Case Report

Neostigmine induced coronary artery spasm: A case report and literature review

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Abstract

Neostigmine is a cholinesterase inhibitor which does not cross the blood brain barrier and a commonly used for reversal of nondepolarizing muscle relaxants. In the following case report, we present a patient who developed coronary artery spasm, after the administration of repeated doses of neostigmine. Ours is the first case to demonstrate such a longstanding coronary artery vasospasm that lasted several hours in response to neostigmine, resulting in myocardial damage and left ventricular dysfunction. We would like to draw the attention of the anesthesiologists to this rare effect that may lead to perioperative cardiac complications.

Keywords: Anesthesia, cardiology, complication, muscle relaxants, postoperative care

Introduction

Neostigmine is a commonly used drug in anesthesiology, meant for reversal of nondepolarizing muscle relaxants. In the following case report, we present a patient who developed coronary artery spasm, after the administration of repeated doses of neostigmine. Following the case report, we present a review of the literature for known cases of neostigmine induced coronary artery spasm, in order to draw the attention of anesthesiologists to this rare phenomenon, which may lead to perioperative complications.

Case Report

A 72-year-old white male with a history of heavy smoking, essential hypertension, hypercholesterolemia, depression and chronic back pain, presented to the emergency room for pain in his right groin, which started on the day of his admission. He had a known right inguinal hernia. Six weeks prior to his admission he was hospitalized due to right lower abdominal pain. Abdominal computerized tomography scan at that time demonstrated fat blurring, and he was diagnosed as having acute colitis. He was discharged home and then with antibiotics.

On the current admission, the patient was diagnosed as suffering from an incarcerated inguinal hernia, and he was sent urgently to the operating room. Medications on his admission included citalopram 20 mg, fluoxetine 20 mg, ramipril 5 mg, hydrochlorothiazide 12.5 mg, simvastatin 20 mg and tramadol hydrochloride 100 mg, once a day each.

The patient had an uncomplicated right inguinal hernia repair, in which a mesh was placed. The operation was performed with general endotracheal anesthesia. For induction, propofol 200 mg, fentanyl 100 ug and rocuronium 50 mg were given. Maintenance of anesthesia was with 2% sevoflurane and 50% nitrous oxide/oxygen mixture. During the 45 min operation, the patient also

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received morphine 10 mg and secondary to an incomplete muscle relaxation, 2 additional doses of rocuronium (10 mg each dose) were administered. At the end of the operation, neuromuscular blockage (NMB) was reversed with neostigmine 2.5 mg and atropine 1 mg and extubation was performed successfully.

In the recovery room, the patient's blood pressure was 190/100 mmHg, the pulse was 110 beats per minute (BPM) and regular, oxygen saturation 98% with a non-re-breathing face mask. The patient demonstrated muscle weakness, due to residual NMB, thus additional doses of neostigmine 2.5 mg and atropine 0.5 mg were given. Immediately afterward, the patient's blood pressure increased to 220/110 mmHg and his pulse increased to 140 BPM, with significant ST segment elevations seen on a single lead continuous electrocardiogram (ECG) monitoring, the patient was anxious with chest pain. An ECG showed sinus rhythm and a 1 mm ST segment elevation in leads II, AVF, and 2 mm ST elevation in chest leads V5 and V6 [Figure 1]. Due to anxiety, blood pressure elevation, and excessive tachycardia, the patient was given propofol 50 mg and labetolol 40 mg intravenous (IV). On a follow-up ECG, 40 min later, all ECG changes were sustained. The patient had no chest discomfort at that time, the patient was anxious, he had a regular pulse, no murmurs were heard, both lungs were clear to auscultation, his abdomen was soft and not tender to palpation, both legs were without edema. Repeat ECG 30 min later revealed sustained ST segment elevations in leads II, AVF, V5, V6.

An echocardiogram demonstrated hypokinesia of the inferior and lateral walls with a good contraction of the apex. At that point, the patient was suspected of having acute coronary syndromes, and was, therefore, given acetylsalicylic acid 300 mg PO, and heparin 5000 units IV and was transferred to the catheterization laboratory. Two hours after hernioplasty, the patient underwent coronary angiography through the right radial artery, which revealed nonsignificant coronary artery narrowing. The patient was diagnosed as having a coronary artery spasm due to repeated doses of neostigmine.

After the cardiac catheterization, the patient was transferred to the intensive cardiac care unit (ICCU) where he was treated with acetylsalicylic acid 100 mg, clopidogrel 75 mg, ramipril 5 mg and citalopram 20 mg orally. Repeat ECG demonstrated ST segment elevation of less than 1 mm in leads II, aVF, V_5, V_6. On the next day, an echocardiogram examination demonstrated a mildly reduced left ventricular function with hypokinesia of the mid inferior wall. Troponin levels increased to a peak of 1.243 ug/L on the 2nd postadmission day and were back to normal on the 4th postadmission day.

During the following days, the patient was well with no abdominal or cardiac complications and was discharged from the hospital on the 5th postadmission day.

Discussion

After having screened the available literature through PubMed, this is the third reported case of coronary artery spasm in humans as a result of neostigmine usage during reversal of neuromuscular block of anesthesia and the fifth case of coronary artery spasm in humans reported as a result of anticholinesterase medication usage. Kido *et al.*[1] described a coronary vasospasm as a result of neostigmine usage in anesthesiology that lasted 5 min with ST segment elevation on ECG and no documented myocardial damage on follow-up ECG or on blood tests. Hayashida *et al.*[2] described a case of coronary artery vasospasm that lasted several minutes after a prolonged operation of a cancer of the tongue.

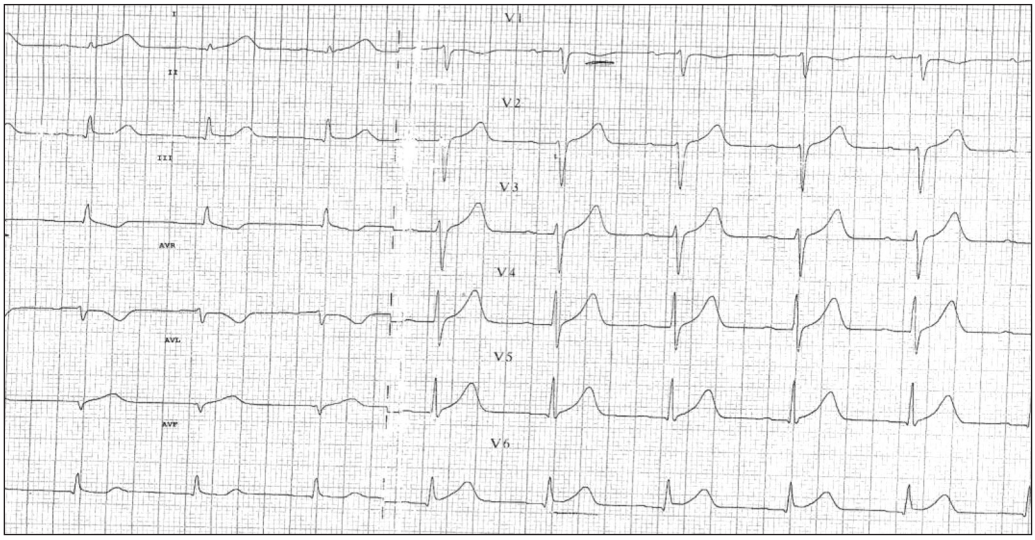

Figure 1a: 12 lead electrocardiogram taken at the recovery room during the patient's acute presentation with chest pain, with ST segment elevations in leads II, V_5 and V_6

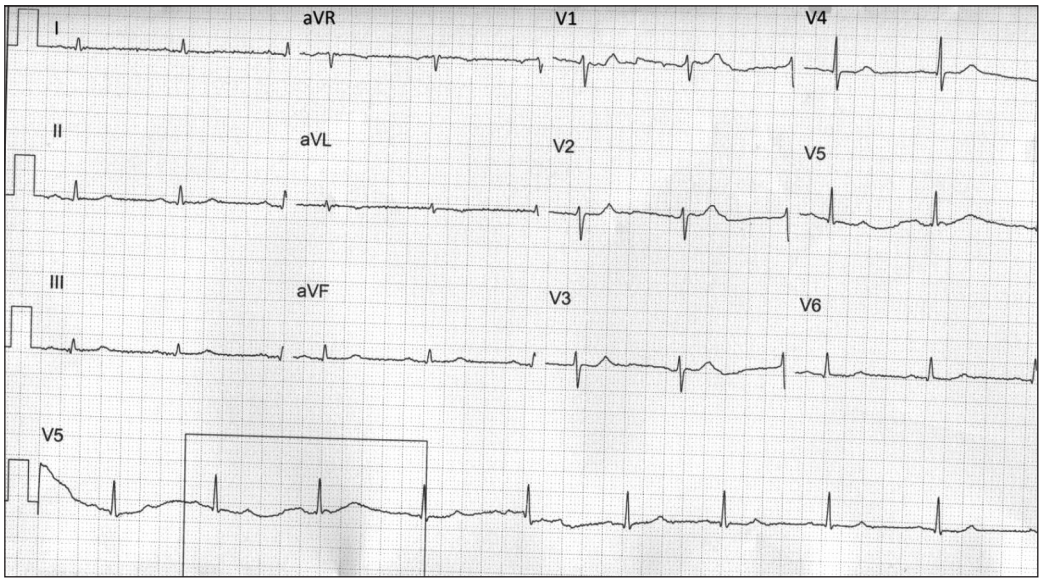

Figure 1b: 12 lead electrocardiogram taken after immediately after coronary catheterization, in the coronary care unit, ST segments in leads II, V_5 and V_6 returned to the normal isoelectric line

Comerci *et al.*[3] and Suzuki *et al.*[4] reported in addition to the known side effects of cholinergic medications (such as diarrhea, bronchospasm, salivation) rare side effects of coronary artery spasm in 2 cases in response to anticholinesterase drugs used to treat myasthenia gravis without residual left ventricular damage. Yamabe *et al.*[5] reported a case of coronary artery vasospasm that lasted 2 min with chest pain that resolved with the administration of nitroglycerin.

Ours is the first case to demonstrate such a longstanding coronary artery vasospasm that lasted several hours in response to neostigmine, resulting in myocardial damage and left ventricular dysfunction.

Neostigmine is a cholinesterase inhibitor which does not cross the blood brain barrier. By inhibiting acetycholinesterase, more acetylcholine is available at the synapse. Acetylcholine is expected to dilate normal coronary blood vessels by promoting the release of vasorelaxant substances from the endothelium. By contrast when the endothelium is damaged as in patients with atherosclerosis, acetylcholine paradoxically constricts coronary blood vessels.[6]

In this patient, inadequate reversal of NMB was diagnosed according to clinical symptoms. After the first dose of neostigmine, the patient was able to take normal respiratory tidal volumes and to lift and to hold his head up, however in the recovery room, the patient expressed symptoms of rebound muscle paralysis, such as an inability to lift his arms and head up and difficulty breathing. We did not have a neurostimulator in the recovery room; however, the clinical symptoms were so clear that we had no doubts regarding the diagnosis.

Sugammadex is a first pharmacological representative of a new class of selective muscle relaxant binding agents.[7] Sugammadex is used for the reversal of neuromuscular drug blockage by agents such as rocuronium and vecuronium, without any significant side effects. The relatively high cost of sugammadex limits its widespread use. However, it might be appropriate to use this drug in cases where repeated doses of neostigmine are administered.[8]

In our differential diagnosis, we considered the possibility of Takotsubo cardiomyopathy as a cause for this patient's clinical presentation; however, the echocardiogram of this patient was lacking the typical findings of Takotsubo cardiomyopathy: With apical ballooning and hypercontractile function of the base.

In addition, we considered a demand, supply mismatch as a cause of the patient's presentation, however such a clinical scenario usually happens in patients with diseased, atherosclerotic coronary arteries, in the presence of hypoxia or anemia, however our patient has been catheterized and nonsignificant narrowing were diagnosed, thus a demand supply mismatch doesn't seem likely in this patient. In case of a coronary spasm blood supply in the artery with spasm could be totally or partially reduced and in such a case a demand supply mismatch could occur, resulting in ischemia, and myocardial infarction with elevation of troponin and regional wall motion abnormalities on echocardiogram, this is also the reason why we decided to treat this patient with double antiplatelet therapy in (acetylsalicylic acid + clopidogrel) in the ICCU, he was discharged from the hospital with aspirin only.

Conclusions

We described a case of a patient who developed coronary artery spasm, associated with ST elevation and left ventricular dysfunction. The patient received repeated doses of neostigmine in order to reverse the effect of a nondepolarizing muscle relaxant. We would like to draw the attention of the anesthesiologists to this rare effect that may lead to perioperative cardiac complications. In this situation, sugammadex may be used to reverse the NMB without any significant side effects.

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Conflict of interest
There are no conflicts of interest.

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