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SHORT COMMUNICATION

USE OF A LIVE VARICELLA VACCINE FOR ACUTE LEUKEMIC CHILDREN SHORTLY AFTER EXPOSURE IN A CHILDREN'S WARD

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Varicella infection is often severe, or even fatal, in children with leukemia and in those with other immunocompromized conditions. Izawa et al. (1977) reported that children with acute leukemia in remission were immunized with a live varicella vaccine without troublesome clinical reactions. In their study, anticancer medication was suspended for two weeks before and after vaccination.

This paper reports clinical findings on vaccination of hospitalized children including those with acute leukemia shortly after close contact with cases of varicella, when anticancer medications were continued before and after vaccination.

On Nov. 21, 1976, the typical exanthem of varicella developed in a child with acute lymphatic leukemia. He had been admitted to the hospital on Oct. 7, 1976 and was then in complete remission, receiving consolidation therapy with methotrexate and 6-mercaptopurine. As he had been allowed to walk about freely in the hospital and was very popular, the other five children in the same room and four children across the passage seemed to have been in close contact with him.

Seven of the nine children had no history of varicella. Their diagnoses of underlying diseases, clinical conditions at the time of exposure and treatments are listed in Table 1.

The index case was isolated immediately, and 3 children, with their parents' consent, were given live varicella vaccine on the following day: the other four children remained unvaccinated. The live varicella vaccine used was the Oka strain of varicella virus (Takahashi et al., 1975) passaged in human embryo lung cells 11 times, guinea pig embryo cells 12 times and human diploid cells (WI-38) 11 times, and it was given at 400 PFU/dose.

After vaccination, clinical observations were made daily by the staff and specimens for routine laboratory examinations were taken frequently to test for adverse effects on underlying diseases attributable to the vaccine. Treatments for underlying diseases were not discontinued in any of the cases.

Serum samples for serological tests were obtained from all the eight children at the onset of the index case and also four weeks later from the 3 vaccinees. Convalescent sera were taken four weeks after the onset of varicel-

TABLE 1. *Underlying diseases and treatments of exposed children*

Case No.	Age & Sex	Underlying disease and clinical condition	Treatment for underlying disease
1[a]	5 M	ALL[b]: In complete remission	Consolidation therapy; MTX[e]+6MP[f]
2	2 M	Nephrotic syndrome; Onset; 4 months before. In partial remission	Paramethasone+CPM[h]
3	9 F	AML[c]: In incomplete remission Onset; 2 months before	Induction therapy; VCR[g]+CPM+PDN[i]+CAR[j]
4	2 M	ALL: In complete remission	Consolidation therapy; MTX+6MP
5	3 M	ALL: In complete remission	Consolidation therapy; MTX+6MP
6	3 M	ALL: In complete remission	Consolidation therapy; MTX+6MP
7	4 F	ALL: In complete remission	Consolidation therapy; MTX+6MP
8	3 M	JRA[d]; Onset; 11 months before. In partial remission	Steroid dependent; PDN+gold salt

[a] Index case. [b] ALL: Acute lymphatic leukemia. [c] AML: Acute myeloblastic leukemia.
[e] MTX: Methotrexate. [f] 6MP: 6-mercaptopurine. [g] VCR: Vincristine.
[i] PDN: Prednisolone. [j] CAR: Cytosine arabinoside. [h] CPM: Cyclophosphamide.

TABLE 2. *Clinical course of varicella and serological findings in unvaccinated and vaccinated*

Case No.	Underlying disease	Vaccination	Onset of varicella (Days after the index case)	Duration of fever (Maximum temp. C)
1	ALL	−	index case	8 days (39.9 C)
2	Nephrotic syndrome	−	4	4 days (38.0 C)
3	AML	−	21	2 days (40.2 C)
4	ALL	−	24	15 days (39.7 C)
5	ALL	−	24	3 days (39.2 C)
6	ALL	+	4	1 days (39.4 C)
7	ALL	+	10	0
8	JRA	+	16	0

[a] CAR: Cytosine arabinoside. [b] Antibody titers on the day of death.

la in the unvaccinated children.

The neutralization (NT) and complement fixation (CF) tests were carried out as described previously (Asano and Takahashi, 1978).

During 24 days after the onset of the index case, all seven children exhibited very mild to severe symptoms of varicella. Clinical and serological findings are summarized in Table 2. Treatments for varicella started immediately after the onset of eruption with cytosine arabinoside (2 mg/kg/day) and gammaglobulin (2.5 g/day) as described in the Table.

The clinical symptoms of the five unvaccinated children were generally severe. Three children with acute leukemia (case 1, 4, 5)

Laboratory findings
Peripheral blood picture: Normal Bone marrow findings: Normal
Albuminuria: 0.3-2.0 g/day
Bone marrow findings: Cell count $8.2\times10^4/mm^3$ Myeloblast; 5.2%
Peripheral blood picture: Normal Bone marrow findings: Normal
Peripheral blood picture: Normal Bone marrow findings: Normal
Peripheral blood picture: Normal Bone marrow findings: Normal
Peripheral blood picture: Normal Bone marrow findings: Normal
Erythrocyte sedimentation rate: elevated

[d] JRA: Juvenile rheumatoid arthritis.
[h] CPM: Cyclophosphamide

(elevation of blood urea nitrogen, oliguria and edema) during the eruptive stage and this renal dysfunction lasted for a long time. Bone marrow aspirates of the two unvaccinated leukemic patients, case 1 and 4, suggested relapse of the underlying disease during the acute stage of varicella. The relapse was transitory in case 4, but long-lasting in case 1.

In contrast, the clinical course of varicella in the three vaccinated children was very mild and the underlying diseases were not affected.

Serologically, all the children exhibited CF and NT antibody responses.

In the present study, 5 unvaccinated children in immunologically impaired conditions developed severe varicella and one case was fatal. Administration of cytosine arabinoside and commercially available gammaglobulin was seemingly ineffective for varicella in these cases. On the contrary, in the 3 vaccinated children the clinical symptoms of varicella were mild without any unfavorable effects on

children

Eruption	Treatment of varicella		Summary of clinical course	Antibody titer (CF/NT)	
	CAR[a] (days)	γ-Gl (days)		Prior to infection or vaccination	4 weeks after varicella or vaccination
Generalized confluent large vesicles	5	8	severe	<4/<4	16/8
Generalized typical vesicles	4	4	moderate	<4/<4	16/8
Progressive hemorrhagic	2	2	fatal	<4/<4	<4/<4[b]
Generalized confluent large vesicles	4	11	severe	<4/<4	32/≧64
Generalized typical vesicles	5	3	severe	<4/<4	16/≧64
22 small vesicles	4	3	mild	<4/<4	4/8
10 small vesicles	3	4	mild	<4/<4	16/8
5 small maculopapular rashes	0	0	very mild	<4/<4	4/32

developed confluent large vesicles in all over the body with high febrile reactions. One child with acute myeloblastic leukemia (case 3) contracted rapidly developing, hemorrhagic generalized varicella and died after three days. In another child with the nephrotic syndrome (case 2), the clinical course of varicella was moderate, but renal function became worse

underlying diseases. Judging from observations on unvaccinated children, it is unlikely that the administered cytosine arabinoside and gammaglobulin played a major role in alleviating the clinical symptoms in the vaccinated children. One of vaccinated children (case 6) developed mild varicella symptoms 4 days after vaccination. It is uncertain whether in

this case the symptoms of varicella were naturally mild or whether they were reduced by vaccination. Baba et al. (1978) noticed that the skin reaction with varicella antigen became positive as early as 5 days after vaccination, 7 to 9 days before the appearance of neutralizing antibody. This indicates that cellular immunity appears very early after vaccination. Therefore, it is possible that the vaccination modified the course of varicella symptoms in case 6. This case (case 6) and case 2 seemed to have been infected with varicella before the time of onset of the indicator case.

Although the present study is not conclusive because of the small number of the vaccinated cases, it provides additional examples of effective use of live varicella vaccine, especially for children with acute leukemia.

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