DHE-Induced Peripheral Arterial Vasospasm in Primary Raynaud Phenomenon: Case Report

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Abstract

Dihydroergotamine (DHE) is primarily a serotonin 5HT_{1B} and 5HT_{1D} receptor agonist used for acute migraine treatment. It is associated with acute vasoconstriction mediated through the 5HT_{1B} receptor and is contraindicated in patients with history of cardiac disease and peripheral vascular disease. We present a case of acute peripheral arterial vasospasm in a patient with primary Raynaud phenomenon while receiving inpatient treatment for status migrainosus with intravenous (IV) DHE. The patient is a 35-year-old female with a history of chronic migraine and primary Raynaud phenomenon. After 15 doses of IV DHE, the patient reported paresthesias of the right hand and was noted to have absent right radial and ulnar pulses to palpation. Portable arterial Doppler study demonstrated abnormal flat line pulse volume recordings (PVRs) in the right second, third, and fourth digits, with markedly dampened PVR in the right thumb and fifth finger along with no ulnar PVR detectable at the wrist. Duplex revealed bilateral severely diminished flow in the right ulnar and radial arteries without acute occlusions. Computed tomography angiogram of right upper extremity visualized arteries through the mid-forearm but not distally. Dihydroergotamine was discontinued, and the patient was started on oral amlodipine and aspirin. Repeat Doppler ultrasound 3 days later revealed normal arm and digital waveforms bilaterally consistent with resolution of vasospasm. This case highlights a potential complication of IV DHE therapy. Risk may be increased in patients with primary Raynaud phenomenon. We suggest cautious use of IV DHE in this population.

Keywords

dihydroergotamine, migraine, Raynaud, vasospasm, status migrainosus

Introduction

We present a case of acute peripheral arterial vasospasm in a 35-year-old female with primary Raynaud phenomenon (RP) while receiving inpatient treatment for status migrainosus with intravenous (IV) dihydroergotamine (DHE). Like migraine, RP is more prevalent among young women and is more likely to affect those with a family history of the disease.^{1,2}

Case Description

A 35-year-old woman, nonsmoker, with history of RP, intractable chronic migraine, and a family history of migraine was admitted to our inpatient headache center for status migrainosus. Her outpatient medication regimen included sumatriptan, nadolol, and topiramate. She tends to get bilateral RP triggered mainly by cold weather. Her last RP episode was about 4 years ago. She was started on a treatment regimen for

migraine including IV DHE, IV lidocaine infusion, IV promethazine, IV magnesium, and IV ketorolac, administered through a right arm peripherally inserted central catheter (PICC). She had not been treated with IV DHE in the past. The vasoconstrictive effects of DHE were discussed with the patient, and given that she has tolerated triptans in the past, the decision was made to use DHE for headache relief. The past history of RP was not taken into consideration given that it was not disclosed on admission and she was not screened for it. Intravenous DHE was started at 0.25 mg every 8 hours and increased by 0.25 mg increments daily over the course of the

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Figure 1. Upper extremity CT angiogram showing contrast through radial artery in the forearm which is not seen distally.

following few days, reaching the dose of 1 mg every 8 hours on hospital day 4. On hospital day 6, about 1 hour after completing her 15th dose of IV DHE at the standard administration rate, the patient reported right-hand numbness and tingling. Examination of the right hand revealed a dusky appearance with reduced capillary refill and absent radial and ulnar pulses to palpation. Peripheral pulses of the other extremities were intact. Portable arterial Doppler study showed abnormal flat line pulse volume recordings (PVR) tracings in the right second, third, and fourth digits, with markedly dampened PVR tracings in the right thumb and fifth finger along with no ulnar PVR detectable at the wrist. There was also abnormal left finger PVR. Duplex showed bilateral diminished flow in ulnar and radial arteries, severe on right, without acute occlusions. Computed tomography angiogram of right upper extremity visualized arteries through the mid-forearm that were not seen distally (see Figure 1). Dihydroergotamine was discontinued, and the PICC was removed. Differential diagnosis included vasospasm related to RP, vasospasm induced by DHE, arterial thrombosis, and possibly carpal tunnel syndrome, given sensory complaints. She was started on 5 mg oral amlodipine daily and 81 mg aspirin daily. Her paresthesia subsided and repeat Doppler ultrasound 3 days later revealed normal arm and digital waveforms bilaterally consistent with resolution of vasospasm.

No further imaging was performed following the resolution of symptoms (see Table 1 for case timeline).

Discussion

This case report highlights the effects that DHE therapy could have on arterial circulation in patients with a previous diagnosis of RP. Dihydroergotamine is primarily a serotonin 5HT1B and 5HT1D receptor agonist used for acute migraine treatment. Dihydroergotamine is also an agonist at 5HT1A, 5HT1F, 5HT2A, 5HT2C, 5HT3, 5HT4, α 1, α 2, β , muscarinic, D1, and D2 receptors. Vasoconstriction is mediated through the 5HT1B receptor, and antimigraine activity is mediated through the 5-HT1D receptor by decreasing the release of neurogenic inflammatory agents such as Calcitonin gene-related peptide and by disrupting trigeminal nerve-mediated nociception.^{3,4} Dihydroergotamine binds to both adrenoceptors and 5-HT1, which are present on veins, making it a stronger venous constrictor. Although DHE-driven arterial vasoconstriction is cranioselective, it also causes cardiac artery vasoconstriction, distally more than proximally. In addition, diffusion of DHE from its receptors is slow leading to longer lasting vasoconstricting effects.⁵ Hence, use of DHE is contraindicated in the presence of cardiac disease (uncontrolled hypertension, ischemic heart disease, angina, history of MI, and coronary vasospasm), peripheral vascular disease as well as severe hepatic and renal dysfunction due to concerns of possible cerebral, cardiac, or peripheral ischemia secondary to vasoconstriction.⁶

Raynaud phenomenon is characterized by an abnormal local vascular response to environmental stress (cold and emotions), causing vasoconstriction of digital arteries and cutaneous arterioles. Raynaud's phenomenon may be primary (Raynaud's disease) or secondary to an underlying disease. The Food and Drug Administration package insert for DHE mentions: "patients who experience other symptoms or signs suggestive of decreased arterial flow, such as ischemic bowel syndrome or Raynaud's syndrome following the use of any 5-HT agonist, are candidates for further evaluation."⁷ However, the effects of DHE have not been investigated in patients with a history of RP. The 1-year prevalence of migraine in the United States is 17.1% in females and 5.74% for RP.⁸ A systematic review demonstrated a significant positive association between migraine and RP with a pooled odds ratio of 4.02 (95% confidence interval: 2.62-6.17).⁸ This is relevant because IV DHE is commonly used for acute migraine treatment, and risk of arterial vasospasm may be increased in patients with RP.

The case report is important because this complication has not previously been reported in a patient with migraine and RP. However, given this is a single case, we are unable to draw any strong conclusion regarding whether the presence of RP increases the risk of vasospasm in migraine patients using IV DHE. The lack of reported vasospasm in patients with RP and migraine suggests that use of DHE

Table 1. Case Timeline.

Hospital Day	1	2	3	4	5	6	7	8	9
IV DHE dose	0.25 mg q8h	0.5 mg q8h	0.75 mg q8h	1 mg q8h	1 mg q8h	Discontinued			
Aspirin						81 mg	81 mg	81 mg	81 mg
Amlodipine						5 mg	5 mg	5 mg	5 mg
Arterial Doppler						Abnormal			Normal
CTA upper extremity							Abnormal		

Abbreviations: DHE, dihydroergotamine; IV, intravenous; q8h, every 8 hours.

may be very low risk, as both entities are common. We are not endorsing the use of DHE in patients with any peripheral vascular disease. Categorizing RP as an absolute rather than relative contraindication to DHE use would exclude many patients with migraine, and the risk may not outweigh the benefit.

Conclusion

To our knowledge, we present the first reported case of IV DHE-induced peripheral arterial vasospasm in a patient with primary RP. We suggest using DHE with caution in patients with RP and counseling the patient regarding a potentially increased risk of vasospasm. Prospective studies are necessary to evaluate the safety of using IV DHE in patients with RP.

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Informed consent was obtained from the patient for the publication of this case report.

Declaration of Conflicting Interests

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Clinton Lauritsen has received honoraria from Cefaly technologies.

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