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PREVENTION OF VARICELLA IN IMMUNOCOMPROMISED PATIENTS ON UNPREDICTABLE OCCURRENCE OF THE DISEASE IN A CHILDREN'S WARD: VACCINE-BOOSTERED IMMUNE WHOLE BLOOD TRANSFUSION (VIB) METHOD

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For prevention of secondary varicella infection in patients whose immunities were extremely impaired by intensive chemotherapy or immunosuppressive agents, we have been using the vaccine-boostered immune whole blood transfusion (VIB) method when there was an unpredictable case of varicella in the children's ward. By this method passive transfer of humoral and cellular immunity is achieved. There have been 25 unpredictable occurrences of varicella or herpes-zoster in the ward of our children's hospital between April 1977 and May 1983 and during these episodes 16 patients, mostly with malignant diseases, have been treated by this method. There has been no case of secondary varicella infection among these patients and no serious troubles associated with the VIB method.

Varicella infection may be fatal in children whose immunity is extremely impaired by intensive chemotherapy or immunosuppressive agents.

So when such children have contact with varicella, especially when it occurs in a children's ward, emergency measures for protection against secondary infections must be taken as soon as possible.

This report describes clinical experience on protection against secondary varicella infection in children in this hospital whose immunities were thought to be extremely impaired by intensive chemotherapy or immunosuppressive agents. The method used was vaccine-boostered immune whole blood transfusion (VIB).

METHOD AND PATIENTS

1. *Vaccine-boostered immune whole blood transfusion (VIB) method*

Live varicella vaccine, kindly provided by Prof. Takahashi, was inoculated into a blood-type matched healthy adult donor, who had a history of varicella or gave a positive skin reaction to varicella antigen. Several days after vaccination, fresh whole blood from the boostered donor was transfused into the immunocompromised patient who had had contact with a case of varicella.

2. *Patients*

During 17 episodes of unpredictable occurrence of varicella in the children's ward, 16 patients whose immunities were extremely impaired by intensive chemotherapy or immunosuppressive agents were treated by this method. Of these patients, eleven had acute leukemia, and one patient each had Wilms tumor, neuroblastoma, embyonal tumor of the testis,

TABLE 1. *Summary of cases transfused with vaccine-boostered immune whole blood*

Case	Name	Sex	Age (yr)	Basic disease	Immunosuppressive drugs	Donor	Vaccination		Transfusion		Use of Ig. iv.	Contracted varicella
							Day[a]	Dose (PFU)	Day[a]	Volume (ml)		
1	T. T.	M	2	AML, Down syndrome	CS	Father	0	3,000	4	150	+	−
2	M. W.	F	1	ALL	CS, VCR	Father	0	3,000	4	150	+	−
									13	150		
3	N. M.	M	1	Nephrotic syndrome	CS EDX	Mother	2	3,000	8	100	−	−
									13	100		
4	A. W.	M	14	SLE	CS (pulse)	Father	3	1,000	5	100	−	+ 5 days[a]
5	K. K.	F	2	ALL	MTX (high dose)	Relative	1	3,000	5	150	+	−
6	S. T.	M	4	ALL	CS, ADM	Mother	1	1,000	5	150	+	−
7	H. I.	M	4	Embryonal tumor of testis	ADM	Father	2	3,000	5	200	+	−
8	H. K.	M	8	Neuroblastoma	VCR, EDX, ADM	Mother	1	1,000	5	200	−	−
9	S. N.	F	2	Wilms tumor	VCR, AcMD	Father	1	1,000	6	200	−	−
10	K. O.	M	1	ALL	CS, VDS	Father	1	1,000	4	200	+	−
11	Y. S.	F	14	APL	CS, 6MP, BH-AC, ACM	Unrelated	0	1,000	4	200	+	−
12	Y. A.	F	8	APL	CS, 6MP, BH-AC, ACM	Unrelated	0	1,000	5	200	+	−
13	S. N.	F	2	Wilms tumor	VCR, AcMD	Father		Convalescent	0	100	−	−
14	S. T.	M	6	ALL	CS, 6MP, VDS	Mother	0	900	4	200	+	−
15	T. S.	M	2	AMoL	CS, 6MP, VCR, MTX	Mother	0	900	4	200	+	−
16	N. K.	F	4	ALL	MTX	Father	0	900	4	200	+	−
17	S. T.	M	6	ALL	6MP, MTX	Father	1	900	4	200	+	−

[a] Days after contact with an infectious patient.

AML: Acute myelocytic leukemia
ALL: Acute lymphocytic leukemia
APL: Acute promyelocytic leukemia
AMoL: Acute monocytic leukemia
SLE: Systemic lupus erythematosus
CS: Corticosteroid
EDX: Endoxan
VCR: Vincristin
MTX: Methotrexate
ADM: Adriamycin
AcMD: Actinomycin D
VDS: Vindesin
ACM: Acracinomycin

the nephrotic syndrome and systemic lupus erythematosus.

RESULTS

From the time of opening of Shizuoka Children's Hospital in April 1977 until May 1983, there have been 25 unpredictable occurrences of varicella or herpes-zoster in the ward. On seven of these occasions, we used the VIB method and treated 16 patients (Table 1). In this series, only one child (case 4) developed clinical varicella on day 5 after contact with the index patient. In this child, symptoms appeared before the boostered fresh whole blood transfusion had been given. Judging from the latent period of varicella, infection in this child was not secondary from the index patient in the ward, but from the same source as for the index patient. Thus, there was no case of secondary varicella infection in immunocompromised patients who were treated by the VIB method after unpredictable occurrence of varicella in the ward.

Data on vaccination and boostered fresh whole blood transfusion are summarized in Tables 2 and 3. Most of the vaccinated donors were parents, and all the donors were vaccinated within 3 days after the unpredictable occurrence of varicella in the ward. Vaccine was used mainly at a dose of 900 to 1,000 PFU.

Transfusions were given 4 to 8 days after exposure using boostered fresh whole blood withdrawn 4 to 6 days after vaccination.

No serious side effects were seen in any cases treated by this VIB method.

DISCUSSION

When immunocompromised children come in contact with varicella, especially on unpredictable occurrence of a case in a children's ward, emergency measures for protection against secondary varicella infection must be taken as soon as possible, because otherwise the patients may contract varicella with fatal consequences.

Immediate administration of zoster immune globulin (ZIG) or zoster immune plasma (ZIP) has been reported to be effective for emergency protection against varicella infection (Brunell et al., 1972; Balfour, 1979). But both cellular

TABLE 2. *Summary of vaccination*

Donor	No. of cases	Day after exposure	No. of cases	Dose (PFU)	No. of cases
parent	14	0	8	—	1
relative	1	1	5	900	4
unrelated	2	2	2	1,000	7
		3	1	3,000	5

TABLE 3. *Summary of boostered fresh whole blood transfusions*

Day after exposure	No. of cases	Volume	No. of cases
0	1	100 ml once	2
4	8	150 ml once	3
5	6	200 ml once	10
6	1	100 ml twice	1
8	1	150 ml twice	1

immunity and humoral immunity are thought to be important in preventing varicella infection. Immediate vaccination by a live varicella vaccine is reported to be effective for preventing spread of varicella in a ward or hospital (Asano et al., 1977). However, when given live varicella vaccine, patients who are in an immunocompromised state may develop clinical varicella with side effects at high frequency (Ha et al., 1980), and may also suffer from relapse of malignancy triggered by the vaccine.

So, in such situations in this children's hospital, we use the VIB method with or without additional intravenous administration of gamma globulin with a large quantity of antibodies to varicella-zoster virus, for protection of immunocompromised patients. Until now, we have had no cases of secondary varicella infection among immunocompromised patients treated by the VIB method.

We have also used this VIB method for 5 outpatients who were receiving strong immunosuppressive agents and who came in close contact with cases of varicella. Two of these 5 patients developed clinical varicella, but had a very mild course. One patient received a transfusion of fresh whole blood 3 days after vaccination to the donor. Another patient was transfused with blood from her father who had been vaccinated 2 months previously on the day of visit to the outpatient clinic, when it was learned that the patient had been in contact with a case of varicella.

There are two problems with outpatients. The first is that we receive information about contact with cases of varicella from the patient or his family too late. The second is that the contact with varicella is often close and continuous because the infectious patient is usually a sibling. These problems make it difficult to prevent secondary varicella infection completely, though our cases showed that there is room for improvement with respect to the dose of vaccine and the time of blood transfusion.

For emergency protection against varicella, procedures must be taken as soon as possible. A good point about the VIB method is that vaccination can usually be done on the same day or the day after occurrence of a case of varicella in the ward using blood of a parent, whose blood-type is almost always matched with that of the patient. We vaccinated all the donors within 3 days and transfused boostered fresh whole blood into the patients within 8 days after exposure.

With this VIB method, no serious side effects, such as the graft-versus-host reaction were seen in any cases. Patients with malignant diseases usually receive successive blood transfusions without trouble. So, fresh whole blood transfusion should also be safe.

Thus, passive transfer of humoral and cellular immunity by vaccine-boostered fresh whole blood transfusion (Baba et al., 1980) is considered to be a safe, convenient and effective method for preventing varicella infection in children whose immunities are extremely impaired.

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