t is illegal to post this copyrighted PDF on any website. Rare Side Effects of Stimulants: Raynaud's Phenomenon

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Psychostimulants (Adderall, Dexedrine, and Ritalin) are a US Food and Drug Administration–approved treatment for attention-deficit/hyperactivity disorder (ADHD).¹ According to the US Centers for Disease Control and Prevention, approximately 3.5% of children between the ages of 0 and 11 years and 6.2% (most common) between 12 and 19 years are prescribed stimulants.² Secondary Raynaud's phenomenon³⁻⁶ is a rare but distressing adverse effect of stimulants.

Case Report

The patient was a 15-year-old girl with a diagnosis of oppositional defiant disorder, ADHD combined type, and Raynaud's phenomenon. She was initially treated with 10 mg of Adderall with the plan to increase to 20 mg after 2 weeks. One week after the initiation of treatment, she began to experience daily recurrence of Raynaud episodes. The patient reported that prior to starting the psychostimulant, her Raynaud episodes were triggered after showers and during the winter season about 3 times per week. These episodes presented as a purple fourth finger bilaterally and purple feet and legs bilaterally with mottling.⁷ However, while she was taking Adderall, these symptoms would present every day in the evening before her shower and manifested in the same fashion as her "regular" Raynaud episodes.8 Each episode lasted for approximately 2 hours with no sensory changes or weakness. Her family physician decided to refer her to the child psychiatry clinic. After carefully reviewing the history, it was decided to take her off Adderall. Four days after the medication was stopped, the evening episodes of Raynaud subsided. She was investigated for collagen vascular disease to rule out any medical cause, but all the results were negative. The patient was switched to guanfacine extended release 2 mg after 1 month. At the time of this writing, she is well maintained on this dose with moderate reduction in her symptoms.

Discussion

Raynaud's phenomenon has been previously reported with the use of psychostimulants. Raynaud's phenomenon

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To cite: Gupta M. Rare side effects of stimulants: Raynaud's phenomenon. *Prim Care Companion CNS Disord*. 2021;23(5):20102857. *To share:* https://doi.org/10.4088/PCC.20102857 is primarily caused by peripheral release of catecholamines, which leads to vasoconstriction.9 The empirical evidence has linked more cases with mixed salt amphetamines compared to methylphenidate.¹⁰ These differences may be due to their distinct pharmacodynamic profiles. Methylphenidate is primarily a reuptake inhibitor of catecholamines, but mixed salt amphetamines, in addition to reuptake inhibition, also release catecholamines.¹¹ Mixed salt amphetamines also have higher potency compared to methylphenidate, which is established in vivo12 and in cross-over studies. The European Society of Vascular Medicine¹³ published expert's consensus guidelines defining mild symptoms including Raynaud's phenomenon and severe manifestations, which need immediate tertiary-level interventions. A recent 2020 case series¹⁴ reported 3 cases of methylphenidate-induced life-threating systematic sclerosis. All these patients had Raynaud's phenomenon and were positive for anti-nuclear antibodies. Another case of dose-dependent Raynaud's phenomenon in an adult patient was reported in which symptoms improved with reduction of the dose.¹⁵ The peripheral manifestations of stimulants are worse in patients with underlying rheumatologic disease, including development of gangrene and need for amputations.¹⁶ Therefore, careful history and screening for rheumatologic disorders are recommended. The clinician's awareness of these adverse effects is critical in effectively addressing these conditions and modifying the treatment.

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