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Hydroxyzine-Induced Supraventricular Tachycardia in a Nine-year-old Child

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ABSTRACT

Hydroxyzine is a first generation antihistamine widely used in the paediatric population for a variety of conditions. A nine-year-old girl presented with supraventricular tachycardia while on clinical doses of hydroxyzine for pruritis. On arrival at the hospital, she was diaphoretic, with cool peripheries, poor peripheral pulses and a heart rate of 250/minute. There was a history of three palpitation episodes with chest tightness during the five months she was taking hydroxyzine. The supraventricular tachycardia eventually reverted to sinus rhythm with intravenous verapamil. Relevant cardiac examination and investigations had not shown any cardiac abnormalities. After discontinuing hydroxyzine, she had no further episodes of supraventricular tachycardia. To our knowledge, this is the first report of hydroxyzine induced-supraventricular tachycardia in the medical literature.

Keywords: antihistamine, drug complication, hydroxyzine, supraventricular tachycardia

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INTRODUCTION

Supraventricular tachycardia (SVT) is generally accepted to be any tachycardia arising from or above the atrioventricular (AV) node, excluding sinus tachycardia. It results mainly from disturbances in conduction, automaticity or both. Estimates of its prevalence in childhood ranges from one in 25,000 to one in 250 individuals[1]. Supraventricular tachycardia can be incited by factors such as alcohol, stress, caffeine, cocaine, tobacco and various medications. Sympathomimetics such as salbutamol, phenylephedrine and the second generation antihistamines are known to be associated with both SVT and ventricular tachycardias[2]. We present a case of a nine-year-old girl who developed episodes of palpitations and proven SVT while on therapeutic doses of hydroxyzine.

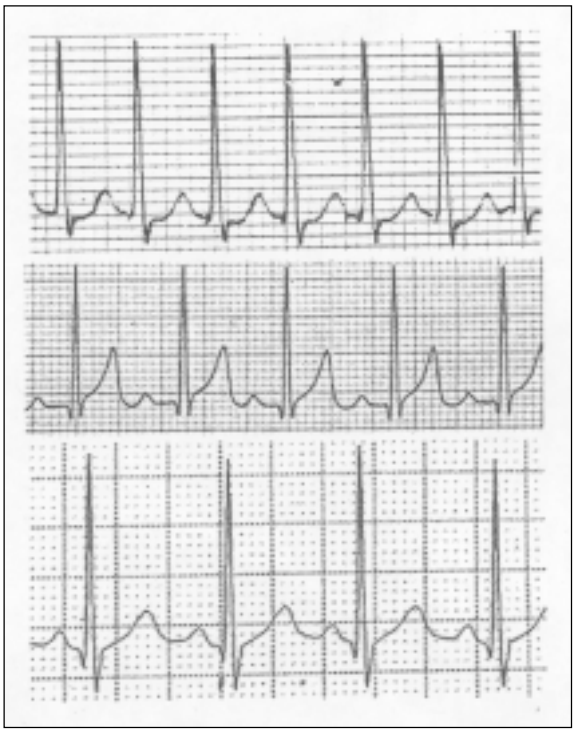

Fig. 1 Serial ECG recordings obtained during treatment.

Top ECG strip shows supraventricular tachycardia with a rate of about 250/min. There is no visible P wave, strongly suggesting atrioventricular nodal reentry tachycardia (AVNRT).

Middle ECG strip obtained after second dose of intravenous verapamil shows sinus tachycardia with prolonged PR interval (1st degree heart block) and a rate of 120/min.

Bottom ECG strip shows normal sinus rhythm with a rate of about 100/min.

CASE REPORT

A nine-year-old girl presented to our casualty department with symptomatic SVT. She had previously complained of nocturnal itch in the perianal region to her general practitioner. She was referred to a gynaecologist, and then a dermatologist, for treatment. When the itch did not settle with chlorpheniramine, she was started on hydroxyzine (Atavan) 12.5 mg nocte orally, and had been on this medication for the last five months prior to her admission for SVT. During that period, she complained, for the first time in her life, of three short-lived episodes of palpitations that were associated with chest tightness. These settled with massage of her chest and were

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not thought to be of any significance by her parents. On the day of admission, she complained of palpitations with severe excruciating central chest pain, while watching television. The pain did not disappear with massage and local ointment. This lasted for three hours before she was brought to the hospital. Her past history also includes infrequent episodic asthma for which she was prescribed salbutamol via metered dose inhaler (Respolin) as needed. She reported that she last used salbutamol two days prior to her admission, but had continued taking hydroxyzine at the prescribed dose every night.

On arrival at our hospital, she was diaphoretic, having cool peripheries, poor peripheral pulses and an unrecordable blood pressure (BP). Noticeably, she did not have tremors nor signs of an acute asthmatic attack. Heart rate was recorded at 250/minute, which corresponded with the ECG monitor. There were no noticeable P waves (Fig. 1). Vagal manoeuvers were tried without success. Thus, intravenous verapamil 4.5 mg as a slow intravenous bolus was administered which resulted in a slowing of her heart rate to 190/minute. This dose of verapamil was repeated and she went into sinus rhythm with first-degree heart block at a rate of 120/minute (Fig. 1) and a recordable BP of 110/70 mmHg. Her serum electrolyte (sodium, potassium, calcium) and blood glucose levels were normal. She was afebrile and a full blood count was also normal. Based on her history, hydroxyzine was discontinued. Over the next 48 hours, the abnormal rhythm did not recur. Verapamil was not further administered and her rhythm returned to normal sinus rhythm with a rate of 100/minute.

She was submitted to further cardiac investigations. A modified Bruce protocol stress test, a Holter monitor and an echocardiogram were all unremarkable. She was also investigated further for her perianal itch with urticaria. Stool examination for ova, cyst and parasites did not reveal any abnormalities; however she had mild eosinophilia (eosinophil differential count was 8%). Mild eosinophilia is commonly seen with worm infestation in our country. Tests for blood erythrocyte sedimentation rate (21 mm/hr), screening for urinary tract infection and connective tissue disorders (antinuclear antibodies, rheumatoid factor), random blood sugar and modified oral glucose tolerance test were unremarkable. Although her stool samples did not reveal any abnormality, she was treated with chlorpheniramine and albendazole (Zentel). With this treatment, her perianal itch settled. She was not put on any antiarrhythmics since the initial two doses of verapamil, and has been free of chest pain and SVT for the last two years.

DISCUSSION

Hydroxyzine is a first generation sedating antihistamine in the piperazine chemical class. It is one of the most potent histamine 1 (H1) receptor antagonists, has strong antipruritic effects and is widely used for skin allergies. In the pediatric age group, its perceived low toxic-to-therapeutic index has contributed to its versatile use in treating allergic conditions, pruritis, urticaria, motion sickness, and as preoperative medication, among other uses. Hydroxyzine is rapidly absorbed from the gastrointestinal tract with a peak blood level of about two hours after oral administration. Plasma half-life is about seven hours in children[3]. It has a long biological action, with pruritis being reported to be significantly suppressed 1-24 hours after administration of a dose[3]. It is mainly eliminated by metabolism, being more rapid in young children compared to adults. Common adverse effects of hydroxyzine in children include adverse central nervous system effects[4] causing sedation, decreased cognitive function and increased subjective somnolence. Even though hydroxyzine is widely used for a variety of conditions, there are very limited reports of its toxicity or overdose.

Cardiac toxicity is a very rarely reported adverse effect associated with hydroxyzine, although certain antihistamines, especially the second generation terfenadine and astemizole, are known to produce cardiac toxicity, mainly in the form of increased risk of ventricular tachyarrhythmias (torsades de pointes). There are no reported incidences of supraventricular tachycardia due to hydroxyzine or its active metabolite, cetirizine. There is, however, one report of sinus tachycardia occurring in accidental ingestion of hydroxyzine in a 13-month-old child[5]. Predominant symptoms in this child were generalised seizures with sinus tachycardia, mydriasis and peripheral vasodilation. Occurrence of SVT and ventricular arrhythmias with another first generation antihistamine, pheniramine, which is of a different chemical class, has been reported in a 27-year-old man presenting with pheniramine overdose[6].

The possible mechanisms whereby hydroxyzine induce SVT in this child are outlined below. Pharmacodynamically, the first generation antihistamines, including hydroxyzine, have anticholinergic properties and this theoretically could cause an increase in heart rate. However, at the dosage given to this child, it is unlikely that marked increase in heart rate occured due to its anticholinergic effect. She was given only 12.5 mg/day of hydroxyzine, and based on her weight, this is not higher than what is recommended. Theoretically, pharmacodynamic interaction may occur between hydroxyzine, which possesses

anticholinergic properties, and salbutamol, a beta-receptor agonist that can cause tachycardia. However, we could not find reports of hydroxyzine and salbutamol interactions causing SVT, despite many asthmatic children being given hydroxyzine. It is also unlikely that this interaction contributed to SVT because she is not on high dose salbutamol, as she administered it via the metered dose inhaler, not taking it orally or via the nebuliser. She also did not display clinical side effects such as tremors, nor did she have laboratory parameters such as hypokalaemia, which could be attributed to recent high dose use of salbutamol.

We also could not explain any pharmacokinetic interaction causing an increased hydroxyzine blood level in our patient. The only other medication she was on at the same time was salbutamol, but as this was taken via a metered dose inhaler, high levels will not be achieved in her blood. Unfortunately, we are not able to do tests for blood hydroxyzine levels at our hospital. We also could not find reported drug interactions with hydroxyzine that cause cardiac dysrhythmia. A drug interaction between hydroxyzine and cimetidine has been reported, where simultaneous administration significantly increased hydroxyzine blood level and decreased its conversion to cetirizine[7]. This interaction, however, has not been associated with any cardiac symptoms.

In summary, this girl presented with SVT while taking hydroxyzine at night for pruritis. Her clinical course suggests that the supraventricular episodes occurred in association with hydroxyzine. It is noteworthy that symptomatic SVT could occur with therapeutic doses of hydroxyzine in a child who did not have cardiac abnormalities nor predisposition for SVT.

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