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Prinzmetal's variant angina during laparoscopy: a case report of vasospasm in the context of cardiac arrest

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Abstract: We report the case of a 43-year-old male patient who experienced cardiac arrest during two elective laparoscopies for cholecystectomy. The first procedure was prematurely interrupted after the return of spontaneous circulation (ROSC) while the other was continued under intravenous (IV) perfusion of nitrates (isosorbide dinitrate). At each time, after a cycle of cardiopulmonary resuscitation (CPR) and injection of atropine 0.5 mg, sinus rhythm was restored. Only 3-lead electrocardiogram (ECG) outlines were recorded, showing ST-elevation in lead II. During the first incident, a coronary angiography was performed showing a vasospasm of the left anterior descending (LAD) coronary artery, reversible upon intracoronary injection of nitrates. ECG during catheterization showed ST-elevation in the anterior coronary territory. Calcium-channel blockers (CCB) were prescribed, and oral nitrates were added after the second episode. Cardiovascular prevention consisted in smoking cessation, aspirin and statins. Reporting this case seems to be relevant due to its unusual presentation: Prinzmetal's angina is usually described as morning chest pains, and it rarely concerns Caucasian men. Moreover, the vasospasm was associated with cardiac arrest and ECG changes suggestive of ST-elevation myocardial infarction (STEMI). The final diagnosis was myocardial infarction with non-obstructive coronary arteries (MINOCA) due to coronary vasospasm, a few minutes after insufflation of pneumoperitoneum. So far, few cases have been described during non-cardiac surgery, and even fewer during laparoscopy. Sharing our experience seems important to attract attention to cardiovascular events that can occur under general anesthesia, especially when clinical presentation is rare.

Keywords: case report; Prinzmetal's angina; general anesthesia; laparoscopy; cardiac arrest.

Introduction

By reporting the case of Prinzmetal's variant angina in a 43-year-old patient who suffered from cardiac arrest during elective surgery, we would like to attract attention to the presentation, the differential diagnosis, risk factors, diagnostic strategies and therapeutic ways to prevent any cardiovascular complications.

The particularity of our case lies in the absence of any cardiac history in a Caucasian male patient. Also, to our knowledge, Prinzmetal's variant angina has rarely been reported during laparoscopy for non-cardiac surgery: as patients under general anesthesia cannot complain about any chest discomfort, only a few cases of ECG changes triggering a coronary angiography showing findings consistent with located vasospasm, have been described. However, the hypothesis that in our case, the coronary vasospasm was a consequence and not the cause of the cardiac arrest, may not be completely ruled out. Transient severe bradycardia, even sinus arrest, may indeed occur during insufflation of the pneumoperitoneum. In this precise case, due to the recurrence of the incident despite a deep level of anesthesia and the response to IV infusion of nitrates, ECG changes and cardiac arrest could reasonably be attributed to a severe vasospasm of the LAD.

Narrative

A 43-year-old Caucasian man was admitted to the day case surgery center to undergo a laparoscopic cholecystectomy for recurrent cholecystitis. He had had a preoperative anesthesia evaluation a few days earlier. The medical history was clear for any cardiac or respiratory symptoms or events. The patient had stopped smoking a few years earlier (10 pack years). He also confessed drinking approximately seven energy drinks every day. He had no allergies and

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had undergone multiple shoulder surgeries under general anesthesia without any complications, but he had never undergone laparoscopic surgery. His medical treatment consisted of proton pump inhibitors (pantoprazol 20 mg, once a day). His physical examination was normal. Blood sample tests only showed hypercholesterolemia.

Therefore, institutional criteria for one-day surgery were met.

On the day of surgery, the NPO status was confirmed and pre-narcosis was administered (melatonin 2 mg and atropine 0.5 mg orally). Induction of anesthesia was performed by an experienced anesthesiologist. An opioid-free protocol was chosen as part of Enhanced Recovery After Surgery (ERAS). The goal was to allow the patient to recover more quickly after his operation and to reduce the length of his stay. It included: lidocaine, ketamine, propofol, clonidine, rocuronium and magnesium, weight-adjusted doses. A first-generation cephalosporin was injected after successful intubation (Cormack I, one attempt). Non-steroidal anti-inflammatory drugs (NSAIDS) and dexamethasone were administered as part of the multimodal pain management and prevention of postoperative nausea and vomiting (PONV). The pneumoperitoneum was insufflated, with pressures not exceeding 15 mmHg. No hemodynamic modifications were observed. The patient was then installed in Fowler's position. At the time of inserting the camera trocar, the patient went into cardiac arrest: at the scope, lead II showed an absence of atrial or ventricular activity, suggesting ventricular asystole. The loss of the end-tidal carbon dioxide ($EtCO_2$) and pulsoxymetry signals strengthened the diagnosis of cardiac arrest. Oxygen was administered at high inspiratory fractions while the surgical resident started CPR. After 2 minutes of CPR and injection of atropine 0.5mg, a sinus rhythm was restored, pulsoxymetry was above 90% and $etCO_2$ went back to previous values (above 30mmHg). In ECG lead II, an ST-elevation was noticed. Unfortunately, a 12-lead ECG was not available in the operating theater. There was no hemodynamic instability, and the patient was brought under general anesthesia to the adjacent facilities to perform a coronary angiography, where a 12-lead ECG was recorded. The exam revealed a thin aspect of the LAD artery in its middle and last myocardial parts (Fig. 1-3), that could be reversed by intra-arterial administration of nitrates (Fig. 4). There were no significant atherosclerotic lesions (luminal narrowing <40%) that could have justified a stent implantation. Echocardiography showed no signs of regional wall motion abnormalities. The ultra-sensitive troponin was negative at the time of procedure.

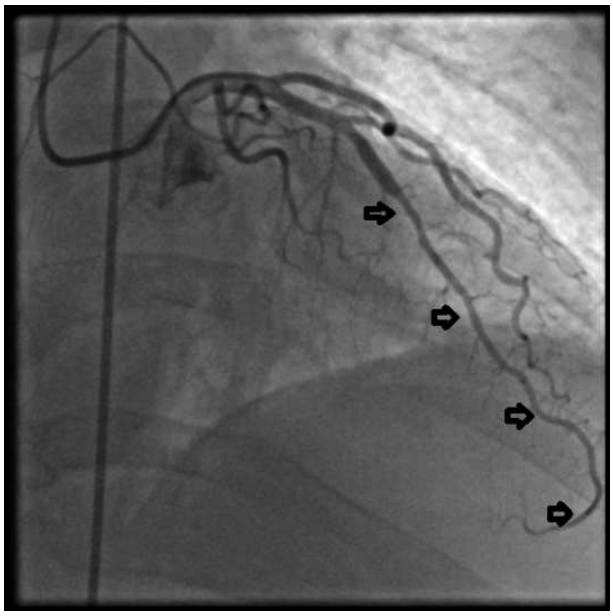

Fig. 1. — Thin aspect of the AIV in its intramyocardic part during catheterization.

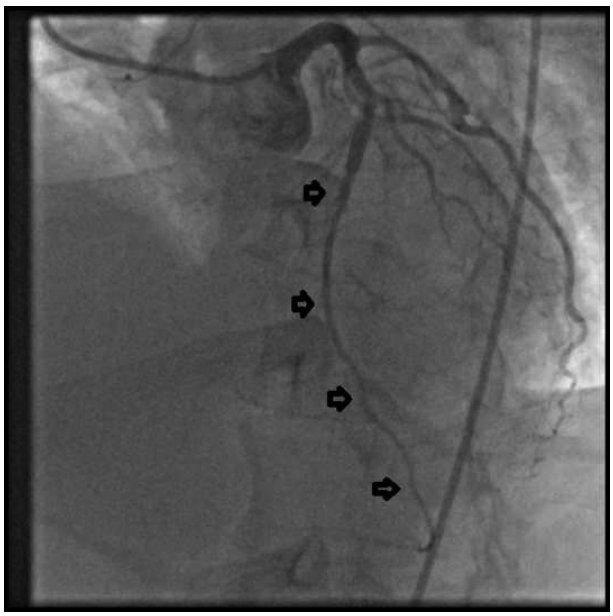

Fig. 2. — Milking aspect of the IVA in its intramyocardic part during catheterization.

After a short stay in the intensive care unit (ICU), the patient was discharged with a new adjusted treatment: a CCB was prescribed (diltiazem, 180 mg once a day). A follow-up appointment showing no sign of relapse allowed to re-perform the cholecystectomy.

During the rescheduled surgery, the exact same sequence happened despite deep relaxation and narcosis (bispectral index (between 40-60) and Train-Of-Four (at 0)). The pneumoperitoneum

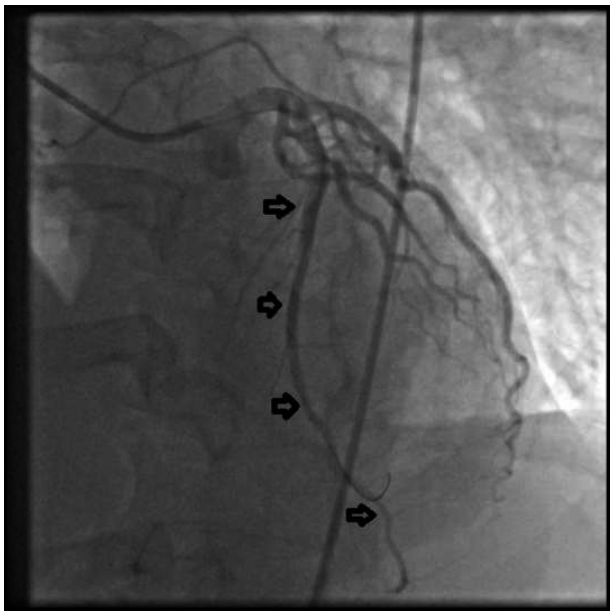

Fig. 3. — Per-catheterization of the milking AIV.

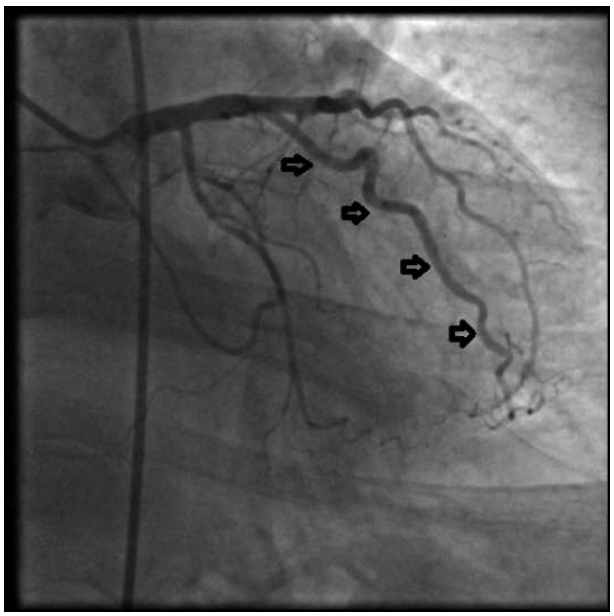

Fig. 4. — Overall view of the left coronary artery branches after the procedure.

was slowly insufflated, with low pressure (less than 12 mmHg). As during the previous time, insufflation and Fowler's position did not trigger any hemodynamic alterations. Loss of $etCO_2$ and pulsoxymetry signals happened at the introduction of the first trocar (Fig. 5). ROSC was obtained after CPR and IV atropine 0.5 mg. Oxygen was also administered with high inspiratory fractions. However, the ST-elevation was significant in lead II, as shown by 3-lead ECG outlines. Given the patient's hemodynamic restoration, the decision was taken to start a continuous infusion of nitrates

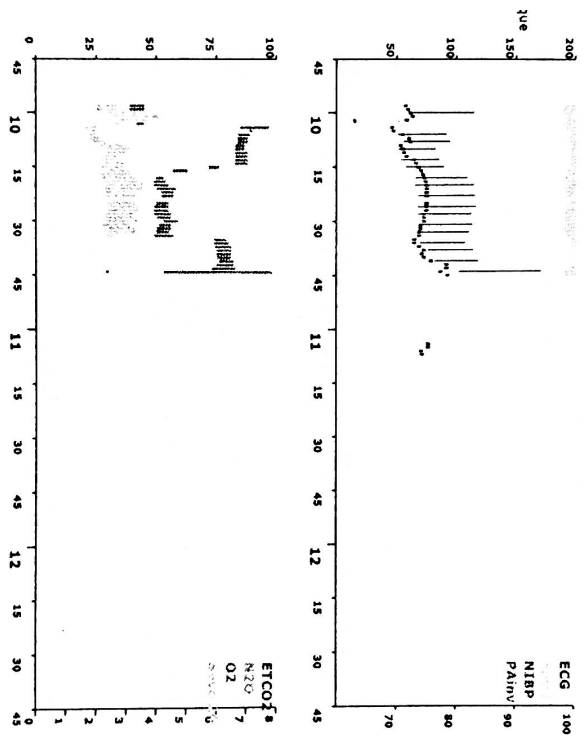

Fig. 5. — Peroperative vitals.

(isosorbide dinitrate). ST-changes progressively regressed. At awakening, the patient had no complaints. Echocardiography and follow-up ECG did not show any ischemic sequelae. Biomarkers stayed negative.

Discussion

In 1959, Dr. Myron Prinzmetal and colleagues published in the American Journal of Medicine a preliminary report about a new form of angina pectoris. The characteristic pain initially described by Heberden was here present at rest (or with light activity) and associated with transient ST-elevation that resolved with nitrates (1). The postulate was made that the clinical syndrome was caused by a spasm of a coronary artery, transiently occluding it and resulting in ischemia of the dependent myocardial territory (1, 2).

Nowadays, vasospastic angina is part of the MINOCA entity: myocardial infarction with non-obstructive coronary atherosclerosis (3). This re-groups myocardial infarction with angiography showing non-stenotic coronary arteries (≤50% stenosis) and without an overt cause for myocardial infarction, such as cardiac trauma or injury (4). Multiple entities can lead to this presentation, coronary vasospasm being one of them (3, 4). Three signs define the diagnosis: (1) nitrate-responsive angina, (2) transient ischemic ECG changes in the

absence of obvious causes for increased myocardial oxygen demand, and (3) angiographical evidence of coronary artery spasm (3, 5, 6).

Clinical presentation consists of typical chest pain, at rest, often in the early morning. It is relieved by sublingual nitrates (1, 2, 3). However, some patients have no complaint at all (1, 7). As for the diagnosis, a 12-lead ECG during the attack may show ST-elevation in the corresponding territory (3), but some cases of ST-depression have also been reported. Troponin C and creatinine kinase are not always as elevated as in STEMI in a context of obstructive coronary atherosclerosis (4, 8). The gold standard for diagnosis is coronary angiography (3, 5, 8) revealing the vasospastic epicardial part of the artery, either spontaneously or induced by the intra-coronary administration of acetylcholine. A positive test for vasospastic angina is defined as: (1) reproduction of chest pain, (2) ECG changes and (3) >90% narrowing of the artery (3, 8).

Vasospastic angina is multifactorial and has been attributed to a disequilibrium between the parasympathetic and orthosympathetic systems, endothelial dysfunction, oxidative stress, chronic low-grade inflammation (due to smoking for example), smooth muscle cell hypercontractility and genetic (3, 5, 7-9). It is triggered by the interaction of hyperreactivity of vascular smooth muscle cells and a transient vasoconstrictor stimulus acting on them, such as physical/emotional stress, stimulant drugs, para and ortho-sympathomimetic drugs, vasoconstrictor agents, ergot alkaloids and magnesium deficiency (5, 8, 9).

Prinzmetal's angina is more common among women, in the Japanese population (5, 9, 10) and between the age of 40 and 70 (3). As for all cardiovascular pathologies, smoking is a risk factor (7, 9). High levels of high - sensitivity - C - Reactive - Protein (CRP) have also been shown to be a risk factor, especially when associated with diabetes mellitus and in women (11).

Complications include life-threatening arrhythmias (bradycardia, sinus arrest, complete atrioventricular block, atrial fibrillation, ventricular tachycardia, ventricular fibrillation, asystole), myocardial infarction (as part of the MINOCA) and sudden cardiac death (8).

The treatment aims at preventing the recurrence of episodes of angina, and at preventing any complications. Two classes of drugs have proved effectiveness in treating vasospasm: calcium-channel blockers and nitrates (3, 5, 7, 8). By their vasodilator effects on both coronary arteries and the systemic circulation, CCB reduce oxygen demand and enhance oxygen supply to the myocardium (8). Either dihydropyridine or non-dihydropyridine CCB can be prescribed, taking into account side effects and the patient's profile (5). On the other hand, nitrates act mostly as systemic vasodilators, reducing myocardial oxygen demand (3, 5). Both therapies can be combined in case of refractory vasospasm (3, 7). Stent implantation can also be considered in patients resistant to drug therapy (3, 8). However, even if the location of the spasm is fixed over time, fluctuations can occur, including in segments adjacent to the stent (3). Implantable cardioverter defibrillators (ICD's) are still debated in patients with ventricular tachycardia or fibrillation (3, 7). Other medications are part of the secondary prevention of cardiovascular disease, such as statins. As for aspirin, its benefits are still debated, even in low doses (3, 5, 8). Moreover, a more global management must be set, including smoking cessation, prohibition of alcohol consumption, emotional stress, magnesium deficiency and vasoconstrictor drugs (5).

Recurrent episodes occur in about 4-19% (8). In patients presenting with acute coronary syndrome, advanced age and left ventricular dysfunction are poor predictive factors (8). By contrast, if the patient is on CCB or nitrates and risk factors are appropriately addressed, the prognosis is favorable (5, 8).

Interesting in our case was the patient's sex and ethnic group: most patients are women or Japanese men (5, 9, 10). Also, Prinzmetal's angina is characterized by morning chest pains (1). Our patient had been interviewed at multiple times and never reported any symptoms, the vasospasm being silent. One may not forget that under general anesthesia, no complaint can be expressed. However, at awakening, the interrogation did not reveal any symptom of chest pain.

Also, our patient presented ECG changes suggestive for ST-elevation myocardial infarction (STEMI) after cardiac arrest and ROSC. The only performed coronary angiography did not show significant atherosclerotic lesions (luminal narrowing <40%), which leads to classifying this event as part of the MINOCA entities (3, 4). Another argument in favor of a vasospasm was the response to continuous IV nitrates perfusion. Unfortunately, no 12-derivation ECG was available at the time of the events, but only during angiography and ICU stay (Fig. 6). Only 3-derivation ECG outlines could have been recorded, likely leading to misdiagnose the territory of the ischemia.

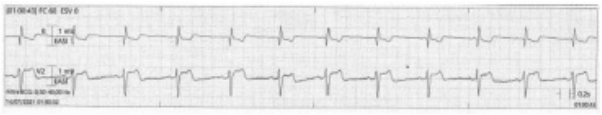

Fig. 6. — Postprocedure ECG showing persistent ST-elevation in the anterior territory.

Concerning the etiology of the spasm, one may think that it could be attributed to both surgical stress and hemodynamic modifications due to coelioscopy. Indeed, insufflation is well known to be a touchy phase during laparoscopy: both mechanical and neurohumoral factors alter hemodynamics as the pneumoperitoneum is administered (12). As a result, there is an imbalance between the para- and ortho-sympathetic systems (12). Transient severe bradycardia, even sinus arrest, may then occur during the insufflation of the pneumoperitoneum. Atropine was thus injected in first intention. However, in more reactive vascular smooth muscle cells, this imbalance may lead to a coronary vasospasm (3, 5, 7-9). In our case, sinus arrest happened in a situation where hemodynamic modifications due to coelioscopy and personal susceptibility interacted, and distinguishing whether the cardiac arrest was caused by a vasospasm or by the pneumoperitoneum seems difficult. However, all the drugs used for induction and maintenance of anesthesia – especially clonidine – aimed to reduce the orthosympathethic tone and the vasoconstrictive response that could trigger such a spasm. While ketamine has stimulating properties, but was here administered at a co-analgesic dose of 0.25 mg kg^{-1}. Also, during the second episode, depth of anesthesia and neuromuscular relaxation were monitored throughout the whole procedure to exclude inappropriate depth of anesthesia that could have resulted in reflex bradycardia during insufflation.

It may as well not be forgotten that the patient was a smoker, and that dyslipidemia had not been treated, both being relevant factors of general cardiovascular risk. He also drank many energy drinks a day, which are often listed as potent sympathetic drives.

As part of suspected myocardial ischemia management, a coronary angiography was immediately performed by a senior interventional cardiologist. At the time of the procedure, vasospasm was objectified in the middle part of the LAD artery and could be reversed with intracoronary injection of nitrates (Figure 4). The cardiologists concluded to Prinzmetal's angina. At the end of the procedure, it was decided not to place an intracoronary stent because of the absence of culprit atherosclerotic lesions.

As for the ultra-sensitive troponin, blood samples were negative at each time, being <1.5 ng L^{-1} the day of the surgery, and peaking at day 1, with a maximum of 16.42 ng L^{-1}. It slowly returned to baseline during the next days.

At last, the patient's treatment was revised: long-term CCB were prescribed (Diltiazem, 180mg, once a day), as well as aspirin 100 mg, once a day, and atorvastatine 40mg, once a day. Facing an early relapse, oral nitrates (isosorbide dinitrate 20 mg) were added on a daily basis. Lifestyle improvement was also advised.

Currently, the patient remains asymptomatic and does not suffer any secondary effects of his medications.

Conclusion

In conclusion, by reporting this case, we attract attention to cardiovascular events that can happen under general anesthesia, and particularly in laparoscopic surgery. Even patients presenting with only few cardiovascular risk factors may develop a perioperative cardiac event that can lead to dramatic consequences. Also, it is important to be aware that myocardial ischemia may be silent and may only become overt in specific situations. In our case, coronary angiography was the key exam to diagnose the coronary spasm and response to intravenous nitrates strengthened the first diagnostic hypothesis. Due to an effective communication between all actors – anesthesiologists, surgeons, cardiologists, and intensivists – the patient did not suffer any complication. The cholecystectomy could finally be performed.

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