Lisdexamfetamine and Secondary Raynaud's Phenomenon

To the Editor: Raynaud's phenomenon is a clinical disorder characterized by episodic spasm or vasoconstriction of the arteries and smaller arterioles of the extremities, such as the fingers and toes or ears and nose, usually in response to cold or emotional stimuli. This disorder is also exacerbated by smoking. A classic attack is evidenced by the pallor of the distal extremity followed by cyanosis and then redness and paresthesia. When the episode occurs with no apparent cause, it is called primary Raynaud's phenomenon. When the episode is associated with a specific disease or disorder, it is called secondary Raynaud's phenomenon.[1] Secondary causes can include various connective tissue disorders as well as medications that may produce vasoconstriction including ergotamine, β-adrenergic antagonists, and sympathomimetic drugs. This case report describes a 16-year-old boy who developed secondary Raynaud's phenomenon while taking lisdexamfetamine, a medication commonly used in the treatment of attention-deficit/hyperactivity disorder (ADHD).

Case report. The patient presented to the neurodevelopmental clinic at 13 years of age with prominent hyperactivity, poor attention span, and high impulsivity that was clearly evident in school, at home, and elsewhere. He was diagnosed with ADHD, moderate in severity (*DSM-5* criteria). He was started on immediate-release methylphenidate, which was gradually optimized to an adequate dose (30 mg/d). He responded well to this medication for the next 2 years, and then the medication gradually became ineffective. Thus, the medication was discontinued and the patient was started on a longer-release preparation of methylphenidate (Medikinet XL 30 mg/d). He had a positive response and was maintained on the medication for the next year. He developed no significant adverse effects with either short-acting or long-acting methylphenidate. After this period, both his parents and school officials noted that the medication was gradually becoming ineffective. It was decided to discontinue Medikinet XL and start the patient on lisdexamfetamine 30 mg/d. While he had a good response to lisdexamfetamine, it was noted that around a week after starting the medication, he began to experience episodes of pallor of his fingers followed by cyanosis and then redness accompanied by a tingling sensation. These episodes would last around 5 to 10 minutes, and he found them distressing. The episodes occurred at a frequency of 1 to 2 per day and were usually precipitated by stressful events at home or school (eg, when he engaged in arguments). There was no history of substance use including smoking.

He was examined by his general practitioner and screened for collagen vascular diseases, including autoantibody screen. No physical cause was identified. There was no family history of collagen vascular diseases or autoantibody disorders. He was referred to our neurodevelopmental team to consider the possibility of medication-induced adverse effects. According to Naranjo's algorithm,[2] the possibility of lisdexamfetamine-associated secondary Raynaud's phenomenon was "probable" (score of 6). Lisdexamfetamine was discontinued and atomoxetine was initiated. This medication change was followed by complete remission of these episodes gradually over the next 2 weeks. He continues to be maintained on atomoxetine.

Secondary Raynaud's phenomenon has been described as a dose-related adverse effect of methylphenidate.[3] There is also a case series[4] on methylphenidate and dextroamphetamine-associated secondary Raynaud's phenomenon. A case-control study[5] in a pediatric rheumatology practice clearly demonstrates that use of stimulant medication is associated with the phenomenon. However, the present case, to the best of the author's knowledge, is the first to report an association between lisdexamfetamine and secondary Raynaud's phenomenon. Although uncommon, clinicians should be aware of this potential adverse effect with lisdexamfetamine, which could possibly impact medication compliance and further planning for management.

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