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. Lymphadenopatathies 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.

INTRODUCTION

Gianotti-Crosti syndrome (GCS) is a disease of self-limiting 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
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.

REFERENCES

1. Lacour M, Harms M. Gianotti-Crosti syndrome as a result of vaccination and Epstein-Barr virus infection. Eur J Pediatr 1995; 154: 688-9.
2. Gianotti F. Papular acrodermatitis of childhood: an Australian antigen disease. Arch Dis Child 1973; 48: 794-9.
3. Hofmann B, Schuppe HC, Adams O, Lenard HG, Lehmann P, Ruzicka T. Gianotti-Crosti syndrome associated with Epstein-Barr virus infection. Pediatr Dermatol 1997; 14: 273-7.
4. Velangi SS, Tidman MJ. Gianotti-Crosti syndrome after measles, mumps and rubella vaccination. Br J Dermatol 1998; 139: 1122-3.
5. Baleviciene G, Maciuleviciene R, Schwartz RA. Papular acrodermatitis of childhood: Gianotti-Crosti syndrome. Cutis 2001; 67: 291-4.
6. Lowe L, Herbert AA, Duvic M. Gianotti-Crosti syndrome associated with Epstein-Barr virus infection. J Am Acad Dermatol 1989; 20: 336-8.
7. Carrascosa JM, Just M, Ribera M, Ferrandiz C. Papular acrodermatitis of childhood related to poxvirus and parvovirus B19 infection. Cutis 1998; 61: 265-7.
8. Yasumoto S, Tsujita J, Imayama S, Hori Y. Gianotti-Crosti syndrome associated with human herpesvirus-6 virus infection. J Dermatol 1996; 23: 499-501.
9. Di Lemia V. Gianotti-Crosti syndrome related to rotavirus infection. Pediatr Dermatol 1998; 15: 485-6.
10. Stratte EG, Esterly NB. Human immunodeficiency virus and the Gianotti-Crosti syndrome. Arch Dermatol 1995; 131: 108-9.
11. Haki M, Tsachida M, Kotsuji M, Iijima S, Tanura K, Koike K, Izumi I, Tanaka M, Hirano T. Gianotti-Crosti syndrome associated with cytomegalovirus antigenemia after bone marrow transplantation. Bone Marrow Transplantation 1997; 20: 691-3.
12. Cambiajdi S, Scarabelli G, Pistrillo G, Gelmetti C. Gianotti-Crosti syndrome in an adult after influenza virus vaccination. Dermatology 1995; 191: 340-1.
13. Caputo R, Gelmetti C, Ermacora E, Gianni E, Silvestri A. Gianotti-Crosti syndrome: a retrospective analysis of 308 cases. J Am Acad Dermatol 1992; 26: 207-10.
14. Drijkoningen M, De Wolf-Peeters C, Snaauwaert J, De Greef H, Desmet V. Immunohistochemical study of epidermal Langerhans cells and dermal dendritic cells in benign and malignant skin lesions characterized by a dermal lymphoid infiltrate consisting either of B-cells or T-cells. Virchows Arch A Pathol Anat Histopathol 1987; 411: 337-43.
15. Magyarlaki M, Drobnitsch I, Schneider I. Papular acrodermatitis of childhood: Gianotti-Crosti syndrome. Pediatr Dermatol 1991; 8: 224-7.
16. Takahashi H, Pool V, Tsai TF, Chen RT. Adverse events after Japanese encephalitis vaccination: review of post-marketing surveillance data from Japan and the United States. The VAERS Working Group. Vaccine 2000; 18: 2963-9.
17. Thomas RE. Preparing patients to travel abroad safely Part 2: Updating vaccinations. Can Fam Physician 2000; 46: 646-52, 655-6.
18. Reflecting the extraordinary pace of change. Canadian Immunization Guide. Laboratory Centre for Disease Control, Health Protection Branch, Health Canada. Can Fam Physician 1999; 45: 135-8.
19. Soln TM. Japanese encephalitis immunization in South Korea: past, present, and future. Emerg Infect Dis 2000; 6: 17-24.
20. Andersen MM, Ronne T. Side-effects with Japanese encephalitis vaccine. Lancet 1991; 337: 1044.
21. Nazareth B, Levin J, Johnson H, Begg N. Systemic allergic reactions to Japanese encephalitis vaccines. Vaccine 1994; 12: 666.
22. Berg SW, Mitchell BS, Hanson RK, Olafoxon RP, Williams RP, Tueller JE, Burton RJ, Novak DM, Tsai TF, Wignall FS. Systemic reactions in U.S. Marine Corps personnel who received Japanese encephalitis vaccine. Clin Infect Dis 1997; 24: 265-6.
23. Ruff TA, Eisen D, Fuller A, Kass R. Adverse reactions to Japanese encephalitis vaccine. Lancet 1991; 338: 881-2.