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Case Report

Anaphylactic reaction to praziquantel following schistosomiasis treatment

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ABSTRACT

Praziquantel (PZQ) is a medication used to treat several parasitic infections, including human schistosomiasis. Although this drug commonly causes transient adverse effects, severe hypersensitivity is rare, and only eight cases have been reported worldwide. Herein we report a case of a 13-year-old Brazilian female who developed anaphylaxis, a severe hypersensitive reaction, after taking praziquantel to treat *Schistosoma mansoni* infection. During a mass drug administration event in a socially vulnerable endemic area of Bahia (Brazil), after taking 60 mg/kg of praziquantel the patient developed rash and generalized edema an hour later, evolving to somnolence and hypotension. Following the anaphylactic episode, she received adequate treatment and recovered approximately 1 day later. Although praziquantel is considered safe, health professionals should be aware of potential life-threatening adverse events.

Introduction

Schistosomiasis, an infectious disease caused by parasites of the genus *Schistosoma*, is a persistent public health problem worldwide, resulting in up to 200 000 deaths annually [1]. Approximately 779 million people live in areas where they are at risk of acquiring infection [2].

Of the six species of *Schistosoma* that parasitize humans, only *Schistosoma mansoni* has been reported in Brazil [3]. Higher prevalence has been reported in the northeast and southeast regions, with 54 026 and 2 480 cases notified, respectively, between 2018 and 2021 [4]. Inadequate hygiene, poor sanitation, and a lack of awareness about the danger of schistosomiasis contribute to the persistent transmission of this parasitic infection [3].

The World Health Organization (WHO) recommends prophylactic administration of praziquantel (PZQ) as a method of controlling schistosomiasis. This drug commonly causes transient adverse effects, such as nausea and abdominal pain [2]. Hypersensitive reactions appear to be rare, with a search of the literature revealing just eight reported cases worldwide [5–12]. Herein, we describe a case of anaphylaxis following PZQ intake in the context of *Schistosomiasis mansoni* treatment in Brazil.

Case

The subject was a 13-year-old-female, weighing 67 kg, who resided in an area endemic for schistosomiasis in the state of Bahia, Brazil. In the rural village where she lived, local surveillance revealed that 56.6% of the population tested positive for schistosomiasis. In accordance with the recommendations outlined by the Brazilian Ministry of Health, mass drug administration (MDA) was indicated for this region [3].

On December 2, 2021, the patient attended an MDA event hosted by the local municipal government. She denied any comorbidities, while drug contraindications, such as gestation, lactation, renal or hepatic insufficiency, or hypersensitivity to the medication, were not evidenced. In accordance with a recommended dosage of 60 mg/kg for PZQ, she took six tablets (600 mg each) of praziquantel (Farmanguinhos, Fiocruz) under direct observation.

About an hour later, the patient experienced rash, pruritus, and generalized edema, evolving into dizziness and somnolence. Fexofenadine hydrochloride (120 mg) was administered, and she was taken to the local municipal health clinic.

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Table 1
Reported cases of hypersensitivity reactions to praziquantel.

Author, year	Country	Sex	Age	Disease	PZQ dose	Period	Symptoms	Outcome
[5] Liu T, et al., 1984	China	Female	46	Schistosomiasis	NA	NA	NA	NA
[6] Shorter D, et al., 2006	Tanzania (refugee camp)	Male	11	Schistosomiasis	20 mg/kg	Symptoms started 2 hours after 1st dose	Pruritic urticaria on arms and chest, cervical lymphadenopathy, and mild expiratory wheeze	Recovery with no sequelae
[7] Huang SW, 1992	USA	Male	10	Neurocysticercosis	600 mg	Symptoms started after 2nd dose	Severe generalized urticaria, difficulty swallowing, and chest tightness	Recovery with no sequelae
[8] Lee JM, et al., 2011	Korea	Female	54	Clonorchiasis	25 mg/kg	Symptoms started 2 hours after 1st dose	Generalized pruritic rashes, facial flushing, nausea, and dyspnea	Recovery with no sequelae
[9] Kyung SY, et al., 2011	Korea	Female	46	Paragonimiasis	1200 mg	Symptoms started 20 minutes after 1st dose	Generalized pruritic urticaria, painful swelling on both eyelids and upper lip	Recovery with no sequelae
[10] Patel TA, et al., 2016	UK	Female	31	Schistosomiasis	40 mg/kg	Symptoms started 1 hour after 1st dose	Generalized migratory urticaria	Recovery with no sequelae
[11] Shen C, et al., 2007	China	Male	35	Clonorchiasis	1200 mg	Symptoms started 30 minutes after 1st dose	Hypotension, tachypnea, generalized pruritic urticaria, chest tightness, and dizziness	Recovery with no sequelae
[12] Shindo T, et al., 2019	Japan	Male	30	Diphyllobothriasis	600 mg	Symptoms started 1 day after 1st dose	Pruritic generalized maculopapular erythematous eruptions	Recovery with no sequelae
Present study	Brazil	Female	13	Schistosomiasis	60 mg/kg	Symptoms started 1 hour after 1st dose	Generalized pruritic rash, edema, hypotension, tachycardia, tachypnea, somnolence, seizure	Recovery with no sequelae

NA = information not available

Upon arrival, physical examination revealed tachycardia (131 bpm), tachypnea (27 BPM), somnolence, and 90% O_2 saturation. Prednisone (20 mg) was administered. Around 40 minutes later, the patient experienced an episode of seizure, followed with hypotension and sweating, prompting the intramuscular administration of 0.6 ml (0.01 mg/kg) of epinephrine in the thigh. To improve the patient's circulation, her lower limbs were elevated. The patient presented a second convulsive episode lasting 3 minutes, with the maintenance of tachycardia and tachypnea.

Due to the severity of her symptoms, the patient was transferred to a regional hospital (15 kilometers away) and remained in the emergency department until discharge. Unfortunately, it was not possible to review the patient's medical records following her hospitalization. The next day, after improvements in signs and symptoms, she was discharged and recovered without sequelae. Both she and her family members were advised to not take PZQ again, and she was also referred to an immunologist and allergist for follow-up.

Prior to receiving PZQ, Kato–Katz (KK) testing of her stool revealed negativity for helminth infection, yet positivity was identified for point-of-care circulating cathodic antigen (POC-CCA) in her urine.

This adverse event was notified on the Brazilian pharmacovigilance platform VigiMed (notification number 11-963-685-188).

Discussion

According to the literature, this case report represents the ninth case of anaphylaxis to praziquantel worldwide, and the first reported case in Brazil. Here we evidenced clinical features compatible with anaphylaxis, including skin rash, dyspnea, tachycardia, desaturation, and generalized edema, following PZQ intake for treatment of schistosomiasis. On a single day at the MDA event, 261 residents (aged 4–70 years) from the same region were treated with an identical product, following the same regimen, yet this teenager was the only case associated with a serious adverse effect.

PZQ is the treatment recommended by the WHO for managing a range of parasitic infections, including human schistosomiasis. Although the medication is considered safe and effective, it has been known to cause diverse neurological and gastrointestinal adverse reactions, which are generally transient and well tolerated. In Brazil, the standard posology used to treat *Schistosoma mansoni* is a single dose of 50 mg/kg for adults, while 60 mg/kg is recommended for children aged 4 years or older [3].

Despite widespread PZQ use since the 1980s, few cases of hypersensitivity have been reported for this medication. Most cases have occurred in countries in East Asia, including China, Korea, and Japan, as shown in Table 1. In contrast, in Africa and South America, in which elevated schistosomiasis transmission has been noted and endemic areas are regularly targeted with large-scale treatment programs, just one case of severe hypersensitivity to PZQ has been reported to date — in Congo. Furthermore, of all the cases identified in the literature, only three occurred in the context of schistosomiasis treatment [5,6,10].

PZQ therapy has been observed to result in hypersensitive reactions induced by the sudden release of antigens into the bloodstream from hatched parasitic eggs, teguments, and fluids discharged by dying worms, especially when used to treat schistosomiasis [13]. However, it can be inferred that the anaphylactic reaction evidenced in the present case did not arise from parasitic-antigen-release immunopathology, but was directly related to the intake of PZQ. Although orally administered PZQ is rapidly absorbed by the gastrointestinal tract, maximal plasma concentration is only achieved within 1–3 hours [14]. Accordingly, hypersensitivity due to antigen release would have occurred at a much later time than was observed in the present case, and therefore the relatively abrupt response post-ingestion seems highly suggestive of drug allergy. In the previously reported cases, the allergic symptoms started between 20 minutes and 1 day after PZQ intake (Table 1).

The subject of this study had no prior history of PZQ intake or any medical allergies. She received PZQ treatment because she lived in an endemic area for schistosomiasis, and began to present signs of severe hypersensitivity about an hour after intake. Fortunately, the patient evolved with no sequelae, and experienced a relatively rapid recovery. Since she resides in an endemic area, additional treatment could be indicated, in which case it would be necessary to carry out a PZQ desensitization protocol, because no other drugs are available for schistosomiasis treatment in Brazil [10].

Even though WHO recommends prophylactic PZQ therapy to control schistosomiasis, this strategy alone has not demonstrated efficacy in the Brazilian epidemiological context. In addition to prophylaxis, public policies aimed at vector control, treating drinking water supplies, and educating affected populations are necessary to eliminate this persistent public health problem [15].

Despite the rare occurrence of hypersensitive reactions to PZQ, these can be associated with severe symptoms and outcomes, such as hypotensive shock and airway obstruction. Therefore, health professionals must be aware of potential life-threatening adverse effects. Considering that MDA for schistosomiasis is a common event in difficult-to-reach rural regions affected by endemicity, it is necessary to properly train medical personnel and local support staff, as well as to implement appropriate infrastructure to deal with any adverse events that may occur as a result of PZQ administration.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical approval

This case report was conducted in the context of a cohort study approved by the Institutional Review Board of the Gonçalo Moniz Institute (CAAE no. 77287417.8.0000.0040). Written informed consent was obtained from all participants and their legal representatives for participation in the present study. The minor participant also provided an assent form.

Author contributions

ICS and RRO contributed to the study design. GAV, BGGC, CDF, FARSN, YJM, RRO, and ICS contributed to data analysis and writing of the manuscript. GAV, BGGC, ACC, MVLM, TRSF, RAS, KRS, and BSSO contributed to participant enrolment, review of medical records, and collection of samples and data. RAS and RRO contributed to laboratory analysis.

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