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Paralytic Poliomyelitis in a Child with Agammaglobulinemia

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Abstract. This paper gives the clinical, immunological and virological data on a patient with agammaglobulinemia who developed paralytic poliomyelitis. The patient was a 3 year-old boy who had a typical B-cell defect without a T-cell defect. He had profound hypogammaglobulinemia and defective plasma cells and had repeated pyogenic infections which were controlled by gammaglobulin replacement therapy. At 3 years of age, he was admitted to our hospital with suspected meningitis. He had fever, tremor and neck stiffness for 3 days and subsequently developed paralysis in his left arm and right leg. There was lymphocytosis in the cerebrospinal fluid. A non vaccine-like strain of poliovirus type 2 was isolated from the stool.

Key words: Poliomyelitis – Agammaglobulinemia.

Introduction

Advances in antibiotic and gammaglobulin therapy have allowed adequate control of most infectious complications in patients with agammaglobulinemia. Pyogenic organisms are the main cause of repeated infections in such patients and viral infections usually take a normal course. However, disseminated vaccinia [7], severe poliomyelitis [4, 5, 6, 15, 17, 18], viral hepatitis [8], pneumocystis carinii [11], echovirus [16], and generalized cytomegalovirus infections [10] have been reported in patients with intact T-cell systems, as evaluated by the present methods. This paper reports a patient with agammaglobulinemia who developed paralytic poliomyelitis. Gammaglobulin replacement therapy did not alter the course of his illness.

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Case Report

The patient was born by normal delivery at full term on December 10th, 1974 and weighed 3060 g at birth. He had otitis media at one and 11 months of age, and had frequent colds and diarrhea associated with high fever, between the ages of 1 and 2 years. At 2 years of age, the child was admitted to Sapporo Medical College Hospital because of increased susceptibility to infection (Fig. 1). He had no siblings and there was nothing unusual in the family history except that the 2 male cousins died before 5 years of age from unknown causes. His past history revealed that he had received two doses of trivalent oral poliovaccine on May 17, 1975, and April 16, 1976, without

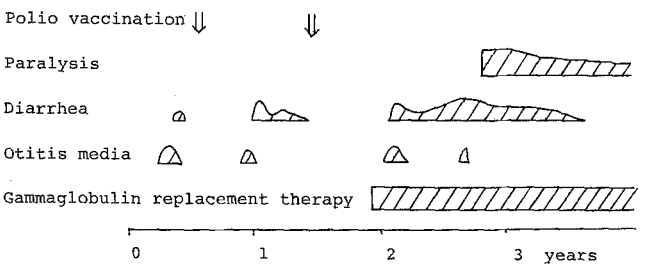

Fig. 1. Summary of clinical course of the patient with agammaglobulinemia

Table 1. Immunological investigation

Total protein	5.8 g/dl
γ-fraction	0%
Serum immunoglobulins	
IgG	0 mg/dl
IgM	< 10 mg/dl
IgA	0 mg/dl
Auto hemaggulutinin titer	
anti-A (−) anti-B (−)	
Plasma cell: Bone marrow	0%
Rectal biopsy	rare
Skin test	
Tuberculin test	(+)/16×17
Candida	(+)/10×10
SK/SD	(−)/ 2× 2
PHA	(−)/ 2× 2
Lymphocyte subpopulation	
T-cell: E-RFC	90.2%
B-cell: Fc-receptor	13.6%
C_3-receptor	2.0%
SIg-cell	0 %
Lymphocyte transformation to PHA	
S.I. = 128.0	

Table 2. Data on the identification of the poliovirus strain isolated from the patient

Case K.W.	rct/40 marker test				Intratypic serodifferentiation test				
	TCD_{50}/0.2 ml			Evaluation[a]	Wecker test			McBride test	
	Low T 35°C	High T 40°C	Difference		$Ratio_{YST}$	Normalized ratio	Antigenic character[b]	Normalized K value	Antigenic character[c]
Isolated strain (Identified an polio type 2)	8.50	8.33	0.17	+	0.25	89	Heterologous	29	Heterologous
Attenuated strain (Sabin type 2)	7.50	0.00	7.50	–	0.01	0	Isologous	100	Isologous
Virulent strain (MEF 1)	8.00	6.50	1.50	+	0.28	100	Heterologous	34	Heterologous

[a] Difference $\leqq 2.0$ (+), $\begin{matrix} > 2.0 \\ < 5.0 \end{matrix}$ (±), $\geqq 5.0$ (–)

[b] N. Ratio $\leqq 25$ (Homologous), $\begin{matrix} > 25 \\ < 75 \end{matrix}$ (±), $\geqq 75$ (Heterologous)

[c] N.K Value $\leqq 60$ (Heterologous), $\begin{matrix} > 60 \\ < 80 \end{matrix}$ (Intermediated), $\geqq 80$ (Homologous)

any apparent trouble. Serum protein electrophoresis demonstrated hypogammaglobulinemia. Rectal biopsy showed no plasma cells, bone marrow examination revealed the absence of plasma cells, and his serum was devoid of immunoglobulins (IgG; 0, IgA; 0, IgM; 10 mg/dl). Autohemagglutinin titer to types A and B was not detectable. In vitro lymphocyte transformation with PHA was normal. Delayed hypersensitivity detected by skin tests (Candida, SK/SD and PHA) was normal. Although he had no serum immunoglobulins and no surface immunoglobulin-positive cells, normal numbers of EA cells were presented (Table 1). These immunological studies supported the diagnosis of agammaglobulinemia. He subsequently received monthly intravenous injections of 100 mg/kg of gammaglobulin.

The patient did well except for otitis media and frequent diarrhea until the age of 2 years and 10 months when he had tremor, fever and neck stiffness. A lumbar puncture revealed a normal pressure and produced clear fluid containing 323/3 white blood cells (80% mononuclear cells), with a glucose content of 82 mg/dl on a protein value of 41 mg/dl (41% gammaglobulin). Cultures for bacteria, viruses and fungi were negative. The electroencephalogram was normal, and CT-scan revealed no abnormality. No heart murmur was audible. The liver and spleen were palpable at the costal margin. The cranial nerves were normal. There was moderate flaccid paralysis in the left arm and right leg, but no sensory abnormalities. The left biceps and radial reflexes were reduced and the right knee reflex was absent. Therapy consisted of bed rest, wet packs and positioning of limbs to prevent contractures. Passive and active physiotherapy was initiated and the weakness of the left arm and right leg gradually improved. The patient was discharged from hospital after 6 weeks. Follow up revealed that muscle activity in the left hand and right foot had improved slightly after approximately 6 months.

Virologic Studies

Type 2 poliovirus was isolated from the stool obtained 1 week after the onset of paralysis, and even after 1 year the patient was found to excrete type 2 poliovirus. Attempts to isolate poliovirus from the cerebrospinal fluid were unsuccessful. A more detailed characterization of the virus was attempted. As shown in Table 2 the strain was classified as non vaccine-like type 2, based on the results of two different sero-differentiation tests. The Wecker test (the mean percentage plaque break-through) gave a normalized ratio of 89%. The McBride test (the ratio of values reflecting the kinetics of neutralization of the unknown and the homologous vaccine strain) gave a normalized K value of 29. Rct marker (the reproductive capacity at 35 and 40° C) was also found to be positive. Convalescent serum was examined for neutralizing antibodies to polioviruses types 1—3. A low level of antibody titer (1 : 8) was detectable only to type 2 poliovirus.

Discussion

With few exceptions, patients with agammaglobulinemia generally show a surprising ability to resist viral infections, and usually have a normal response to vaccination. The cell mediated defence mechanism is possibly the essential one against most viral infections, and humoral antibody is not so important [2, 9].

Immunological studies revealed that the patient had agammaglobulinemia. The disorder of the B-cell systems in this patient was probably congenital and serum immunoglobulins were absent (Table 1). Studies of lymphocyte membrane markers revealed a B-cell defect which was supported by the absence of surface-bearing immunoglobulins (SIg), normal cell-mediated immunity, and undetectable tissue plasma cells.

On the basis of the clinical and virological findings, there appears to be little doubt that the patient had paralytic poliomyelitis. Although isolation of poliovirus from the cerebrospinal fluid (CSF) was not successful, isolation of

poliovirus from his stool was considered to provide strong presumptive evidence of infection by this agent. The virus strain isolated from the stool of the patient was found to be non vaccine-like poliovirus type 2.

It was demonstrated that the patient continued to excrete type 2 poliovirus of the same character one year after the onset of his illness, although his clinical symptoms were not progressive.

A question can be raised concerning the origin of the non vaccine-like type 2 poliovirus isolated from this patient. Surveillance of poliomyelitis and poliovirus in Japan has been carried out extensively since the introduction of mass vaccination with Sabin vaccine in 1961 [12, 13, 14]. It has been reported that wild poliovirus has been eradicated from Japan, although there were several poliovirus isolates which were considered non vaccine-like several years after mass vaccination [13]. Cases of paralytic poliomyelitis from which non vaccine-like poliovirus was isolated have been reported on only two occasions, one in 1968 with type 1 poliovirus, and the other in 1971 with type 3 poliovirus. The first case was a boy of 3 years without vaccination against poliomyelitis, who was admitted to Sapporo Medical College Hospital in March 1968. Type 1 poliovirus was isolated from stool and proved to be non vaccine-like. The second case was a boy of 5 years who had received one dose of trivalent Sabin vaccine 4 years before, and was admitted to the Akita Red Cross Hospital in March 1971. Type 3 poliovirus was isolated from his stool and proved to be non vaccine-like. These cases were not immunologically deficient and responded with serum neutralizing antibodies against the serotype of the isolated poliovirus. No epidemiological data supported the possibility that these cases were infected with wild virulent poliovirus imported from abroad. The possibility cannot be excluded that such non vaccine-like polioviruses were derived from Sabin strains by variation.

The present patient received two doses of trivalent Sabin vaccine in 1975 and 1976, without any apparent side effects. Although the excretion of vaccine-derived poliovirus from this child was not detected until 28 October 1977, when he was admitted to the hospital because of flaccid paralysis, it is likely that he had been excreting type 2 poliovirus since his first dose of Sabin vaccine because of his agammaglobulinemia. It is generally said that the incubation period of vaccine-associated paralytic cases with hypogammaglobulinemia is longer than that usually accepted for natural or vaccine-associated poliomyelitis, although the period from the first dose of Sabin vaccine to the appearance of paralysis in the present case was extremely long. The possibility that vaccine-derived poliovirus undergoes variation during long-lasting multiplications in immunodeficient children, resulting in the isolation of non vaccine-like poliovirus strains, has also been reported [5, 17]. In spite of the expectation that sero-diagnostic tests would not be possible in this case because of generalized hypogammaglobulinemia, neutralizing antibody to poliovirus type 2 was detectable in the convalescent serum. This patient had received monthly injections of gammaglobulin. If the neutralizing antibody titer in the convalescent serum was due to the injected gammaglobulin, antibody to all types should have been detected in the serum. Only a type 2 titer was detectable, so it was thought that this neutralizing antibody was produced by the patient himself. It is unusual to detect serum antibody in patients with agammaglobulinemia, but in some instances minute quantities of

antibody to enteroviruses may be detectable in such patients when a highly sensitive method is employed [1, 3].

The association of poliomyelitis and agammaglobulinemia with virtual absence of B-cells and plasma cells provides a clinical enigma of unusual interest.

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