Reversible ischaemic neurological deficit associated with short-term methylphenidate medication

Methylphenidate is a central nervous system stimulant pharmacologically related to amphetamines frequently used in attention deficit hyperactivity disorder (ADHD) and narcolepsy. Haemorrhagic stroke is a rare but well-known potential side-effect of amphetamine abuse, however, cerebral ischaemia has been reported casuistically (Rothrock et al., 1988). Here, we present incidence of a reversible ischaemic neurological deficit during short-term methylphenidate treatment.

Case report

A 21-yr-old male suffering from ADHD but otherwise healthy was treated with methylphenidate for the first time. The dose was titrated to 50 mg/d orally (given b.i.d., 30 mg at 08:00 hours and 20 mg at 12:00 hours) within 19 d. At day 20, in the afternoon he complained of numbness of the left hand for about 1 min recurring twice within the following hour and reported a similar episode 1 wk previously. Except for hypesthesia of the hand neurological examination was normal. The next day, in the evening, numbness of the left hand again occurred and spread over the whole left arm and the left half of the face combined with paresthesia and slight clumsiness of the hand. Simultaneously, he reported right frontotemporal dull headache without nausea or photo-/phonophobia. Methylphenidate medication was discontinued, and 300 mg acetylsalicylate per day was prescribed. Without further treatment all symptoms resolved completely within 3 d.

Cerebral MRI scan including diffusion weighted imaging was normal as were electrocardiography, electroencephalography and blood pressure. Transoesophageal echocardiogram, being an invasive procedure, was not performed as the uniformity of the episodes argued against cardioembolic insults. Thrombophilia was ruled out (antithrombin III, protein C and S, activated protein C-resistance, factor V Leiden and prothrombin mutation as well as antiphospholipid antibody tests yielded negative results). Drug screening was negative apart from methylphenidate. Doppler and duplex sonography of extra- and intracranial arteries showed no evidence for artery dissection, stenosis or atherosclerosis but showed increased cerebral blood flow volume normalizing within 1 wk. In the past, the patient regularly consumed marijuana and nicotine. He had a family history of coronary heart disease and migraine.

The patient most probably suffered transient right-hemispheric ischaemic attacks. The last episode almost lasted 3 d and, therefore, is classified as reversible ischaemic neurological deficit. The semiology of the events argues against epileptic seizures. Considering the family history of migraine a forme fruste of migraine associated with dopamine hypersensitivity cannot be completely excluded, but seems to be less probable because of the simultaneous appearance of headache with the deficits without delay. The close temporal coincidence of this event in an otherwise healthy man and complete remission following methylphenidate discontinuation render an adverse drug effect likely. Ischaemic strokes as well as cerebral haemorrhage are well-known adverse events of amphetamine or cocaine abuse due to vasculitis and vasospasm (Fredericks et al., 1991; Rothrock et al., 1988). Intravenous methylphenidate was shown to cause vessel irregularity in animal models (Rumbaugh et al., 1976), providing a theoretical rationale for cerebrovascular side-effects of methylphenidate. Stroke due to artery occlusion presumably caused by vasculitis during long-term methylphenidate medication was reported twice in children (Schteinschnaider et al., 2000; Trugman, 1988), whereas lacunar infarction of unknown aetiology was described after long-term oral methylphenidate abuse (Sadeghian, 2004). In our case, the coincidence of neurological deficits with headache and increased cerebral blood flow volume indicating reactive hyperemia points towards vasospasm causing the attack. Additional risk factors (nicotine and drug abuse, family history of atherosclerosis) may have contributed to a predisposition towards this adverse effect. Taking into consideration that additional risk factors tend to increase with age, the occurrence of this
adverse effect may be more frequent in adults than in children. Since the event had already occurred during short-term treatment, patients with additional risk factors should be monitored carefully for neurological deficits following the introduction of oral methylphenidate.

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Statement of Interest

None.

References


Christine Leonhard¹, Andreas Reif², Marcus Beck³, Christian Jacob³, Klaus-Peter Lesch¹
¹ Department of Psychiatry and Psychotherapy
² Department of Neurology, University of Würzburg, Germany