CASE REPORT

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A Fatality Due to the Intranasal Abuse of Methylphenidate (Ritalin®)

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ABSTRACT: A fatality in a teenager from the recreational intranasal abuse of methylphenidate (Ritalin®) is reported. The prescribed use of methylphenidate (Ritalin®) in the treatment of attention deficit and/or hyperactivity disorder is widespread. The intranasal abuse of methylphenidate (Ritalin®) among teenagers is becoming increasingly more recognized. Previous deaths from the parenteral abuse of methylphenidate (Ritalin®) have been reported. This fatality is the first reported from its intranasal abuse.

KEYWORDS: forensic science, forensic pathology, forensic toxicology, fatality, death, methylphenidate, Ritalin®, intranasal, teenage, drug abuse

A 19-year-old white male was reported to have been ''snorting'' methylphenidate (Ritalin®), several times in one evening, and ''drinking ale'' with other friends at a party. He was seen to come out of a bathroom, suddenly lose consciousness and fall, striking his head on a doorknob as he did so. He was immediately picked up by friends and driven approximately 2 miles (3.2 km) to a nearby hospital. By the time he arrived, he was noted to be in full cardiopulmonary arrest. He was placed on a ventilator and given intravenous epinephrine, bicarbonate, atropine, and lidocaine. Pulse and blood pressure were restored without electrical defibrillation. The patient was, however, deemed to have sustained severe hypoxic brain damage. Following admission, he developed fever and tachycardia. Temperatures ranged from 100.5° to 104°F (38° to 40°C), and pulse rates in the range of 150 to 160 were noted over the next several hours. An echocardiogram revealed left ventricular segmental hypokinesis with a low ejection fraction, consistent with a congestive cardiomyopathy or global myocardial ischemia. Serum CK-MB concentrations were elevated. After approximately 16 h, he was noted to have become asystolic and was declared dead.

Witnesses at the scene reported to police that ''lines'' of powder from crushed methylphenidate tablets, brought by several teenagers, had been seen at the party. The decedent's medical history was negative. Witnesses who knew the decedent said that he did not regularly take methylphenidate as a part of any therapeutic regimen. He was also not known to abuse the drug on a regular basis.

Autopsy and Toxicological Findings

Postmortem examination demonstrated microscopic foci in the heart of individual myocardial fiber necrosis surrounded by degenerating polymorphonuclear leukocytic and histiocytic cells (Fig. 1). This cardiac lesion appeared similar to catecholamine cardiomyopathy, although contraction bands were not noted. The autopsy was otherwise negative. Traditional anatomic findings of chronic drug abuse (chronic phlebitis, pulmonary granulomata, hepatic portal triaditis, etc.) were absent.

Methylphenidate (Ritalin®), a basic compound, can be analyzed by standard liquid-liquid (1,2) or solid-phase extraction (3) procedures. The solid-phase C-18 extraction procedure was chosen due to the amphoteric nature of the principal metabolite, ritalinic acid, derivatized with BSTFA containing 1% TCMS trichloromethylsilane, and analyzed by gas chromatography/mass spectrometry (GC/MS). Toxicological analyses revealed the presence of methylphenidate at a concentration of less than 0.05 mg/L in the fluoride preserved admission blood sample only. This concentration was within the therapeutic range reported in a study of adult subjects after a single 20 mg oral dosage (4). Methylphenidate itself was not detected in the postmortem blood sample. However, the concentration of ritalinic acid, the principal metabolite of methylphenidate, was 0.4 mg/L in the admission blood sample and 0.24 mg/L in the postmortem sample. This concentration was 2 to 3 times higher than reported therapeutic concentrations from the same study (4). Neither methylphendiate nor its metabolite was detected in the postmortem vitreous humor sample. While a 0.10 % w/v concentration of ethanol was also found in the admission blood sample, no other drugs were detected.

Discussion

Methylphenidate (Ritalin®) is a phenylethylamine derivative used in the treatment of depression, narcolepsy and attention deficit disorder with or without hyperactivity (ADD or ADHD) (4,5). A recent report showed that 4% of the students in one school district receive medication at school for ADD or ADHD. More than 90% of all the medications given in school in this same district are specifically for this disorder (6). This drug is structurally similar to the amphetamines (4). It is rapidly absorbed on an empty stomach. Its half-life is short (between 0.5 and 4 h) (4,7), necessitating

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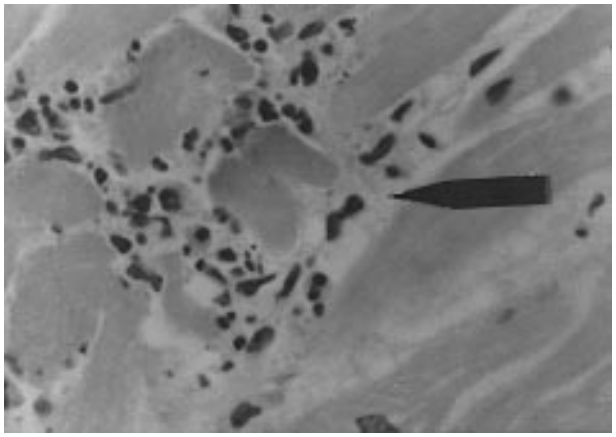

FIG. 1—*Myocardium (hematoxylin and eosin stain, ×40 magnification). Isolated cardiac muscle cell in cross section (indicated by pointer) demonstrates eosinophilic change and surrounding interstitial infiltrate of histiocytic cells.*

more than one daily dose for the patient. Overdosage is known to cause manifestations typically associated with stimulant drugs. These include nausea, vomiting, agitation, tremors, twitching, delirium, hallucinations, sweating, flushing of the skin, headache, tachycardia, hyperpyrexia, cardiac arrhythmias, hypertension, convulsions and coma (4).

Methylphenidate was first synthesized in 1944. It was initially thought to be nonaddictive (8). In 1960, Roux raised the question of the addictive potential of this drug when he reported a patient taking 125 tablets orally each day (12). The parenteral abuse of this drug and its attendant complications were first reported in 1971 when it was referred to as ''West Coast'' by prisoners (8–10). The drug, unclassified as a controlled substance at that time, was often readily obtained from physicians by simply asking for it. Tablets were then crushed and the powder was injected intravenously (10). In 1986, Levine et al. reported a death occurring in an adult female after the intravenous injection of 40 mg of methylphenidate. In this case, blood concentrations of methylphenidate approximately 40 times greater than therapeutic were found (11). In 1991, a case of adolescent dependency resulting from intranasal methylphenidate abuse was reported (5). The drug-dependent individual in this study was reported to have used as much as 200 mg at once intranasally. A ''high, speedy feeling'' was said to have occurred with each use. Numerous other teenagers at a private special-education boarding school were also reported in this study to have regularly abused methylphenidate by the intranasal route (5). Today, teenagers themselves report that the intranasal abuse of methylphenidate by other teenagers is commonplace (13).

This case report patient presented with a history and clinical signs, including hyperpyrexia and tachycardia, characteristic of methylphenidate abuse. The left ventricular dysfunction and elevated C.-MB concentrations noted clinically have been noted in acute amphetamine cardiomyopathy (14,15). Pathologically, the microscopic foci of myocardial necrosis identified in this case were much like the lesions produced experimentally in rats following the intraperitoneal injection of methamphetamine (16). Similar microscopic lesions, with contraction bands, myocardial fiber necrosis and inflammatory cellular infiltrates (17–19) have been noted as well, experimentally and clinically, in states where catecholamine hypersecretion has been known or believed to exist (17–19). Such states include pheochromocytoma, isoproterenol infusion, hypertension, cocaine abuse and intravenous drug abuse (19–21).

The abuse of methylphenidate, parenterally, orally and intranasally, has been documented over a period of several decades. Methylphenidate is now available to significant numbers of school-age children and adolescents as prescription medication for the treatment of ADD or ADHD. The effects of this drug are well known to these young patients. Its recreational intranasal abuse by school-age children and adolescents is now known to exist. This case demonstrates that the recreational intranasal abuse of this widely available drug can have sudden and unexpected fatal consequences.

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