Evidence for human immunodeficiency virus (HIV) infection of the brain in a patient with aplastic anemia*

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Summary. A young female patient with a long history of intravenous drug abuse died after a fulminant course of aplastic anemia. At postmortem examination, she was found to have multinucleate giant cells and immunocytochemical evidence of human immunodeficiency virus (HIV) infection of the central nervous system. This case raises the possibility that HIV infection contributed to the patient's aplastic anemia, and suggests that HIV-associated giant cells might be found retrospectively or prospectively within the brains of patients who die of conditions other than those narrowly defined as acquired immune deficiency syndrome (AIDS) or AIDS-related complex (ARC). It furthermore emphasizes that HIV infection of the nervous system is not necessarily accompanied by clinically apparent neurological disease.

Key words: Human immunodeficiency virus (HIV) - Multinucleate giant cells - Aplastic anemia - Acquired immune deficiency syndrome (AIDS)

In the course of a systematic review of autopsy material derived from the nervous system of patients who died after bone marrow transplantation [13], we have encountered a patient not specifically known to have acquired immune deficiency syndrome (AIDS) or AIDS-related complex (ARC), in whom several organs—most prominently the brain—showed evidence of infection by the human immunodeficiency virus (HIV).

Case report

A 25-year-old woman with a 5-year history of intravenous drug abuse came to autopsy (in June, 1984) 3 1/3 months after the diagnosis of aplastic anemia was made. Initial therapy for the anemia had consisted of a course of antithymocyte globulin (20 mg/kg intravenous for 8 days) shortly after that diagnosis was confirmed. A bone marrow transplant from an HLA identical brother was performed three months after the diagnosis of aplastic anemia, and one day after total lymphoid irradiation (300 rads). Medications received prior to and after the transplant included Piperacillin, Amphotericin B, Vancomycin, Polymixin, cyclophosphamide, cyclosporin and methotrexate. Several blood transfusions were performed. There was no indication by history or physical examination that the patient had experienced clinical neurological morbidity. Four days after the transplant, the patient became comatose following an unexplained cardiac arrest, but retained significant brain stem function. One day prior to death, she experienced abnormal movements that were thought to indicate a hemorrhage or an infarct within the basal ganglia. An electroencephalogram showed severe diffuse bilateral slowing. The patient died 8 days following the cardiac arrest and 12 days following the bone marrow transplant.

Necropsy findings included multiple petechial hemorrhages throughout many organs, including subendocardial hemorrhages within the heart, severe cytomegalovirus (CMV) and Pneumocystis carinii pneumonia, right ventricular hypertrophy and dilatation of the heart, chronic passive congestion with centrilobular necrosis and early fibrosis of the liver, and lymphoid depletion of the lymph nodes and spleen. The brain showed slight cerebral edema at the time of cutting after routine formalin fixation, and narrowing and elongation of the brain stem, but no other focal abnormalities. Histological sections of brain showed changes of severe diffuse anoxic-ischemic encephalopathy in all regions, consistent in age with anoxia having occurred at the time of cardiac arrest 8 days before death. Sections of the diencephalon showed many multinucleate cells including multinucleate giant cells, usually in a perivascular distribution (Fig. 1) and scattered perivascular mononuclear inflammatory cells. The cells showed either a small amount of cytoplasm, which was finely granular or foamy, or a negligible amount of cytoplasm, i.e., the nuclei themselves seemed to form an aggregate (Fig. 1).

An immunocytochemical staining procedure (avidin-biotin-peroxidase) similar to one described previously [27], but instead performed using a mouse monoclonal antibody to HIV Gp41 envelope protein (obtained from K. Shriver and L. Goldstein, Genetic Systems, Seattle, Washington) was carried out on paraffin sections of brain, lung and bone marrow. Positive controls included tissues known to be infected by HIV and HIV-infected HUT 78 cells. Negative controls included tissue sections stained after omission of the primary antibody. Sections of the diencephalon showed numerous strongly staining macrophages.
Fig. 1A, B. Microscopic sections of diencephalon show prominent perivascular multinucleate cells (arrows, A) with either a small amount of granular or foamy cytoplasm or negligible cytoplasm (B). Other scattered inflammatory cells are seen. Hematoxylin and eosin, A × 425, B × 714