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Epidemiologic Notes and Reports Pneumocystis carinii Pneumonia among Persons with Hemophilia A

CDC recently received reports of three cases of Pneumocystis carinii pneumonia among patients with hemophilia A and without other underlying disease. Two have died; one remains critically ill. All three were heterosexual males; none had a history of intravenous (IV) drug abuse. All had lymphopenia, and the two patients who were specifically tested have had in vitro laboratory evidence of cellular immune deficiency. The case reports follow.

Patient 1: A 62-year-old resident of Westchester County, New York, with a history of chronic hepatitis had received frequent injections of Factor VIII concentrate for severe hemophilia for many years. In February 1981, he began to experience weight loss and vague right upper quadrant abdominal discomfort associated with laboratory evidence of increasing hepatic dysfunction. In December 1981, while hospitalized in Miami, Florida, for elective knee surgery, he complained of cough and fever. He was lymphopenic, and chest X-ray revealed interstitial infiltrates compatible with viral pneumonia. He was discharged in late December after a brief course of corticosteroids associated with overall clinical improvement. He returned in severe respiratory distress a few days later. Open lung biopsy on January 5 revealed P. carinii, for which he received sulfamethoxazole/trimethoprim (SMZ/TMP) during the 2 weeks before death. P. carinii pneumonia and micronodular cirrhosis were documented at post-mortem examination.

Patient 2: A 59-year-old lifelong resident of Denver, Colorado, noted the onset of gradual weight loss, dysphagia associated with pharyngitis, aphthous-like ulcers, and anterior cervical adenopathy beginning in October 1980. As a patient with severe hemophilia, he had received frequent injections of Factor VIII concentrate for several years. Weight loss continued over a period of months. Oropharyngeal candidiasis was diagnosed in February 1982. He was hospitalized in May 1982 with symptoms including nausea, vomiting, and recurrent fever. Pneumonia was diagnosed, and P. carinii and cytomegalovirus (CMV) were repeatedly identified from lung tissue or bronchial secretions using histopathologic and culture techniques. Therapy with SMZ/TMP and pentamidine isethionate continued until death on July 5, 1982. Laboratory evidence for cellular immune dysfunction included absent mitogen responses and depletion of the T-helper lymphocyte cell population, relative increase in T-suppressor cells, and resultant inverted T-helper/T-suppressor ratio.

Patient 3: A previously healthy 27-year-old lifelong resident of northeastern Ohio developed fever, urinary frequency and urgency, and extreme lassitude in July 1981. He had frequently received parenteral Factor VIII concentrate for severe hemophilia. Bilateral pneumonia was diagnosed in October 1981, and open lung biopsy revealed P. carinii. He responded

successfully to a 3-week course of SMZ/TMP. In February 1982, he received ketoconazole to suppress repeated episodes of oral candidiasis. He was hospitalized again in April with fever, splenomegaly, anemia, and lymphopenia. An extensive tumor work-up (including laparotomy) did not uncover an underlying malignancy. Cultures of bone marrow, liver, mesenteric lymph nodes, and blood grew Mycobacterium avium. In vitro immunological testing in March indicated a reduction in absolute number of circulating T-cells. Subsequent, more extensive testing documented the lack of lymphocyte responsiveness to mitogens, absolute and relative decrease in T-helper cells, relative increase in T-suppressor cells, and resultant inverted T-helper/T-suppressor ratio.

For each patient, records of the administration of Factor VIII concentrate were reviewed to determine manufacturer and lot numbers. No two of the patients are known to have received concentrate from the same lots. Reported by: NJ Ehrenkranz, MD, South Florida Hospital Consortium for Infection Control, J Rubini, MD, Cedars of Lebanon Hospital, Miami, R Gunn, MD, State Epidemiologist, Florida Dept of Health and Rehabilitative Svcs; CR Horsburgh, MD, T Collins, MD, U Hasiba, MD, W Hathaway, MD, University of Colorado School of Medicine, W. Doig, MD, R Hopkins, MD, State Epidemiologist, Colorado Dept of Health; J Elliott, MD, W Hoppes, MD, I Patel, MD, Aultman Hospital, Canton, CE Krill, MD, Children's Hospital, Akron, T Halpin, MD, State Epidemiologist, Ohio Dept of Health; Field Services Div, Epidemiology Program Office, Div of Host Factors, Center for Infectious Diseases, Task Force on Kaposi's Sarcoma and Opportunistic Infections, CDC.

Editorial Note

Editorial Note: Pneumocystis carinii pneumonia has not been previously reported among hemophilia patients who have had no other underlying diseases and have not had therapy commonly associated with immunosuppression. A review of the Parasitic Disease Drug Service's records of requests for pentamidine isethionate for 1980-1982 failed to identify hemophilia among the underlying disorders of patients for whom pentamidine was requested for Pneumocystis carinii therapy.

The clinical and immunologic features these three patients share are strikingly similar to those recently observed among certain individuals from the following groups: homosexual males, heterosexuals who abuse IV drugs, and Haitians who recently entered the United States.(1-3) Although the cause of the severe immune dysfunction is unknown, the occurrence among the three hemophiliac cases suggests the possible transmission of an agent through blood products.

Hemophilia A is a sex-linked, inherited disorder characterized by a deficiency in Factor VIII activity. There are an estimated 20,000 patients with hemophilia A in the United States (4). Severity of disease is classified according to percentage of endogenous Factor VIII activity. Approximately 60% of the 20,000 are classified as severe, and 40% are classified as moderate (4). Factor VIII deficiency can be treated with intravenous administration of exogenous Factor VIII as either cryoprecipitate made from individual units of fresh frozen plasma or lyophilized Factor VIII concentrate manufactured from plasma pools collected from as many as a thousand or more donors.

CDC has notified directors of hemophilia centers about these cases and, with the National Hemophilia Foundation, has initiated collaborative surveillance. A Public Health Service advisory committee is being formed to consider the implication of these findings. Physicians diagnosing opportunistic infections in hemophilia patients who have not received antecedent immunosuppressive therapy are encouraged to report them to the CDC through local and state health departments.

References

1. CDC. Follow-up on Kaposi's sarcoma and Pneumocystis pneumonia. MMWR 1981;30:409-10.

2. CDC. Update on Kaposi's sarcoma and opportunistic infections in previously healthy persons--United States. MMWR 1982;31:294,300-1.

3. CDC. Opportunistic infections and Kaposi's sarcoma among Haitians in the United States. MMWR 1982;31:353-4,360-1.

4. Petit CR, Klein HG. Hemophilia, hemophiliacs and the health care delivery system. National Heart and Lung Institute, Division of Blood Diseases and Resources, Office of Prevention, Control, and Education. DHEW Publication No. (NIH) 76-871, 1976