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PASSIVE IMMUNIZATION AGAINST VARICELLA IN SICK NEONATES BY TRANSFUSION FROM DONORS IMMUNOLOGICALLY ENHANCED BY PREVIOUS VACCINATION WITH LIVE VARICELLA VACCINE

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Twenty-six sick children in a neonatal unit received passive immunization against varicella shortly after close contact with varicella in the ward, with the aim of preventing nosocomial infection. Because zoster immune globulin was not available at the time, the babies were given transfusion of whole blood from donors. All these donors had a history of varicella in childhood, and had received live varicella vaccine, Oka strain, to increase their immunological status before use of their blood for transfusion. Only one of the recipients contracted varicella after the passive immunization. No adverse reaction attributable to the transfusion was observed.

INTRODUCTION

Varicella in newborn infants is usually mild, but it may be fulminent, with extensive visceral infection and be fatal. After the neonatal period, varicella infection can be protected safely and effectively by vaccination with live varicella vaccine, Oka strain (Takahashi et al., 1974; Asano et al., 1977). However, the safety and effectiveness of immunization of sick neonatal children with live vaccines is still controversial. This paper reports a trial of prevention of nosocomial spread of varicella in a neonatal care unit by passive immunization.

MATERIALS AND METHODS

1. *Study design*

On Feb. 2, 1980, typical vesicular exanthema of varicella developed in a 7-month-old girl who had been admitted to the Neonatal Unit of the Central Hospital in Aichi Prefectural Colony for Disabled Children. At the time there were 29 children in the unit with the underlying diseases shown in Table 1.

The index case was isolated immediately. Six children were considered to have been in close contact with the index case; four in the same ward and two in the nextdoor ward. These six children were also isolated immediately and their nursing staff and

TABLE 1. *Patients in the neonatal unit*

Classification	No. of cases	Age	Body weight when exposed
VLB[a]	9	0 days-1 mo	800–1,720 g
Surgical illness[b]	5	24 days-7 mo	2,025–3,800 g
Neonatal illness[c]	15	4 days-4 mo	1,930–4,030 g
Total	29	0-7 mo	800–4,030 g

[a] Very low weight baby, with/without respiratory distress syndrome.
[b] Four cases of congenital atresia of alimentary truct, one case of Hirschsprung disease.
[c] Nine cases of low birth weight baby, with/without complications, 3 cases of neonatal sepsis, 3 cases with miscellaneous diseases.

supply systems were subsequently separated from those of other wards.

We tried to obtain zoster immune globulin (ZIG) commercially for these exposed patients to prevent their contraction of varicella. But the amount of ZIG available was sufficient for only one patient, who was treated with it the day after onset of disease in the index case.

A schedule of passive immunization for the other five children was designed as follows: (1) A live varicella vaccine, Oka strain, was inoculated into adult donors. All the donors had an apparent history of varicella in their childhood. (2) Seven to ten days after vaccination, whole venous blood was withdrawn from the donors and transfused into the patients, at a rate of 10 ml/kg. (3) Serum samples for tests on circulating antibody titers against varicella zoster virus (VZV) were collected from donors at the time of vaccination and blood transfusion and from recipients as frequently as possible after blood transfusion.

The other 22 patients were observed without specific preventive measures. On day 15 after the onset of the index case, typical varicella developed in another child. The child had been considered not to have been in contact with the index case, but reexamination of his chart revealed that he had been in the same ward as the index case until three days before onset of disease in the latter. Two days later (17 days after onset of disease in the index case), one of the nursing staff contracted regular varicella. Therefore, during the next week the other patients also received passive immunization by the schedule described above.

2. *Vaccine*

Live attenuated varicella vaccine of the Oka strain of varicella virus was inoculated subcutaneously in a volume of 0.5 ml, containing 2,500 plaque forming units/dose of the virus.

3. *Tests on circulating antibody*

For detection of antibody activities, a neutralization (NT) test and a test of fluorescent antibody to membrane antigen (FAMA) were performed as described by Yamada et al. (Yamada et al., 1979).

RESULTS

1. *Contraction of varicella after passive immunization*

In all, 26 patients received passive immunization from vaccinated donors. Of these recipients, one patients contracted varicella the day after transfusion (on day 17 after contact). Clinical manifestations in this case were those of regular, uncomplicated varicella. The other recipients did not contract varicella.

No adverse reaction referable to blood transfusion was observed in the recipients and no side effects of the vaccine were observed.

2. *Serological studies*

As the volume of venous blood sample available from neonates are extremely small, serial serological studies could not be done in all children. Representative results of NT and FAMA tests on the children examined are shown in Table 2. All the donors had already had antibody against VZV before vaccination. Fourfold or more increases in antibody titers

TABLE 2. *Antibody titers in donors and recipients*

Case		Donor		Recipient					
		Pre-vacc.	Post-vacc.	Pre-transfusion	Post-transfusion (days)				
					1	2	7	14	120
YANO	NT	×8	×32	<×4	×4	<×4	<×4	ND	<×4
	FAMA	×8	×64	<×2	×8	×2	×2	×2	×4
HASUKO-I[a]	NT	×16	×32	<×4	×4	×4	<×4	ND	<×4
	FAMA	×32	×64	×2	×2	×2	<×2	ND	<×2
HASUKO-II[a]	NT	×16	×32	ND[b]	ND	ND	ND	ND	ND
	FAMA	×32	×64	<×2	×8	×2	<×2	ND	<×2
IWASAKO	NT	×16	×128	ND	ND	ND	ND	ND	ND
	FAMA	×16	×256	<×2	×16	×4	<×2	<×2	<×2
TAKEMURA	NT	×16	×64	ND	ND	ND	ND	ND	ND
	FAMA	×16	×256	<×2	×16	×4	<×2	<×2	<×2

[a] Twins with the same donor.
[b] Not done.

in seven to ten days after vaccination were observed in three of four vaccinees. All five recipients studied showed antibody activities after transfusion. These activities decreased in seven to 14 days after the transfusion, but one patient (case Yano in Table 2) had detectable antibody activity four months after the transfusion.

DISCUSSION

Neonatal varicella is usually mild, self-limiting disease. However, it may sometimes be a fulminent, fatal illness. Because it is so contagious, immediate preventive measures should be taken once a case of varicella is imported into a neonatal care unit, where there are many low weight babies and neonates with surgical illnesses in pre-operative or post-operative condition.

ZIG should be the first choice for the purpose of passive immunization. However, highly immune globulin for varicella zoster virus is often not available in Japan, because there is no system for its supply. In this series of studies, adult whole blood was transfused into patients shortly after their exposure to varicella. Considering the harmful effect of transfusion of a large volume of blood into very low weight babies, we increased the immunological level of the donors by inoculating them previously with live varicella vaccine. Consequently, the recipients could be protected from varicella by transfusion of only a regular volume of blood.

Adult donors hematologically matched to the patients were prepared at the time of admission of the patients. In fact, many of the patients studied had received blood transfusion from the donors one or more times before this trial of passive immunization. No clinical findings suggestive for host*vs*graft reactions were observed after the transfusion aimed to induce passive immunization.

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