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■ Case report ■

Herpes zoster complicated by deep vein thrombosis : a case report

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= Abstract =

Varicella zoster virus (VZV) causes two diseases: *Varicella*, a generalized, primary infection, and *herpes* zoster (zoster), a secondary infection caused by latent VZV reactivation. Zoster can also be caused by latent VZV reactivation after a varicella vaccination. The complications associated with varicella include cutaneous infections, which are the most common, as well as pulmonary and neurological involvement. However, a deep venous thrombosis (DVT) has been rarely described as a varicella-associated complication. Here, we describe the case of a child with varicella zoster who developed a DVT that completely resolved after intravenous acyclovir and subcutaneous low-molecular-weight heparin treatment. **(Korean J Pediatr 2009;52: 607-610)**

Key Words : Varicella zoster virus, Herpes zoster, Varicella vaccine, Deep venous thrombosis

Introduction

Varicella-zoster virus (VZV) causes two diseases. *Varicella*, is a generalized illness and a primary infection, and *herpes zoster* (zoster) is a secondary infection, caused by reactivation of latent VZV. VZV becomes latent after a *varicella* infection and usually persists silently and indefinitely. Zoster can be caused by reactivation of latent VZV after a varicella vaccination. Among vaccine recipients, zoster has an incidence of 14 cases per 100,000 person-years[1]. Although most complications associated with varicella infection are cutaneous, pulmonary and neurological, deep venous thrombosis (DVT) occurred in the patient reported here. The patient was treated with intravenous acyclovir and subcutaneous low molecular weight heparin (LMWH) and the DVT completely resolved.

Case report

A 6-year-old previously healthy boy was admitted to the hospital because of pain in the right hip and skin eruptions at the right tibial area. Pain and erythema in the right hip developed first. Three days later, skin eruptions with prickly pain appeared at the right tibial area. These skin lesions consisted of grouped vesicles on an erythematous base and were localized to the L5 dermatome, involving the right knee and shin (Fig. 1).

On presentation the body temperature was 36.7℃ with a pulse rate of 116 beats/min, a respiratory rate of 24 breaths/min and a blood pressure of 100/60 mmHg. Physical examination revealed no specific findings with the exception of

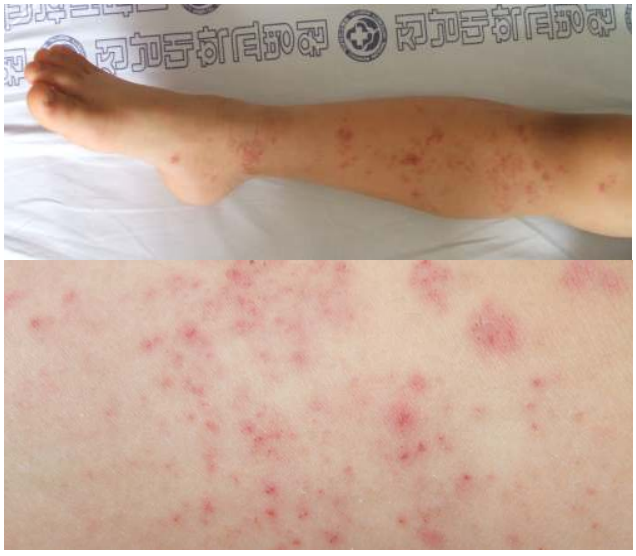

Fig. 1. Skin lesions consisting of grouped vesicles on an erythematous base localized to the L5 dermatome, involving the right knee and shin.

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typical eruptions of herpes zoster on the right lower leg. The patient complained of gait disturbance due to aggravation of the right hip pain. However, his right hip and calf were not swollen; but severe tenderness at the right inguinal area was present .

The results of the laboratory studies were as follows: white blood cell count 5,900/mm^3, platelet count of 245,000/mm^3 and a hemoglobin 14.8 g/dL. The activated partial thromboplatin time and prothrombin time were normal (35 seconds, 10.6 seconds respectively). The Antithrombin III test (38.7 mg/dL) was normal. The renal and liver function tests and the C-reactive protein were within normal range.

The immunization record indicated that the patient had received a single dose of the varicella vaccine at one year of age. The patient had not developed chicken pox prior to or after the vaccination. The patient did not have a history of thromboembolic diseases except for Henoch-Schonlein purpura five years previously.

The inguinal pain was evaluated for a thrombophlebitis or thromboembolism by computed tomographic (CT) venography. The results showed a segmental thrombotic filling defect from the right iliac vein to the right common femoral vein (Fig. 2). We evaluated the patient for underlying thromboembolic risk factors. The protein C, protein S and homocysteine values were all normal. The anti-cardiolipin Ab, anti-phospholipid Ab, lupus anticoagulant, and ANA were negative. The factor 5 Leiden mutation was also normal. The 2-D echocardiogram showed normal cardiac structure and function without intracardiac or pulmonary thromboemboli.

For evaluation of the skin lesions, the Tzanck smear preparation revealed multinucleated giant cells, supporting a clinical diagnosis of herpes zoster. The serology for herpes zoster IgM and IgG were both positive. Given the diagnosis of Herpes zoster with deep vein thrombosis, we started intravenous acyclovir 240 mg/m^2, q8h along with subcutaneous low molecular weight heparin (LMWH, Crexan prefilled syringe□) 0.1 mg/kg q 12 hours.

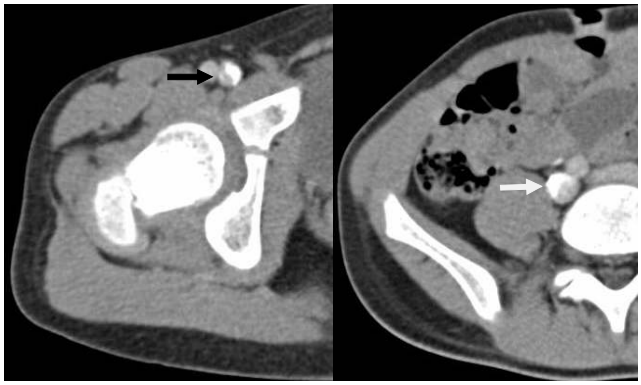

Fig. 2. Computed tomographic venography showed a segmental thrombotic filling defect from the right iliac vein (arrow) to the right common femoral vein (white arrow).

On the second hospital day, the right tibial erythematous skin lesions subsided but the vesicles spread to the right great toe. The right inguinal pain, tenderness and skin eruptions gradually improved. On the fifth hospital day, a second CT venography showed that the segmental thrombotic filling defect improved but was still present. The acyclovir was discontinued, and the LMWH was continued for 10 days. On the tenth hospital day, the lower extremity ultrasound showed no evidence of a DVT in the right iliac or femoral vein. Therefore, the LMWH was changed to oral warfarin sodium. During the anticoagulation treatment, the patient did not have any symptoms or signs of a pulmonary thromboembolism.

On the twelfth hospital day, the patient was discharged after a complete recovery from both the herpes zoster and the DVT. The oral warfarin sodium was continued for the next month. The patient remained free of any clinical symptoms of a thrombotic disorder.

Discussion

VZV is the causative agent of *varicella* a primary infection that occurs in susceptible individuals. After the primary infection, the virus establishes a lifelong latent infection in the dorsal root ganglion cells. Its reactivation causes herpes zoster, which is characterized by unilateral neuralgia followed by vesicular eruptions in a dermatome distribution[2].

The incidence of zoster in healthy children who have had natural varicella infections has been reported by Hope-Simpson[3] to be 0.74 cases per 1,000 children per year, during the first 10 years of life. The incidence of zoster among immunocompromised children immunized with live attenuated varicella vaccine has been reported by many observers[4,5]. However, the incidence of zoster among healthy children immunized with live attenuated varicella vaccine remains to be determined. The occurrence of herpes zoster after immunization with live varicella vaccine among healthy children has been very rarely reported[6-8].

Confirmation of zoster can be obtained by immunofluorescence or immunoperoxidase staining of vesicle scrapings or viral cultures of vesicle fluid. However, the sensitivity of

these diagnostic methods is limited and highly dependent on the quality of the scrapings, handling time of the vesicle fluids and stage of the skin lesions. Nevertheless, a serology diagnosis of VZV reactivation remains useful for the confirmation of the clinical diagnosis, particularly when vesicle specimens are of poor quality or not available at all, which is usually the case in routine diagnostic laboratories. The majority of laboratories therefore perform serological IgM antibody determination and look for a rise in the IgG or the complement fixation test[9,10]. However, in children with herpes zoster subsequent to an immunization, it is difficult to tell whether this results from a vaccine-type or a wild-type virus, in cases where the VZV cannot be differentiated. Several methods including restriction fragment length polymorphism[11], and PCR[12], are available for differentiation of the wild-type from the vaccine derived VZV strains.

Umberto and Fabio[13] reported, in adult zoster cases that the overall rate of complications was 26.1%. The most common herpes zoster complication is post herpetic neuralgia with an overall rate of 19.6% and ocular complications as high as 5.7%. The complication rates are significantly higher in people 65 or older and in those with two or more affected dermatomes. DVT is a rare complication of adult varicella zoster virus infection, mainly affecting the major veins of the legs. In 1984, Ali[14] described a case of iliofemoral vein thrombosis in a patient with chickenpox and considered this as a direct result of the VZV infection. Since then, some reports have supported that VZV infections were related to thrombotic complications[15,16]. In 1970 Minick et al.[17] first noted that viruses may induce atherosclerosis, and a relationship was proposed between viruses, vasculitis and possibly thrombosis[18]. VZV infection has been found to induce endothelial damage in blood vessels[19, 20].

Early diagnosis and initiation of anticoagulant therapy is recommended during the course of varicella. Gogos et al[3] treated one case of varicella pneumonia with DVT using acyclovir 500 mg i.v, t.i.d., along with heparin, 30,000 IU/day i.v. for the first seven days and wafarin sodium p.o. for the next three months; the other case of varicella with DVT was treated with heparin 35,000 IU/day i.v. only for 10 days followed by wafarin sodium p.o.. These cases are both adult patients with varicella complicated by DVT.

In the present case we describe a child who had simultaneous varicella zoster – VZV reactivation and developed deep venous thrombosis.

한 글 요 약

대상포진에 합병된 심부정맥혈전증 1예

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수두 바이러스는 두 가지 임상 증후군을 유발하는 데, 초회 감염되면 수두를, 지각 신경절에 잠복해 있다가 재발하면 대상포진을 일으킨다. 수두백신이 널리 이용되면서 수두 이후의 대상포진 뿐만 아니라 수두백신 접종 후 발생한 대상포진도 관찰되고 있다. 수두바이러스에 의한 합병증으로는 2차 세균감염에 의한 농가진, 연조직염 등의 피부감염이 가장 흔하며 이외에도 호흡기계와 신경계의 합병증이 잘 알려져 있다. 또 수두 바이러스 감염 후의 합병증으로 심부정맥혈전증이 매우 드물게 보고되고 있다. 주로 혈관벽의 손상과 관련된 것으로 여겨지며 하지 정맥을 침범한다. 수두 감염된 심부정맥혈전증 증상을 보이는 환자에서 합병증을 의심하고 조기 진단하여 항응고치료를 하는 것이 추천된다. 이에 저자들은 수두 백신만 1회 접종한 환아에서 심부정맥혈전증을 동반한 대상포진이 발생하여 acyclovir 정맥주사와 저분자량 헤파린 피하주사로 회복되어 보고한다.

References

1) Leung AK, Robson WL, Leong AG. Herpes zoster in childhood. J Pediatr Health Care 2006;20:300-3.
2) Arvin AM. Varicella-zoster virus. Clin Microbiol Rev 1996; 9:361-81.
3) Hope-Simpson RE. The nature of herpes zoster: a long-term study and a new hypothesis. Proc R Sco Med 1965;58:9-20.
4) Katsushima N, Yazaki N, Sakamoto M. Effect and follow-up study on varicella vaccine. Biken J 1984;27:51-7.
5) Lawrence R, Gershon AA, Holzman R, Steinberg SP. The risk of zoster after varicella vaccination in children with leukemia. N Engl J Med 1988;318:543-8.
6) Hammerschlag MR, Gershon AA, Steinberg SP, Clarke L, Gelb LD. Herpes zoster in an adult recipient of live attenuated varicella vaccine. J Infect Dis 1989;160:535-7.
7) Johnson C, Rome LP, Stancin T, Kumar ML. Humoral immunity and clinical reinfections following varicella vaccine in healthy children. Pediatrics 1989;84:418-21.
8) Arbeter AM, Starr SE, Plotkin SA. Varicella vaccine studies in healthy children and adults. Pediatrics 1986;78:748-56.
9) Schmidt NJ, Arvin AM. Sensitivity of different assay systems for immunoglobulin M responses to varicella-zoster virus in reactivated infections (zoster). J Clin Microbiol 1986; 23:978-9.
10) Gershon AA, Steinberg SP, Borkowsky W, Lennette D, Lennette E. IgM to varicella-zoster virus: demonstration in patients with and without clinical zoster. Pediatr Infect Dis 1982;1:164-7.

11) Gelb LD, Dohner DE, Gershon AA, Steinberg SP, Waner JL, Takahashi M, et al. Molecular epidemiology of live, attenuated varicella virus vaccine in children with leukemia and in normal adults. J Infect Dis 1987;155:633-40.
12) Takada M, Suzstani T, Yoshida I, matoba M, Azuma M. Identification of varicella zoster virus strains by PCR analysis of three repeat elements and a PstI-site-less region. J Clin Microbiol 1995;33:658-60.
13) di Luzio Paparatti U, Arpinelli F, Vison G. Herpes zoster and its complications in Italy: an observational survey. J Infect 1999;38:116-20.
14) Ali MS, Kutty MS, Corea JR, Kutty K. Iliofemoral thrombosis in a case of chicken pox. Angiography 1984;35:577-8.
15) Gogos CA, Apostolidou E, Bassaris HP, Vagenakis AG. Three cases of varicella thrombophlebitis as a complication of varicella zoster virus infection. Eur J Clin Microbiol Infect Dis 1993;12:43-5.
16) Bodensteiner JB,Hille MR,Riggs JE. Clinical features of vascular thrombosis following varicella. Am J Dis Child 1992;146:100-2.
17) Minick CR, Fabricant CG, Fabricant J, Litrenta MM. Atherosclerosis induced by infection with a herpesvirus. Am J Pathol 1979;96:673-706.
18) Gunby P. Viral infection may lead to vessel wall problems. J Am Med Assoc 1984;251:1131-2.
19) Johnson HN. Visceral lesions associated with varicella. Archives of Pathology 1940;30:292-307.
20) Sargent EN, Carson MJ, Reilly ED. Roentgenographic manifestations of varicella pneumonia with postmortem correlation. Am J Roentgenol Radium Ther Nucl Med 1966;98:305-17.