CASE REPORT

Myocardial Infarction after Taking Zolmitriptan

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We report the case of a patient with mild non-obstructive coronary artery disease who sustained an inferior wall myocardial infarction shortly after taking zolmitriptan as abortive therapy for migraine headaches. A Medline search was performed to review all reported cases of myocardial infarction related to migraine therapy with zolmitriptan and related medications. Zolmitriptan may cause myocardial infarction (MI) even in the absence of significant coronary artery disease.

INTRODUCTION

Zolmitriptan belongs to the class of anti-migraine medications that targets the 5-hydroxytryptamine (5-HT) serotonin receptor (triptans). When this class of drugs was conceived, the 5-HT1 receptor was thought to abort migraines by causing vasoconstriction solely in the cerebral vasculature. However, vasoconstrictive effects on the coronary circulation have been widely documented in vivo and in vitro, due to either the presence of 5-HT1 receptors, other 5-HT1-type receptors in coronary arteries, or ranging degrees of receptor reactivity of these drugs [1-3].

Although chest symptoms, including chest pressure, tightness, and pain, have been described in up to 15 percent of patients taking these drugs, cardiovascular adverse events such as myocardial infarction (MI) have rarely been reported in the literature [3-10]. The mechanism for these events is thought to be related to vasoconstriction superimposed on a pre-existing coronary lesion.

REPORT OF A CASE

This 68-year-old woman had a history of migraines with visual aura since she was 48 years of age. She averaged one to two attacks every week and had been taking zolmitriptan for six years. She routinely took 5 mg orally for every episode and had an adequate response, rarely requiring a second dose. There was no history of hypertension, diabetes, hyperlipidemia, ischemic heart disease, cerebrovascular disease, smoking, or family history of premature atherosclerotic disease. She had never experienced any chest pain prior to this episode.

On the day of admission, the patient experienced a typical migraine attack around 11 a.m. and took 5 mg of zolmitriptan. Five
hours later she had sudden onset of chest pain while lying in bed. She described the pain as pressure which was localized to the retrosternal area and radiated to the left breast, neck, and left arm. The pain was severe in intensity (8/10) initially and decreased gradually over the next three hours to a moderate pain (4/10). At that time, she repeated the dose of zolmitriptan for cephalgia, while still having chest pain. Soon thereafter, she presented to the emergency department, where she had normal vital signs, a normal electrocardiogram, and normal cardiac enzymes. Another set of enzymes was drawn four hours later, revealing a troponin I of 2.36 ng/ml. The patient was chest-pain free by that time and was taken to the catheterization laboratory 10 hours later.

Angiography revealed mild two-vessel coronary artery disease with several stenoses, none of which was greater than 30 to 40 percent. Left ventriculography demonstrated severe diaphragmatic hypokinesis, and the troponin I level later peaked at 7.99 ng/mL (Figure 1).

**COMMENT**

Zolmitriptan, a 5HT1 agonist, belongs to a class of anti-migraine drugs that are known to cause vasoconstriction, precipitating chest pain in up to 15 percent of patients, but rarely causing serious cardiovascular events. Several reports of MI in patients receiving sumatriptan, a close relative to zolmitriptan, appear in the literature. However, a patient with confirmed MI by elevated cardiac enzymes and a wall-motion abnormality demonstrated by left ventriculography with non-obstructive coronary disease on coronary angiogram had not been reported until a recent case report by Mikhail et al. involving zolmitriptan [10]. Our case represents the second such documented MI attributable to zolmitriptan in a similar patient without known coronary artery disease.

As was the case in Mikhail et al.’s case of MI due to zolmitriptan, we demonstrated non-obstructive coronary artery disease with coronary angiography performed the morning after symptom onset. Both troponin I elevation and a hypokinctic diaphragmatic segment on left ventriculography confirmed the presence of MI (See Figure 1). Given the known vasoconstrictive effects of the triptans and the temporal relationship between our patient's self-administration of zolmitriptan and her clinical presentation, this case implies a
causal relationship between zolmitriptan and MI even in the absence of significant coronary artery stenoses.

In two of the earlier reported cases of triptan-induced MI, there was no enzymatic evidence of myocardial necrosis [4, 5]. Coronary angiography revealed normal coronary arteries and minor luminal irregularities, respectively. In a third case, an inferior MI was diagnosed shortly after sumatriptan use, but coronary angiography was not performed [6]. In a fourth case, the patient had severe underlying coronary artery disease and a history of cocaine abuse [7]. Another case described a patient with moderate atherosclerotic disease and an anterior wall MI after sumatriptan and methysergide use [8].

In a sixth case, the patient presented with polymorphic ventricular tachycardia and an inferior ST-elevation MI with troponin I elevation to 31.9 ng/ml. Angiography revealed a totally occluded non-dominant right coronary, and the patient's history of diabetes mellitus and tobacco abuse make underlying coronary artery disease probable [11].

While almost all previously reported MIs thought secondary to triptan use have occurred after administration of sumatriptan, recent reports involving tegaserod [9] and zolmitriptan [10] point to a possible class effect for these anti-migraine medications. This class effect is not unexpected, as Zolmitriptan has a similar mechanism of action to other triptans [12]. Vijayan et al. reported a case of ischemic spinal cord infarction thought secondary to zolmitriptan [13]; Carnero et al. described angina related to zolmitriptan use [14]; and ours is now the second case of zolmitriptan-induced MI in the literature [10].

Our case highlights the significant challenge in identifying patients at risk for adverse cardiovascular events with this class of drugs. Evans et al. suggest a strategy for assessing this risk [15], including ascertaining cardiac risk factors, screening electrocardiograms, and non-invasive ischemia evaluations with stress testing. However, non-invasive screening tests, such as nuclear or echocardiographic stress tests or even invasive diagnostic procedures, may not be sensitive enough to detect all patients at risk, as these tests typically only detect more severe coronary lesions. A potential role for CT or MR angiography in screening patients may eventually give physicians a non-invasive tool for screening prior to prescribing triptans, but the technology and evidence for such an approach are currently lacking.

As pointed out by Evans et al. [14], physicians should attempt to use other abortive therapies for migraines in patients with any cardiovascular risk factors. In those patients for whom no other effective options exist for migraine therapy, specific counseling regarding symptoms of myocardial ischemia should be given by physicians prescribing these medications. Our patient took the maximal allowable dose in a 24-hour period, two 5 mg tablets, the second of which was taken in the throes of her cardiac event. More effective education of our patient concerning the potential cardiac effects of zolmitriptan may have dissuaded her from taking the second pill, which likely exacerbated the situation. Finally, our patient had frequent headaches and took zolmitriptan one to two times per week. The safety of zolmitriptan in patients with frequent headaches requiring abortive therapy three or more times a week is uncertain.

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