Brief communications

Pneumocystis carinii pneumonia in an infant with X-linked agammaglobulinemia

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X-linked agammaglobulinemia (XLA) is characterized by severe congenital hypogammaglobulinemia with marked reduction in the number of pre-B and mature B cells. *Pneumocystis carinii* pneumonia (PCP) is an opportunistic pulmonary infection that occurs mainly in patients with T-lymphocyte defects. We report the unusual occurrence of PCP in an infant with XLA.

Abbreviations used
IVIG: Intravenous immunoglobulin G
PCP: *Pneumocystis carinii* pneumonia
XLA: X-linked agammaglobulinemia

CASE REPORT

A 4-day-old male was diagnosed with XLA because of a family history of the disease in two male cousins whose genomic DNA had shown a mutation in exon 8 of the Bruton's tyrosine kinase locus (unpublished communication from Mary Ellen Conley, MD, St. Jude Children's Research Hospital, Memphis, Tenn.). Low serum immunoglobulins and absent B lymphocytes were consistent with the diagnosis (Tables I and II). Intravenous immunoglobulin G (IVIG; 0.4 gm/kg) given every 3 to 4 weeks was started at 5 weeks of age, when the serum IgG level was 0.44 gm/L. Trough serum IgG after the third IVIG infusion was 0.59 gm/L (normal, 0.18 to 0.53 gm/L). At 4 months of age, 2 weeks after the fourth IVIG infusion, the patient developed a dry cough, anorexia, and fussiness. Despite a normal physical exam and chest roentgenogram, he was given an additional dose of IVIG. His symptoms persisted during the following week, and he developed an acute onset of tachypnea and grunting. For the previous 3 months, the patient had been in close contact at home with his recently deceased grandfather who had a lung malignancy that had rendered him unfit for therapy. The patient's physical exam showed weight of 5.5 kg, temperature of 37° C, pulse of 135 beats/minute, blood pressure of 99/35 mm Hg, respiration of 60 breaths per minute, oxygen saturation on room air of 89%, absent tonsils, lower intercostal and subcostal retractions, and normal lung auscultation. Chest radiography showed diffuse haziness with hyperinflation. A complete blood cell count showed white blood cells of 15,200 cells/mm^3 (normal range, 6000 to 17,000 cells/mm^3), an absolute neutrophil count of 3340 cells/mm^3 (normal range, 1000 to 8500 cells/mm^3), and an absolute lymphocyte count of 8820 cells/mm^3 (normal range, 4000 to 13,500 cells/mm^3). The patient's serum IgG level was 0.79 gm/L. Silver staining of bronchoalveolar lavage fluid showed a positive result for *Pneumocystis carinii*. No other organisms were isolated. Results of a polymerase chain reaction and culture for the human immunodeficiency virus were negative, and results of cultures for cytomegalovirus were also negative. He was treated with intravenous trimethoprim sulfamethoxazole, methylprednisolone, and 0.4 mg/kg weekly IVIG. After initial improvement, the hospital course was complicated on the tenth day by a recurrence of tachypnea and an increased oxygen requirement and the appearance of extensive oral thrush. A repeat bronchoalveolar lavage fluid culture grew *Candida albicans*, and the patient was treated with Amphotericin B. His condition eventually improved, and the oxygen requirement resolved. During recovery, at 6 months of age, T-lymphocyte subpopulations (Table II), cytotoxic T-cell function assays, and natural killer cell function assays were normal. Proliferative responses were transiently decreased but normalized 2 weeks later (Table III) and remained normal 3 months later.

DISCUSSION

There are several reports of PCP in infants with hypogammaglobulinemia and normal T-lymphocyte function.[1, 2] The number of circulating B lymphocytes in these infants was either not reported[1] or was normal.[2] In two patients with hypogammaglobulinemia and normal T- and B-lymphocyte numbers, PCP was ascribed to depressed natural killer cell function.[3, 4] In a series of 96 patients with XLA, a 21-year-old patient receiving IVIG developed PCP as a near-terminal complication of chronic pulmonary disease.[5] Except for a transient suppression during treatment with steroids and during recovery, our patient had normal T-lymphocyte and natural killer cell numbers and function, although a decrease in T-lymphocyte response because of his young age at the onset of the infection could have contributed to his susceptibility to *P. carinii*.

TABLE I. Serum immunoglobulin levels

Age	IgA (gm/L, 0.13-0.52)*	IgM (gm/L, 0.19-0.83)	IgG (gm/L, 0.24-0.9)
4 days	< 0.06	0.07	0.89

*Values in parentheses indicate normal range.

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TABLE II. Lymphocyte subpopulation analysis

	Total lymphocyte	CD3		CD4		CD8		CD19		CD16	
Age	Absolute cells/mm³ (3610-8840)*	% (45-79)	Absolute cells/mm³ (2280-6450)	% (36-61)	Absolute cells/mm³ (1690-4600)	% (16-34)	Absolute cells/mm³ (720-2490)	% (14-39)	Absolute cells/mm³ (600-3000)	% (2-14)	Absolute cells/mm³ (100-1300)
4 days	6940	87	6041	65	4514	26	1805	<1%	<69	10	694
4 mo	1450	78	1131	44	636	34	493	<1%	<14	21	304
6 mo	7370	91	6708	60	4423	29	2138	<1%	<74	7	516
6½ mo	4536	95	4309	64	2903	29	1315	0	0	4	181

*Values in parentheses indicate normal range.

TABLE III. Mitogen stimulation assays

	Spontaneous (404 cpm)*		Phytohemagglutinin (235,464 cpm)		Concavalin A (145,551 cpm)		Pokeweed (35,725 cpm)	
Age	Patient (cpm)	Control (cpm)	Patient (cpm)	Control (cpm)	Patient (cpm)	Control (cpm)	Patient (cpm)	Control (cpm)
6 mo	438	582	90,471	188,149	58,381	246,263	94,067	32,559
6½ mo	170	240	419,707	249,194	222,489	144,129	48,272	35,725

*Numbers in parentheses indicate mean normal response.

Infants with hypogammaglobulinemia may be unable to produce protective immunoglobulins against *P. carinii*.[2] However, recurrent PCP has been reported in a patient with hypogammaglobulinemia while receiving IVIG therapy.[4] Our patient had PCP while regularly receiving IVIG with adequate trough levels, and he was replenished at the earliest onset of symptoms. Because most healthy individuals develop antibodies to *P. carinii* by 2 years of age, IVIG preparations pooled from healthy adult donors should have provided him with adequate amounts of IgG antibodies to *P. carinii*, although he remained IgA and IgM deficient.

In our patient the occurrence of PCP can not be explained by a deficiency in IgG antibody; T-lymphocyte number, proliferation, or cytotoxic function; or natural killer cell function. Possibly, the contact with the patient's terminally ill grandfather had provided an exposure to the organism. The diagnosis of PCP should be considered in patients with XLA who are first seen with symptoms or signs of respiratory distress, and patients with immunodeficiencies should not be exposed to other ill immunocompromised individuals.

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