CASE REPORT

Lacunar Stroke Associated with Methylphenidate Abuse

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ABSTRACT: ***Background:*** Methylphenidate is a central nervous system stimulant used for the treatment of attention deficit hyperactivity disorder and narcolepsy and like other psychostimulants has a potential for abuse. ***Case study:*** A young man with a cerebral lacunar infarction following chronic oral abuse of methylphenidate is presented. ***Conclusions:*** The experience of our patient and a review of the literature suggest that cerebral infarction is a potential side effect of chronic consumption of methylphenidate.

RÉSUMÉ: Accident vasculaire cérébral associé à l'utilisation abusive de méthylphénidate. ***Introduction:*** Le méthylphénidate est un stimulant du système nerveux central utilisé dans le traitement du syndrome d'hyperactivité/déficit d'attention et de la narcolepsie et, comme d'autres psychostimulants, peut entraîner des abus. ***Présentation de cas:*** Il s'agit d'un jeune homme qui a subi un infarctus cérébral lacunaire suite à l'abus oral chronique de méthylphénidate. ***Conclusions:*** L'expérience de notre patient et une revue de la littérature suggèrent que l'infarctus cérébral puisse être un effet secondaire de la consommation chronique de méthylphénidate.

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Methylphenidate is a piperidine-derived central nervous system (CNS) stimulant.[1] It is commonly used for the treatment of attention deficit hyperactivity disorder (ADHD) in children and narcolepsy in adults.[1] Some studies suggest possible therapeutic uses for methylphenidate in elderly patients with depression,[2] patients with post-stroke depression,[3] those with traumatic brain injury,[4] cancer patients,[5] and those with human immunodeficiency virus infection.[6] This drug is related to amphetamine and other psychostimulants. Methylphenidate blocks the dopamine transporters in the presynaptic cell membrane, leading to increased extra cellular levels of dopamine.[1,7,8] This mechanism is shared by amphetamine and cocaine, which are well-known for their addictive properties and neurologic complications following their abuse.[7,9] The abuse potential of methylphenidate is a problem that has received considerable attention, especially in recent years.[8,10,11] This report describes a young man who suffered an ischemic stroke following chronic methylphenidate abuse and suggests a causal association between ingestion of methylphenidate and the occurrence of cerebral infarction.

Case History

A 24-year-old university student suddenly developed left-sided weakness without loss of consciousness while attending a class. His weakness progressed over the next twenty minutes, then became fixed. He was in good general health before the incident, had no significant medical history and denied any similar symptoms in the past. His family history was unremarkable and there were no risk factors for vascular disease in his family members. He had used methylphenidate hydrochloride tablets 60 mg per day by mouth for the past six months. He was not addicted to any other drug of abuse and denied using methylphenidate by other routes.

General physical examination with emphasis on the cardiovascular system showed no abnormalities. His blood pressure was 115/75 mmHg at admission, and it never exceeded 130/80 mmHg during hospitalization. There was no evidence of needle puncture, superficial venous thromboses over the extremities, nasal mucosal ulceration or septum perforation. At neurologic examination, mental state and speech were normal. Cranial nerves were intact. There was a left central facial palsy. Funduscopic examination showed a normal vascular pattern and optic disc. There was no visual field defect. Right upper and lower extremities had normal muscle tone and strength, whereas the left extremities had decreased muscle tone. Left upper extremity strength was 4+/5 both proximally and distally. Left lower extremity strength was 4/5 at proximal and 3/5 distally. Muscle bulk was normal. Muscle stretch reflexes were diminished throughout on the left side in comparison to right. There was no sensory loss or extinction. The plantar reflex was upgoing on the left. There were no primitive reflexes. There was no evidence of limb incoordination or cerebellar ataxia out of proportion to weakness. He was not able to walk at the time of presentation.

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The following laboratory tests or investigations showed normal results: complete blood count with differential; sedimentation rate; blood chemistry and electrolytes, plasma homocysteine level, C-reactive protein and lipid profile; serum protein electrophoresis; serum VDRL, anti-HIV, anticardiolipin, antinuclear and ds DNA antibodies; serum protein C, protein S, antithrombin III, factor V Leiden, and activated partial thromboplastin time; liver enzymes; urinalysis; CSF analysis including electrophoresis; ECG, chest x-ray, and transesophageal echocardiography with intravenous bubble contrast.

Brain CT scan performed with and without injection of intravenous contrast media showed a lacunar infarction involving the head of right caudate nucleus and adjacent anterior limb of the internal capsule (Figure). Magnetic resonance imaging (MRI) study as well as MR angiography were not performed due to the patient's severe claustrophobia. Conventional four vessels cerebral angiography, however, was normal. The course of recovery was uneventful and after six weeks he was able to return to university. After neurologic improvement, he was referred to a specialized facility for further psychiatric evaluation and therapy.

Discussion

Methylphenidate, like other psychostimulants, has a potential for abuse, especially among student populations who use it for nonmedical purposes.[12] Abuse liability in controlled use of methylphenidate for ADHD in children and adolescents, is considered to be rare;[7] however, illicit use occurs frequently among middle and high school students without history of ADHD.[12,13] Most individuals abuse it for stimulant effects, mainly wakefulness, suppression of appetite, increased attentiveness and euphoria.

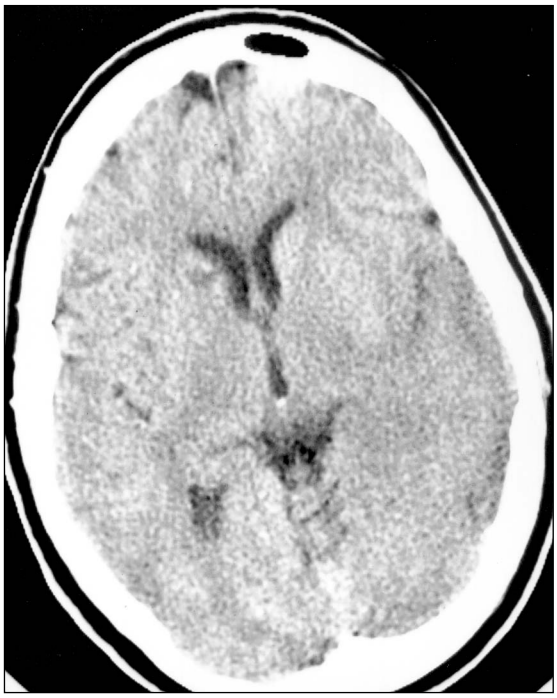

Figure: *Computerized tomographic scan shows a lacunar infarction in the right caudate nucleus and adjacent part of anterior limb of the internal capsule.*

Although methylphenidate has been abused less frequently than other CNS stimulants, a wide range of complications are reported following its abuse, which in part depends on its route of administration. This spectrum of complications differs from side effects of therapeutic use of methylphenidate that includes nervousness, headache, insomnia,[14] and movement disorders.[15] Methylphenidate has been abused intravenously,[16] intra-arterially,[17] and intranasally[18] using tablets crushed into powder, in addition to oral route. Intravenous abuse of methylphenidate has been followed by CNS toxicity with multiple organ failure,[19] myelopathy,[20] deep neck abscesses,[21] and precocious emphysema.[22] Occasional fatal outcome has occurred following intranasal abuse of methylphenidate.[23]

It is widely known that the chronic use of amphetamine, among many other detrimental effects, may result in cerebral vasculitis with consequent ischemic or hemorrhagic strokes.[24,25] Ischemic and hemorrhagic stroke is also frequently seen in those who use cocaine. These complications are presumably the result of vasospasm caused by the sympathomimetic effects of cocaine and induced hypertension.[26] Other stimulants like phenylpropanolamine,[27] methamphetamine[28] and 3,4-methylenedioxymethamphetamine (Ecstasy)[29] have also been incriminated as a cause of cerebral vascular insults. Intravenous methylphenidate can produce angiographic changes such as decreased vascular diameter and filling defects in experimental models.[30]

A clinical report by Trugman[31] described a patient with hemidystonia, a few years after experiencing ischemic cerebral infarction. The patient was diagnosed with ADHD at age five and treated with methylphenidate 20 mg per day until age 12 when right hemiparesis and aphasia suddenly developed. Cerebral angiography showed occlusion of the left anterior cerebral artery and a branch of the left middle cerebral artery. Brain MRI confirmed infarction in the left striatum and internal capsule. Schteinschnaider et al[32] reported an eight-year-old boy with ADHD who developed repeated episodes of hemidystonia and ataxia, while receiving methylphenidate 20 mg daily for 18 months. An MRI showed thalamic infarction and an angiogram revealed occlusion of both posterior cerebral arteries.

The occurrence of lacunar infarction following chronic oral abuse of methylphenidate in our patient who did not have any known risk factor for cerebrovascular disease, suggests an association between this drug and cerebral infarction. It is possible that the observed lacunar infarct in the right caudate nucleus is old and another infarct in the posterior limb of the internal capsule, which is too small or too early to be seen in the CT scan accounts for patient's symptomatology. Nonetheless, it seems justified to consider methylphenidate abuse as a potential predisposing factor for stroke in this patient.

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