Atrial fibrillation with rapid ventricular response in a case with piperazine citrate intoxication: A rare manifestation

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Summary

Background: Atrial fibrillation is one of the most vexing cardiovascular conditions and is induced by various factors. The emergence of new culprits for this expensive health problem results in its increased prevalence.

Case Report: This is the case of a 29-year-old male whose chief complaints were fatigue, weakness, and palpitation. He was a previously healthy man who had been prescribed piperazine citrate for the treatment of oxyuriasis two days prior to admission. He became symptomatic after the unintentional ingestion of half of the bottle of piperazine citrate. On admission he was hypotensive with detectable irregularly irregular pulse. Atrial fibrillation with rapid ventricular response was diagnosed by electrocardiography. The patient responded well to fluid therapy and rate control measures. Laboratory data were indicative of early stages of primary hypothyroidism, but the patient's condition was not in favor of overt hypothyroidism. In echocardiographic evaluation, no clot or structural heart disease was found. The patient was discharged with sinus heart rhythm.

Conclusions: Atrial fibrillation with rapid ventricular response is a rare manifestation of piperazine citrate toxicity. Piperazine citrate should be considered as a possible cause of atrial fibrillation in poisoning centers.

Keywords: atrial fibrillation • rapid ventricular response • piperazine citrate

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BACKGROUND

Atrial fibrillation (AF) is one of the most vexing cardiovascular conditions [1] and it may coexist with both cardiovascular and non-cardiovascular conditions [2]. The emergence of new culprits for this expensive health problem is a cause of its increased prevalence. Since AF is associated with considerable morbidity and mortality [2], the identification of potential risk factors is of great value. Here we report a new risk factor for this common rhythm disorder.

CASE REPORT

The patient was a 29-year-old Afghan male who was referred to our center with the chief complaints of fatigue, weakness, and palpitation two hours prior to admission. He was a previously healthy male who had been prescribed piperazine citrate (Antepar, Elixir 60 ml, 583.5/5 ml; Iran Pharma Inc., Iran) for the treatment of oxyuriasis two days earlier. Expelling the worms in feces, he was encouraged to consume more syrup to clear all worms via the intestinal route. About 6 hours after drinking half of the bottle of piperazine citrate (total: 8 grams), he became symptomatic. He experienced just one episode of vomiting at home. On admission he was conscious, but partly weak. His vital signs were blood pressure: 80 mmHg/pulse, heart rate: 140 beat per minute, respiratory rate: 18/min, and oral temperature: 37°C. His heart rate and pulses were both irregularly irregular. No other finding was detected on physical examination. ECG showed atrial fibrillation with rapid ventricular response (Figure 1). Other electrical parameters such as duration of the QRS complex and QT-interval were within the normal ranges. The patient had no predisposing factor for such an event, as hypertension, smoking, alcohol drinking, or hyperthyroidism, and no metabolic or electrolyte abnormalities were found in his lab data. Cardiac troponin levels, assessed semi-quantitatively, were negative.

Fluid therapy was started and 0.5 mg digoxin was injected intravenously for rate control under heart monitoring. Heparin infusion was also started. His blood pressure reached 114/78 mmHg and rate control was achieved about 4 hours later. With rate control, two tablets of flecainide acetate 100 mg was prescribed. He achieved sinus rhythm about 2.5 hours later (Figure 2). Heparin infusion was discontinued with the normal heart structure and absence of clot on echocardiography evaluation (Figure 3). Half a tablet of metoprolol tartrate 25 mg was prescribed to the patient as the loading dose. Incidentally, his lab data were relevant for the early stages of primary hypothyroidism (TSH: 9.53 IU/l, T4: 6.07 IU/l, and T3: 1.8 IU/l), but the patient’s clinical conditions were not confirmatory for the lab data. Lipid profile was normal (HDL: 43 mg/dl, LDL: 100 mg/dl, TG: 64 mg/dl). He was referred to an endocrinologist for further approaches. He was discharged with the half tablet of metoprolol tartrate (Iran Pharma, Iran) 25 mg twice daily. On follow-up visit he was symptom free and reported no episode of palpitation.

Discussion

Atrial fibrillation, the most common type of cardiac arrhythmia in clinical practice, accounts for approximately one third of the hospitalizations due to cardiac rhythm disturbances [3]. This straightforwardly diagnosed arrhythmia imposes great costs on patients and healthcare systems [4]. Greater risks of ischemic stroke [5], systemic thromboembolic events, and heart failure and a twofold increase in mortality rate threaten the affected patients. Palpitation and exercise intolerance are also disturbing facts [6].

Risk factors attributed to the development and progression of AF are mainly considered to be hypertension, hyperthyroidism, coronary artery disease [7], diabetes mellitus [8], smoking [9], alcohol consumption [10], advanced age [11], structural heart disease [12], major cardiovascular surgery [13], obesity [14], sleep apnea [15], and drug-induced cases [16]. Interestingly, the constellation of some risk factors, such as metabolic syndrome [17], endurance sport practice [18], and genetic predisposition [19], draw our attention to the emergence of new risk factors which are not totally identified. Drug-induced atrial fibrillation, as a matter of fact, is attributed mainly to drugs with the potential of sympathetic excitation, such as amphetamines [16], or having major effects on the heart ion channels, such as antiarrhythmic agents [20]. The mechanism of AF induction by some drugs, including biphosphonates, is not well understood [21].

Piperazine citrate is an anthelminthic agent used in the treatment of pinworms and intestinal nematodes [22], but other drugs are usually preferred due to its poor efficacy and adverse effects [23]. No significant side effect was seen with this drug when applied in anthelminthic doses [24]. The reported side effects are dizziness, drowsiness, headache, muscle weakness, tremors [25–27], abdominal cramps

Figure 1. ECG strip demonstrates atrial fibrillation with rapid ventricular response.
or pain, diarrhea, nausea, and vomiting [25,27,28,30–33]. Muscle weakness of the extremities [34], respiratory depression, and seizures [28,32,34] are reported manifestations of acute drug overdose. A dose-dependent reduction in blood pressure, attributable to its quinidine-like actions, was also reported recently in anesthetized cats [35]. Significant reduction in heart rate and increased QT/JT intervals were seen in normal healthy volunteers, without any effect on the QRS complex and T wave. In this subject group, average prolongation of the PR interval with maintenance of the sinus rhythm was also seen [36]. Piperazine citrate has similar effects on rat heart, in addition to the dose-dependent increase in QT interval and the occurrence of sino-atrial suppression and various atrioventricular blocks at high doses [37]. Despite the mentioned alterations in the ECG profile similar to potent antiarrhythmic agents, no dysrhythmic phenomena were seen with piperazine citrate per se [36].

One interesting matter is the protective role of piperazine citrate in cases with ouabain toxicity in toads. This
antiarrhythmic effect was demonstrated to be comparable to that of lignocaine hydrochloride, but with less potency and side effects. Some anesthetizing potencies were also detected for piperazine citrate [37]. The mechanism of this protective action is not yet determined, but, as other antiarrhythmic drugs, this effect may lower the threshold of arrhythmogenicity. The neuro-stimulatory effects of piperazine-derivate compounds may be associated with the increased rate of arrhythmogenicity [38], such as the induction of AF in our presented case, but this is not observed with piperazine citrate.

Our case is an interesting one, with paroxysmal AF in a cases with background of piperazine citrate toxicity in the setting of hypothyroidism and the presence of no precipitating factor. The effect of piperazine citrate on the heart conduction system or atrial electrical cells needs to be determined. The importance of considering AF as a manifestation of piperazine citrate toxicity may be a lowering of the seizure threshold, regarding seizure as an adverse effect of this drug.

CONCLUSIONS

Atrial fibrillation with rapid ventricular response is a rare manifestation of piperazine citrate toxicity and piperazine citrate should be considered as one of the causes of atrial fibrillation in poisoning cases.

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