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USE OF LIVE VARICELLA VACCINE IN CHILDREN WITH ACUTE LEUKEMIA AND MALIGNANT LYMPHOMA

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Live varicella vaccine was given to 7 children with acute leukemia and 1 child with non-Hodgkin's lymphoma. Seroconversion without any clinical reactions was observed in 4 children in remission from acute leukemia without interruption of anticancer medication. These children have been free from varicella for 5 to 11 months after vaccination.

Mild to severe clinical reactions developed in 3 of 4 children who were receiving remission induction chemotherapy.

It is concluded that live varicella vaccine is effective in children with acute leukemia without interrupting anticancer medication, but that it is not suitable for children with leukemia and lymphoma who are receiving remission induction chemotherapy with antileukemic agents.

INTRODUCTION

A live varicella vaccine developed by Takahashi and his colleagues (Takahashi et al., 1975) has been used to prevent the spread of varicella cases of leukemia and other malignancies. Izawa et al. (1977), Ha et al. (1980) and Nakagawa and Katsushima (1978) reported protective effects of the live varicella vaccine against varicella and they recommended use of this vaccine for prevention of varicella in patients with leukemia and other malignancies. We recently experienced nine cases of acute leukemia and malignant lymphoma with the complication of varicella. Of these nine children, three had severe varicella and died, although we treated them with zoster immune globulin (ZIG), zoster immune plasma (ZIP) and cytocine arabinoside (Ara-C). So we tested the effect of live varicella vaccine in children with acute leukemia and malignant lymphoma for prevention of varicella.

MATERIALS AND METHODS

Seven children with acute lymphocytic leukemia (ALL) and one child with non-Hodgkin's lymphoma (NHL) were given live varicella vaccine. Four of them were in remission and had been receiving 6-mercaptopurine and methotrexate as maintenance therapy and vincristine, cyclophosphamide and steroids as reintensification therapy. Four of them were at the onset of disease or in relapse and had been receiving remission induction chemotherapy with vincristine, daunorubicine, L-asparagenase and steroids. Treatments of underlying diseases were

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TABLE 1. *Effects of live varicella vaccine in patients with leukemia and lymphoma*

Case	Age	Sex	Underlying disease	Stage of disease	Titer of antibody (IAHA)		Clinical reactions
					Before	After	
1. Y. Y.	2 yr	F	ALL	Remission	<2X	4X	−
2. S. F.	7 yr	M	ALL	Remission	<2X	16X	−
3. A. R.	6 yr	F	ALL	Remission	<2X	2X	−
4. O. K.	2 yr	M	ALL	Remission	<2X	32X	−
5. K. T.	6 yr	M	ALL	Onset	<2X	16X	+ Fever, Rash, Hepatitis
6. W. C.	5 yr	F	ALL	Relapse	<4X[a]	64X[a]	+ Fever, Rash
7. S. S.	7 yr	M	ALL	Relapse	<2X	16X	− Natural varicella?
8. O. M.	9 yr	F	NHL	Onset	<2X	128X	+? Fever, Rash, Hepatitis, Encephalopathy, Ileus

F, female; M, male; ALL, acute lymphocytic leukemia; NHL, non-Hodgkin's lymphoma; IAHA, immune adherence hemagglutination.
[a] CF, complement-fixation.

not suspended before or after vaccination in any case.

Live attenuated varicella vaccine of the Oka strain (lot 8202) (Takahashi et al., 1975) was supplied from Dr. Takahashi, Osaka University. A virus dose of 1,000 plaque forming units in 0.5 ml was injected subcutaneously into each vaccinee. Serum samples were obtained just before and 2 to 6 weeks after vaccination and tested for immune adherence hemagglutination (IAHA) antibody and complement fixation (CF) antibody.

RESULTS

The results are summarized in Table 1. No clinical reactions were observed in four children in remission and in one in relapse. Seroconversion occurred in all the children and they have been free from varicella for 5 to 11 months after vaccination.

Fever and rash were observed in three (cases 5, 6 and 8) of four children at the onset of disease or in relapse who had been receiving remission induction chemotherapy with antileukemic agents. In case 5, high fever and moderate numbers of vesicles developed 4 weeks after vaccination. The fever continued for 8 days and the vesicles disappeared in 26 days. This case also had mild liver dysfunction, but the underlying disease did not become worse. Case 6 had fever and a rash 4 weeks after vaccination. The rash was minute and soon disappeared. On March 31, 1983, there was a case of varicella in the pediatric ward of Hirosaki University Hospital. Case 8 was vaccinated with live varicella vaccine on April 1. Fever and large vesicles appeared 12 days after vaccination. She developed hepatitis, encephalopathy and functional ileus as visceral involvements of varicella. But in spite of her serious condition, she recovered after rash and fever for 12 days.

DISCUSSION

Varicella has been thought to be severe or even fatal in children with leukemia and other malignancies receiving immunosuppressive therapy. It was reported that prophylaxis with ZIG and ZIP significantly reduced the incidence of clinical varicella and attenuated the severity of its course (Brunell et al., 1969; Geiser et al., 1975). But we could not prevent the spread of varicella in our pediatric ward or decrease the severity of its course by using ZIG and ZIP. In this study, we used live varicella vaccine for preventing varicella in eight children

with ALL or NHL.

Four children in remission received the live varicella vaccine without suspension of anti-leukemic agents before or after vaccination. All of them showed seroconversion 2 to 6 weeks after vaccination. They showed no clinical reactions to the vaccine and have been free from varicella for 5 to 11 months after vaccination.

Among 4 children who received live varicella vaccine at the onset or during relapse of acute leukemia while receiving induction chemotherapy, 3 children (cases 5, 6 and 8) showed symptoms; these were very mild in case 6, moderate in case 5 and severe in case 8. The underlying disease was not affected in any case. In case 8, who was exposed to natural varicella the day before vaccination, it was uncertain whether clinical symptoms were caused by natural infection or by vaccination. Judging by the incubation period of varicella, her infection was probably due to infection with natural varicella, though this was not confirmed by virus isolation. We conclude that it is undesirable to use a live varicella vaccine for children with leukemia and lymphoma who are receiving remission induction chemotherapy with anti-leukemic agents, but that live varicella vaccine is safe and effective for preventing spread of varicella in children with leukemia in remission. Izawa et al. (1977) recommended suspending anticancer medication from one week before vaccination to one week after vaccination. Ha et al. (1980) reported immediate use of varicella vaccine without suspension of chemotherapy in children with acute leukemia or other malignancies if they are not in an extremely immunologically suppressed condition. In our study, no clinical reactions were observed and seroconversion occurred in all children who were in remission and received live varicella vaccine without suspension of anticancer medication. Thus we conclude that live varicella vaccine can safely and effectively be used in children with acute leukemia for prevention of varicella.

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