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Postinduction Paced Pulseless Electrical Activity in a Patient With a History of Oropharyngeal Instrumentation–Induced Reflex Circulatory Collapse

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Background: Reflex hypotension and bradycardia have been reported to occur following administration of several drugs associated with administration of anesthesia and also following a variety of procedural stimuli.

Case Report: A 54-year-old postmenopausal female with a history of asystole associated with sedated upper gastrointestinal endoscopy and post–anesthetic-induction tracheal intubation received advanced cardiac resuscitation after insertion of a temporary transvenous pacemaker failed to prevent pulseless electrical activity. The patient's condition stabilized, and she underwent successful cataract extraction, intraocular lens implantation, and pars plana vitrectomy.

Conclusion: Cardiac pacemaker insertion prior to performance of a procedure historically associated with reflex circulatory collapse can be expected to protect a patient from bradycardia but not necessarily hypotension.

Keywords: *Anesthesia–general, heart arrest, pacemaker–artificial, shock*

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INTRODUCTION

Reflex hypotension and bradycardia have been reported to occur following administration of several drugs commonly used in association with the administration of anesthesia (Table 1)[1-19] and in association with a wide array of medical procedures (Table 2).[4,5,7,8,13,14,17,20-34] We report a case in which the preoperative insertion of a temporary transvenous cardiac pacemaker (TTvP) prevented asystole but did not prevent (paced) pulseless electrical activity.

CASE REPORT

A 54-year-old postmenopausal female was scheduled to undergo cataract extraction, intraocular lens implantation, and pars plana vitrectomy under general anesthesia. Her preprocedural medical problem list and treatment regimen are shown in Table 3.

The patient had had 4 prior episodes of medical procedure–related reflex asystole (confirmed by pulselessness and, if awake, loss of consciousness) during 3 anesthetic inductions. Following rapid-sequence general anesthetic induction (fentanyl, propofol, succinylcholine) and tracheal intubation for a (canceled) cataract extraction, the patient experienced asystole requiring cardiopulmonary resuscitation (CPR) and intravenous (IV) administration of epinephrine. She had had 3 episodes of severe bradycardia during 2 upper gastrointestinal (GI) endoscopic examinations under IV sedation without topical anesthesia. During one (canceled) procedure 12 months prior to the present admission, the sedative medication used was etomidate (total dose of 20 mg). The same procedure 5 days later was successfully completed following preprocedural insertion through a femoral vein of a VVI TTvP programmed to ensure a heart rate of at least 70 bpm (sensitivity 3 mA, output current 10 mA). Doses of sedative medication during this second attempt at upper GI endoscopy were midazolam 2 mg, propofol 50 mg, and ketamine 100 mg. Also during this second attempt at GI endoscopy, IV atropine (0.1-0.2 mg) was administered on 3 occasions in response to the occurrence of a paced cardiac rhythm, each dose returning the patient to sinus rhythm at her baseline rate of 90-100 bpm.

The patient's surgical/procedural history included uneventful colonoscopy 2 years prior, 2 cesarean sections, and bilateral tubal ligation. Anesthesia records for these procedures were not available.

The patient had no known allergies. Her preanesthetic physical examination was unremarkable except for morbid obesity with concerns for possible difficult mask ventilation and difficult tracheal intubation. Results of relevant preoperative tests are shown in Table 4. The patient's vital signs at the time of presentation to the preoperative nursing unit

Table 1. Drugs and Administration Techniques Employed in Association With Administration of Anesthesia Reported Capable of Causing Severe Bradycardia/Asystole and Hypotension

Central Nervous System Depressants	Neuromuscular Blockers and Reversal Agents	Other Agents
Propofol[1,2]	Succinylcholine[9]	Local anesthetics (local,[13] regional,[14] neuraxial[15,16]; also insufficient local anesthesia[17,18])
Fentanyl[3] and analogues[4-6] (also insufficient fentanyl[7])	Vecuronium[4,5]	Beta blockers[4]
Dexmedetomidine[8]	Neostigmine (heart transplant recipient[10,11] or child[12])	Diltiazem[4]
		H2 antagonist antacids[19]

Note: Bradycardia/asystole and hypotension events often involve multiple drugs, procedural stimulation, or preexisting cardiac disease.[7]

were noninvasive blood pressure (NIBP) of 142/69 mmHg, heart rate of 71 bpm, respiratory rate of 20 breaths per minute, and oral temperature of 36.9°C. Cardiac and respiratory examinations were unremarkable. Point-of-care blood glucose was 168 mg/dL (not treated).

After completion of all preoperative checks, the patient was taken to the operating room without sedation according to the surgical suite policy requiring the patient to speak with the surgeon before any sedative drug can be administered. Standard noninvasive monitors were attached, and readings were logged every minute into an electronic medical record. The first NIBP reading was 234/117 mmHg. The electrocardiogram (ECG) monitor showed sinus rhythm with no change in heart rate. Because of a hospital no-sedation-prior-to-proceduralist-arrival policy, the increase in blood pressure was treated with reassurance and commencement of IV nitroglycerine titrated to a final infusion rate of 33 mcg/min; the treatment achieved an NIBP of 173/92 mmHg with no change in heart rate.

After the required patient-surgeon discussion, the patient received a total of 3 mg of titrated midazolam sedation during insertion of a TTvP. After internal jugular cannulation, a 0.5-mg prophylactic dose of atropine was administered prior to pacemaker wire insertion with no change in heart rate. During wire insertion, the patient suddenly announced that she "felt funny" and lost consciousness. The ECG monitor showed asystole, so CPR was started, and a 1-mg IV bolus of atropine was administered. Within a minute, the patient regained full consciousness with a heart rate and pulse rate of 85 bpm. Soon after, the pacing wire was connected to the pacemaker and the current was adjusted to 10 mA to achieve ventricular capture at a heart rate of 60 beats per minute.

Table 2. Medical Procedures Associated With Severe Bradycardia/Asystole and Hypotension

Laryngoscopy[4,7,20]
Liver biopsy[5]
Sigmoidoscopy[21]
Periosteal stimulation (even with effective spinal anesthesia)[22]
Skull base surgery (including transsphenoidal)[5,23]
Abdominal surgery (open or laparoscopic)[5,24-26]
Patient movement to beach chair position[8,27,28]
Eye surgery,[5] orbital surgery,[13] eyelid surgery,[13] and retrobulbar block[13]
Facial or maxillofacial surgery,[5,29,30] dental extraction,[17] and mouth prop insertion[31]
Electroconvulsive therapy[32,33]
Hypodermic needle puncture[14,34]

After uneventful completion of TTvP insertion, the patient was preoxygenated with 100% oxygen delivered via face mask. Immediate preinduction vital signs were NIBP of 177/112 mmHg and heart rate of 72 bpm (sinus rhythm). A rapid-sequence anesthetic induction regimen was chosen out of concern for possibly difficult mask ventilation and intubation and obesity-related and diabetic gastroparesis–related increased risk of regurgitation of gastric contents. To achieve rapid hypnosis, lidocaine (50 mg), fentanyl (250 mcg), and propofol (150 mg) were administered along with continuation of the nitroglycerine infusion at 33 mcg/min prior to succinylcholine (120 mg). Propofol was selected instead of etomidate to prevent exacerbation of hypertension after tracheal intubation. Tracheal intubation was quickly and atraumatically achieved with the aid of a plastic Eschmann-type tracheal tube introducer (bougie) used to overcome a Cormack-Lehane Grade 3 view of the larynx.

Immediately after confirmation of the presence of end-tidal carbon dioxide ($ETCO_2$) (39 mmHg) and equal bilateral breath sounds, NIBP was 119/90 mmHg, and heart rate was 62 bpm (paced rhythm). Two minutes later, NIBP dropped to 88/76 mmHg. Four minutes after induction, the physician attempting to insert a radial artery catheter noted a lack of vessel pulsation on the ultrasound screen. Carotid and femoral arterial pulses were immediately checked and found to be absent.

Despite the ECG monitor showing a paced ventricular rhythm at 60 bpm, chest compressions were commenced, and the nitroglycerine infusion was discontinued. $ETCO_2$ during compressions was 23 mmHg. A 1-mg bolus of IV epinephrine was administered. Within 2 minutes, the patient's cardiac rhythm had returned to sinus with a rate of 112 bpm (this rate diminished without additional intervention to her original heart rate within 10 minutes), and $ETCO_2$ increased to 46 mmHg. CPR was discontinued, and the next NIBP reading was 145/121 mmHg, prompting cautious introduction of sevoflurane. Seven minutes after induction, invasive radial arterial pressure was 233/97 mmHg, and heart rate was 97 bpm. Sevoflurane concen-

Table 3. Preprocedural Problem List and Current Therapy[a]

Condition	Present Treatment
Systemic arterial hypertension	Losartan 50 mg with hydrochlorothiazide 12.5 mg qd, carvedilol 25 mg bid, amlodipine (dosage prior to surgery no longer accessible in the electronic medical record)
Hypercholesterolemia	Atorvastatin 10 mg qd
Type II diabetes mellitus complicated by • Proliferative retinopathy • Peripheral neuropathy (especially severe in lower extremities) • Charcot arthritis affecting ankles • Intermittent foot ulcers • Gastroparesis • Chronic kidney disease, stage III	Diabetic diet Insulin glargine 28 units at night; insulin aspart 10 units before meals (modifiable based on capillary blood glucose level) Gabapentin 300 mg qid (for neuropathy)
Morbid obesity (height 1.7 m; weight 122 kg; body mass index 43)	Low-calorie diet (presumed noncompliant)
Coronary artery disease	Clopidogrel 75 mg, aspirin 81 mg (both discontinued 7 days prior to surgery) Carvedilol 25 mg bid Nitroglycerine 0.4 mg sublingual as needed
Peripheral arterial disease (lower extremities)	Clopidogrel 75 mg, aspirin 81 mg (both discontinued 7 days prior to surgery)
Gastroesophageal reflux disease • History of *Helicobacter pylori* hemorrhagic gastritis	Pantoprazole 40 mg qd Had completed triple antibiotic therapy
Borderline microcytic anemia	Oral ferrous sulfate (dosage prior to surgery no longer accessible in the electronic medical record)
Mild exertional shortness of breath (considered multifactorial)	Weight control and exercise
Severe bradycardia or asystole (confirmed by pulselessness and, if awake, loss of consciousness) following medical procedures involving oropharyngeal stimulation	Scheduling the presence of a member of anesthesia department for such procedures; preprocedural temporary transvenous pacemaker placement

[a]All medications were taken within 24 hours of surgery unless otherwise specified. bid, twice daily; qd, daily; qid, four times daily.

tration was slowly increased to 0.6% (dial) during the subsequent 5 minutes.

An emergency transthoracic echocardiogram was interpreted by the cardiologist as normal and showing no evidence of pacemaker wire insertion–induced tamponade. No evidence of a decrease in myocardial contractility was observed. By 17 minutes postinduction, invasive blood pressure had dropped to 105/65 mmHg. During the following 30 minutes, repeat IV boluses of phenylephrine (40-80 mcg) maintained invasive systolic blood pressure at 105-150 mmHg despite administration of 0.4% sevoflurane (vaporizer reading), which proved sufficient in the presence of residual fentanyl to produce electroencephalogram evidence of adequate anesthetic depth: a bispectral index (BIS) of 28-52.

At 45 minutes postinduction, the patient's vital signs and ECG tracing remained stable despite frequent episodes of paced rhythm. Low-dose sevoflurane supplemented by midazolam was sufficient to maintain a BIS between 40-60 (general anesthetic level), and the only hemodynamic support required was a phenylephrine infusion (0.5-6.0 mcg/min). The issue of whether or not to proceed with surgery was considered. A decision to proceed was made based on the following considerations: (1) the patient was already blind in one eye, and the procedure on the fellow eye was considered potentially sight saving; (2) the patient had stabilized hemodynamically; (3) a 12-lead ECG showed no changes from the preoperative tracing; (4) the patient had suffered no lasting ill effects of vasovagal attacks requiring advanced life support occurring during previous anesthesia or sedation and oropharyngeal or laryngeal stimulation; (5) the patient's strong tendency to experience vasovagal pulselessness made a smoother course during a subsequent anesthetic administration unlikely; and (6) the majority of severe intraoperative vasovagal events reported in the literature are followed by a benign clinical course.

The patient tolerated the procedure well. Despite a total midazolam dose of 17 mg, she awakened and was extubated within 20 minutes after discontinuation of sevoflurane. By this time, phenylephrine was no longer needed, and preoperative hypertension did not recur.

The patient was taken to the intensive care unit where she maintained sinus rhythm and normal blood pressure. She denied all cardiac symptoms (shortness of breath, chest

Table 4. Preoperative Tests

Days[a]	Test	Result(s)
350	Stress echocardiogram	Poor exercise tolerance
		Resting hypertension
		Inability to achieve target heart rate (limiting sensitivity for detection of ischemia)
345	Cardiac catheterization	Non–ST-elevation myocardial infarction 2 years prior to proposed procedure, treated with bare metal stent in third obtuse marginal branch of the left circumflex coronary artery
		Residual 80% occlusive disease of distal left anterior descending artery—not amenable to percutaneous coronary intervention; nonobstructive disease of right and left circumflex arteries
		Left ventricular pressure at the time of stent placement 134/14 mmHg
30	Chest x-ray	Lungs clear
		Mildly enlarged cardiac silhouette unchanged from examination 1 year prior
30	Electrocardiogram	Sinus rhythm
		First degree atrioventricular block (PR interval 0.22 seconds); no change from previous tracings
30	Nuclear cardiac stress test	Reversible ischemia at the left ventricular apex and inferolateral aspects of the periapical left ventricle in the distribution of the circumflex and anterior descending branches of the left coronary artery
		No wall motion defects identified
2	Transthoracic echocardiogram	Normal chamber sizes except left atrial enlargement
		Normal valves and wall thicknesses
		Normal systolic function (ejection fraction >55%)
		Diastolic filling pattern considered normal for age
		Estimated right atrial pressure 3 mmHg
		Estimated pulmonary artery systolic pressure <35 mmHg
2	Hemoglobin and hematocrit	10.2 g/dL and 30.8%
2	Serum biochemistry	Sodium 141 mEq/L, potassium 4.7 mEq/L, urea nitrogen 33 mg/dL, creatinine 1.7 mg/dL, glucose 140 mg/dL

[a]Expressed as number of days prior to present admission.

discomfort, palpitations, dizziness, and light-headedness). She also denied any recall of intraoperative events. On postoperative day 1, pacemaker settings were reduced to a demand rate of 40 bpm and output of 5 mA. Absence of any bradycardia or symptoms prompted pacemaker removal, and the patient was transferred to a medical floor bed on postoperative day 2. She was discharged the following day and has had no cardiac symptoms for 1 year.

The patient denies having ever had any symptoms of bradycardia, either spontaneous or induced by neck stimulation, outside the setting of a medical procedure requiring oropharyngeal stimulation. For this reason, our cardiology team has not recommended Holter monitoring or insertion of a permanent pacemaker. The patient has been advised to notify future anesthesia personnel involved in her care that she has a history of vasovagal reaction to oropharyngeal/laryngeal instrumentation during sedation or general anesthesia and that she may be intolerant to ordinary doses of fentanyl, propofol, and succinylcholine either singly or in combination.

DISCUSSION

Depending on the degree of bradycardia exhibited, vasovagal reflex circulatory collapse in response to instrumentation in the presence or absence of anesthetic drug administration may be classified (analogous to vasovagal syncope) as (1) cardioinhibitory, (2) vasodepressor, or (3) mixed.[35] Cardiac slowing during such events can be because of sinus or nodal bradycardia,[35] varying degree of atrioventricular heart block,[15,26,36] or complete cardiac electrical silence (asystole).[20,29,31,36] From prior experience, an important factor of our patient's episodes was known to be cardioinhibitory. The consistent occurrence of severe bradycardia leading to asystole concealed the vasodepressor factor that was revealed by the presence of the pacemaker.

That the patient had recently undergone an ultimately successful diagnostic upper GI endoscopy with TTvP support, in retrospect, offered false reassurance that the same intervention might permit uneventful administration of general endotracheal anesthesia and performance of cornea and retina surgery. Recent evidence suggests that permanent pacemaker insertion can reduce the probability

of a syncopal attack in patients with documented vasovagal ("neurally mediated") syncope.[37] However, the cardiology literature warns that such pacing, while preventing the cardioinhibitory component of a vasovagal reflex, cannot be relied upon to prevent the vasodepressor component, which may be dominant.[35,38-40]

Because our patient's pacemaker maintained a (sometimes pacemaker-captured) ventricular rate of at least 60 bpm, we conclude that (1) laryngoscopy and tracheal intubation were capable of prompting a stronger vasodepressor response than oral insertion of a gastroscope, or (2) one or more of the agents used in the rapid anesthetic induction sequence—fentanyl, propofol, and/or succinylcholine—augmented vasodilation enough to cause pulselessness. Considering that it took 2-4 minutes for the patient to become pulseless, perhaps placement of the arterial line preoperatively could have permitted administration of a vasopressor/inotropic drug (small doses of epinephrine) and avoided the second episode of chest compressions.

Prophylactic vagolytic premedication (eg, hyoscine, atropine, glycopyrrolate) has been recommended in high-risk situations (such as eye surgery)[41,42] but also discouraged[13] due to ineffectiveness[28] or out of concern that effective doses are often sufficient to cause troublesome tachycardia.[13] Our patient received an advanced cardiac life support dose of atropine (1 mg) in response to the first pulseless event (with asystole). However, this atropine administration did not cause tachycardia or prevent the need for pacing at various times during the rest of the patient's intraoperative course.

Preoperative administration of a beta-blocking drug has been suggested as potentially useful in preventing bradycardia and hypotension.[28] Our patient did not take her morning dose of carvedilol. We opted not to administer the dose because her heart rate was normal and did not increase with an effective antihypertensive dose of nitroglycerine (suggesting residual beta blockade) and because beta blockade to prevent vasovagal attacks is controversial and can be counterproductive.[43,44] We were prepared to treat tachycardia with esmolol and metoprolol, but tachycardia did not occur except for 7 minutes following IV epinephrine administration.

The first step in treating vasovagal bradycardia, heart block, or asystole is usually stopping the responsible stimulation. In our patient's case, abandoning pacemaker insertion was not considered, and immediate extubation in a patient with a high probability of difficult mask ventilation was not considered an option. We realize that other anesthesiologists might have canceled the surgical procedure that we allowed to proceed. Perhaps the best defense of our admittedly controversial management is the patient's excellent short-term and long-term cardiac and ocular outcomes.

If this patient returns to our institution for a subsequent operative procedure, the anesthesia team will face several issues. Recommendations placed in the patient's electronic medical record are the following: (1) to consult cardiology regarding TTvP insertion and if none is recommended to have an external pacemaker available; (2) because rapid-sequence induction with fentanyl, propofol, and succinylcholine has twice been followed by cardiovascular collapse, to consider another induction drug combination; (3) to complete insertion of an arterial catheter prior to oropharyngeal instrumentation and/or pacemaker insertion to permit a more rapid pharmacologic response to hypotension; and (4) if the patient undergoes repeat upper GI endoscopy, to apply oropharyngeal topical anesthesia prior to gastroscope insertion to allow a reduction in sedative drug dosage.

CONCLUSION

In a patient with a history of instrumentation-induced reflex circulatory collapse, preoperative cardiac pacemaker insertion may provide insufficient protection against recurrence. Preparation should also be made for immediate diagnosis and treatment of the syndrome's vasodepressor component.

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