

Hypersensitive Reaction to Praziquantel in a Clonorchiasis Patient

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Abstract: Praziquantel is the drug of choice for clonorchiasis. Since clonorchiasis is endemic in most river basins, praziquantel has been widely used for 30 years in Korea. A 54-year-old Korean woman suffered from hypersensitive reactions, such as nausea, dyspnea, rash, and urticaria after taking the first dose of praziquantel to treat clonorchiasis. She ingested one dose again and the same symptoms appeared, and she was treated at a clinic with anti-histamines. She tried one more dose with anti-histamines but found the same symptoms. Later, she was found to pass eggs of *Clonorchis sinensis* and medicated with flubendazole. The hypersensitive reaction to praziquantel is rare but occurs. This is the 5th case report in the world.

Key words: *Clonorchis sinensis*, clonorchiasis, praziquantel, hypersensitive reaction

INTRODUCTION

Praziquantel (PZQ) is the drug of choice for treatment of parasitic infections by trematodes or cestodes. Since the parasitic infections are common in many countries, PZQ is widely used. It is estimated that about one hundred million people take PZQ over the world every year. PZQ is safe enough for the global use even though it has some known adverse effects, such as abdominal pain, diarrhea, sleep disorder, dizziness, and headache. These adverse effects are common but mild and transient, and require no specific medical intervention [1].

In addition to the common adverse effects, rather severe reactions to PZQ have been recognized. The severe reactions are drug eruptions, including skin rash or urticaria, dyspnea, and hypotensive shock. They are serious to require specific medical care. These serious symptoms or signs are induced by hypersensitive or anaphylactic reaction of individuals to most of drugs. At present, 4 cases of PZQ hypersensitive reactions have been reported worldwide [2-5].

The hypersensitivity reaction is rare but serious when it occurs. The present case report describes clinical findings of a clonorchiasis patient who had hypersensitive reactions after PZQ ingestion in Korea.

CASE REPORT

The patient was a 54-year-old-female who was running a dairy farm in Gyeongju, Korea. She had eaten raw trout a few times and cooked freshwater fish frequently but not enjoyed eating raw freshwater fish. She was found to pass eggs of *Clonorchis sinensis* through her feces when she was examined by a program of parasitic infection survey for dairy farmers in 2009. She was recommended to take PZQ with a dosage of 25 mg/kg × 3. On 25 August, 2010, she took the first dose of PZQ (Dis-tocide®, Shin Poong Pharmaceutical Co. Ltd., Seoul, Korea), and felt an itching sensation and noticed skin rashes on her hands and then on her entire body about 2 hr after the ingestion. She realized other symptoms of facial flushing, nausea, and dyspnea as well. The rashes ranged in their diameter from 3 to 10 mm. The patient assumed that these symptoms had been caused by some kinds of food and the symptoms subsided during sleeping. She took the second dose of PZQ on the next day after eating breakfast. After the second ingestion, she experienced the same symptoms. She realized that PZQ might have caused the skin rash, and visited a local clinic. According

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to the record of the local clinic, the symptoms slightly subsided compared from the beginning but body itching and skin rashes persisted. Blood pressure was 116/64 with heart rate 64, and she was diagnosed as acute gastritis with Distocide® allergy. The doctor prescribed chlorpheniramine maleate 0.5 ample (anti-histamine) followed by bepotastine besilate 10 mg (second generation anti-histamine), methylprednisolone 4 mg, and metoclopramide HCl 3.84 mg for 2 days. The symptoms disappeared after a few hours. At 14:30 she took 1 dose of PZQ with the prescribed medicines. After 2 hr, similar reactions of mild degree appeared again. Itching and skin rashes were present but dyspnea was not. She consulted her medical problems with Prof. Lim and was recommended to stop taking PZQ.

She had no specific medical history. She had been healthy without any experience of drug eruptions. She denied taking any other drugs simultaneously.

She was examined of her feces at Department of Parasitology and Tropical Medicine, Seoul National University. Her feces were confirmed to pass a few eggs of *C. sinensis* on 9 September, 2010. She was treated with flubendazole (Zelcom®, Chong Kun Dang Pharm. Seoul, Korea) 400 mg/day for 14 days as a substitute. Her feces were re-examined and no eggs were found in April 2011.

DISCUSSION

The present case demonstrated skin rashes and other symptoms of nausea, dizziness, and dyspnea after PZQ ingestion, which were compatible with those by hypersensitive reactions. She recognized the same drug reactions repeatedly after ingestion of PZQ. Therefore, it is evident that the present case had hypersensitive reactions to PZQ.

Both PZQ and parasites are foreign bodies and become potential allergens for a human body. In schistosomiasis, dead parasite bodies and eggs were recognized to induce the hypersensitive reaction after PZQ medication [6]. PZQ kills *S. japonicum* in the blood vessel, and the disintegrated dead worms may suddenly release much amount of allergens into the blood. The suddenly increased allergens should trigger the anaphylactic reaction after PZQ medication. Nonetheless, the present case is regarded as a patient of hypersensitive reaction which was induced by PZQ itself. There is only one recorded case of PZQ anaphylaxis in clonorchiasis [3]. That was a case of reaction to PZQ not to the worms.

Since *C. sinensis* live in the intrahepatic bile duct, PZQ which is metabolized in the liver and excreted into the bile can kill the worms [7]. Since T_{max} of PZQ is 2 hr after ingestion in humans, it takes more time than 2 hr to kill the worms [7]. Furthermore, *C. sinensis* live in the bile duct and pass down to the intestine through the bile duct lumen after paralysis or death of worms by PZQ [8]. Since most of the dead worms of *C. sinensis* are discharged from the body, they have little chance of allergic stimulation within 2 hr after PZQ medication. Contrary to this, allergens from the dead worms of *Schistosoma* or *Paragonimus* are directly exposed to immune cells in the blood or tissue [2,6]. In this context, it is evident that the present case showed hypersensitive reactions to PZQ not to the parasite.

The hypersensitive or allergic reaction requires a primary sensitization to the allergen. It is uncertain when the present case had been previously exposed to PZQ. Although she denied ingestion of the PZQ before, she had been exposed to PZQ in an unnoticed occasion.

Since the present case was unable to finish whole dosage of PZQ therapy, she was examined and found still positive for *C. sinensis* eggs. She took flubendazole for 2 weeks, and became egg negative. Recently a hypersensitive case to PZQ has been reported in pulmonary paragonimiasis [2]. The case was treated with PZQ after desensitization. Desensitization is a good choice for cure of those hypersensitive or allergic patients of a certain drug.

The cases of hypersensitive reaction to PZQ may have occurred more than reported. Most cases of mild reactions have recovered without specific medical care. They have been unnoticed by physicians and therefore not reported. Only the cases of serious reactions have been selectively reported. There have been only 4 reported cases as hypersensitive or anaphylactic reaction to PZQ although it has been globally used for more than a billion people during the last 30 years.

In conclusion, PZQ is a safe anti-helminthic but hypersensitive reaction may rarely occur. This is the 5th case of hypersensitive reaction to PZQ as literature concerned.

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