Case Report

Complete Remission of Human Parvovirus B19 Associated Symptoms by Loxoprofen in Patients with Atopic Predispositions

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1. Introduction

The classic symptoms of human parvovirus B19 (HPV-B19) infection include fever, rash, arthralgia, and edema [1]. In children, the symptoms are usually self-limited, resolving spontaneously within a few weeks [2]. In adults, however, they are often prolonged, sometimes causing serious complications, such as chronic arthritis, myocarditis, and meningitis [3–5], or triggering the onset of autoimmune diseases [6]. According to previous studies, the direct cytotoxicity of the virus has been ascribed to the pathogenesis of the symptoms [7, 8]. However, due to the absence of drugs that are effective for the virus, there is no causal treatment. To relieve the symptoms, analgesics or antipyretics are generally used [9], although they do not shorten the duration of the disease. Here, we experienced two cases of HPV-B19 infection in adult patients with past histories of atopic dermatitis and allergic rhinitis [10]. According to our previous studies, the direct cytotoxicity of the virus has been ascribed to the pathogenesis of the symptoms [7, 8]. However, due to the absence of drugs that are effective for the virus, there is no causal treatment. To relieve the symptoms, analgesics or antipyretics are generally used [9], although they do not shorten the duration of the disease. Here, we experienced two cases of HPV-B19 infection in adult patients with past histories of atopic dermatitis and allergic rhinitis [10]. In those cases, due to the atopic predispositions of the patients, an increased immunological response was more likely to be involved in the pathogenesis of the symptoms. In such cases, a nonsteroidal anti-inflammatory drug (NSAID), loxoprofen, dramatically improved their deteriorating symptoms immediately after the administration. The immunomodulatory property of this drug was thought to repress the lymphocyte activity and thus provided a rapid and sustained remission of the disease.

2. Case Presentation

2.1. Case 1. A 38-year-old woman with a childhood history of atopic dermatitis and allergic rhinitis came to our outpatient clinic because of polyarthritis due to a low-grade fever and edema (Figure 1). Oral administration of 400 mg acetaminophen relieved her symptoms. However, five days prior to her visit, she developed upper respiratory symptoms and a lower grade fever. Oral administration of 400 mg acetaminophen relieved those symptoms. Then, however, she developed a butterfly-shaped erythema on her face and swelling of her fingers. Three days later, although the facial erythema had improved, she developed joint pain in her fingers, wrists, shoulders, and knees, for which acetaminophen did not work. On physical
examination, the patient looked tired. Her body temperature was 36.7°C, blood pressure was 94/50 mmHg, and pulse rate was 61 beats/min. She weighed 48 kg and was 153 cm tall. She had no rash except for a malar erythema that was faint at that time. All her fingers were swollen, but her wrist, shoulder, and knee joints were not. Both her legs had pretibial pitting edema. Laboratory data showed mild hypoprofibrinemia (serum protein 6.4 g/dL) and slightly decreased peripheral white blood cell count (4,100/µL). However, other hematologic parameters were relatively normal (hemoglobin 11.2 g/dL, hematocrit 35.2%, reticulocyte 1.4%, and platelet count 230,000/µL). Liver enzymes and C-reactive protein levels were not elevated. Regardless of hypocomplementemia (C3 72 mg/dL, C4 9 mg/dL, and CH50 18.6 U/mL), the tests for serum antinuclear antibodies and rheumatoid factor were negative. Although the IgG antibody was not examined, a positive result for HPV-B19 IgM antibody (index 7.97) indicated a recent infection of the virus [10]. Since microbiological tests for other viruses, such as measles and rubella, were negative, a diagnosis of HPV-B19 infection was finally made. Because her symptoms deteriorated despite the use of acetaminophen, oral administration of loxoprofen (180 mg/day) was alternatively started immediately after the diagnosis (Figure 1). The symptoms, including facial erythema, polyarthralgia, and the swelling of her fingers, rapidly disappeared within 12 hours after the initiation of the drug. No recurrence of the symptoms or signs was noted afterwards, indicating the complete remission of the disease.

2.2. Case 2. A 36-year-old woman with a past history of allergic rhinitis came to our outpatient clinic because of polyarthralgia and swelling of her fingers. Ten days prior to her visit, she had a low grade fever (Figure 2) when her 9-year-old son was diagnosed as having erythema infectiosum because of his slapped cheek rash. Seven days later, she developed a butterfly-shaped erythema transiently on her face that disappeared the next day. Then, she developed swelling of her fingers and joint pain in her shoulders, ankles, and knees. Since oral administration of acetaminophen did not relieve her symptoms, she came to our clinic. On physical examination, the patient looked tired. Her body temperature was 37.0°C, blood pressure was 110/72 mmHg, and pulse rate was 66 beats/min. She weighed 52 kg and was 160 cm tall. At that time, she presented no malar erythema and no rash in her body. Although all her fingers were swollen, the swelling of her shoulder, ankle, and knee joints was not obvious. Laboratory data showed normal hematologic parameters (white blood cell count 6,300/µL, hemoglobin 12.6 g/dL, hematocrit 37.6%, and platelet count 264,000/µL). Liver enzymes and C-reactive protein levels were not elevated. Regardless of hypocomplementemia in Case 1, which occurs in both SLE and HPV-B19 infection [14], indicated the activation of the classical complement pathway caused by the increase in
immune complexes. Therefore, in our cases, such enhanced immunity was more likely to be involved in the pathogenesis of the symptoms. According to previous studies, patients with atopic dermatitis and allergic rhinitis are prone to develop autoimmune diseases due to the hypersensitivity of T-helper 2 lymphocytes [15, 16] or the dysregulated activity of B-lymphocytes [17]. In our cases, since both patients were predisposed to atopic disorders, such as atopic dermatitis and allergic rhinitis, the HPV-B19 infection may have triggered the activity of the lymphocytes.

For adult patients with HPV-B19 infection, NSAIDs are often used to provide symptomatic relief for arthralgia and myalgia [12, 18]. However, since these drugs do not shorten the duration of the disease, the patients have to wait at least 1 to 2 weeks for the spontaneous remission of the disease [19, 20]. In our cases, although acetaminophen failed to ameliorate the patients’ symptoms, loxoprofen completely removed their deteriorating symptoms quickly after the administration (Figures 1 and 2). Therefore, in our cases, loxoprofen was thought to be responsible for the complete remission of the disease. NSAIDs are the most commonly used anti-inflammatory, analgesic, and antipyretic drugs. Additionally, due to their immunomodulatory properties [21], they have also been used in the treatment of autoimmune diseases, such as SLE [22] and rheumatoid arthritis [23]. Studies have revealed that NSAIDs inhibit the migration of leukocytes or their cytokine production, either cyclooxygenase (COX) dependently [24] or independently [25, 26], and thus exert immunomodulatory effects. In the present cases, since the increased activity of lymphocytes was mainly involved in the pathogenesis, the immunomodulation by the NSAID was thought to be responsible for the rapid removal of the symptoms and the complete remission of the disease. Recently, we have demonstrated in a basic study that NSAIDs repress the activity of lymphocytes by the functional inhibition of delayed rectifier K+-channels (Kv1.3) [27]. Since T-lymphocytes highly express the channels in their plasma membranes [28], such mechanism may have greatly contributed to the immunomodulatory effect of NSAID in our patients. In this regard, besides the short-term use of immunosuppressive agents or steroids, the use of selective Kv1.3-channel blockers may also be useful. The early administration of such drugs would not only shorten the duration of the disease, but also prevent the serious complications caused by HPV-B19 infection or the onset of autoimmune diseases triggered by the virus.

In summary, this is the first report of HPV-B19 infection in adult patients with atopic predispositions showing the usefulness of NSAID for the quick removal of the symptoms. The immunomodulatory property of NSAID was thought to repress the increased lymphocyte activity and thus provided a rapid and sustained remission of the disease.

**Conflict of Interests**

The authors declare no conflict of interests.

**References**

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