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Observations on Coronary Spasm Complicating Non-Cardiac Surgery

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Abstract

For patients with pre-existing vasospastic angina, the risk of perioperative coronary artery spasm (PCAS) complicating non-cardiac surgery has not been quantified. Why PCAS occurs at all in patients without pre-existing vasospastic disease is unclear. The occurrence of PCAS was studied in 31 patients with a preoperative diagnosis of variant angina who underwent 54 non-cardiac surgical procedures. An extensive review of published literature was undertaken to summarize current knowledge of PCAS complicating non-cardiac surgery. In 31 patients with preoperative diagnosis of variant angina, in 54 non-cardiac surgeries, 9 morbid cardiac events occurred in 7 cases related to PCAS. In a larger group of patients with a diagnosis of variant angina, 7 were found who did not have a preoperative diagnosis of coronary disease, but who had their first episode of coronary spasm in the form of PCAS. In the medical literature describing cases of PCAS related to non-cardiac surgery, the incidence of PCAS in patients without preoperative coronary vasospasm was somewhere between 0.2 and 0.02 percent of cases undergoing non-cardiac surgery. In 40 of such cases, postoperative coronary angiography with provocative testing was positive for coronary spasm in 38 (95%). Thus, PCAS occurs rarely in the setting of non-cardiac surgery in cases without pre-existing coronary vasospasm. But it can cause potentially life threatening complications. In patients with pre-existing coronary vasospasm, PCAS is common and special preventive measures are justified to reduce the risk of its occurrence.

Keywords

Coronary artery spasm; Coronary vasospasm; Non-cardiac surgery; Perioperative coronary spasm

Abbreviations

- AV: Atrioventricular
- CPR: Cardiopulmonary resuscitation
- ECG: Electrocardiogram or electrocardiographic
- ISDN: Isosorbide dinitrate
- PCAS: Perioperative coronary spasm
- TEE: Transesophageal echocardiography
- VF: Ventricular fibrillation
- VT: Ventricular tachycardia

Introduction

This study is an attempt to shed light on several aspects of attacks of perioperative coronary spasm (PCAS) complicating non-cardiac surgery that have not been emphasized in the medical literature. First, what is the risk of such a complication of non-cardiac surgery in patients with prior proven vasospastic angina? Second, are there clues to an increased risk of PCAS in the preoperative evaluation of patients without a prior history of ischemic heart disease? Third, in retrospect is there something unusual about patients suffering PCAS in the absence of preoperative ischemic heart disease.

Methods

Patients studied

Prinzmetal's variant angina is part of the spectrum of coronary vasospastic disease [1-3]. Of 84 patients with variant angina first seen by me at the UCLA Medical Center between July 1963 and November 1989, 31 underwent a non-cardiac surgical procedure subsequent to the onset of their symptoms of vasospastic angina, and their experiences were studied in detail. The circumstances surrounding the very first episode of angina were examined in 100, personally studied variant angina patients, and 7 cases without a prior history of ischemic heart disease or anginal symptoms, but who first presented with PCAS related to non-cardiac surgery, are briefly described. Clinical information on these cases had previously been accomplished by review of pertinent hospital records, periodic examination

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of the patients, by phone calls to them or their physicians, or by a combination of these means. This study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in prior approval by the institution's human research committee. A requirement of informed consent from patients was waived because the data used was already in the author's possession from a prior approved study before this study commenced.

Definitions

Variant angina was defined as a transient, self-limited anginal discomfort accompanied by greater than 0.1 mv of ST segment elevation in at least one ECG lead, which disappeared promptly with subsidence of the episode, which was not associated with organic coronary arterial obstruction sufficient to account for this clinical picture, and which was not associated with evidence of myocardial infarction within two weeks of the termination of such an episode. Patients were considered in an active phase of their disease if they had at least one attack of spontaneous angina within the 6 months prior to their non-cardiac surgery.

Statistical analysis

Data means are expressed ± one standard deviation. Data were analyzed for level of significant differences with Fisher's exact test utilizing BMDP statistical software. Threshold for significance was set at $p<0.05$.

Literature review

In addition to my own collection of references on the subject, PubMed was searched for publications dealing with coronary spasm related to non-cardiac surgery and associated anesthesia starting with June 01, 2017 and going back as far as 1966. References in these publications were checked for additional information about the subject not obtained from the PubMed search.

Results

Patient characteristics

There were 12 men and 19 women with a preoperative diagnosis of variant angina who underwent 54 non-cardiac surgical procedures. Their average age at the time of surgery was 56 ± 10.0 years. The general nature of the procedures is listed in Table 1. At the time of surgery, 16 patients were in an active phase of their vasospastic disease, and the other 15 were in an inactive phase.

Type of anesthesia

The nature anesthetics used is summarized in Table 1. The general anesthetics usually included thiopentol or thioamytol, fentanyl, nitrous oxide and oxygen, with another inhaled anesthetic such as isoflurane or ethrane, and often a neuromuscular blocking agent such as succinylcholine or pancuronium.

Perioperative antianginal medication

Many of these procedures were carried out before 1980 when calcium channel blocking agents began to become available for general use in this country. Of the 25 instances where patients received some antianginal medication to cover them during their surgery, a calcium channel blocker was given by mouth shortly before the start of anesthesia in 18 cases, and was resumed as soon as possible postoperatively; in 12 of these instances oral isosorbide dinitrate (ISDN) or nitroglycerin ointment was also given at the same time as the calcium channel blocker; and in three cases intravenous nitroglycerin was also used throughout the procedure. In six instances only ISDN or nitroglycerin ointment was given at the start of the procedure and in the immediate postoperative period. In one case intravenous nitroprusside was used throughout the operative procedure. In 29 instances no antianginal medication was used peri-operatively.

Morbid events

There were 9 morbid cardiac events believed due to PCAS in 7 patients during or within 10 days after the 54 surgical procedures. During or within several hours following the procedure there were three events: intraoperative ventricular tachycardia (VT); hypotension with ST-segment elevation and asystolic cardiac arrest immediately postoperatively; postoperative ST elevation and shock (one case of each, and each recovered). There were additionally four cases of one or more uncomplicated, spontaneous anginal attacks 8 hours to 10 days postoperatively. One other patient died suddenly and unexpectedly on the second postoperative day, and yet another had an acute but nonfatal myocardial infarction on her 6th postoperative day.

Serious, non-fatal but potentially life-threatening events during surgery or within the first 6 post-operative days were more common in instances where no perioperative antianginal medication was used than in patients who did receive such treatment (5 of 29 versus 0 of 25; p=0.04). There was also a trend toward fewer perioperative morbid cardiac events for procedures done during an inactive phase of vasospastic disease compared with those done during an active phase (3 of 24 versus 6 of 30; p=0.24), but in this case the number of patients is too small to show statistical significance. There was no apparent relation between the severity of organic coronary artery disease on the most recent angiogram, or the presence of left ventricular wall motion abnormality and the risk of perioperative cardiac morbidity. Of interest

	Number of Procedures	Number of Patients	Type of Anesthesia*
Chest or lung surgery	4	4	G (4)
Abdominal surgery	12	8	G (12)
Peripheral vascular surgery	15	7	G (14)
Brain surgery	6	4	G (6)
Breast surgery	3	2	G (6)
Face lift surgery	3	2	G (3)
Eye surgery	3	3	G (1), L (2)
Lumbar spine surgery	1	1	G (1)
Thyroidectomy	1	1	L (1)
Carpal tunnel surgery	1	1	L (1)
Cystoscopy	2	2	G (1), L (1)
D & C	1	1	G (1)
Delivery of infant	1	1	E (1)
New pacemaker insertion	1	1	L (1)

Table 1: Types of surgery and anesthesia in 31 patients with Variant Angina.
*G=General anesthesia
L=Local anesthesia
E=Epidural block

was that there was no intraoperative or immediate postoperative cardiac morbidity in 13 of the 15 instances (87 percent) where patients were in an active phase of their disease but received no perioperative antianginal medication. Also of note is that the cases of death and myocardial infarction postoperatively occurred in two patients in an "inactive" phase of their vasospastic disease and who had received no perioperative antianginal medication.

Patients with no past history of coronary disease

Out of a group of 100 patients with a diagnosis of variant angina, 7 patients (not included in the 31 cases described above) were observed who had no past history of ischemic heart disease or anginal symptoms, but whose first episode of myocardial ischemia manifested as PCAS during non-cardiac surgery. None had evidence of perioperative myocardial infarction, and only one experienced anginal symptoms after recovering from the effects of anesthesia and surgery.

Literature Review and Discussion

Incidence

In a general population of patients undergoing non-cardiac surgery, the risk of PCAS is very low, and there is no justification for any special precautions against it. In the experience of one Japanese hospital only 18 episodes of PCAS were documented (0.02 percent of a total of 77,745 procedures), including 2 arrhythmic deaths [4]. Eight of these 18 had a diagnosis of angina pectoris (type unspecified) preoperatively. In another study, in 454 patients having lung surgery under cervical epidural blockade supplemented by light general anesthesia, Mizuyama et al. [5] found only one case (0.22 percent) complicated by PCAS. The present report indicates a much greater incidence of PCAS in subjects with the preoperative diagnosis of a form of vasospastic angina, and in such cases there is a need for special prophylactic perioperative precautions.

Nature of patients whose non-cardiac surgery was complicated by PCAS

In a major review of articles on the subject published between 1966 and 1998, Koshiba and Hoka [6] identified 104 cases of PCAS in Japanese patients undergoing non-cardiac surgery. Another review (in Japanese with English abstract) found 56 case reports of PCAS [7]. My own review identified 134 cases [4,8-102], many of which are likely duplicates of those reported by Koshiba and Hoka [6] and by Chang and Hanoaka [7], but supplemented by 64 cases published after 1998. Many cases of PCAS are not included in my review because the journal articles were unavailable to me or were in Japanese without a satisfactory English summary.

Some characteristics of these cases are shown in Table 2. A predominance of men, mean age over 56 years, and the great majority of cases in subjects without prior ischemic heart disease were similar to the findings of others [6,7]. Presence of risk factors for coronary atherosclerosis (e.g., smoking, high lipid levels, hypertension, diabetes) were common, especially in older patients, but many cases had none of these risk factors. Most attacks of PCAS occurred during the surgical procedure, but some happened during induction of anesthesia, and others in the immediate postoperative period.

	n*	
Age	102	Mean of 56.6±14,1 (SD) years; Range 18-80 years
Gender	119	78 Male; 41 Female
Presence of preoperative angina pectoris	133	15 with vasospastic angina; 10 with type unclear
Type of anesthesia	126	
General alone		74
General with epidural		21
Epidural alone		10
Spinal w/wo general or epidural		12
Local		9

Table 2: Characteristics of Patients with PCAS Reported in the Literature.
*n: Number of cases for which this information was available.
PCAS=Perioperative coronary artery spasm
w/wo=With or Without.

	n*	Observed in Cases	Percent
ECG changes on monitored lead(s)	103		
ST segment elevation only		85	82.5
ST elevation and depression		6	5.8
ST depression only		11	10.7
T inversion only		1	1
Complications of PCAS			
Hypotension	109	70	64.2
Ventricular tachycardia	110	37	33.6
Ventricular fibrillation	132	22	16.7
Complete AV block	127	12	9.4
Biomarker indicated myocardial infarction	130	20	15.4
Q wave myocardial infarction	130	2	1.5
Death	133	3	2.3
Postponement or cessation of incomplete surgery	120	27	22.5

Table 3: ECG findings during and Complications of PCAS in published case reports.
n*=Number of cases for which information available.
ECG=Electrocardiogram.
PCAS=Perioperative coronary artery spasm.

Diagnosis of PCAS and accompanying ECG changes and complications

Table 3 summarizes ECG findings during and complications of PCAS. As expected, acute and transient ST segment elevation in the monitored lead(s) was by far most common, but only ST segment depression was found in a minority of cases, and both ST elevation and depression at different times were also occasionally seen. Such ST segment shift is the most useful sign to suggest presence of PCAS. Which ECG lead or leads to monitor can be debated. The most common lead used appeared to be some form of modified lead II, and one similar to V_5 was a frequent second lead. Additional information might be obtained from a third lead similar to V_2 or V_3 to detect an ST injury vector directed anteriorly or posteriorly [103]. Some have advocated the use of intraoperative transesophageal echocardiography (TEE) in order to assist in early detection of PCAS; new regional ventricular wall motion abnormalities may appear before ST segment shift is seen on the surface ECG. [71,82].

Significant hypotension was the most common complication, and often was the presenting finding even before ST segment shift was recognized. In some such cases it is difficult to rule out a role for the vasoactive medications used to treat the hypotension (often ephedrine, epinephrine, dopamine, phenylephrine or methoxamine) in the production of the PCAS.

Arrhythmias were common and often of a life-threatening nature (e.g., VT, ventricular fibrillation (VF), complete AV block). Occurrence of VF almost always required a period of cardiopulmonary resuscitation (CPR) and use of direct current electrical cardioversion. Episodes of complete AV block were usually transient and did not require emergency cardiac pacing. The three deaths resulting from PCAS were due to VF, and in one of these death occurred despite implantation of a cardiac defibrillator in a patient with a history of preoperative coronary spasm [43].

In 19 cases surgery was postponed or aborted because of PCAS; this was due wholly or in part to the occurrence of VT (9 cases), VF (7 cases), or complete AV block (2 cases). In 16 instances in 14 cases, the surgery was repeated 1 week to 3 months after the first try. In 8 instances in 7 patients, the same type of anesthesia without prophylactic coronary vasodilators was repeated, and in 6 of these instances, PCAS recurred. None of these 6 patients had a history of ischemic heart disease prior to their first surgery, and none experienced anginal symptoms in the interval between surgeries. In 4 instances in 3 patients repeat surgery with the same anesthetic was done, but with perioperative coronary vasodilators (usually intravenous nitroglycerin and a calcium channel blocker), and in 4 instances a different anesthetic method was used on the second try, and PCAS recurred in none of these.

Treatment of PCAS

Once PCAS was suspected, addition of intravenous nitroglycerin or ISDN was frequently effective in resolving the vasospasm, but occasionally addition of an intravenous calcium channel blocker (e.g., diltiazem or nicardipine) was required. Additional boluses of nitraoglycerin, ISDN, or calcium channel blockers may be needed in patients whose PCAS occurs while on continuous intravenous infusions of these agents. Special treatment of complicating arrhythmias usually required addition of intravenous lidocaine and/or CPR measures. Use of amiodarone can be considered if latter measures fail to abort VT or VF; it was developed initially as a coronary vasodilator and has been used to treat variant angina [104]. If the procedure must be postponed or aborted, it is likely that it could be successfully carried out in the near future with a different approach to anesthesia and suitable precautions against coronary spasm [16,20,25,47,48,52,61,70,98].

Specific conditions provoking PCAS

In a few cases, specific stimuli were believed to have triggered the PCAS. These included anaphylactic reactions to a medication [40,50], or to a blood transfusion [41]; respiratory alkalosis secondary to either accidental or purposeful hyperventilation [57,90]; use of cocaine for local anesthesia [30]; use of the non-selective beta-adrenergic blocker propranolol to treat epinephrine-induced tachycardia [94]; use of ergonovine or sulprostone with or without ergonovine for postpartum uterine atony [31,59,76]. In most cases of PCAS, however, there was no clear precipitant, and common speculation was that the event was triggered by reflex increase in vagal tone produced by manipulation of a part of the body.

Postoperative management

Postoperative check of biomarkers of myocardial cell death seemed worthwhile, as this allowed a diagnosis of non-q wave myocardial infarction in about 1 out of every 6 cases. These were usually small infarcts but often associated with modest and transient regional wall motion abnormalities. Non-invasive, radionucleide-based studies of myocardial sympathetic receptor activity with ^{123}I-β-methyl-iodophenyl pentadecanoic acid and ^{123}I- metaiodobenzylguanidine may be useful in some cases, as abnormalities in this regard may persist for a week following a bout of transmural myocardial ischemia [22,105,106].

Coronary arteriography to help diagnose and evaluate the substrate for PCAS was done immediately post-procedure to several weeks postoperatively in 73 patients, and it seemed to be a useful diagnostic adjunct. Coronary anatomy was described as normal or "no stenoses" in 25 cases. "Non-obstructive" or "non-critical coronary disease was noted in 37 cases. Only 3 subjects had the presence of one or more greater than 50 percent fixed stenosis of a major coronary artery. Eight additional cases showed significant coronary stenoses on initial angiography that proved to be due to coronary spasm as in all the coronaries appeared to be normal following intracoronary nitroglycerin or ISDN.

Of special interest is that out of the 40 of the cases having a postoperative coronary angiogram accompanied by a provocative test for coronary spasm days or weeks after the surgery, 38 (95 percent) had a positive provocative test [4,8,9-19,21-26].

Long-term follow-up of cases without preoperative coronary spasm

Long-term follow-up information on these case is limited. Including the 7 cases presented in the present study, 26 cases were found with follow-up information after their PCAS extending from 3 weeks to more than 1 year post-operatively. Of these, only two patients experienced chronic anginal symptoms following recovery from the surgical procedure. Given the very high rate of positive provocative tests for coronary spasm in cases with PCAS which did not have preoperative evidence of ischemic heart disease, and given the rarity of clinical coronary vasospasm after recovery from the precipitating surgery and anesthesia, it seems likely that these cases of PCAS are occurring in patients with an inherent predisposition for coronary spasm at that time in their lives, which however is unmasked by the special stresses of the anesthesia and surgery, but not by those of daily life. The cause and duration of this predisposition are unknown. The limited data on long-term follow-up of these patients also leaves unknown whether they are a greater than average risk for subsequent development of clinical ischemic heart disease or sudden death, and whether any special postoperative treatment is warranted.

Long-term follow-up studies on these patients are needed. Where available, genetic studies on such patients are also needed to seek the presence of hypofunctioning alleles of genes involved in production of endothelial nitric oxide synthase or hyperfunctioning ones involved in regulating Rho-kinase activity [107,108]. Presence of such genetic factors would suggest additional means for preoperative screening for risk of PCAS, and for preventive treatment. Prudence suggests that subjects having PCAS be placed on coronary vasodilator therapy including a calcium channel blocker for at least a few months postoperatively, and then be considered for tapering off such medication if no anginal symptoms have occurred and long-term ECG monitoring documents the absence of asymptomatic ST segment

shifts and significant arrhythmia. Control of risk factors for coronary atherosclerosis such as smoking, diabetes, hypercholesterolemia is important. In patients with vasospastic angina, the use of statin therapy may reduce the risk of anginal attacks if a favorable effect is achieved on hyperlipidemia [3].

Long-term follow-up of patients with preoperative vasospastic disease

There is no evidence that the occurrence of PCAS in patients with a pre-procedure diagnosis of vasospastic disease alters the course of their disease unless a major myocardial infarction or death occurs, or the event prompts a major change in the treatment of their vasospastic disease.

Prevention of PCAS in high risk subjects

In patients with a known propensity to coronary spasm (e.g., variant angina as demonstrated in this study, or subjects who had previously experienced an episode of PCAS), special precautions are justified in view of the relatively high risk of PCAS. Consider scheduling elective surgery in the afternoon rather than the morning because of the circadian distribution of spontaneous coronary spasm [3]. Effective coronary vasodilators should be continued throughout the perioperative period. Consider use of continuous intravenous nitroglycerin at dosage of 1.0 μg/kg/min starting before anesthesia induction and continuing into the postoperative period with gradual tapering off [109]. If, because of the length or nature of the surgery, continuous therapeutic levels of a calcium channel blocker cannot be maintained with perioperative oral medication, use should be made of intravenous infusions (e.g., diltiazem or nicardipine). Any electrolyte abnormality should be corrected before surgery if possible, particularly hypomagnesemia [3]. If it can be done without sacrificing patient safety and comfort, epidural and spinal anesthesia should be avoided because of the theoretical reflex increase in alpha-adrenergic vasoconstrictor activity in the upper part of the body (including coronary arteries) when sympathetic activity is blocked in lower portions of the body. There should be avoidance of respiratory alkalosis due to hyperventilation [3]. As noted above, where possible, vasoconstrictor agents should be avoided. Patients should be kept warm unless hypothermia is required for the procedure [3]. Special care is needed when manipulating organs or stimulating regions likely to result in reflex increase in vagal tone (e.g., near the carotid sinus in the neck or abdominal viscera).

Limitations of the study

Retrospective analysis of data on occurrences of PCAS are not as reliable as would be data obtained prospectively, but such has so far not been available. The incidence of PCAS is probably underestimated, as its occurrence may not be recognized, especially if ST segment shifts on the monitored ECG are very transient and not accompanied by fall in blood pressure or arrhythmia. The incidence of serious complications of PCAS, arrhythmic and otherwise, is probably overestimated by a literature review, as the presence of such complications are more likely than their absence to prompt publication of case reports. The paucity of long-term follow-up information on patients having PCAS really limits our understanding of its possible prognostic significance. As most cases of PCAS reported in the literature are Japanese, there has been speculation that racial/genetic factors predispose subjects from the Far East to coronary spasm, and therefore the conclusions reached from the above literature review would not necessarily be valid for Western populations [3]. On the other hand, my own observations suggest that physicians in the West (particularly the United States) shy away from performing provocative tests for coronary spasm, and do them far less often than physicians in Japan. If you don't compulsively look for something, you're less likely to find it. Coronary spasm is still a significant problem in Western populations. A recent study involving patients from Western countries found a 33.4% incidence of positive intracoronary acetylcholine tests for spasm of epicardial coronary arteries in a large group of patients having angiography for evaluation of angina-like chest pain but who had no obstructive coronary lesions [110].

Summary and conclusions

Coronary spasm during non-cardiac surgery and the associated anesthesia can be complicated by potentially life-threatening dysrhythmias and rarely myocardial infarction or death. In patients with no prior history of ischemic heart disease or anginal symptoms, coronary spasm is a very rare complication of such procedures. There is no practical means of predicting before the surgical procedure which of such subjects will have this complication. However, patients with preexisting vasospastic angina are at much greater risk for perioperative attacks, and special precautions are justified to reduce this risk. Special methods for diagnosing and treating PCAS are available. Most subjects having PCAS in the absence of preoperative vasospastic disease may have a constitutional predisposition to coronary spasm which is only unmasked by the unusual stresses of anesthesia and surgery, but not provoked by the stresses of daily life. Although little data is available on the long-term prognosis of such patients, most, in the absence of repeated anesthesia and surgery, seem not to have recurrence of coronary spasm following recovery from the non-cardiac surgery.

As mentioned above, there is need for further research in this area. Formal, prospective studies are needed on the risk of PCAS in patients with pre-existing coronary vasospasm undergoing non-cardiac surgery with appropriate perioperative prophylactic vasodilator treatment. Unmedicated controls in such studies would not be possible, given considerations of patient safety. Additional information is needed on the incidence of PCAS in patients without pre-existing coronary vasospasm undergoing non-cardiac surgery. Such patients suffering this complication need to be studied more intensively to determine whether there are factors present that might allow pre-operative prediction of the likelihood of PCAS, whether they need any special treatment following their recovery from the surgery and associated anesthesia, and whether they are at increased risk of subsequent development of some form of coronary heart disease or sudden death.

Conflict of interest

The Author declares that there is no conflict of interest.

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