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Phentermine and Coronary Vasospasm–Induced Myocardial Infarction

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Abstract

Women presenting to the cardiac catheterization laboratory with normal coronary arteries without significant atherosclerotic disease is a common presentation. In such patients, it is important to maintain a wide differential and consider alternate diagnoses. We present two cases of women presenting with chest pain found to have severe coronary vasospasm in the setting of recent initiation of phentermine. Phentermine may have vasospastic proprieties which are important to consider when prescribing to patients.

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We present 2 cases of women presenting with chest pain and acute coronary syndrome who had a history of both nicotine dependence and recent initiation of phentermine. Both patients were found to have severe coronary vasospasm–induced myocardial infarction.

Case 1

The first patient was a 48-year-old woman who presented to the emergency department with several episodes of severe substernal chest pain over the previous few weeks. She had no history of coronary artery disease, but had a long-standing history of hypertension secondary to renal fibromuscular dysplasia with plans for renal angioplasty. Her home medications included lisinopril, hydrochlorothiazide, as well as initiation of phentermine 3 weeks before admission. Her vital signs revealed an elevated blood pressure of 172/57 mm Hg. On physical examination, no notable abnormalities were found.

Her initial electrocardiogram did not reveal any evidence of ischemia, and her troponin levels were within normal limits. She underwent coronary computed tomography angiography that revealed multiple moderate coronary stenoses of the proximal left anterior descending artery and the proximal circumflex coronary artery as well as severe stenosis of the right coronary artery. She was admitted for observation; however, she subsequently had a repeated episode of chest pain, at which time an electrocardiogram exhibited significant ST-segment elevations (Figure 1A). Troponin levels remained within normal limits. She was taken to the cardiac catheterization laboratory emergently where she was found to have severe coronary vasospasm of the proximal right coronary artery relieved with intracoronary nitroglycerin (Figure 1B).

Case 2

The second patient was a 47-year-old woman who presented on the same day with substernal chest pain and ST-segment elevation myocardial infarction. She had severe episodic chest pain upon the initiation of phentermine several months before admission. She had been taking phentermine intermittently for years. A discrete lesion was noted in the distal right coronary artery, and she underwent percutaneous intervention; however, she continued to have symptoms of unremitting chest pain over the next 12 to 24 hours. This was relieved by nitroglycerin, but not associated with any electrocardiographic changes. The troponin level was elevated to 1.3 ng/mL. She was taken back to the cardiac catheterization laboratory the next day where repeat coronary angiography revealed vasospasm of the proximal

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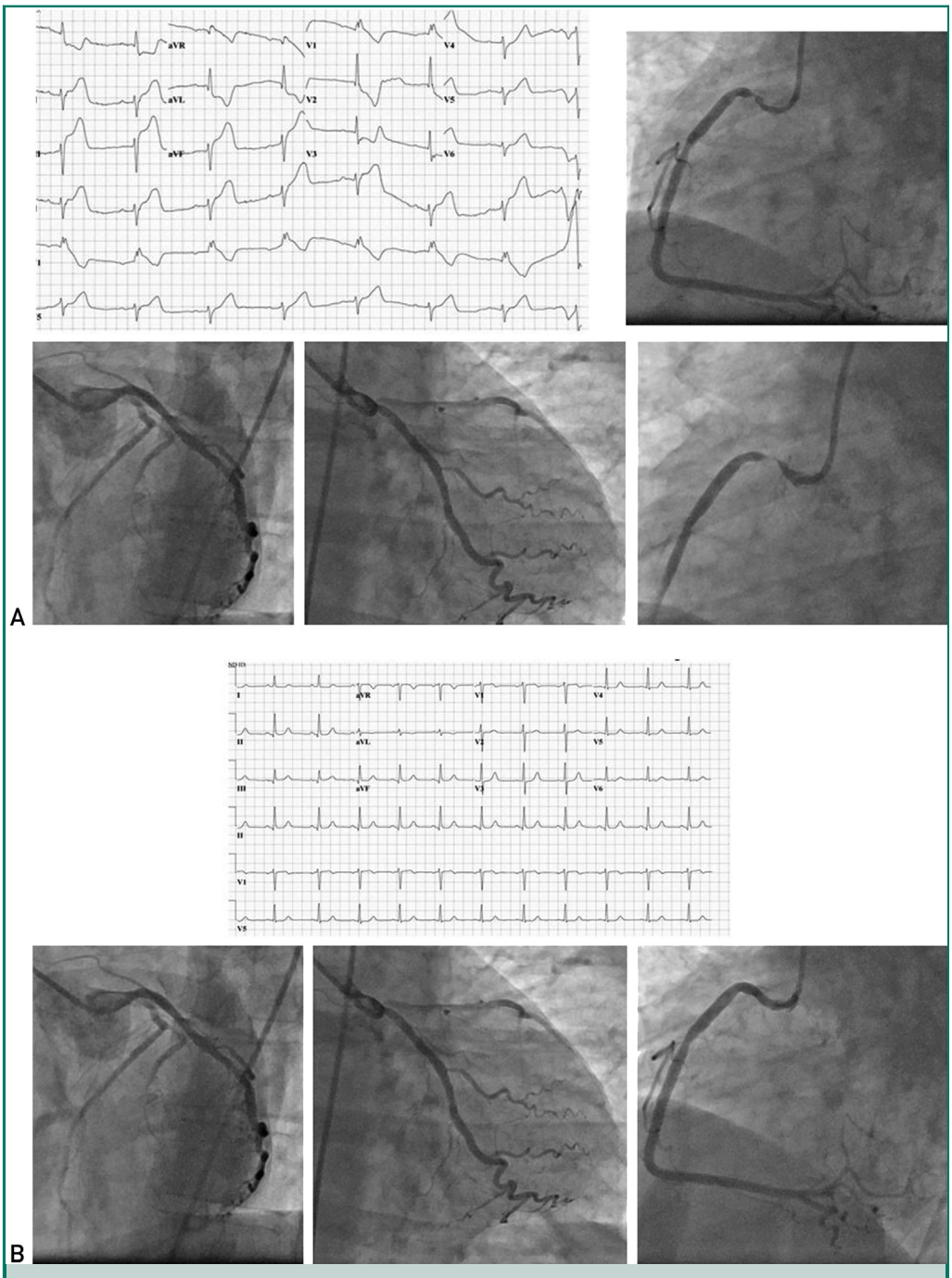

FIGURE 1. A, Electrocardiogram consistent with inferior ST-segment elevation myocardial infarction. Coronary angiography reveals proximal narrowing of the right coronary artery. B, Electrocardiogram and angiogram after the administration of intracoronary nitroglycerin. There is resolution of the narrowing noted in the proximal right coronary artery with concomitant normalization of the electrocardiogram.

circumflex coronary artery not seen on the initial angiogram (Figure 2).

Both patients were initiated on L-arginine, long-acting nitrates, and calcium channel blockers for their underlying coronary vasospasm. Both patients were advised to discontinue phentermine. These patients had improvement in their symptoms and

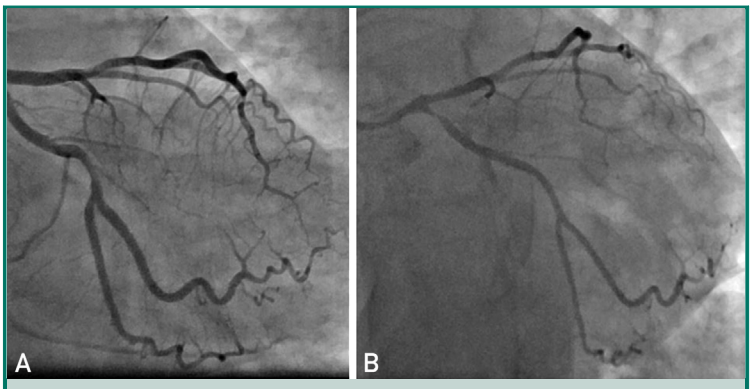

FIGURE 2. A, Initial coronary angiogram of the second patient. There is no evidence of narrowing of the proximal circumflex artery. B, Proximal narrowing of the circumflex artery with otherwise normal coronary vasculature suggestive of proximal circumflex artery spasm not present on the initial angiogram performed on the previous day.

were discharged with close outpatient follow-up.

DISCUSSION

We present 2 cases of women presenting with coronary vasospasm—induced myocardial infarction who had a history of nicotine dependence and recent use of phentermine for weight loss in the absence of any history of coronary disease. We hypothesize that phentermine, an amphetamine analogue, may be associated with increased coronary sensitivity and predisposition to coronary vasospasm. Identification of this potential life-threatening adverse effect is important to alert patients who may be taking phentermine and physicians who may be prescribing this weight loss medication.

Phentermine is an analogue of amphetamine that acts by up-regulating the noradrenergic and the dopaminergic central nervous system by increasing release of norepinephrine and inhibiting uptake. Weight loss is thought to be secondary to central and sympathetic nervous system activation. At this time, phentermine is the most widely used weight loss pharmacotherapy in the United States and is approved for the short-term treatment of obesity because of its effectiveness in helping patients lose weight.[1]

Phentermine was initially marketed as "Fen-Phen," which was a compound of fenfluramine and phentermine and a commonly used weight loss agent 20 years ago. In 1997, this medication was taken off the market because of concerns for increased risk of valvular heart disease.[2,3] This was thought to be secondary to fenfluramine as opposed to phentermine, and phentermine monotherapy has continued to be commonly prescribed for weight loss.[4]

Coronary spasm and acute myocardial infarction have been previously cited in patients taking amphetamines, an analogue of phentermine, and it is thus plausible that certain patients may present with similar adverse effect profiles. In addition, there have been sparse reports of phentermine causing acute coronary syndrome, cardiac arrest, and ischemic stroke.[5-9] Specifically, Azarisman et al[10] have reported 2 cases of phentermine-associated myocardial infarction in women with normal coronary arteries. These patients may have had acute coronary syndrome secondary to coronary vasospasm that subsequently resolved and thus was not detected by coronary angiography. There has also been reports of 2 patients without ischemic risk factors taking phentermine presenting with ischemic stroke.[7] This may have been secondary to cerebrovascular vasospasm leading to ischemia and subsequent neurological deficits as has been described in patients taking amphetamines.[11] Thus, phentermine may be associated with life-threatening consequences including cardiovascular and cerebrovascular vasospasm, yet the drug continues to be widely prescribed. We believe that a potential association between phentermine use and coronary vasospasm exists and patients should be counseled about these adverse effects. Although unlikely, it is important to note that our findings are limited in that we cannot exclude catheter-induced spasm in both these cases.

Although many patients with obesity-related cardiovascular risk factors associated with diabetes, hypertension, and hyperlipidemia may benefit from phentermine because of weight loss and improved metabolic panels, it is unclear which patients may develop coronary sensitivity and subsequent coronary vasospasm. The underlying mechanism is unclear, but increased adrenergic response in response

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to increased norepinephrine and increased coronary sensitization has been postulated as a potential mechanism leading to vasospasm in patients taking vasospastic drugs such as cocaine.[12] Mechanistically, phentermine may have vasospastic properties that need further exploration.

CONCLUSION

Phentermine is a commonly prescribed drug traditionally thought to have minimal adverse effects, especially in patients without a history of cardiovascular disease. We, however, present 2 cases and note several other potentially related cases in the literature, suggesting a risk of arterial vasospasm secondary to phentermine. It is important to note that these patients are relatively healthy with few other risk factors. We believe patients should be counseled about such potential adverse effects and shared decision making be implemented when advising patients on weight loss. Although these reports do not prove causation, this potential association must be further investigated with larger studies to better understand this possible association and to ensure the safety of weight loss medications such as phentermine. As providers, it is important that we have heightened awareness of potential adverse effects of phentermine so that we are able to best manage and advise our patients' weight loss endeavors.

Potential Competing Interests: The authors report no competing interests.

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