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Letters to the Editor

Successful Use of Ranolazine in a Patient With Vasospastic Angina

To the Editor:

Vasospastic angina, previously described as variant or Prinzmetal angina, is caused by coronary spasm. A sudden occlusive vasoconstriction of an epicardial artery generally causes transmural ischemia and is revealed as angina with ST-segment elevation on electrocardiogram.

The most widely accepted treatment regimens of vasospastic angina are nitrates and calcium channel blockers. However, in some cases, first-line treatment with these agents has poor success rates in symptom relief. We report the successful use of ranolazine to relieve the symptoms of vasospastic angina.

A 57-year-old woman was admitted to the emergency department with the complaint of chest pain for the past several hours before admission. Electrocardiogram revealed T-wave inversion in the precordial leads (Fig. 1A). Furthermore, troponin I levels were high; therefore, the initial diagnosis was non–ST-segment elevation myocardial infarction. Subsequent angiography demonstrated an 80% focal stenosis in the mid-left anterior descending artery, which reduced after administration of intracoronary nitrate (Fig. 1B). Medical treatment for vasospastic angina was regulated, including daily diltiazem 120 mg and isosorbide mononitrate 40 mg po. Subsequently, oral nitrate therapy was stopped because of a severe headache and was replaced by amlodipine 10 mg. The maximum-tolerated doses were determined as diltiazem 180 mg and amlodipine 10 mg according to the patient's pulse rate and blood pressure. In hospital follow-up, an ST-segment elevation in anterior leads was observed that promptly responded to intravenous infusion of nitrate (Fig. 1, C and D); however, the patient experienced severe headaches again. Considering the patient's resistant symptoms, we administered an off-label, additional treatment of ranolazine at a dose of 375 mg twice a day. Given the inhibition by diltiazem of both CYP3A4 metabolism and p-glycoprotein transport of ranolazine, initial doses were kept low. In addition, the QT interval was closely followed because ranolazine may cause prolongation of the QT interval, especially in patients who use other medications that may affect the QT interval or CYP3A4. After ranolazine treatment, the patient reported pain relief. She is currently being followed with amlodipine, diltiazem, and ranolazine treatment and has been free of symptoms for the past 5 months.

Vascular smooth muscle hyper-reactivity resulting from increased calcium sensitivity plays a key role in the pathogenesis of large epicardial vessel spasm.[1] Ranolazine decreases intracellular calcium overload due to inhibition of the late

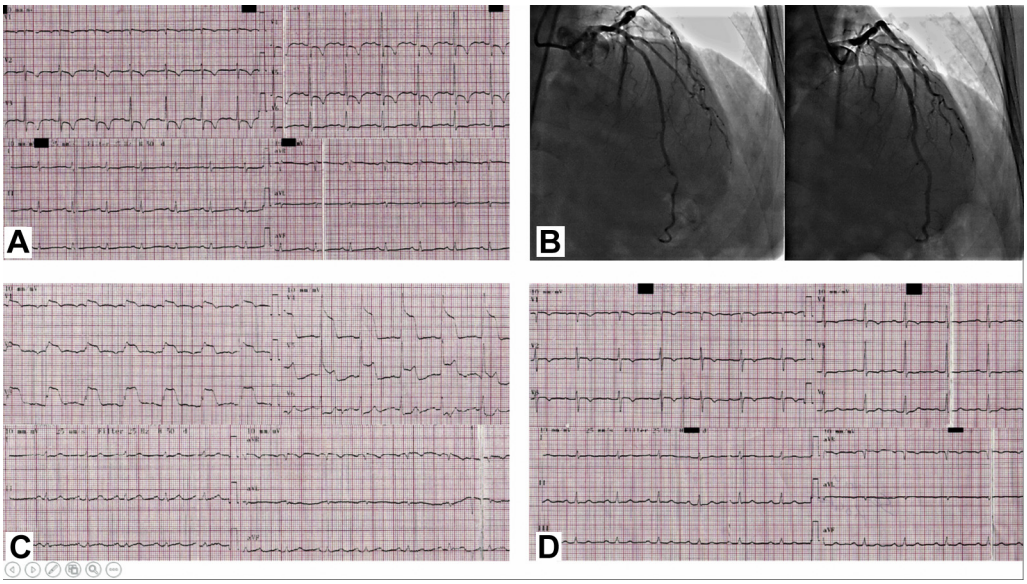

Figure 1. (**A**) Electrocardiogram on admission revealed T-wave inversion in the precordial leads. (**B**) When the patient's symptoms were reduced, coronary angiography demonstrated an 80% stenosis in the mid-left anterior descending artery, which reduced after administration of intracoronary nitrate. (**C**) Precordial ST-segment elevation was seen in hospital follow-up although the patient was under first-line vasospastic angina treatment. (**D**) Rapid response to intravenous nitrate treatment was obtained.

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inward sodium channel. Nieminen et al.[2] demonstrated in anaesthetized pigs that intracoronary administration of ranolazine resulted in an increase in the left anterior descending coronary artery flow and a reduction in the coronary vascular resistance. In addition, it has been shown that microvascular spasm also exists at a significant proportion in patients with vasospastic angina.[3] Ranolazine has been shown to improve symptoms in patients with microvascular angina,[4] and our patient who has been diagnosed with vasospastic angina had a clinical response coincident with ranolazine treatment. This may have been a primary beneficial effect of ranolazine, or possibly potentiation of the mechanisms already exerted by calcium channel blockers, but also possibly a temporal coincidence. A challenge of ranolazine withdrawal in this patient or a case series might be helpful to evaluate the efficacy of ranolazine in patients with vasospastic angina.

Omer Faruk Cirakoglu, MD
omerfcirakoglu@hotmail.com

Selim Kul, MD
Muhammet Raşit Sayın, MD

Disclosures

The authors have no relevant conflicts of interest to disclose.

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