Case Report: Acute Generalized Exanthematous Pustulosis Caused by Praziquantel

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Abstract. Praziquantel is widely used for treating parasitic infections globally, especially in countries with endemic schistosomiasis. However, severe hypersensitivity to praziquantel has rarely been reported. We report the case of a 30-year-old Japanese man who developed acute generalized exanthematous pustulosis (AGEP), which is a rare and severe cutaneous reaction usually triggered by drugs, after taking praziquantel. During medical examination, eggs of *Diphyllbothrium nihonkaiense* were found in his stool. He took praziquantel 600 mg for 1 day and developed skin rashes and fever the next day. Pruritic generalized maculopapular erythematous eruptions were observed over the entire body. He had elevated white blood cell count, liver enzymes, and C-reactive protein level. We prescribed acetaminophen, fexofenadine hydrochloride, loxoprofen sodium, and topical ointments including difluprednate and hydrocortisone. Over the next 3 days, he developed pinhead-sized, non-follicular pustules on his diffusely erythematous skin. Histological findings of the pustular lesion showed spongiform subcorneal pustules with perivascular inflammatory cells. Approximately 8 days after taking praziquantel, the pustules resolved with desquamation. He became afebrile on day 9 and his laboratory parameters returned to normal levels on day 16. He was diagnosed with AGEP caused by praziquantel. Physicians need to be aware that praziquantel could cause AGEP, although it is generally considered a safe drug.

CASE REPORT

A 30-year-old Japanese man presented to our hospital for anthelmintic medication. He was a chef on a luxury cruise ship and had undergone annual stool examinations for pathogenic bacteria and parasites conducted by his company. Three days before his visit, eggs of *Diphyllbothrium nihonkaiense* were found in his stool. Although he was asymptomatic, he was required to receive anthelmintic therapy according to his company's regulations. He had no notable medical history, previous drug allergy, or personal/family history of skin disease. We prescribed praziquantel 600 mg for 1 day.

The next day, he returned to our hospital because of skin rashes and fever. We suspected that he had a severe drug reaction to praziquantel and he was admitted. On physical examination, he was conscious and alert. His blood pressure was 119/51 mmHg, pulse rate 98 beats/minutes, respiratory rate 18 cycles/minutes, and temperature 39.2°C. The patient's breath and heart sounds were normal, and the abdomen was soft and flat. Pruritic generalized maculopapular erythematous eruptions were observed on his face, neck, trunk, and extremities, without mucosal involvement and urticarial lesions (Figure 1). He had a white blood cell (WBC) count of 10,800/μL (with 8,964/μL of polymorphonuclear neutrophils), hemoglobin level of 15.0 g/dL, platelet count of 184,000/μL, aspartate aminotransferase of 833 IU/L, alanine aminotransferase of 841 IU/L, total bilirubin of 1.5 mg/dL, alkaline phosphatase of 468 IU/L, gamma-glutamyl transpeptidase of 197 IU/L, blood urea nitrogen of 9.2 mg/dL, serum creatinine of 0.68 mg/dL, and C-reactive protein (CRP) level of 10.96 mg/dL. Serologic tests for cytomegalovirus, Epstein-Barr virus, human herpesvirus-6, and hepatitis B and C viruses were negative. Antinuclear antibody, myeloperoxidase anti-neutrophil cytoplasmic antibody, proteinase-3-antineutrophil

cytoplasmic antibody, and anti-Jo-1 antibody were also negative.

We prescribed acetaminophen 2,400 mg/day, fexofenadine hydrochloride 120 mg/day, loxoprofen sodium 60 mg/day, and a topical ointment including difluprednate and hydrocortisone. Over the next 3 days, he developed pinhead-sized, non-follicular pustules on his diffusely erythematous skin, especially in the intertriginous area (Figure 2). The results of blood and pustule cultures were negative. Skin biopsy of the pustular lesion was conducted, and the histological findings showed spongiform subcorneal pustules with perivascular inflammatory infiltrates consisting of neutrophils, eosinophils, and lymphocytes (Figure 3). Eggs and segments of *Diphyllbothrium* were not detected in his stool samples which were collected before and after he took the praziquantel. Capsule endoscopy did not show any abnormal lesions in the gut. Approximately 8 days after taking praziquantel, the pustules resolved without additional treatment, and desquamation followed (Figure 4). We stopped the regular medication. He became afebrile on day 9 without any medication and was discharged the next day. Subsequently, all cutaneous lesions cleared. His WBC count, liver enzymes, and CRP level returned to normal on day 16. He was diagnosed with acute generalized exanthematous pustulosis (AGEP) caused by praziquantel. There has been no recurrence for 12 months.

DISCUSSION

Praziquantel is widely used for treating parasitic infections and is considered to be a safe drug. It is estimated that about 100 million people take praziquantel globally every year.¹ However, only five cases of hypersensitivity reaction caused by praziquantel have been reported.^{1–5} Acute generalized exanthematous pustulosis is a rare and severe cutaneous reaction and is mostly caused by drugs. Acute generalized exanthematous pustulosis sometimes leads to multiple organ dysfunction. The mortality rate of AGEP estimates approximately 5%.⁴ Acute generalized exanthematous pustulosis is defined by 1) several small, mostly non-follicular

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FIGURE 1. Pruritic generalized maculopapular erythematous eruptions on the thighs (A) and abdomen (B). This figure appears in color at www.ajtmh.org.

pustules arising on a widespread edematous erythema; 2) typical histopathological changes; 3) fever $> 38^{\circ}\text{C}$; 4) blood neutrophil counts above $7 \times 10^9/\text{L}$; and 5) acute evolution with spontaneous resolution of pustules in less than 15 days.⁶ In the present case, the patient met all the criteria for AGEP. Moreover, according to an AGEP validation score developed by the EuroSCAR group to confirm the diagnosis of AGEP,⁷ the patient scored 12, which indicated a definitive diagnosis of AGEP. The acute dermatological reaction after taking praziquantel might have been caused by the killing of the parasite, which in turn released parasitic antigens to which the patient had been sensitized. However, in the present case, reexamination for eggs and segments of the parasite in the stool before and after taking praziquantel was negative, and endoscopic examination of the gastrointestinal tract did not show abnormal lesions. We think that the result of the first stool examination was false positive. To the best of our knowledge, this is the first case of AGEP caused by praziquantel.

In the treatment of AGEP, the usefulness of corticosteroids has not been fully established. The use of potent topical corticosteroids might be associated with a decreased duration of hospitalization.⁸ However, it is not clear whether systemic corticosteroids are beneficial with regard to the disease course.^{9,10} Systemic corticosteroids should be carefully used, as AGEP is not only caused by drugs but also by infections.^{11,12}

In conclusion, hypersensitivity to praziquantel has rarely been reported; however, physicians should be aware that praziquantel could cause AGEP, which may lead to serious conditions.

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FIGURE 2. Pinhead-sized, non-follicular pustules on erythematous skin. This figure appears in color at www.ajtmh.org.

FIGURE 3. Histological findings of the pustular lesions showing spongiform change (black circle), papillary edema with eosinophilic infiltration (black triangles), and subcorneal pustules (white circle). This figure appears in color at www.ajtmh.org.

FIGURE 4. The erythematous eruption and pustules were resolved, followed by desquamation. This figure appears in color at www.ajtmh.org.

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