J Anesth (2012) 26:905–909
DOI 10.1007/s00540-012-1442-2

CLINICAL REPORT

A case of coronary artery spasm caused by manipulation of the neck: heart rate variability analysis

Hirotsugu Miyoshi · Noboru Saeki · Ryuji Nakamura · Shigeaki Kurita · Masashi Kawamoto

Received: 19 December 2011 / Accepted: 19 June 2012 / Published online: 17 July 2012

Abstract A 66-year-old man with no history of ischemic heart disease underwent cervical lymph node dissection. General anesthesia was induced and maintained with remifentanil, along with propofol. With manipulation of the neck and a subcutaneous injection of lidocaine supplemented with adrenaline before the operation, a sudden decrease in blood pressure (BP) and elevation of the ST-T segment appeared on the monitoring electrocardiogram (ECG). Ephedrine, phenylephrine, adrenaline, and nitroglycerin were administered; however, the hypotension was sustained and the ECG abnormalities progressed, along with further elevation of the ST-T segment and a complete atrioventricular block. Following an injection of atropine, the changes in ECG and BP were attenuated. Heart rate variability (HRV) was analyzed using fully recorded monitor variables, and revealed an increase in the high-frequency domain at the time of the cervical manipulation, suggesting simultaneous vagal stimulation and coronary artery spasm. We concluded that the cervical manipulation had increased the vagal tone and we note that HRV analysis was useful to interpret this coronary event.

Keywords Coronary artery spasm · Heart rate variability analysis · Vagal stimulation · General anesthesia

H. Miyoshi (✉)
Department of Anesthesiology and Critical Care,
Hiroshima University Hospital, 1-2-3 Kasumi, Minami-ku,
Hiroshima, Hiroshima 734-8551, Japan
e-mail: h-miyoshi@hiroshima-u.ac.jp

N. Saeki
Department of Anesthesiology and Critical Care,
Hiroshima University, Hiroshima, Japan

R. Nakamura · M. Kawamoto
Department of Anesthesiology and Critical Care,
Graduate School of Biomedical Sciences,
Hiroshima University, Hiroshima, Japan

S. Kurita
National Hospital Organization Kure Medical Center
and Chugoku Cancer Center, Kure, Japan

Introduction

Coronary artery spasm is a rare but life-threatening complication during anesthesia. Various causes of coronary artery spasm are reported, though it is often difficult to determine the specific cause(s) in each case [1]. Manipulation of the neck is known to be one of the causes of coronary spasm during anesthesia [2]; however, the vagal stimulations have not been elucidated in the reported cases. We treated a patient who experienced a coronary artery spasm after cervical manipulation; analysis of heart rate variability (HRV) revealed vagal stimulation by the cervical manipulation as the suspected cause.

Case report

A 66-year-old man (height 165 cm; weight 57 kg) diagnosed with a hard-palate tumor was scheduled for cervical lymph node dissection. The patient had received radiation therapy for tongue cancer at the age of 51, chemotherapy and surgery for a gingival carcinoma at the age of 55, two operations for the hard-palate tumor at the age of 64, and radiation therapy for the hard- palate tumor at the age of 65. He had an treated hypertension; there was no history of tobacco use and no episodes of chest pain such as that caused by angina. No abnormal findings were noted in the preoperative examinations.

Anesthesia management

No medication was given prior to anesthesia. Electrocardiogram (ECG), non-invasive blood pressure (BP), and pulse oximetry were monitored (S/5M™; Datex-Ohmeda Division, GE Healthcare, Little Chalfont, Buckinghamshine, UK). Figure 1a shows the ECG waveform before anesthesia induction, at which time BP was 153/102 mmHg and heart rate (HR) was 55 beats/min. General anesthesia was induced with 50 mg of lidocaine, remifentanil at 0.5 μg/kg/min, and propofol at 3 μg/ml with a target-controlled infusion system (TCI pump TE-371™; Terumo, Tokyo, Japan), and 40 mg of rocuronium. Circulatory status was stable during tracheal intubation, followed by a decrease in BP (95/55 mmHg), which was attenuated (120/70 mmHg) with 6 mg of ephedrine.

Following antibiotic administration (1 g of cefoperazone), the neck was manipulated by the surgeon, and the patient was subcutaneously injected with methylene blue and 20 mg of lidocaine supplemented with 0.001 % adrenaline. Shortly thereafter, the patient's BP decreased from 110/65 to 73/40 mmHg and HR increased from 50 to 66 beats/min. Although cutaneous signs were unremarkable, we suspected anaphylactic shock caused by the antibiotic. We stopped the antibiotic administration and began treatment with vasopressors, fluid resuscitation, and ventilation with 100 % oxygen. However, the BP remained as low as 66/33 mmHg even with 6 mg of ephedrine and 0.7 mg of phenylephrine. The ECG showed ST-T segment elevation and second-degree atrioventricular block at 5 min after the decrease in BP (Fig. 1b). Next, we administered 25 μg of nitroglycerin, 0.1 mg of adrenaline, 20 mg of famotidine, 5 mg of D-chlorpheniramine, and 100 mg of hydrocortisone succinate. Although the BP increased to 94/40 mmHg, the ECG showed a third-degree atrioventricular block (Fig. 1c), which developed into a complete atrioventricular block (Fig. 1d). We then administered 0.5 mg of atropine, and 2 min after this the ECG was normalized (Fig. 1e), and BP and HR increased (175/80 mmHg and 110 beats/min, respectively). The duration of the circulatory collapse was about 20 min, and the volumes of infusions given during that period were 100 ml of extracellular fluid and 200 ml of colloid solution. We thought that coronary artery spasm had occurred although we had first suspected anaphylaxis. We thought that the coronary artery spasm was caused by parasympathetic stimulation induced by the neck manipulation. Because the parasympathetic stimulation had been reversed by atropine and the scheduled surgery was expected to be minimally invasive, we thought that we would be able to perform the surgery safely. Accordingly, the operation was performed as scheduled; emergence from anesthesia was smooth and the patient was extubated without complications. He did not complain of chest symptoms and no abnormal findings were seen on the 12-lead ECG. In addition, blood biochemical examinations, including creatine kinase, creatine kinase MB, troponin I, and human heart fatty acid binding protein, did not reveal any significant elevation at the end of the surgery, and the basophilic leukocyte count was not depleted.

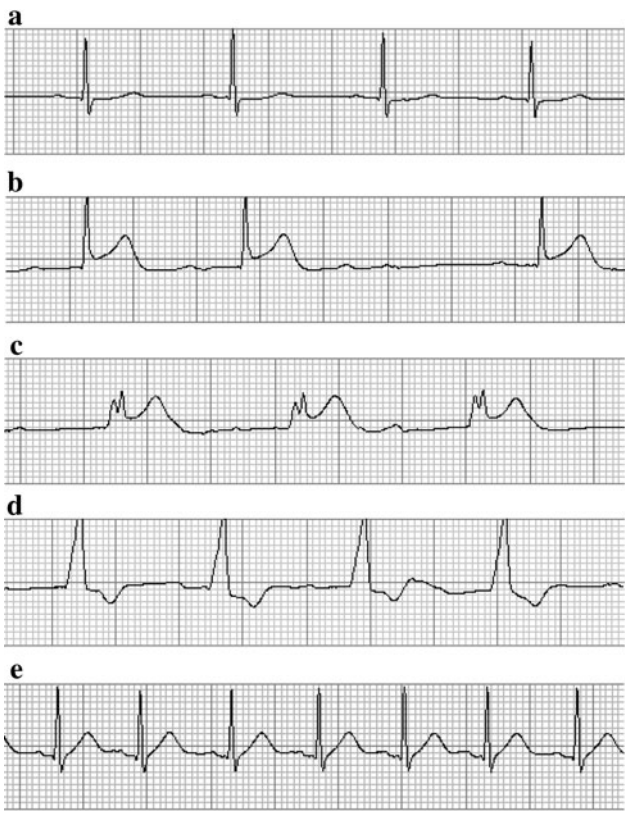

Fig. 1 Electrocardiogram (ECG) during anesthesia. **a** Baseline. **b** Five minutes after blood pressure decreased, ST-T segment elevation and second-degree atrioventricular block were observed. **c** Ten minutes after blood pressure decreased, third-degree atrioventricular block had developed, showing an intraventricular conduction defect. **d** Eleven minutes after blood pressure decreased, complete atrioventricular block had developed. **e** Two minutes after the administration of atropine, sinus rhythm was restored

Postoperative investigations

Coronary angiography was performed 1 week after the operation, with no significant stenosis being noted, indicating that acetylcholine loading had not provoked the spasm. Skin tests performed at 3 weeks after the operation were negative for the antibiotic, intravenous lidocaine, and methylene blue. We also analyzed HRV from the recorded ECG, using a data server (iCentral™, GE Healthcare Japan, Tokyo, Japan), which digitized the samples at 300 Hz, and a MemCalc/Tonam2 device (Suwa Trust, Tokyo, Japan), which analyzes HRV in the frequency

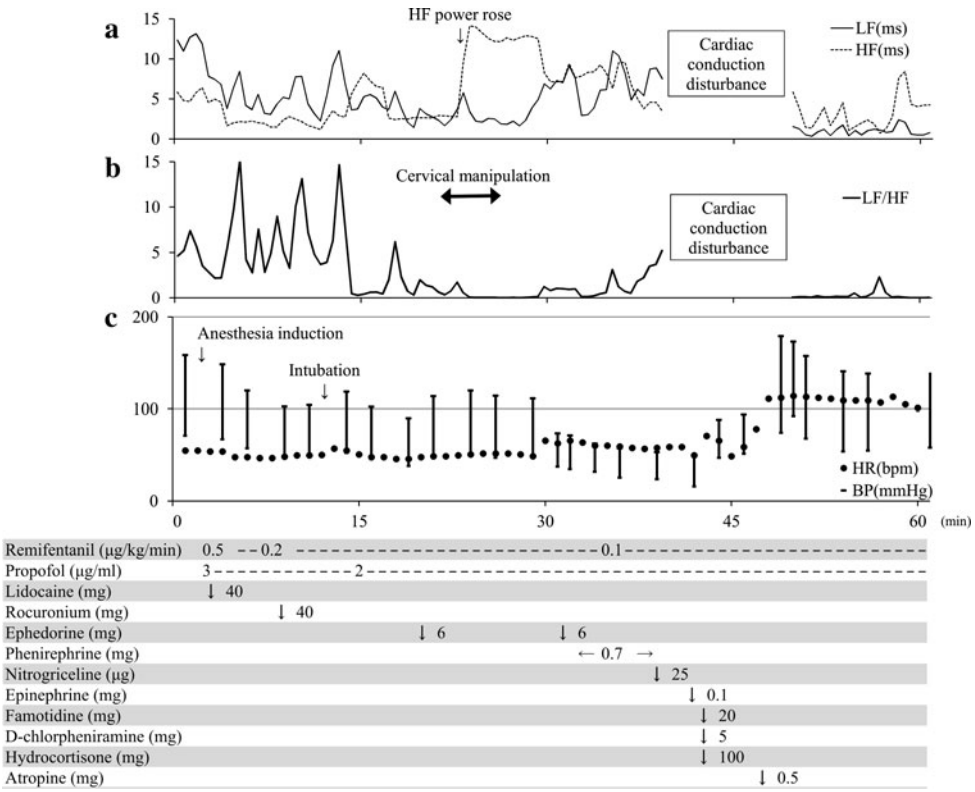

Fig. 2 Changes in heart rate variability (HRV) analysis, heart rate (*HR*), and blood pressure (*BP*). Changes in the spectral power of the low-frequency (*LF*; 0.04–0.15 Hz) and high-frequency (*HF*; 0.15–0.4 Hz) domains, and changes in the LF/HF ratio are shown in **a** and **b**, while the changes in HR and BP are shown in **c**. The *abscissa* represents the time course in minutes and the *ordinates* show the value of each component. Units in **a** and **b** are arbitrary. We could not analyze HRV in the blank periods shown in **a** and **b**, because of cardiac conduction disturbance

domain using a maximum entropy method (Fig. 2). The spectral power of the low-frequency (LF) (0.04–0.15 Hz) and high-frequency (HF) (0.15–0.4 Hz) domains, and the ratio of the spectral power in the two domains (LF/HF) were calculated. The HRV analysis revealed that an increase in HF power and a decrease in the LF/HF ratio had preceded the circulatory collapse. The HF power had remained high until the circulatory collapse occurred. Although HRV could not be analyzed during the period of disturbed cardiac conduction, the changes in HF power and the LF/HF ratio were attenuated following treatment with atropine. These findings suggest that the coronary artery spasm had been caused by vagal stimulation rather than by an allergic reaction.

Discussion

To the best of our knowledge, this is the first reported case of vagal stimulation-induced coronary spasm during general anesthesia documented by HRV analysis. A coronary artery spasm during anesthesia is rare, although studies have shown that it is more likely to occur in Japanese than in Caucasians, and more likely to occur in males, patients in their 60s, and those with no history of angina pectoris [1, 3]; each of these characteristics were present in our patient. Guidelines for the diagnosis of coronary artery spasm in non-anesthetized subjects are based on specific symptoms (chest pain at rest, often in the early morning), ECG findings, and provocation test results [4]. However, in anesthetized patients, a coronary artery spasm can only be diagnosed by ECG findings and a provocation test, because specific symptoms cannot be verbally noted. Reproduction of a coronary artery spasm by acetylcholine has been used for diagnosis [5, 6]. In the present patient, we found no significant stenosis in the coronary artery and could not reproduce the coronary artery spasm with acetylcholine. The sensitivity of variant angina to an acetylcholine load has been reported to range from 89 to 93 % [5, 6]. Thus, the inability to provoke a coronary artery spasm is not conclusive evidence of its absence. In our patient, we suspected the occurrence of a coronary artery spasm based on the decreased BP, disturbed cardiac conduction, and an ischemic pattern on the ECG findings.

Triggers of a coronary artery spasm during anesthesia include epidural anesthesia, the use of vasopressor agents, hyperventilation, hypotension, light anesthesia, vagal stimulation, and allergic reaction [3, 7]. Because of the rapid progression of circulatory derangement seen with this condition, the initial diagnosis and treatment are often based on the presumption of the condition after noting the timing between the initiation of a suspected trigger and the onset of symptoms. In our patient, multiple causes, including allergic reaction, the use of vasopressors, and

vagal stimulation were considered to be possible triggers, while hyperventilation, hypotension, and light anesthesia were not considered to have been possible triggers.

An allergic reaction or anaphylaxis was first suspected as the cause of the coronary artery spasm in our patient. When the event had occurred, the administration of an antibiotic and ephedrine, local anesthesia with lidocaine plus adrenaline, marking of the skin with methylene blue, and neck stimulation were being performed simultaneously. However, these these possible causes (apart from the neck stimulation) were soon considered to have been unlikely causes of the event, because: (1) cutaneous-mucus signs and bronchospasm were absent despite the presence of the severe cardiac symptoms, (2) there was no significant loss of intravascular volume, (3) prompt recovery was obtained with the use of atropine, (4) there was no depletion of the basophilic leukocyte count, and (5) the agents administered just before the hypotension had occurred were shown to be negative for allergic reaction by the results of skin tests.

Vagal stimulation and changes in the balance of the autonomic nervous system have been reported to provoke coronary artery spasm [8]. Therefore, in the perioperative period when the balance of the autonomic system becomes unstable, it is conceivable that a coronary artery spasm can occur. HRV analysis of the frequency domain is a known method for non-invasively evaluating autonomic nervous activity, and has an advantage in that sympathetic and parasympathetic activities can be separately measured [9, 10]. The spectral power of the LF domain reflects the sum of sympathetic and parasympathetic activities, while that of the HF domain reflects parasympathetic activity, and LF/HF is the ratio of the two that reflects the sympathetic and parasympathetic balance [9]. HRV analysis has revealed that parasympathetic activity associated with vasospastic angina is implicated in the development of coronary artery spasm [11]. Additionally, an earlier study revealed that HF power was increased prior to ST-T segment elevation in patients with variant angina [12]; although the patients in that report were not under general anesthesia at the time of the ST-T segment elevation, this finding corresponded to our result. Even in patients under general anesthesia, HRV is said to be useful for the analysis of autonomic balance [13]. In our anesthetized patient, as documented in the above study [12] (which was not carried out in anesthetized patients), increased HF power prior to the coronary spasm indicated that the event was induced by parasympathetic dominance. In our patient, neck manipulation was suspected to have been the trigger of the parasympathetic dominance, because the timing of the increase in HF power corresponded to the timing of the neck manipulation. In addition, after the administration of atropine, the derangements in the circulation and in cardiac conductance were attenuated, suggesting that vagal stimulation had been the cause of the coronary artery spasmt. It has been reported that propofol [14] and remifentanil [15] have an effect that causes parasympathetic stimulation. Thus, together with the use of these agents, the neck manipulation in our patient might have provoked parasympathetic tone.

The use of vasopressors has been reported to trigger coronary spasm [16]. In the present patient, it is possible that adrenaline administration had been one of the causes of the condition. We had administered lidocaine supplemented with adrenaline subcutaneously immediately before the coronary artery spasm occurred. However, based on the HRV analysis and the improvement after the administration of atropine, we considered that the main cause of this event had been increased parasympathetic activity. We note that we had administered ephedrine, which stimulates both alpha and beta receptors, 13 min prior to the event, with a second administration after the event had occurred. These findings suggest that ephedrine was not the cause of the coronary spasm in our patient.

To summarize, we experienced a case of coronary artery spasm just prior to surgery, in which hypotension, elevation of the ST-T segment, and a cardiac conduction defect were manifested. Based on HRV analysis, it appeared that vagal stimulation by cervical manipulation was the cause of the event. We recommend HRV analysis as being useful for investigation of the cause of coronary artery spasm.

Conflict of interest No external funding and no competing interests are declared.

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