus, the rapid onset of severe HIV-polymyositis in our patient during immune restoration with combination antiretroviral therapy is an unresolved finding, as the improved immune status may have contributed to its pathophysiology.

The immune restoration (which has been reported during combination antiretroviral therapy) suggests a complex process involving a fast initial release and redistribution of CD4+ T memory cells, which were sequestrated in lymphoid tissues, and a subsequent and slower regeneration of CD4+ T naive cells (5) from the thymic and extrathymic pools. Finally, almost all the CD4+ T-cell repertoire may be subsequently normalized after combination antiretroviral therapy. We were unable to determine whether any of the reconsti-

Table 1. Plasma HIV RNA Concentrations (Monitor HIV Roche), CD4+ T-Cell Counts, Muscular Enzyme Levels, and Clinical Outcome during Combination Antiretroviral Therapy

	06/97	09/97	10/97	12/97	02/98	05/98	09/98	01/99
Viral load (log 10)	5.2		<2.3	<2.3	<2.3	<2.3	<1.7	<1.7
L ($\times 10^9$/L)	0.38	1.45	1.46	1.31	1.6	2.5	1.5	3
CD4 (per μL)	10	100	140	180	190	410	360	510
CD8 (per μL)	230	890	790	760	1,020	1,310	990	1,690
Creatine kinase level (IU/L)	195	2,442	3,892	272	304	186	149	242
Aldolase level (U/L)	4.4	—	15.9	7.7	6.3	4.3	4.8	3.4
Myalgia	No	No	Severe, diffuse		No	Electromyogram normalized	Mild	No
Therapy	Zidovudine, lamivudine, indinavir	Zidovudine, lamivudine, indinavir	Right deltoid electromyogram Left deltoid biopsy Prednisone (30 mg/d), stavudine, lamivudine, indinavir	Prednisone (10 mg/d)	Prednisone (7.5 mg/d)	Prednisone (5 mg/d)		Prednisone (5 mg/d)

tuted CD4+ T-cell subset was involved in promoting the occurrence of this HIV-polymyositis.

Pierre Sellier, MD
Jean-Jacques Monsuez, MD
John Evans, MD
Catherine Minozzi, MD
Jean Passeron, MD
Daniel Vittecoq, MD
Elisabeth Dussaix, MD
Service de Médecine Interne et Maladies Infectieuses and Laboratoire de Virologie
Hôpital Paul Brousse
Villejuif, France
Guylene Carcelain, MD
Laboratoire d'Immunologie Cellulaire
Hôpital Pitié-Salpétrière
Paris, France
Catherine Lacroix-Jousselin, MD
Laboratoire de Neuropathologie
Hôpital Kremlin Bicêtre
Bicêtre, France

1. Said G, Saimot AG, Lacroix C, et al. Neurological complications of HIV and AIDS. In: Warlow CP, Van Gijn J, eds. *Major Problems in Neurology*. Vol 34. London: WB Saunders; 1997:181–195.
2. Brinkman K, Hofstede HJM, Burger DM, et al. Adverse effects of reverse transcriptase inhibitors: mitochondrial toxicity as common pathway. *AIDS*. 1998;12:1735–1744.
3. Leon-Monzon M, Lamperth L, Dalakas MC. Search for HIV proviral DNA and amplified sequences in the muscle biopsies of patients with HIV polymyositis. *Muscle Nerve*. 1993;16:408–413.
4. Kopelman RG, Zolla-Pazner S. Association of human immunodeficiency virus infection and autoimmune phenomena. *Am J Med*. 1988;84:82–88.
5. Autran B, Carcelain G, Li TS, et al. Positive effects of combined antiretroviral therapy on CD4+ T cell homeostasis and function in advanced HIV disease. *Science*. 1997;277:112–116.

TRANSIENT ANTICARDIOLIPIN ANTIBODY SYNDROME IN A PATIENT WITH PARVOVIRUS B19 INFECTION

To the Editor:

Transient autoantibodies are often produced in response to viral infections (1,2). Although these autoantibodies are usually polyspecific and occur in low titers, some patients develop high-titer antibodies with subtype specificity.

Human parvovirus B19 causes several clinical syndromes including erythema infectiosum, polyarthritis, hepatitis, autoantibody expression, and aplastic crises in patients with hemolytic anemia or hemoglobinopathies (3,4). Anticardiolipin antibodies have been reported infrequently in adults infected with parvovirus B19. We report a patient with transient anticardiolipin antibody syndrome and thrombosis after human parvovirus B19 infection.

A 25-year-old previously healthy man was admitted with left upper-quadrant abdominal pain and a 2-week history of fever. Physical examination revealed a fever of 38.8°C and tender splenomegaly. There was no hepatomegaly or lymphadenopathy, and no other abnormalities were noted.

Splenomegaly (and the absence of hepatomegaly) were confirmed with an abdominal ultrasonography examination. Persistent abdominal pain and worsening splenomegaly prompted a second ultrasound examination with duplex, which revealed a wedge-shaped lesion in the spleen consistent with an infarct and reversed flow in one of the branches of the splenic vein. There was no evidence of thrombosis in the hepatic vein or the main splenic vein. A computed tomographic scan of the abdomen confirmed the infarct area in the spleen and showed mild retroperitoneal lymphadenopathy.

Laboratory studies disclosed normal levels of antithrombin-III, protein C and protein C resistance, protein S, and homocysteine, and elevated titers of anticardiolipin antibody IgG (104 gpl/mL) and IgM (56 mpl/mL). Two weeks after presentation, further tests were strongly positive for IgM antibodies and slightly positive for IgG antibodies for parvovirus B19. There was no evidence of IgM antibodies for cytomegalovirus or Epstein-Barr virus infections.

The patient's condition was diagnosed as acute parvovirus B19 infection with the anticardiolipin antibody syndrome. He was treated with aspirin (100 mg per day) and his fever and upper abdominal pain resolved. An abdominal ultrasonography examination revealed normal flow in the splenic vein. Repeat tests 1 and 2 months later showed decreases in the titers of IgG and IgM anticardiolipin antibodies.

The natural history of human parvovirus B19 infection is biphasic, consisting of a viremic phase and an antibody response phase (3). Some patients are asymptomatic; others have a flulike illnesses. The onset of anti-B19 IgM antibodies is associated with clearance of viremia, and the second phase of the illness is frequently characterized by rash, arthralgia, or arthritis, and less frequently by autoantibodies in the blood (3,5,6).

Moore et al (7) reported 7 patients with parvovirus B19 infection who had a history of malar rash and arthralgia. Six of these patients had antinuclear antibodies, of whom 2 had antibodies to Scl-70, and 4 had antibodies to Sm, RNP, SS-A (Ro), or SS-B (La). Two patients presented with elevated levels of rheumatoid factor, and all had an elevated IgM antibody titer to parvovirus B19 at the onset of their illness. Hansen et al (1) reported a 54-year-old woman who presented with a history of febrile disease and diffuse pruritic rash. Laboratory studies showed evidence of anticardiolipin IgG and IgM. Further investigation revealed IgM antibodies to parvovirus B19.

Anticardiolipin antibodies have been found in a variety of viral illnesses. In one study (8), 40 patients with acute viral infection were tested for anticardiolipin antibodies by enzyme-linked immunosorbent assay. Eight of 10 patients with parvovirus B19 infection, 7 of 10 with Epstein-Barr virus infection, 10 of 10 with hepatitis A virus infection, and 8 of 10 with rubella had anticardiolipin antibodies.

Infection with parvovirus B19 may be associated with the expression of various autoantibodies and clinical events, as in our patient. In patients with prolonged febrile illness and