

Amantadine-Induced Livedo Reticularis in a Child Treated Off Label for Neurobehavioral Disorders

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PRACTICE POINTS

- Amantadine is a generally well-tolerated medication that is more commonly used for off-label treatment of several pediatric neurobehavioral conditions such as attention deficit hyperactivity disorder, autism spectrum disorders, obsessive compulsive disorder, depression, and others.
- Livedo reticularis has known associations with several medications and diseases; however, the most common presentation is cutis marmorata, a benign condition that typically affects newborns.

We report the case of an 8-year-old boy who was taking amantadine off label for multiple childhood neurobehavioral disorders and subsequently developed livedo reticularis. Although this side effect is well-described in adult patients taking amantadine for Parkinson disease, it is now being seen in children as the off-label use of amantadine is expanded to this population.

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Livedo reticularis (LR) is a common dermatologic finding consisting of diffuse, reticulated, violaceous patches. It often is a benign physical finding known as cutis marmorata; however, LR can be associated with other medical conditions as well as with the use of some medications.^{1,2} Amantadine is a common cause

of LR in Parkinson disease patients.^{3,4} We present a rare case of amantadine-induced LR in a pediatric patient and highlight the off-label use of this medication in children.

Case Report

An 8-year-old boy presented with a diffuse rash on the trunk, arms, and legs of 9 months' duration. The patient denied any associated symptoms as well as alleviating or exacerbating factors. He also denied any changes with temperature. He had no recent international travel and no prior drug allergies. His medical history was remarkable for attention deficit hyperactivity disorder (ADHD), bipolar disorder, and autism spectrum disorder. His previously prescribed medications included atomoxetine, quetiapine, and valproic acid. The only new medication that had been started within the last year was amantadine. Physical examination revealed a diffuse, reticulated, erythematous to violaceous, blanching rash that was most notable on the legs (Figure 1A) but also was present on the trunk (Figure 1B) and arms (Figure 1C). The clinical examination was consistent with LR, which was presumed to be secondary to amantadine use. Given the multiple psychiatric diagnoses and medication history in this young patient, a consultation with child psychiatry was facilitated. His medications and diagnosis were reviewed, and amantadine was discontinued. At a follow-up visit 5 months later, the patient's LR had improved (Figure 2).

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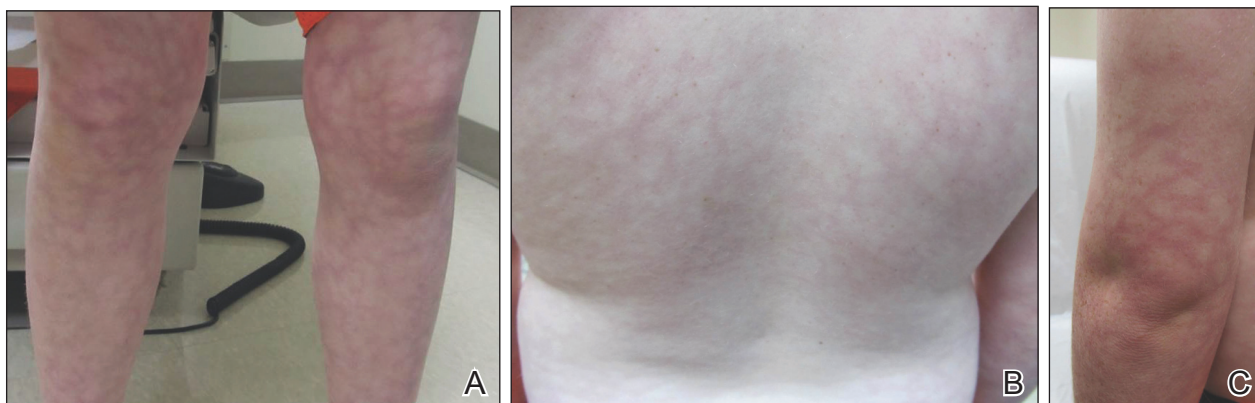


FIGURE 1. Livedo reticularis with a diffuse, reticulated, erythematous to violaceous, blanching rash on the legs (A), trunk (B), and arm (C) in a child undergoing off-label treatment with amantadine for neurobehavioral disorders.



FIGURE 2. Livedo reticularis, which previously was most pronounced on the legs, was minimal 5 months after discontinuing amantadine use.

Comment

Amantadine has a well-documented association with LR in patients with Parkinson disease,^{3,4} which has been reported in up to 40% of those taking amantadine.² More recently, amantadine has been used off label to treat neurobehavioral disorders in children due to beneficial effects including improvement in attention and concentration, distractibility, and fatigue.⁵ Our patient was being treated off label with amantadine for ADHD and bipolar disorder. Amantadine acts as a noncompetitive antagonist of the

N-methyl-D-aspartate receptor, enhancing dopamine release to reduce symptoms of ADHD.^{5,6} Additionally, amantadine can cause a depletion of catecholamines in the peripheral nerve terminals, which may lead to dilatation of dermal vessels.^{4,6} This sequence of events has been proposed as a possible mechanism contributing to amantadine-induced LR, though the pathophysiology is not fully understood.^{1,3,4}

Our case of LR likely was induced by amantadine given the temporal relationship between initiation of the medication, onset of the rash, and the considerable improvement of the rash upon discontinuation of amantadine. Barrera and Browning⁶ reported another case of amantadine-induced LR in a pediatric patient. Because amantadine is increasingly being used off label to treat childhood neurobehavioral disorders, amantadine-induced LR may become more prevalent in patients who do not have Parkinson disease; therefore, physicians who treat pediatric patients must be aware of this side effect.⁵

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