Unusual Presentation of Measles Giant Cell Pneumonia in a Patient with Acquired Immunodeficiency Syndrome

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The typical clinical presentation of measles in a normal immunocompetent host includes cough, coryza, conjunctivitis, Koplik's spots, and rash. However, in an immunocompromised host, measles may have an atypical clinical presentation and may be commonly associated with severe pneumonia or encephalitis. We report a fatal case of measles pneumonia without any clinical features that suggest measles in a patient with acquired immunodeficiency syndrome.

Case report. A 14-year-old hemophilic patient with HIV type 1 (HIV-1) infection and a 10-day history of fever and cough was admitted to Hokkaido University Medical Hospital (Sapporo, Japan) on 25 April 1996. Hemophilia A had been diagnosed at birth and HIV infection had been diagnosed at 4 years of age. He had received trimethoprim-sulfamethoxazole (TMP-SMX) for prophylaxis of Pneumocystis carinii since 1991. Antiretroviral therapy with zidovudine and didanosine had been initiated in 1992. He did not have a history of severe symptoms related to HIV infection before admission. In April 1996, without our knowledge, he stopped taking his medication, because of side effects, such as headache, nausea and anorexia. Ten days before admission, he developed a cough, but a radiograph of the chest showed no abnormalities.

Although therapy with aerosolized pentamidine isothionate was started, severe coughing and fever developed. Antiretroviral therapies could not be continued because of nausea and vomiting. There was no history of measles vaccination or replacement therapy of iv immunoglobulin (IVIG) before admission.

The results of a retrospective serological study for measles, which was done by use of an ELISA, showed no IgG or IgM antibodies to measles.

A physical examination performed at the time of admission revealed fever, oral candidiasis, and purpurigo nodularis on his legs. Breathing sounds were normal by auscultation. Results of laboratory examination showed a hemoglobin concentration of 10.4 g/dL, a hematocrit level of 32.3%, a platelet count of 478,000 cells/mm³, and a WBC of 3600 cells/mm³ (49% segmented neutrophils, 5% bands, 21% lymphocytes, 24% monocytes, and 1% basophils) with a CD4⁺ lymphocyte count of 5 cells/mm³. A radiograph of the chest revealed bilateral diffuse interstitial and alveolar infiltrates. Sputum specimens tested negative for Pneumocystis carinii on silver staining but tested positive for Streptococcus pneumoniae on culture.

Antibacterial therapy with fosfomycin and minocycline was started. After TMP-SMX therapy was discontinued, the patient developed cough and fever. Thus, in view of the possibility of Pneumocystis carinii infection, he was given iv pentamidine isothionate. However, further clinical deterioration necessitated administration of oxygen by means of a mask on the 11th hospital day. IVIG was also administered on the 13th and 14th hospital days. Because of the side effects of pentamidine isothionate, such as hypoglycemia and arrhythmia, treatment was changed to iv TMP-SMX on the 15th hospital day. Despite such treatments, respiratory distress subsequently developed, and a radiograph of the chest revealed progression of bilateral diffuse interstitial and alveolar infiltrates. In view of the possibility of cytomegalovirus, he was treated with ganciclovir on the 26th hospital day. However, he became progressively hypoxemic and hypotensive, and he died of pneumonia of unknown origin on the 27th hospital day. There was no history of rash before or after the onset.

Postmortem examination of lung tissue was performed. Pathological examination showed interstitial pneumonia with multinuclear giant cells that contained numerous intranuclear and intracytoplasmic inclusions, and alveolar damage, a finding consistent with measles giant cell pneumonia. The cytoplasms of alveolar epithelial cells, macrophages, and multinuclear giant cells reacted positively to a mouse monoclonal antibody to measles hemagglutinin (Chemicon International) by means of indirect immunoperoxidase staining (figure 1). To confirm the diagnosis of measles pneumonia, reverse transcriptase–PCR study was performed; the results revealed the presence of measles RNA in lung tissue specimens.

Discussion. Pneumonia is an important complication of
measles infection in immunocompromised hosts. It appears that cell-mediated immunity is more important than humoral immunity in the defense against measles infection. Patients with an abnormality in cell-mediated immunity have severe illness, frequently with the absence of rash, whereas those with an abnormality in humoral immunity appear to have typical measles illness. The clinical course of measles in HIV-infected patients has been reported to be similar to that in patients with depressed cell-mediated immunity [1–5]. Twelve cases of measles pneumonia in children with HIV-1 infection have been reported [1–5]. Six of the 12 children died of measles pneumonia. Although 5 of 12 children had a characteristic measles rash, 2 children presented with no rash. Five children exhibited a delayed or transient rash [1–5]. It is conceivable that measles rash may be due to a cell-mediated hypersensitivity reaction.

For our patient, the direct cause of death was giant cell pneumonia caused by measles, as defined by pathological, immunological, and molecular examinations. However, the source of measles infection in our patient was not determined. The development of a severe cough after discontinuation of TMP-SMX therapy and the absence of a rash made the diagnosis of measles difficult. In fact, we never considered the possibility of measles infection. The relationship between the severity of measles and the degree of HIV-induced immunosuppression has not been well characterized. CD4+ and CD8+ lymphocyte counts in our patient were only 5 cells/mm³ and 270 cells/mm³, respectively; these counts indicate that cell-mediated immunity was completely destroyed. Although reports of measles in HIV-infected patients are limited, severe measles infection has been reported to have occurred in patients with a CD4+ lymphocyte count of ≥200 cells/mm³ [6]. Although the relevance of CD46 for the entry of wild-type measles virus remains controversial, measles virus may infect HIV-infected CD4+ lymphocytes [7]. Measles may exacerbate the immunosuppression caused by HIV, which would alter the clinical presentation of measles.

We propose that measles pneumonia should be considered as one of causes of respiratory disease even in HIV-infected patients without known exposure to measles. Suspicions of measles pneumonia in HIV-infected patients will prevent the delay of diagnostic examination and allow for earlier initiation of treatment. However, since there are limited therapies available for the treatment of severe measles infections, measles vaccination is recommended for all HIV-infected children with the exception of those with severe immunosuppression [6].

References