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RECURRENT/PERSISTENT PNEUMONIA IN A 3 1/2-YEAR-OLD-GIRL DUE TO ACQUIRED IMMUNE DEFICIENCY SYNDROME

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INTRODUCTION

Acquired Immune Deficiency Syndrome (AIDS) is now a very well known illness. Since the first cases reported in 1981¹ in homosexual males in California, many more cases have been reported in intravenous drug abusers, certain Haitian immigrants, recipients of HIV infected blood transfusions or blood products and sexual partners of patients with the syndrome. In 1982²⁻³ the first two cases of pediatric AIDS were reported in the same journal. One was a 20-month-old white male who had received multiple blood transfusions including a platelet transfusion from a person later found to have AIDS. The other child, in a different report, was a 10-year-old hemophiliac patient who had received factor VIII concentrate in a home care program. In children the disease occurs in offspring of women in high risk groups and in recipients of infected blood or blood products.^{4,5} The etiologic agent of Acquired Immune Deficiency Syndrome is a lymphotropic retro-virus designated as Human T-cell Lympho-

trophic Virus Type III; Lymphadenopathy-associated virus (HLTV-III/LAV).⁶ As of June, 1984, 57 cases of AIDS in children have been reported to CDC.⁷ Most of the reported cases have been from three states: New York, New Jersey, and Florida. The prognosis in children with AIDS is poor. Fifty-eight percent of the cases reported to CDC have died; half of them died the first nine months after diagnosis and half of the children under one year of age died within six months after the diagnosis.

The following is the report of the first case of a Delaware born child who developed AIDS, born from a mother who was not in a high risk group.

CASE REPORT

This is a 3 1/2-year-old Hispanic female born in Delaware from parents of Puerto Rican origin. She was delivered after a full-term pregnancy by repeat cesarean; the mother was Gravida III, Para II with the first pregnancy producing a still born. Her Apgar scores at birth were 9/9, birth weight was 7 lbs 10 oz with no complications during the pregnancy, labor, or delivery. The baby had a normal neonatal period. Her older sister is five years old and healthy; her mother is 27 years old, and her father is 32 years old, both being apparently healthy. They have never received any blood transfusions or blood products and both parents denied any drug use. The father denied homosexuality or bisexuality but did have several sexual partners. The patient was formula fed

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and during the first 2 1/2 years she had a normal development and was in good health. During this time she received three DPT vaccines, three Oral Polio vaccines and an MMR vaccine without any problems or serious side effects. Two tuberculosis skin tests were negative. During this time she was never hospitalized, never received any blood transfusions or blood products, and never had any surgical procedures. At two years of age, she had a chest x-ray which was normal. At age 2 1/2 she started having multiple infections for which she visited the local hospital emergency rooms on at least 12 occasions. During this time, according to the mother, she developed high evening fevers and productive cough. Nine months ago another chest x-ray showed nodular bibasilar infiltrates. She was treated with oral antibiotics and did improve. Following this, she was hospitalized on three occasions because of recurrent pneumonia. She was treated with IV antibiotics, postural drainage, and symptomatic medications, She clinically improved each time, but her radiological picture remained the same. During the same time period she developed both tinea corporis which resolved with medications, and oral moniliasis which did not improve with topical medications. Prior to this time her weight and length were in the 50th percentile, but since then her weight and length had dropped to below the fifth percentile. She developed a moderate microcytic hypochromic anemia with a hemoglobin of 10 gms and a hematocrit of 32%. During these three hospital admissions several tests were done and found to be normal: sweat tests x 2, N.B.T. test, alpha 1 anti-trypsin, barium swallow, gastric aspirate to rule out hemosiderosis, PPD, gastrographic examination of the esophagus to look for a tracheoesophageal fistula, stool for ova and parasites, and a lactic dehydrogenase (LDH). During her previous hospitalization all the physical findings had been localized to the pulmonary system with the presence of crepitant rales at both bases. These improved with therapy but did not disappear. On this admission her physical examination again showed the presence of crepitant rales at both bases. There was also an enlargement of the liver which was firm and palpable 6 cm. below the right costal margin; the spleen was also firm and palpable 3 cm. below the left costal margin. There was generalized lymphadenopathy (axillar, inguinal, submaxillary, etc). The lymph nodes were 1 cm in diameter, mo-

bile and non-tender. There was moderate enlargement of the parotid glands with atypical dermatitis of the face plus the presence of oral moniliasis. The rest of the physical examination, including a neurological evaluation, was normal.

The following tests were found to be abnormal: sedimentation rate was 135, rheumatoid factor was positive 1:280, ANA was positive 1:80, total protein was 10, albumin 4.2, globulin increased to 5.8, and the albumin/globulin ratio was 0.7. The patient had polyclonal hypergammaglobulinemia: IGA was 708 mgs/dl (normal for age 22-159), IGG was 3,900 mgs/dl (normal for age 400-1100), IGM 453 mgs/dl (normal for age 47-200). The elisa antibody was repeatedly reactive; the Western blot was reactive to the major HIV specific antigens: the core (P24), as well as the envelope (Gp41,GP120/160). These results indicated an infection with retrovirus HIV. Lymphocyte function studies were done showing the following values:

	RESULTS	REFERENCE RANGE
Total WBC	7,800	4,000-11,000/cu mm
Total lymphocyte count	3,016	800-2,600/cu mm
Total B lymphocytes	211	100-600 cu mm
% of	7%	5-20%
Total T lymphocytes	2,564	800-2,200 cu mm
% of	85%	65-85%
Helper-inducer	452	more than 400
% of	18%	45-75%
Suppressor-cytotoxic cells-T8	2,051	250-750/cu mm
% of	80%	18-40%
Helper-suppressor ratio	0.22%	more than 1.0%

At this time, other titers were also performed: CMV elisa value was 0.06, measles-rubella was 0.00, indicating that no antibody was detectable in any of them.

Epstein-Barr virus titers were:

EBV viral capsid IGM: titers less than 1:10

EBV viral capsid IGG: titer 1:640

EBV early diffuse AG: titer 1:40

EBV early restrict AG: titer less than 1:10

EBV nuclear AG: titer 1:20

EBNA control: titer less than 1:10

The titer results are suggestive of an Epstein-Barr virus infection in the past. EBV associated lymphoproliferative disease is an important and common complication in children with AIDS.⁸ Two types of lymphoproliferative diseases are associated with EBV-DNA: a) central nervous system lymphoma b) chronic lymphocytic interstitial pneumonitis (LIP).

Small bowel and gastric mucosa biopsies were normal, an esophageal mucosa biopsy showed mild esophagitis but the culture was negative for candida and other fungus or bacteria. A bone marrow aspiration examination and cultures were normal. A CAT scan of the head was also normal.

The rest of the family's results were: her five-year-old sister shows a non-reactive elisa antibody in repeated tests, but her mother and father were found reacting positive to EIA: more than 2000 (cut-off = 0.12).

DISCUSSION

Our patient, born by a Cesarean section and formula fed, could have contracted the retro-virus in utero, as was the case in the previous report⁹ in 1985 which described a premature infant of 28 weeks gestation, Cesarean born, with transplacental transmission of HTLV-III virus. Another report¹⁰ in the same year describes the intrauterine transfer in a 20-week-old fetus.

Our patient was healthy until 2 1/2 years of age when she developed recurrent febrile episodes, persistent pneumonia, and later oral moniliasis. Such symptomatology and findings were also encountered in the majority of children with AIDS reported by previous authors.¹¹⁻¹⁴ Failure to thrive, which occurred in our patient, has also been reported in previous cases.¹¹⁻¹⁴

The presence of atopic dermatitis has been previously reported in some of these children.¹¹⁻¹⁴ Our patient also showed a mild enlargement of the parotid glands, hepatosplenomegaly and generalized enlargement of the lymphatic nodes. All of the above findings

have been previously reported.¹¹⁻¹⁵ In regard to the laboratory findings, our patient shows polyclonal hypergammaglobulinemia, a finding present in the majority of children with AIDS, especially children who have Lymphocytic Interstitial Pneumonitis.¹¹⁻¹⁵

About 80% of the total circulating lymphocytes are peripheral T lymphocytes which are divided into two major groups: one with the T4 antigen called a "helper" since it has a helper role in the immune responses; the other with a T8 antigen called a "suppressor" which has cytotoxic and suppressor functions. Changes in the T4/T8 ratio (less than 1.0%) is usually found in children with AIDS¹¹⁻¹⁴ as was the case in our patient.

Lymphocytic Interstitial Pneumonitis (L.I.P.), also called Pulmonary Lymphoid Hyperplasia, and Pneumocytic Carinii Pneumonia are the two most common pulmonary disorders in children with AIDS and AIDS related complex.¹¹⁻¹⁵ Some authors¹⁶ believe that they can make the diagnosis of lymphocytic interstitial pneumonitis based only on x-ray findings. Other authors¹⁷ do not agree that this is possible, but recently Rubinstein¹⁵ has found a perfect correlation between lymphocytic interstitial pneumonitis in children with AIDS with other physical findings and laboratory tests.

In Rubenstein's study, children with AIDS who have pulmonary lymphoid hyperplasia, also exhibit enlargement of peripheral lymph nodes and the parotid glands. Likewise they have a polyclonal hypergammaglobulinemia with marked elevation of IGG. Their serologic assays demonstrate elevated EBV titers suggestive of Epstein-Barr infection. Serum LDH levels in these patients are found to be normal or slightly elevated. By contrast, patients with pneumocytic carinii pneumonia do not have enlargement of the lymph nodes nor their parotid glands; their EBV serum titers are normal, their LDH serum levels are elevated, and their serum IGG levels are normal or slightly elevated. Based on these findings, a differential diagnosis can be made without the need for surgical biopsy.

This is the first case of AIDS in a child born in Delaware by a cesarean section from parents who were not in the high risk categories. Heterosexual partners have also been found to transmit the disease¹⁸ to their spouses through intercourse and oral sex, and to their children by perinatal transmission as it probably was in our patient's

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family. In the above study, the overall rate of transmission of HTLV-III/LAV among heterosexual couples was 58%.

Until this decade a differential diagnosis of AIDS was not considered in a child with recurrent or persistent pneumonia, but the time has come to do so in any child.

As of April, 1988, 934 cases of AIDS in children under 13 years of age had been reported to the CDC, representing about 1 1/2% of all cases of AIDS. Of the 932 cases with known race, 53% were black, 23% hispanic, and 23% white non-hispanic.

In our case the diagnosis was made in July 1988. She is still alive. Since that time, another case of a child with AIDS has been reported in Delaware.¹⁹

ADDENDUM

The numbers of reported cases of AIDS in the United States²⁰ continues to increase every year. As of December 31, 1988, 82,764 cases have been reported to the Center for Disease Control (CDC) and of these cases, more than 46,000 have died. There were 1,346 cases in children less than 13 years of age; of these 52.5% were black, 23.9% were white and 22.9% were hispanic. One of the best latest review articles about pediatric AIDS appears in the January issue of the *Journal of Pediatrics*.²¹

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