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Gianotti-Crosti Syndrome Following Japanese Encephalitis Vaccination

We report a three-year-old Korean boy who presented with itching symmetrical erythematous macules and papules on his face, trunk, and extremities for 1 week. Lymphadenopathies were detected on physical examination. He was vaccinated against Japanese B Encephalitis (JE) 1 day before developing skin rashes. The patient's serum JE antibody titer by hemagglutinin inhibition (HI) test was 1:40. Under the diagnosis of Gianotti-Crosti syndrome following JE vaccination, he was conservatively treated with an antihistamine agent, and his symptoms were all cleared 2 weeks after treatment.

Key Words : *Acrodermatitis; Gianotti-Crosti Syndrome; Japanese Encephalitis Vaccine*

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INTRODUCTION

Gianotti-Crosti syndrome (GCS) is a disease of self-limited acrolocated eruption characterized by acute onset of symmetrical papules over the limbs and face, which may last up to 8 weeks (1). This syndrome is frequently associated with hepatitis B (HB) antigenemia (2), but hepatitis B virus (HBV) antigen-negative cases had been subsequently described by Gianotti (2). A wide spectrum of viral diseases and preceding immunizations are associated with the disease (3, 4).

We report a case of GCS following Japanese encephalitis (JE) vaccination. To our knowledge, this is the first case of GCS associated with Japanese encephalitis vaccine.

CASE REPORT

A three-year-old Korean boy presented with pruritic rashes for 1 week. He was generally healthy and vaccinated against JE 1 day before developing cutaneous manifestations. No drug history was found. Physical examination revealed symmetrical erythematous macules and papules on his face, trunk, and extremities (Fig. 1). Concomitant lymphadenopathies of right postauricular, right axillar, and both inguinal areas were detected. Complete blood cell count was normal except moderate eosinophilia (7.2%). Other laboratory examinations including liver function test, urinalysis and chemical profiles were normal. Skin biopsy from right upper arm revealed focal spongiosis with mild lymphocytic exocytosis in epidermis. Mild superficial and deep perivascular inflammatory infiltrates composed of lymphocytes were noted in dermis (Fig. 2).

Under the impression of GCS, further evaluations were performed to reveal viral etiology. Serum hepatitis B surface antigen (HBsAg) was negative and antibody to HbsAg (HBsAb) was positive due to the routine scheduled vaccination. Serum JE antibody was positive (1:40) by hemagglutinin inhibition (HI) test. His symptoms were all cleared 2 weeks after conservative antihistamine treatment.

DISCUSSION

GCS shows characteristic cutaneous eruption following viral infection or immunization (1). Although HBV is the most common etiologic agent (5), it is now generally accepted that GCS can be triggered by a variety of other viruses, such as Epstein-Barr virus (6), poxvirus (7), parvovirus B19 (7), human herpes virus 6 (8), rotavirus (9), HIV (10), and CMV (11). It is also associated with vaccinations against influenza virus (12), diphtheria (6), pertussis (6), poliovirus (6), measles, mumps, or rubella (MMR) (4).

The precise pathogenic mechanism of GCS remains unclear until now. Caputo et al. suggested that GCS is a self-limiting cutaneous response to different viruses; clinical differences are probably due to individual characteristics of each patient rather than the causative virus (13). However, Drijkoningen et al. suggested that inflammatory infiltrates consisting of dendritic cells and T cells in the skin and around the small vessels in GCS are similar to the reactive lymph node (14). The latter can be correlated with the dendritic cell-T cell clusters of the primary immune response observed in vitro (14). This delayed type of T cell immune response can be

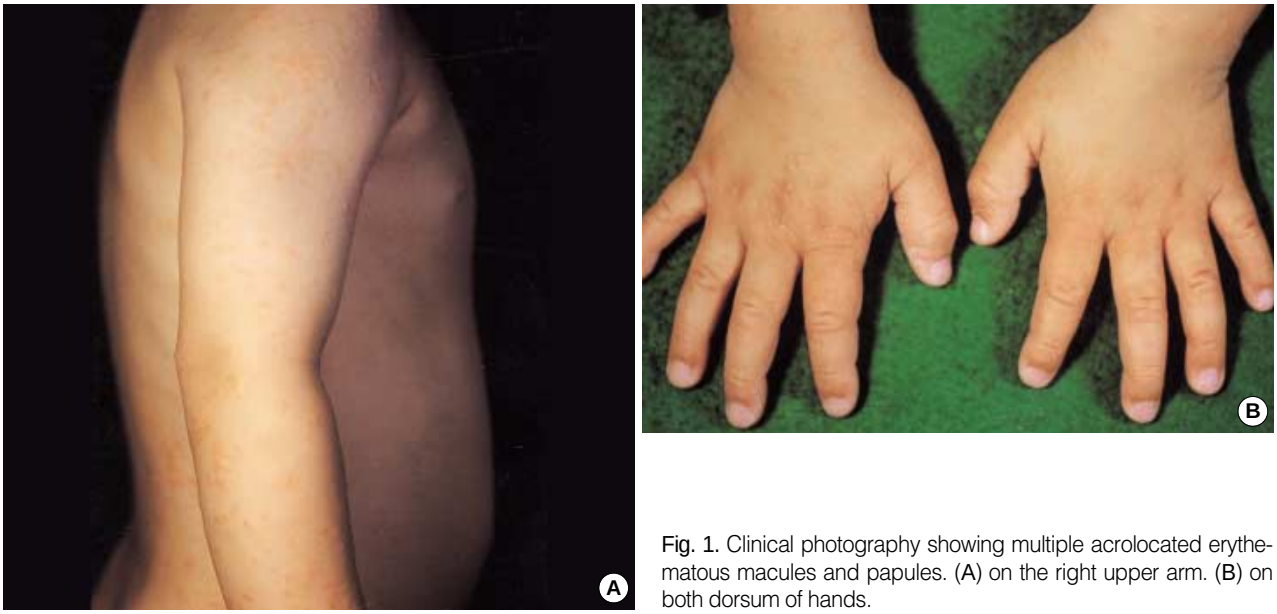

Fig. 1. Clinical photography showing multiple acrolocated erythematous macules and papules. (A) on the right upper arm. (B) on both dorsum of hands.

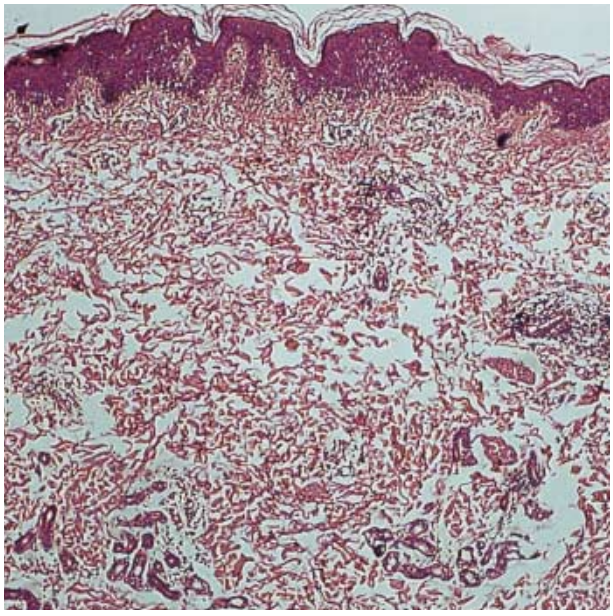

Fig. 2. Focal spongiosis with mild lymphocytic exocytosis in epidermis. Mild superficial and deep perivascular inflammatory infiltrates composed of lymphocytes in dermis (H&E stain, ×40).

induced by a number of chemical and physical stimuli or pathogens. In this regard, Magyarlaki et al. suggested virus-induced type IV cutaneous hypersensitivity (15).

Mostly, GCS is diagnosed by clinical manifestations with specific viral etiology. In our case, physical examination revealed characteristic symmetrical erythematous macules and papules with concomitant lymphadenopathies. His symptoms developed after the first immunization against JE. Inactivated JE virus suspension from infected mouse brain is used for JE immunization in Korea, Japan, and U.S.A. In case of suspicious JE infection, HI test is firstly indicated. Our patient's serum JE antibody titer was 1:40. Following JE vaccination, antibody titer higher than 1:10 indicates successful immunization. If antibody titer is 1:80 or higher, recent JE infections is suspected rather than vaccination and ELISA test to JE antibody is recommended to confirm active JE infection. Hence the HI test titer 1:40 in our patient was considered to result from JE vaccination.

JE is a viral zoonosis spread by Culex mosquitoes in most Asian countries (16). According to the Korean Ministry of Health and Welfare, the estimated coverage rate of this immunization is over 95%. Vaccination against JE is recommended for children aged 3 to 15 yr. The interval of booster vaccination schedule for JE has been changed from every other year to only twice (6th and 12th year) since 2000.

In this case, further recommendation of booster JE vaccination depends on the physician according to the JE prevalence of the area. Studies in the United Kingdom and the United States found that, after two doses, fewer than 80% of patients produced neutralizing antibody. The percentage substantially declined to less than 29% following 6 to 12 months (17). After three doses, 90% produced the antibody (18).

Recently, a few studies on the side effects after JE immunization have been conducted. The side effects are cutaneous, respiratory, cardiovascular, and neurologic symptoms. These symptoms are rare but have been reported by several nations among travelers from Europe, North America, and Australia (19-22). According to a Japanese report, two patterns of systemic immediate type reaction to JE vaccine exist (16). One is associated with cutaneous and respiratory symptoms, and the other with cardiovascular symptom. Cutaneous side

effects are urticaria, angioedema or itching (16). Interestingly, more than half of the cases revealed delayed onset of 1-3 days, and these are the hallmark of the hypersensitivity reactions associated with JE vaccination. The incidence of cutaneous reactions is 15-18 per 10,000 vaccinees (23).

We herein described a patient of GCS following immunization against JE with literature review. Our case represents one of the dermatologic side effects following JE vaccination.

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