CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 22-2023: A 59-Year-Old Woman with Hypotension and Electrocardiographic Changes

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PRESENTATION OF CASE

Dr. Yuefan Chen (Anesthesia, Critical Care, and Pain Medicine): A 59-year-old woman had hypotension and electrocardiographic (ECG) ST-segment abnormalities after the administration of anesthetic agents while she was in the operating room of this hospital.

Eighteen weeks before the current presentation, features of acromegaly were observed on routine physical examination by the patient's primary care provider at another hospital. The blood level of insulin-like growth factor I (IGF-I) was 595 ng per milliliter (reference range, 50 to 317) and the growth hormone level 9.1 ng per milliliter (reference range, 0.0 to 7.1). The patient was referred to the endocrinology clinic of this hospital.

Eleven weeks before the current presentation, the patient was evaluated in the endocrinology clinic. She reported that her shoe size, which had been stable since young adulthood, had recently increased by two sizes. She also reported a deepening of her voice, fatigue, headaches, arthralgias, oily skin, skin tags, and acne on her face and back. She had had an intentional weight loss of 12.7 kg during the previous 9 months. The facial features were coarse, and there was no frontal bossing. Visual fields were full on confrontation testing. The tongue was thick and obscured the soft palate; the lower jaw was enlarged, with increased spacing between the teeth. The hands and feet were large and fleshy. Scattered skin tags were present on the neck. Auscultation of the heart and lungs revealed no abnormalities. Imaging studies were obtained.

Magnetic resonance imaging (MRI) of the head revealed a normal-sized pituitary gland with a well-circumscribed area of hypoenhancement that measured 9 mm by 7 mm by 10 mm. The patient was referred to the neurosurgery clinic of this hospital, and an elective microscopic transsphenoidal hypophysectomy was subsequently recommended.

Seven weeks before the current presentation, an extensive preoperative evalua-

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tion was performed, given the patient's diagnosis of acromegaly. As part of the preoperative evaluation, additional history was obtained. The patient's medical history included hypertension, prediabetes, obesity, obstructive sleep apnea, polycystic ovary syndrome, rheumatoid arthritis, osteoarthritis, and scoliosis. Physical activity was limited by pain in the knees; she could climb a flight of stairs but did so very slowly because of knee pain. She had no chest pain or dyspnea. Medications included hydrochlorothiazide, olmesartan, and ibuprofen and acetaminophen as needed for joint pain. Hydroxychloroquine had caused leukopenia, and meperidine had caused gastrointestinal upset. The patient lived in a rural area of New England with her husband and worked in an office. She did not smoke cigarettes or use illicit drugs; she drank alcohol rarely. Multiple maternal and paternal family members had cardiovascular disease.

ECG revealed sinus rhythm with nonspecific ST-segment and T-wave abnormalities, including a T-wave inversion in lead III. A transthoracic echocardiogram (TTE) showed normal left ventricular volume and systolic function, with a left ventricular ejection fraction of 55%, and there were no wall-motion abnormalities. The right ventricular volume and systolic function were normal; the estimated right ventricular systolic pressure was 28 mm Hg. Mild mitral regurgitation and tricuspid regurgitation were present. A pharmacologic stress test, with myocardial perfusion imaging performed after the administration of regadenoson, revealed no evidence of ischemia.

Three weeks before the current presentation, the patient was taken to the operating room for transsphenoidal hypophysectomy. The preoperative temporal temperature was 36.7°C, the heart rate 72 beats per minute, the blood pressure 131/69 mm Hg, and the oxygen saturation 97% while she was breathing ambient air. The body-mass index (the weight in kilograms divided by the square of the height in meters) was 35.7. Midazolam was administered, and anesthesia was induced with fentanyl, propofol, lidocaine, and rocuronium. Tracheal intubation was moderately challenging because of the presence of redundant tissue in the supraglottic region. During intubation, the oxygen saturation decreased to 79% but normalized in less than 1 minute. Inhaled sevoflurane (an anesthetic) and dexamethasone and piperacillin–tazobactam were administered, remifentanil and phenylephrine infusions were started, and the patient was placed in a level, supine position for the procedure.

After the induction of anesthesia, before the surgical procedure was initiated, the blood pressure gradually decreased (Fig. 1A). Sixteen minutes after induction began, the blood pressure was 96/48 mm Hg and the heart rate 75 beats per minute; 29 minutes after induction began, the blood pressure had decreased to 67/36 mm Hg and the heart rate to 71 beats per minute. Telemetric monitoring (Fig. 2A) showed ST-segment elevations in the inferior leads and ST-segment depressions and T-wave inversions in the anterior and lateral leads. Aspirin was administered rectally, the rate of the phenylephrine infusion was increased, and multiple boluses of phenylephrine and an ephedrine bolus were administered. The blood pressure increased to 110/54 mm Hg and the heart rate to 111 beats per minute. Telemetric monitoring showed resolution of the ST-segment and T-wave abnormalities. Findings on ECG and transesophageal echocardiography (TEE) performed in the operating room were consistent with those of the preoperative ECG and TTE. The procedure was aborted, the patient was weaned from the vasopressor therapies, and the trachea was extubated. She was transferred to the cardiac intensive care unit.

On admission to the cardiac intensive care unit, the blood level of troponin T was 10 ng per liter (reference range, 0 to 9); 1 hour later, the level had decreased to 8 ng per liter. Other laboratory test results are shown in Table 1. Chest radiography was normal. Computed tomographic angiography of the coronary arteries revealed moderate stenosis of the distal left anterior descending coronary artery. The intraoperative ST-segment elevations were attributed to coronary vasospasm. Treatment with amlodipine and isosorbide mononitrate was initiated for coronary vasospasm, and treatment with atorvastatin was started for nonobstructive coronary artery disease. After discussion among the cardiology, neurosurgery, and anesthesia teams, it was determined that the patient remained a candidate for transsphenoidal hypophysectomy, particularly because the surgery could offer a cure for her acromegaly; the procedure was rescheduled. The patient was discharged home on the third hospital day.

During the subsequent 3 weeks, the patient continued taking the newly prescribed medications, and no new symptoms developed. On the day of the current presentation, she was again taken to the operating room to undergo transsphenoidal hypophysectomy. The preoperative blood pressure, as measured through an arterial catheter, was 118/67 mm Hg and the heart rate 88 beats per minute. Sedation with fentanyl and midazolam was started, topical lidocaine was used to anesthetize the airways, and fiberoptic tracheal intubation was performed while the patient was awake. Anesthesia was then induced with propofol, rocuronium, and sevoflurane. A phenylephrine infusion was started, and piperacillin–tazobactam was administered.

The blood pressure decreased abruptly to 54/29 mm Hg (Fig. 1B). Telemetric monitoring (Fig. 2B) showed ST-segment elevations in the inferior leads and ST-segment depressions and T-wave inversions in the anterior and lateral leads.

Management decisions were made, and a diagnostic test was performed.

DIFFERENTIAL DIAGNOSIS

Dr. Wilton A. van Klei: This 59-year-old woman with obesity, hypertension, and obstructive sleep apnea presented for transsphenoidal hypophysectomy. A preoperative cardiac evaluation included echocardiography, which revealed a normal ejection fraction, and a pharmacologic stress test, which showed no evidence of ischemia. After the induction of anesthesia, the blood pressure gradually decreased from 131/69 mm Hg to 67/36 mm Hg, and ECG changes suggestive of cardiac ischemia developed. I will first consider possible causes of the intraoperative hypotension that occurred during the induction of anesthesia that preceded the first attempted procedure.

INTRAOPERATIVE HYPOTENSION

A decrease in blood pressure after the induction of anesthesia is common. The degree of decrease in blood pressure that is considered to be abnormal is not clear, since a single definition of intraoperative hypotension that applies to all patients does not exist. The most commonly used threshold is a mean arterial pressure of less than 65 mm Hg, which is associated with adverse outcomes such as myocardial injury, kidney injury, and death. Nearly two thirds of patients under general anesthesia have at least one episode of intraoperative hypotension when the condition is defined by a mean arterial pressure of less than 65 mm Hg.[1-3] To determine the cause of intraoperative hypotension in this patient, the timing relative to the surgery (between induction and surgery, during surgery, or immediately after surgery), patient risk factors, and procedural risk factors should all be considered.

Timing of Intraoperative Hypotension Relative to Surgery

This patient began to have hypotension during the period between induction of anesthesia and surgery, when the mean arterial pressure decreased to 46 mm Hg. Hypotension that occurs during this period is most commonly due to the sympatholytic effects of anesthetics, whereas hypotension that develops during surgery can also be caused by blood loss or reduced venous return resulting from surgical compression.

Patient-Related Risk Factors for Intraoperative Hypotension

Patient-related risk factors for intraoperative hypotension include age-related physiologic changes, pathophysiological changes due to coexisting conditions, and medication use.[3,4] The physiologic increase in arterial stiffness and decreases in intravascular volume, baroreceptor reflex, and myocardial contractility that occur with older age can result in clinically significant hypotension after the administration of anesthetics; however, such changes would be unlikely causes of hypotension in this 59-year-old patient. In addition, the patient did not have coexisting conditions that are typically associated with intraoperative hypotension, such as heart failure, atrial fibrillation, peripheral vascular disease, diabetes, hypothyroidism, or adrenal insufficiency.

Could the patient's medications have caused intraoperative hypotension? Intravascular volume depletion from the use of hydrochlorothiazide or residual blockade of angiotensin II–mediated vasoconstriction might have contributed to a decrease in blood pressure but would be unlikely to have caused the degree of hypotension that this patient had. She did not take other medications known to contribute to the occurrence of hypotension after induction of anesthesia, such as antiarrhythmic medications, which reduce the heart rate and have a negative inotropic effect.

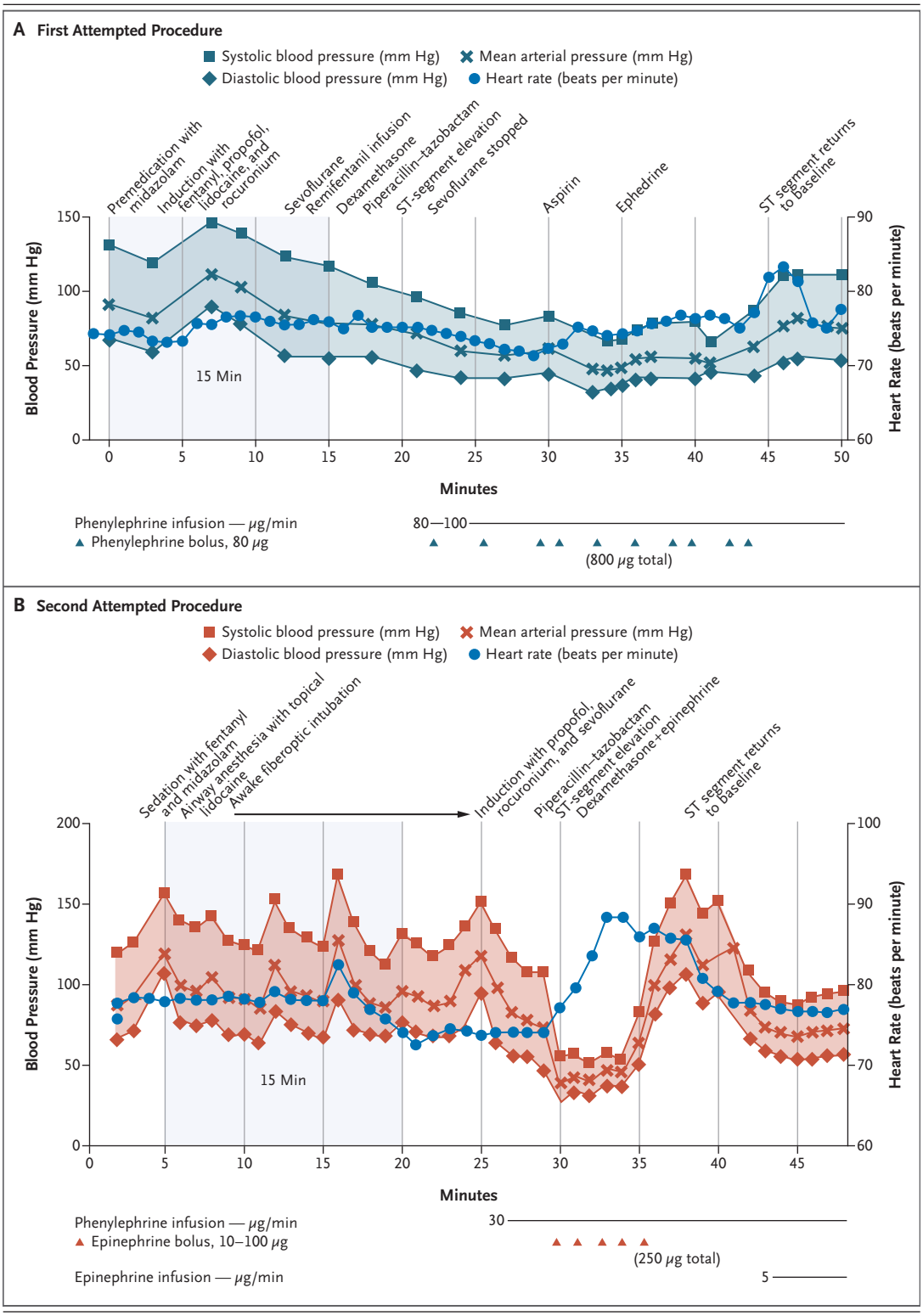

Figure 1 (facing page). Intraoperative Vital Signs.
Vital signs were recorded during two separate episodes of hypotension with concurrent ST-segment elevation after the administration of piperacillin–tazobactam. During the induction of anesthesia that preceded the first attempted procedure (Panel A), there was a gradual onset of hypotension over a period of 10 to 15 minutes for which the patient received doses of vasopressors that were higher than those typically used to restore normotension. During the induction of anesthesia that preceded the second attempted procedure (Panel B), there was an abrupt and profound drop in the systolic blood pressure immediately after the administration of piperacillin–tazobactam. Dexamethasone was administered to treat possible adrenal insufficiency, and epinephrine was administered in escalating doses, followed by an infusion. The systolic and diastolic blood pressure was measured with a sphygmomanometer during the first induction and through an arterial catheter during the second induction.

The fact that the patient had a gradual development of hypotension that abated after the administration of ephedrine and phenylephrine argues against an anaphylactic reaction to other medications such as rocuronium and piperacillin–tazobactam, which were administered during the period of induction of anesthesia.

Procedural Risk Factors for Intraoperative Hypotension

Procedural risk factors for intraoperative hypotension include the type and urgency of surgery, positioning of the patient, blood loss, and type of anesthesic agents administered. Transsphenoidal hypophysectomy was a planned neurosurgical procedure, and the hypotension occurred before the procedure began; therefore, blood loss was not a factor in this case. The patient was placed in the supine position rather than the prone position, the latter of which is more commonly associated with hypotension that is due to reduced venous return.

Could the patient's hypotension have resulted from the administration of the general anesthetics? The use of propofol decreases both systemic vascular resistance and myocardial contractility. The use of remifentanil decreases systemic vascular resistance and reduces the heart rate. Volatile anesthetics used for the maintenance of anesthesia, such as sevoflurane, also cause a decrease in vascular resistance. Rocuronium — a neuromuscular blocking agent — usually does not affect the cardiovascular system, except in the case of an anaphylactic reaction.

This patient's hypotension and ECG changes occurred after the administration of multiple medications to induce general anesthesia and at the start of the maintenance phase of general anesthesia with sevoflurane and infusion of remifentanil but before any painful stimuli were present. The hypotension developed gradually and abated after the administration of ephedrine and phenylephrine. The occurrence of hypotension is not uncommon when the doses of anesthesics are adjusted for an individual patient. If I had been caring for the patient during the first attempted procedure, I would have attributed the hypotension to a side effect of the anesthesics that was greater than expected. However, the ST-segment elevations require additional investigation.

ST-SEGMENT ELEVATIONS

Shortly after the onset of hypotension, telemetric monitoring showed ST-segment elevations in the inferior leads and ST-segment depressions and T-wave inversions in the anterior and lateral leads. These are uncommon intraoperative ECG changes, even though intraoperative hypotension is common among patients under general anesthesia. ST-segment elevations are seen with coronary occlusion but can also occur in patients with takotsubo (stress) cardiomyopathy or coronary vasospasm. No characteristic findings of takotsubo cardiomyopathy were seen on intraoperative TEE, and there was no obvious trigger. I would be very concerned about inferior-wall myocardial ischemia as the cause of the ST-segment elevations. However, additional cardiac investigation revealed only moderate stenosis of the distal left anterior descending coronary artery, and intraoperative ST-segment elevations were attributed to coronary vasospasm.

SECOND ATTEMPTED PROCEDURE

When the patient returned to the operating room for the rescheduled procedure 3 weeks later, she had sudden and severe hypotension, and the mean arterial pressure decreased to 37 mm Hg after

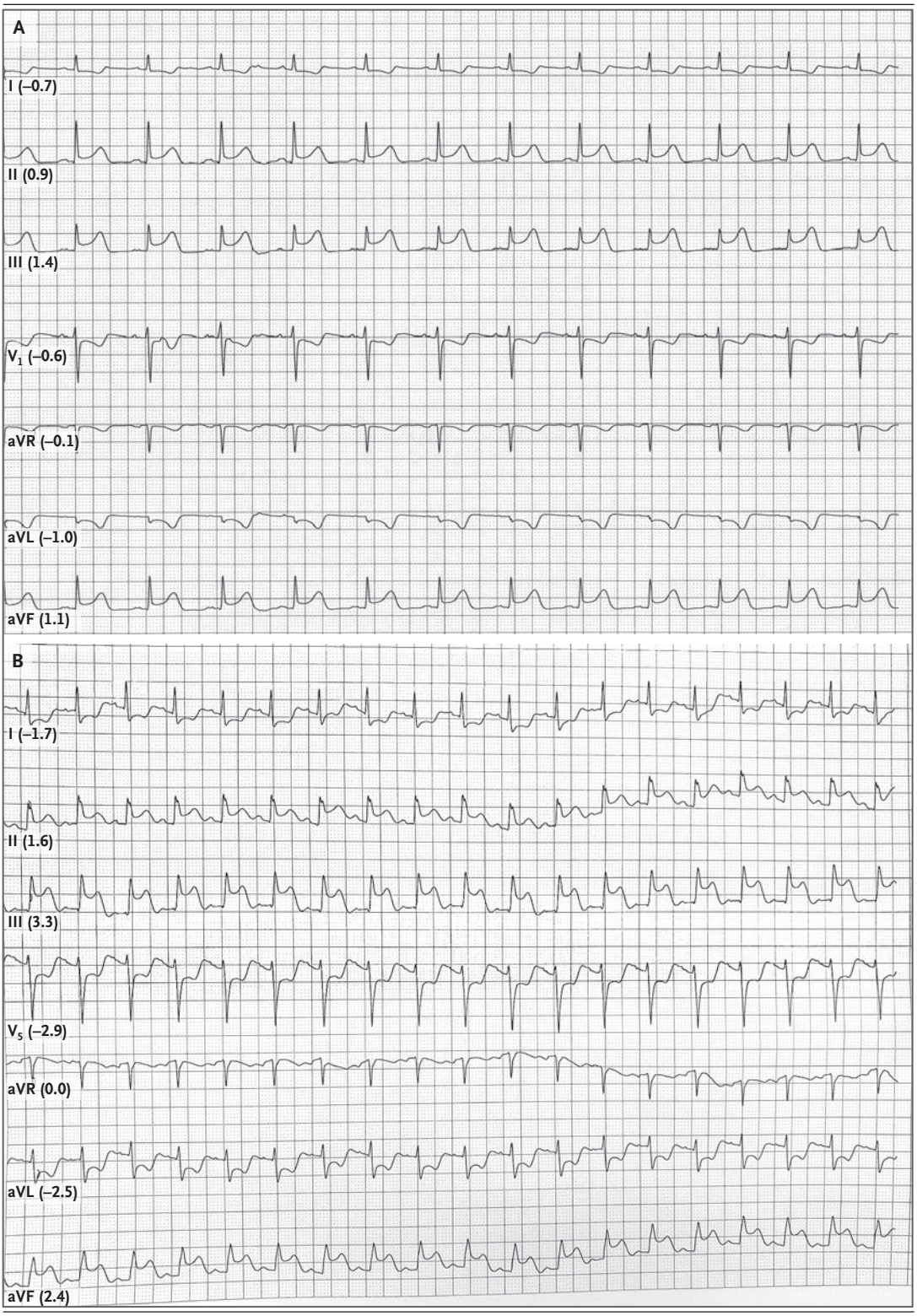

Figure 2 (facing page). Intraoperative Telemetric Monitoring.

Intraoperative telemetric monitoring performed during the patient's hypotensive episodes shows ST-segment elevations in leads II, III, and aVF, with reciprocal depressions in leads I and aVR, during the administration of anesthetics before the first attempted procedure (Panel A) and during the administration of anesthetics before the second attempted procedure (Panel B).

anesthesia was induced. The abrupt nature of the hypotension that developed after induction of anesthesia before the second attempted procedure is highly suggestive of an anaphylactic reaction.

ANAPHYLAXIS

The occurrence of anaphylaxis in the operating room is rare. The incidence is estimated to be one case per 10,000 to 20,000 procedures, and neuromuscular blocking agents such as rocuronium are reported to be the most common cause, accounting for 50 to 70% of cases. The second most common cause is antibiotic agents.[5] This patient was exposed to both a neuromuscular blocking agent and antibiotics before the rapid onset of severe hypotension, which makes anaphylaxis the most likely diagnosis in this case.

Could anaphylaxis also explain the ST-segment changes seen on intraoperative telemetric monitoring? Coronary vasospasm associated with mast-cell activation due to anaphylaxis has been reported and is a clinical entity called the Kounis syndrome.[6] Anaphylaxis could explain both the patient's hypotension and her ST-segment elevations, and I suspect that the diagnostic test that was performed in this case was drug-allergy testing.

CLINICAL IMPRESSION

Dr. Michele D. Szabo: The patient's second intraoperative course was uneventful until the intravenous administration of piperacillin–tazobactam, when the systolic blood pressure decreased from 118 to 54 mm Hg in only 45 seconds. Soon thereafter, the patient had ST-segment elevations in leads II, III, and aVF.

Our differential diagnosis for the cause of this abrupt and profound hypotension included adrenal insufficiency, cardiogenic shock, and anaphylaxis. The patient's small pituitary tumor did not compress the pituitary gland and therefore would be an unlikely cause of adrenal insufficiency. We wondered whether coronary vasospasm could have precipitated cardiogenic shock. Given the localized inferior ST-segment elevations, acute right ventricular failure was considered; however, there was no bradycardia or evidence of jugular venous distention to support this diagnosis. Although no bronchospasm or cutaneous signs of an allergic reaction were present, we thought that the pattern of intravenous exposure to an allergen, immediately followed by hypotension, was strongly suggestive of anaphylaxis.

Dexamethasone was administered for the treatment of possible adrenal insufficiency, but the patient's blood pressure did not improve. Incremental epinephrine boluses were administered for the treatment of presumed anaphylaxis. We had

Table 1. Laboratory Data.*

Variable	Reference Range, Adults†	On Admission, Cardiac ICU
Sodium (mmol/liter)	135–145	137
Potassium (mmol/liter)	3.4–5.0	5.0
Chloride (mmol/liter)	98–108	104
Carbon dioxide (mmol/liter)	23–32	21
Urea nitrogen (mg/dl)	8–25	16
Creatinine (mg/dl)	0.60–1.50	0.58
Glucose (mg/dl)	70–110	102
Calcium (mg/dl)	8.5–10.5	8.2
Lactic acid (mmol/liter)	0.5–2.0	0.9
Alanine aminotransferase (U/liter)	9–32	64
Aspartate aminotransferase (U/liter)	7–33	58
Alkaline phosphatase (U/liter)	30–100	91
White-cell count (per μl)	4500–11,000	4550
Hemoglobin (g/dl)	12.0–16.0	10.4
Hematocrit (%)	36.0–46.0	33.8
Platelet count (per μl)	150,000–400,000	180,000

* To convert the values for urea nitrogen to millimoles per liter, multiply by 0.357. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for glucose to millimoles per liter, multiply by 0.05551. To convert the values for calcium to millimoles per liter, multiply by 0.250. To convert the values for lactic acid to milligrams per deciliter, divide by 0.1110. ICU denotes intensive care unit.

† Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at Massachusetts General Hospital are for adults who are not pregnant and do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.

planned to initiate a nitroglycerin infusion for the treatment of acute coronary syndrome once the blood pressure improved. However, the ST-segment elevations resolved within 10 minutes after administration of the epinephrine boluses. A TEE showed no wall-motion abnormalities and a normal left ventricular ejection fraction. We were concerned that we could not easily explain the concurrent apparently nonrandom, associated ST-segment elevation until a brief literature search linked the entities of allergic reaction and acute coronary syndrome in the Kounis syndrome. A diagnosis of the Kounis syndrome was suspected, the procedure was aborted, and the patient was evaluated by the allergy consult service.

CLINICAL DIAGNOSIS

Kounis syndrome.

DR. WILTON A. VAN KLEI'S DIAGNOSIS

Kounis syndrome due to anaphylaxis.

DIAGNOSTIC TESTING

Dr. Paul E. Hesterberg: I was asked to evaluate this patient for anaphylaxis. Anaphylaxis is a highly likely diagnosis if any of the following three criteria are met: sudden onset of illness with involvement of skin or mucosal tissue and either respiratory symptoms or cardiovascular symptoms; involvement of two or more systems (cutaneous, respiratory, cardiovascular, or gastrointestinal) after exposure to a likely allergen or trigger; or reduced blood pressure alone after exposure to a known allergen for that patient.[7] In patients with perioperative anaphylaxis, cardiovascular symptoms are common and can be the sole feature of anaphylaxis,[8] as was the case in this patient.

The diagnosis of anaphylaxis can be made on the basis of serial measurement of the total tryptase level in blood samples obtained immediately after or shortly after symptoms begin, followed by measurement of the baseline level (in a blood sample obtained >24 hours after symptom resolution). Blood tryptase levels rise rapidly during the first 90 minutes after anaphylaxis, with a plasma half-life of approximately 2 hours.[9] Therefore, tryptase levels for the diagnosis of anaphylaxis should ideally be measured within 4 hours after the onset of symptoms.

In this patient, serial measurement of the tryptase level was performed in blood samples obtained beginning approximately 15 minutes after the onset of hypotension. The initial blood level of tryptase was 7.4 ng per milliliter (reference value, <11.5), with a peak level of 7.8 ng per milliliter occurring 110 minutes after the onset of symptoms. At 27 hours after the onset of symptoms, the baseline tryptase level was 3.4 ng per milliliter.

The minimum acute elevation in the tryptase level that is needed to show clinical significance is determined by a formula ($2+1.2\times$baseline tryptase level)[10] that has been validated in the perioperative setting.[11] In this patient, the peak tryptase level exceeded the calculated cutoff (6.1 ng per milliliter), thereby supporting the diagnosis of anaphylaxis.

The patient was referred to the allergy clinic of this hospital for skin testing. Skin-prick and intradermal testing were performed at established nonirritating concentrations to evaluate for reactions to the suspected culprit medications that were used before the surgical procedures. The medications evaluated included fentanyl, propofol, dexamethasone, rocuronium, lidocaine, midazolam, chlorhexidine, and penicillin derivatives (piperacillin–tazobactam, penicillin, ampicillin, and benzylpenicilloyl polylysine).

Skin-prick testing was negative for all the medications. Intradermal testing was positive for piperacillin–tazobactam (with the wheal measuring 11 mm in diameter and the flare 50 mm in diameter) at a concentration of 1 mg per milliliter, thus establishing the diagnosis of allergy to piperacillin–tazobactam. All the other tests were negative, including those for the additional penicillin derivatives.

DISCUSSION OF MANAGEMENT

Dr. Szabo: Our understanding of the Kounis syndrome is limited, and the precise pathophysiological mechanism is unknown. However, it is generally accepted that an allergic reaction triggers mast-cell degranulation that leads to the release of numerous inflammatory mediators that can have clinically significant effects on coronary arteries. Such mediators include histamine, proteases, and platelet-activating factor, which can

Table 2. Variants of the Kounis Syndrome.

Variant	Pathologic Characteristics of Coronary Arteries	Mechanism of Cardiac Injury	Percentage of Affected Patients
Type I	None	Vasospasm (transient or persistent)	76.6
Type II	Preexisting atheromatous disease	Plaque erosion or rupture, with or without vasospasm	22.3
Type III	Presence of a stent	Stent thrombosis	5.1

induce coronary vasospasm or plaque disruption or can promote stent thrombosis, ultimately leading to one of three variants of the Kounis syndrome (Table 2).[6]

There is no specific test to diagnose the Kounis syndrome; rather, it is a clinical diagnosis based on the identification of the signs and symptoms of an allergic reaction together with the signs and symptoms of acute coronary syndrome. Most patients with the Kounis syndrome present with cutaneous symptoms, bronchospasm, or anaphylaxis. In a review of 175 patients with the Kounis syndrome, 87% had chest pain and more than 95% had abnormal ECG findings, most commonly ST-segment elevation.[12]

Treatment of the Kounis syndrome is challenging because the goal is to treat the allergic reaction and acute coronary syndrome simultaneously in patients in whom the clinical spectrum of both disease entities is highly variable and the effects of cardiovascular medications on both anaphylaxis and coronary lesions need to be considered and balanced. In this case, we determined that the benefits of prompt administration of epinephrine to treat life-threatening anaphylaxis outweighed the risk of adverse cardiac effects in a patient with acute coronary syndrome who was known to have nonobstructive coronary artery disease.

Dr. Hesterberg: Perioperative anaphylaxis can be attributed to IgE-dependent or IgE-independent processes, and both immunologic and nonimmunologic mechanisms have been implicated in these processes. Skin testing is useful only in the evaluation of IgE-mediated hypersensitivity reactions, and culprit medications can be identified in more than 70% of such cases.[8] Although neuromuscular blocking agents and antibiotics are implicated most frequently, a variety of perioperative medications have been associated with anaphylaxis.

Extensive skin testing was performed to assess for hypersensitivity to each medication used during the perioperative induction period. Results were notable for a positive test for piperacillin–tazobactam only, in the absence of sensitization to other penicillin derivatives that were also evaluated as part of the skin-testing process. Cross-reactivity within the penicillin class of antibiotics can be conferred through the shared beta-lactam ring that is present in all semisynthetic penicillins and in benzylpenicillin.[13] However, sensitization to the specific aminopenicillin side chain can occur in the absence of cross-reactivity with other antibiotics in the penicillin class. This phenomenon has been reported specifically for piperacillin–tazobactam; up to two thirds of patients may be selectively sensitized to this medication.[14]

Given that a culprit medication had been identified, it was deemed to be appropriate for the patient to undergo surgery under general anesthesia along with the use of an alternative prophylactic antimicrobial agent. The administration of an alternative penicillin derivative (such as ampicillin, given the patient's negative skin test) could have been considered in this case. However, clindamycin was ultimately chosen.

Dr. Szabo: While the patient was undergoing skin testing to determine her medication allergies, treatment with a somatostatin analogue was initiated to medically manage her acromegaly. Six months after the first episode of intraoperative hypotension, the patient underwent transsphenoidal hypophysectomy and received prophylaxis with clindamycin. The intraoperative course was uneventful, and her acromegaly was cured with the surgical resection.

A physician: Do you think that the Kounis syndrome explains the events that occurred during induction of anesthesia before the first attempted procedure?

Dr. Szabo: The patient had acute coronary syndrome during the first induction. Although evidence for an allergic reaction is subtle and consists only of a gradual onset of hypotension after

induction that was more pronounced than is typical for intraoperative hypotension and required more intense vasopressor therapy than is commonly needed to restore normotension, subsequent identification of a culprit agent suggests that the patient had the Kounis syndrome. Allergic reactions can be difficult to diagnose in patients who cannot report symptoms during anesthesia, when multiple causes of hypotension may confound the diagnosis. A recent review of 35 patients with perioperative Kounis syndrome included 3 patients with intraoperative acute coronary syndrome without a recognized allergic reaction who had anaphylaxis when they were reexposed to the culprit agent during a subsequent surgical procedure, as occurred in this patient.[15] Some clinicians have suggested that a serum tryptase level be obtained in patients with intraoperative acute coronary syndrome to help evaluate for an uncommon allergic cause.[16-18]

FINAL DIAGNOSIS

Kounis syndrome due to exposure to piperacillin–tazobactam.

This case was presented at Anesthesia, Critical Care, and Pain Medicine Grand Rounds.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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