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Abstract

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KEYWORDS: papilar acrodermatitis of childhood, Gianotti's disease, hepatitis B virus, hepatitis B surface antigen subtype.

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DETECTION OF HEPATITIS B SURFACE ANTIGEN SUBTYPE adr IN AN EPIDEMIC OF PAPULAR ACRODERMATITIS OF CHILDHOOD (GIANOTTI'S DISEASE)

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Abstract. Papular acrodermatitis of childhood (PAC) has recently been reported to be associated with hepatitis B surface antigen (HBsAg) subtype ayw. Between September, 1978, and June, 1979, we saw 14 patients with PAC in a small epidemic occurring in Iwakuni City, Japan. HBsAg was detected in sera from all patients. Subtyping of HBsAg in 11 patients showed that 8 had a determinant adr and 3 had no detectable determinant because of low antigen titers. The result suggests that factors other than the specific HBsAg subtype contribute to the development of PAC.

Key words : papular acrodermatitis of childhood, Gianotti's disease, hepatitis B virus, hepatitis B surface antigen subtype.

Papular acrodermatitis of childhood (PAC) is a non-relapsing disease characterized by papular eruptions on the face and limbs, reactive reticulohistiocytic lymphadenitis, and acute anicteric hepatitis. In 1973, Gianotti established a close relation between hepatitis B surface antigen (HBsAg) and PAC (1). Subsequently, Ishimaru *et al.* in 1976 and Colombo *et al.* in 1977 reported that HBsAg subtype ayw is specifically associated with the disease (2, 3). It is, however, still unclear why PAC affects only a limited number of infants and young children. We saw 14 patients with PAC in a small epidemic occurring in Iwakuni City, Japan. HBsAg subtype adr was detected in 8 out of 11 patients. In this report we wish to emphasize that factors other than the specific HBsAg subtype contribute to the development of PAC.

MATERIALS AND METHODS

Between September, 1978, and June, 1979, there was a small epidemic of PAC in Iwakuni City (population about 110,000). A total of 14 patients was admitted to the Department of Pediatrics, Iwakuni National Hospital, during that time. The outbreak was not confined to any specific district of the city. The diagnosis of PAC was based on the following three criteria: (a) characteristic non-relapsing, non-itching erythematopapular eruptions localized to the

face and limbs; (b) acute, usually anicteric, hapatitis; and (c) HBsAg in the serum obtained within the first few days of the dermatitic phase. The presence of lymphadenopathy or hepatomegaly also supported the diagnosis. All serum specimens were tested for HBsAg and the corresponding antiboby (anti-HBs) using radioimmunoassay (4). HBsAg subtypes were determined by inhibition of passive hemagglutination (5). Available family members of the patients were also studied for HBsAg and anti-HBs.

RESULTS

The clinical and serological data from the 14 patients are shown in Table 1. Cases 10 and 14 were siblings. None of the patients had any previous blood transfusion. Of the 14 patients, 6 were male and 8 were female. Their ages ranged from 8 months to 7 years. The mean follow-up time was 5.1 months with a range of 3 to 10 months. We failed to follow the course of Case 1, because the patient moved to a remote region one month after the onset. Definite enlargement of lymph nodes was found only in Case 1, and overt jaundice was present in Case 13. The duration of the dermatitic phase was between 3 and 43 days.

At the time of admission, levels of serum glutamic oxaloacetic transaminase (SGOT) were elevated in all but one patient (Case 13) who, however, showed increased levels later. The highest values of SGOT in the 14 cases ranged from 156 to 830 U/L. In 10 patients, the increased SGOT values returned to normal in an average period of 2.3 months, whereas in 3 patients (Cases 3, 5 and 6) the

TABLE 1. CLINICAL AND SEROLOGICAL DATA IN PATIENTS WITH PAPULAR ACRODERMATITIS OF CHILDHOOD AT THE TIME OF ADMISSION AND AT THE END OF OBSERVATION.

Case no.	Age	Sex	Length of observation (Month)	At the onset of rash				At the end of observation		
				SGOT (U/L)	HBsAg	HBsAg subtype	Anti-HBs	SGOT (U/L)	HBsAg	Anti-HBs
1.	8m	M	1	60	+	ND	−	/	/	/
2.	10m	F	4	166	+	adr	−	36	−	+
3.	1y	M	8	132	+	adr	−	59	+	−
4.	1y	F	3	212	+	ND	−	33	−	+
5.	1y	M	9	110	+	adr	−	233	+	−
6.	1y	M	10	126	+	adr	−	102	+	−
7.	2y	M	3	730	+	/	−	24	−	+
8.	2y	F	3	237	+	adr	−	32	−	+
9.	3y	F	8	245	+	adr	−	38	+	−
10.	4y	M	3	309	+	adr	−	22	−	+
11.	5y	F	4	289	+	/	−	19	−	+
12.	5y	F	3	48	+	ND	−	27	−	+
13.	6y	F	4	21	+	adr	−	23	−	+
14.	7y	F	4	212	+	/	−	20	−	+

SGOT, serum glutamic oxaloacetic transaminase (normal up to 40 U/L); HBsAg, hepatitis B surface antigen; anti-HBs, antibody to hepatitis B surface antigen; ND, could not be determined.

levels of SGOT remained high throughout the observation time.

At the beginning of the dermatitic phase, sera from all patients were positive for HBsAg but negative for anti-HBs. All except four (Cases 3, 5, 6 and 9) eventually became negative for HBsAg. These 4 patients had not acquired anti-HBs, and became chronic carriers of HBsAg. Subtyping of HBsAg in 11 available patients showed that 8 had determinant adr while 3 had no detectable determinant because of low HBsAg titers.

The results of serological studies in 29 available family members of the patients are summarized in Table 2. Exposure to hepatitis B virus (HBV) can be indicated by the presence of HBsAg or anti-HBs. The exposure rates in mothers, fathers and siblings were 42% (5/12), 40% (4/10) and 43% (3/7), respectively. HBsAg was found in sera from 4 family members. Interestingly, one of them, a 3-year-old female sibling of Case 2, became affected with typical acute hepatitis B due to the same HBsAg subtype as Case 2 one month after the onset of PAC in Case 2. The remaining 3 members with HBsAg (the mother of Case 13 and two siblings of Case 12) had normal values of SGOT.

TABLE 2. FREQUENCY OF HEPATITIS B SURFACE ANTIGEN AND ANTIBODY IN FAMILY MEMBERS OF PATIENTS WITH PAPULAR ACRODERMATITIS OF CHILDHOOD.

	Total examined	HBsAg positive	Anti-HBs positive	HBsAg or anti-HBs positive	
	No.	No.	No.	No.	%
Mothers	12	1	4	5	42
Fathers	10	0	4	4	40
Siblings	7	3	0	3	43
Total	29	4	8	12	41

HBsAg, hepatitis B surface antigen ; anti-HBs, antibody to hepatitis B surface antigen.

DISCUSSION

The clinical, laboratory and prognostic data of our patients show no difference from those of the cases reported by Gianotti (1973) (1) except in the frequency of lymphadenopathy. The low frequency of this sign in the present study (7.4%) was distinctive. However, Ishimaru *et al.* (1978) also described the rare occurrence of lymphadenopathy in Japanese patients with PAC (6). Racial differences may be related to the varied manifestation of the sign.

The risk of being exposed to HBV is high in Japan where the overall incidence of a carrier with HBsAg is estimated to be 2.0% (7), and HBV infection is usually manifested as acute hepatitis B. Although an association between PAC and HBV has been well established, why PAC occurs only in a limited number of infants and young children remains obscure. With regard to this question, the following hypotheses have been proposed: (a) PAC occurs only when HBV infects through the skin or mucous membrane (1), (b) the deposition

of HBV antigen-antibody immune complex on the skin is involved in the development of PAC (8), and (c) PAC is a condition caused by the specific HBsAg subtype ayw (2, 3). At present, the last hypothesis is considered the most pertinent explanation. In our study, however, HBsAg subtype adr was detected. Furthermore, Onozuka *et al.* (1978) found the subtype adw in their patients in an epidemic of PAC in Saga City, Japan (9). This suggests that PAC is not necessarily associated with a specific HBsAg subtype. It was reported that cases of Down syndrome are predisposed to PAC (1). Moreover, the present study showed that the sibling of case 2 had acute hepatitis B due to the same HBsAg subtype as her younger sister with PAC. These findings argue strongly for the concept that factors other than the specific HBsAg subtype, perhaps host factors, contribute to the development of PAC. Further studies of host factors such as extensive immunologic investigations including typing of HLA antigens are warranted.

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