Fatal Cytomegalovirus Infection in a Patient without Evidence of Prior Immunodeficiency

Cytomegalovirus (CMV) infection is a common cause of death among immunocompromised individuals, whereas among immunocompetent hosts, CMV infections are generally subclinical. We describe a case of CMV infection with a rapidly fatal outcome in a patient for whom there was no evidence of prior immunodeficiency.

A 62-year-old, previously healthy African man was admitted to the Nairobi Hospital (Nairobi, Kenya) on 1 June 1996 for evaluation of fatigue, fever, cough, and dyspnea of 4 weeks’ duration. Physical examination revealed a very ill-appearing patient who was dyspneic and febrile (temperature, 38.5°C). Bilateral basal crepitus was elicited on auscultation, and hepatosplenomegaly was detected on abdominal palpation; there was no evidence of superficial lymphadenopathy. The patient’s blood pressure was 100/60 mm Hg, his heart rate was 110, and his respirations were 28/min. A chest radiograph showed an interstitial pulmonary process.

Laboratory hemato logic evaluation revealed anemia (hemoglobin level, 8.2 g/dL; RBC count, 3.1/mm³), leukopenia (WBC count, 2.3/mm³ with 32% neutrophils, 62% lymphocytes, and 6% monocytes), a low platelet count (100,000/mm³), and hypoproteinemia (total protein level, 39.5 g/L; normal range, 60–80 g/L). Parameters for liver and renal function were within normal limits. Evaluation of a bone marrow biopsy specimen showed hyperplastic hemopoiesis with abnormal erythropoiesis, granulopoiesis with a left shift (without excess blast forms), and rare micromegakaryocytes with naked nuclei. The patient developed diarrhea, and evaluation of a stool specimen (described as yellow and loose) showed many RBCs, WBCs, and yeasts, but no ova, cysts, or trophozoites were detected. Culture of the specimen was negative for bacteria. Broad-spectrum antibiotic therapy was administered.

Serologies for IgG to CMV were positive (11 au/mL), but those for IgM to CMV were negative, and no specific treatment was initiated for CMV. Serologies for antibodies to HIV-1 and HIV-2 were negative, as assessed by use of ELISA.

The patient’s condition deteriorated suddenly; he developed nau sea and vomiting. Laboratory studies revealed the following values: RBCs, 3.0/mm³; WBCs, 1,300/mm³ with severe lymphocytopenia, 350/mm³; and platelet count, 80,000/mm³. His respiratory symptoms persisted, as did the diarrhea. The patient became confused, having only intervals of lucidity, and his condition continued to deteriorate until he died 10 days after his hospital admission.

At autopsy, the right and left lungs weighed 1,339 g and 1,117 g, respectively. There were fibrinous adhesions on the pleural surfaces. Histological evaluation of lung sections showed bronchiolitis obliterans and marked interstitial fibrosis with type II pneumocyte proliferation. There were numerous CMV inclusions in the alveolar epithelial cells (figure 1).

Gross examination of the spleen at autopsy (weight, 1,220 g) showed focal areas of cortical infarction. Histological evaluation revealed fibrosis and lymphocyte depletion of the white pulp, macrophage hyperplasia with hemophagocytosis, and foci of extramedullary hemopoiesis. The hilar as well as mediastinal and paraortic lymph nodes appeared atrophic with severe lymphocyte depletion, fibrosis, vascular proliferation, and “burnt out” germinal centers. CMV inclusions were evident in some cells.

Immunophenotyping revealed a relative reduction of CD4+ T lymphocytes with a CD4/CD8 ratio of 0.5. Examination of the colonic mucosa showed multiple ulcerations, and characteristic CMV inclusions were detected on histological examination. Careful examination of the remaining viscera showed no relevant pathological findings.

A nested PCR that used universal lentivirus primers was performed on DNA extracted from paraffin-embedded lymph node, spleen, and lung specimens, according to previously published protocols [1]. There was no evidence of HIV-1, HIV-2, or lentivirus-related DNA on repeated assays.

CMV infection is a common cause of death among immunocompromised individuals, whereas among immunocompetent hosts CMV infections are generally subclinical. A mild and self-limiting mononucleosis-like syndrome occurs in ~10% of adults, and severe CMV disease in immunocompetent patients is rare [2–5]. The possibility that a subtle immunologic defect may be recognized in such cases in the future cannot be excluded, but currently there is no evidence to validate this hypothesis.

We described CMV infection with rapid fatal outcome in a patient for whom there was no evidence of prior immunodeficiency. A serology for IgM to CMV was negative in our case, as is usually observed in acute infections among immunocompromised patients or in reactivation of latent infections [6]. In addition, results of histology and immunophenotyping of lymphoid tissue...
were highly suggestive of AIDS. Antibodies to HIV-1 and HIV-2 were not detected by ELISA in the patient’s serum, nor could HIV or lentivirus-related DNA sequences be demonstrated by use of nested PCR on multiple paraffin-embedded samples of lymph node, spleen, and lung specimens.

A number of HIV-negative individuals have been identified worldwide with AIDS-like clinical and laboratory signs in the absence of other causes of immunodeficiency [7–10]. It is not clear whether the immunodeficiency in our patient was due to the CMV infection itself or to other undefined causes.

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Reference

Isolated Thrombocytopenic Purpura Associated with Infection Due to Verocytotoxin (Shiga Toxin)–Producing Escherichia coli Serotype O26:H11

Diarrhea-associated hemolytic uremic syndrome, characterized by acute renal failure, thrombocytopenia, and microangiopathic hemolytic anemia (MAHA), is a complication of infection due to verocytotoxin (VT)–producing Escherichia coli (VTEC) [1]. Occasionally patients present with incomplete hemolytic uremic syndrome consisting of acute renal injury and either thrombocytopenia or MAHA [2,3]. Post-infectious MAHA also occurs without renal injury [2,3], but isolated thrombocytopenic purpura without renal injury and MAHA has not been recognized. We report such a case, associated with infection by VTEC serotype O26:H11. The hospital diagnosis was idiopathic (immune) thrombocytopenic purpura (ITP).

A 21-month-old female presented for evaluation of an 8-day history of nonbloody diarrhea, an ecchymotic rash that developed 1 day after the onset of diarrhea, and a 24-hour history of fever. Physical examination showed an alert, well-hydrated infant with a rectal temperature of 39°C. Ecchymoses were present over the left periorbital area, as well as the thighs, elbows, and shins, and there were scattered petechiae over the trunk and extremities. Physical examination findings were otherwise normal.

Laboratory findings included marked thrombocytopenia (platelet count, 22.0 × 10^9/L); hemoglobin, 12.8 g/dL; hematocrit, 39.1%; WBC count, 11.1 × 10^9/L; and normal prothrombin time and partial thromboplastin time. Microscopic evaluation of a blood smear showed reduced platelet numbers, minimal anisocytosis and poikilocytosis, but no schistocytes. Bone marrow examination showed normal cellularity and unremarkable megakaryocytes. Urinalysis results were normal, and there was no evidence of proteinuria. Blood urea nitrogen and creatinine values were normal. The Coomb’s test, antinuclear factor test, and a complement fixing antibody test for platelet antibodies were negative, and Ig levels were normal. The patient’s serum, obtained 9 days after the appearance of symptoms, was negative for antibodies to Epstein-Barr and varicella zoster viruses, and a test for hepatitis B surface antigen was negative. There was no serological evidence of mumps, measles, or rubella. Tests for antibodies to parvovirus B19 were not performed. Cultures of blood obtained on admission were negative. The serum had a neutralizing antibody titer to VT1 of 16. Management was conservative, and the child did not receive corticosteroids, iv Ig, antibiotics, or platelets. Recovery was uneventful.

Cultures of stool obtained on admission were positive for VTEC serotype O26:H11, but negative for Campylobacter, Shigella, Salmonella, and Yersinia species. Electron microscopic evaluation of stool was negative for viruses.

We tested the patient’s serum sample for antibodies to E. coli O26 lipopolysaccharide (LPS) by use of ELISA [4]. There were markedly elevated levels of IgG, IgA, and IgM antibodies to O26 LPS which were, respectively, 7, 16, and 48 standard deviations above the mean values for sera from 38 control patients aged 1 to 3 years.