



# CASE REPORT

## Coronary Artery Disease in a Young Patient Taking Modafinil

Justin G. Fernandez, M.D.<sup>1</sup>, Mahmoud Farhoud, M.D.<sup>1</sup>, Mona Brake, M.D.<sup>1,2</sup>

<sup>1</sup>University of Kansas

School of Medicine-Wichita

Department of Internal Medicine

<sup>2</sup> Robert J. Dole Veteran's Administration Medical Center, Wichita, KS

### Introduction

Modafinil is a relatively new drug typically used in patients diagnosed with sleep disorders including narcolepsy and obstructive sleep apnea. It has been described as a “stimulant” and can produce cardiac symptoms such as increased blood pressure, asystole, chest pain, and sinus tachycardia.<sup>1,2</sup> There is relatively little data on the correlation between modafinil use and risk for coronary artery disease.

### Case Report

A 37-year-old white male with a history of narcolepsy (on modafinil) and post-traumatic stress disorder (on lamotrigine, sertraline, and temazepam) presented with a chief complaint of chest pain. Aspirin therapy was initiated immediately.

Cardiac and lung exams were unremarkable with clear breath sounds and no murmurs, rubs, or gallops. Initial complete blood count (CBC) showed a slightly elevated white blood cell count at  $13,700 \times 10^3/\mu\text{L}$ , which was attributed to stress reaction. B-type natriuretic peptide (BNP), thyroid stimulating hormone (TSH) and electrolytes were within normal limits. Initial troponin I was unremarkable and electrocardiogram (EKG) did not show any ST-segment elevation or any other changes when compared to previous EKG.

Approximately eight hours after presentation, blood pressure reached 197/128 mmHg and troponin I increased to 9 ng/ml then peaked at 15 ng/ml. A

diagnosis of non-ST elevation myocardial infarction (NSTEMI) was made. The patient was taken for cardiac catheterization, which revealed a 90% occlusion of the left anterior descending artery at the trifurcation of the first major septal artery. A bare metal stent was placed and the patient's chest pain resolved.

Aspirin was continued and a beta-blocker, statin, and clopidogrel were started after the procedure per acute coronary syndrome (ACS) protocol. The patient remained stable and was discharged the following day and was advised not to take modafinil.

### Discussion

Modafinil is the first new psychostimulant medication for narcolepsy in 20 years. It has become popular recently due to its lower abuse potential and is used frequently in the military for soldiers experiencing excessive fatigue. Although the exact mechanism of action is poorly understood, it most likely acts as an agonist on the central alpha-1 adrenergic system or dopamine system producing stimulation-like effects on the central nervous system (CNS) and vasospasm and tachycardia.<sup>2,3</sup>

Potential cardiac side effects include palpitations, chest pain, ischemic EKG changes, and dyspnea.<sup>1,2</sup> There is a limited amount of literature linking the use of modafinil to coronary artery disease (CAD). However, there is a fair amount of evidence

that modafinil should be used with caution in patients with pre-existing heart conditions such as left ventricular hypertrophy and a history of myocardial infarction.<sup>4</sup>

The prevalence of CAD in younger patients is difficult to establish because it is typically a silent process. In an autopsy study<sup>6</sup> involving 760 patients aged 15 to 34 who were victims of accidents, suicides, and homicides, advanced coronary atheromata were seen in two percent of men aged 15 to 19, but no women. An advanced lesion was present in 20 and 8 percent of men and women aged 30 to 34, respectively, while 19 and 8 percent, respectively, had a 40 percent or greater stenosis of the left anterior descending artery.<sup>7</sup>

There are limited data on the frequency of myocardial infarction in younger, healthier patients with few to no risk factors. One study showed that, although serum lipids have a great role in ischemic heart disease, half of patients with acute myocardial infarction had normal lipid profile.<sup>8,9</sup> Lastly, a study on known cases of ischemic heart disease did not show a combination of risk factors such as hyperlipidemia, hypertension, diabetes, and smoking. Fifteen percent of men, 19% of women, and more than half of all patients had only one classic risk factor.<sup>10,11</sup>

Conversely, our patient was a young, non-diabetic, healthy male with no family history of CAD. He did not have

hypercholesterolemia or metabolic syndrome, did not smoke, use cocaine, or other illicit drugs, and should not have been at risk for myocardial infarction. However, he was taking modafinil for narcolepsy for approximately 20 months and we believe this drug could have contributed directly to his in-hospital hypertension, CAD, and ultimate myocardial infarction. Another consideration was that modafinil indirectly caused his CAD as a result of his in-hospital hypertension. For these reasons, modafinil was discontinued upon admission and after discharge for secondary prevention.

### Conclusion

Our patient was young and had minimal risk factors predisposing him to CAD. It is unclear whether the patient's long-term use of modafinil contributed to his course and need for intervention. Further prospective and/or retrospective studies of patients with long-term usage of modafinil may be beneficial to define the advantages and disadvantages of this drug better. Also, further genetic studies may help our understanding of why certain exposures correlate more strongly with CAD in some patients compared to others. Our case demonstrated that modafinil may play a role in the CAD spectrum and that clinicians should keep this in mind when prescribing this drug.

### References

- <sup>1</sup> Broughton RJ, Fleming JA, George CF, et al. Randomized, double-blind, placebo-controlled crossover trial of modafinil in the treatment of excessive daytime sleepiness in narcolepsy. *Neurology* 1997; 49(2):444-51. PMID: 9270575.
- <sup>2</sup> Ballon JS, Feifel D. A systematic review of modafinil: Potential clinical uses and mechanisms of action. *J Clin Psychiatry* 2006; 67(4):554-566.

- <sup>3</sup> Provigil.com. Welcome to the Provigil healthcare professional site. November 2013. Available at: <http://www.provigil.com/hcp.aspx>.

- <sup>4</sup> Kingshott RN, Vennelle M, Coleman EL, Engleman HM, Mackay TW, Douglas NJ. Randomized, double-blind, placebo-controlled crossover trial of modafinil in the treatment of residual excessive daytime sleepiness in the sleep

- apnea/hypopnea syndrome. *Am J Respir Crit Care Med* 2001;163(4):918-923. PMID: 11282766.
- <sup>5</sup> McGill HC Jr, McMahan CA, Zieske AW, et al. Association of coronary heart disease risk factors with microscopic qualities of coronary atherosclerosis in youth. *Circulation* 2000; 102(4):374-379. PMID: 10908207.
- <sup>6</sup> Azar RR. Coronary heart disease and myocardial infarction in young men and women. December 31, 2012. Available at: [http://www.uptodate.com/contents/coronary-heart-disease-and-myocardial-infarction-in-young-men-and-women?source=search\\_result&search=coronary+heart+disease+in+young+men+and+women&selectedTitle=1~150](http://www.uptodate.com/contents/coronary-heart-disease-and-myocardial-infarction-in-young-men-and-women?source=search_result&search=coronary+heart+disease+in+young+men+and+women&selectedTitle=1~150).
- <sup>7</sup> Libby P, Ridker PM, Maseri A. Inflammation and atherosclerosis. *Circulation* 2002; 105(9):1135-1143. PMID: 11877368.
- <sup>8</sup> Buffon A, Biasucci LM, Liuzzo G, D'Onofrio G, Crea F, Maseri A. Widespread coronary inflammation in unstable angina. *N Engl J Med* 2002; 347(1):5-12. PMID: 12097534.
- <sup>9</sup> Ridker PM. Clinical application of C-reactive protein for cardiovascular disease detection and prevention. *Circulation* 2003; 107(3):363-369. PMID: 12551853.
- <sup>10</sup> Pasceri V, Willerson JT, Yeh ET. Direct proinflammatory effect of C-reactive protein on human endothelial cells. *Circulation* 2000; 102(18):2165-2168. PMID: 11056086.

*Keywords:* chest pain, coronary artery disease, narcolepsy, modafinil