CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 23-2019: A 52-Year-Old Man with Fever, Cough, and Hypoxemia

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PRESENTATION OF CASE

Dr. Lila M. Martin (Medicine): A 52-year-old man was transferred to this hospital for evaluation and treatment of hypoxemia.

The patient had been in his usual state of health until 7 days before transfer to this hospital, when nonproductive cough and intermittent fever with temperatures of up to 38.2°C developed. During the subsequent 4 days, these symptoms persisted and were accompanied by malaise, mild anorexia, weakness, and exertional dyspnea. He had no chest pain, palpitations, antecedent respiratory symptoms, rashes, joint symptoms, or weight loss. The administration of dextromethorphan and acetaminophen did not improve symptoms. On the morning before transfer to this hospital, dyspnea occurred with minimal exertion. The patient presented to a local urgent care clinic, where the heart rate was 113 beats per minute and the oxygen saturation was 91% while he was breathing ambient air. He was referred to the emergency department at a local hospital for further evaluation.

On presentation to the other hospital, the temperature was 37.6°C, the heart rate 115 beats per minute, the blood pressure 126/83 mm Hg, and the respiratory rate 18 breaths per minute. The oxygen saturation was 90% while the patient was breathing ambient air and then increased to 93% while he was receiving oxygen through a nasal cannula at a rate of 2 liters per minute. No jugular venous distention or increased work of breathing was reported. Auscultation of the chest revealed rhonchi and occasional wheezes on the right side and a prominent systolic murmur at the right upper sternal border. The remainder of the examination was normal. The N-terminal pro–B-type natriuretic peptide level was 4850 pg per milliliter (reference range, 0 to 900), the D-dimer level 2487 ng per milliliter (reference range, <244), and the lactate dehydrogenase level 458 U per liter (reference range, 110 to 210); other laboratory test results are shown in Table 1. Cultures of the blood were obtained.

Dr. Milena Petranović: Initial posteroanterior and lateral chest radiographs (Fig. 1A and 1B) showed markedly asymmetric lung opacities located predominantly in the central portion of the right upper lobe.

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Table 1. Laboratory Data.*

Variable	Reference Range, Other Hospital	On Presentation, Other Hospital	Reference Range, This Hospital†	On Presentation, This Hospital	4 Hr after Presentation, This Hospital
White-cell count (per mm^3)	4000–11,000	17,300	4500–11,000	24,510	
Hemoglobin (g/dl)	13.5–17.5	16.5	13.5–17.5	14.4	
Hematocrit (%)	38–50	46.9	41.0–53.0	41.6	
Platelet count (per mm^3)	135,000–400,000	307,000	150,000–400,000	294,000	
Neutrophils (%)	40–70	85.2	40–70		
Sodium (mmol/liter)	136–145	138	135–145	138	
Potassium (mmol/liter)	3.5–5.2	4.6	3.4–5.0	4.7	
Chloride (mmol/liter)	95–106	98	98–108	106	
Carbon dioxide (mmol/liter)	20–31	23	23–32	18	
Urea nitrogen (mg/dl)	9–23	24	8–25	25	
Creatinine (mg/dl)	0.50–1.30	1.80	0.60–1.50	1.78	
Calcium (mg/dl)	8.7–10.4	9.1	8.5–10.5	8.1	
Lactate (mmol/liter)	0.5–1.9	2.3	0.5–2.0	2.0	
Troponin T (ng/ml)	0–0.01	0.65	<0.03	0.80	
Central venous oxygen saturation (%)	70–80			79.1	
Arterial blood gas analysis					
Fraction of inspired oxygen				1.0	1.0
pH	7.35–7.45		7.35–7.45	7.24	7.31
Partial pressure of carbon dioxide (mm Hg)	35–45		35–42	48	37
Partial pressure of oxygen (mm Hg)	80–105		80–100	82	151

* 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 calcium to millimoles per liter, multiply by 0.250. To convert the values for lactate to milligrams per deciliter, divide by 0.1110.

† 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.

Dr. Rajeev Malhotra: An electrocardiogram (Fig. 2A) showed sinus tachycardia with left axis deviation, left atrial abnormality, early R-wave progression, and ST-segment depressions in the anterior leads. Bedside ultrasonographic examination of the heart revealed a hyperdynamic left ventricle.

Dr. Martin: Ceftriaxone, azithromycin, aspirin, atorvastatin, and intravenous normal saline were administered, and the administration of supplemental oxygen through a nasal cannula was continued. The patient was admitted to the intensive care unit (ICU) of the other hospital.

That afternoon, 5 hours after presentation to the other hospital, hypoxemia worsened; the oxygen saturation was 86% while the patient was receiving oxygen through a nasal cannula at a rate of 6 liters per minute, and the respiratory rate was 34 breaths per minute. The levels improved after the administration of additional supplemental oxygen; the oxygen saturation increased to 92% while he was receiving oxygen through a nonrebreather face mask at a rate of 15 liters per minute and then increased to 100% while he was receiving oxygen through a high-flow nasal cannula at a rate of 60 liters per minute (fraction of inspired oxygen [F_{IO_2}], 1.0), and the respiratory rate decreased to 28 breaths per minute.

Dr. Petranović: A portable chest radiograph (Fig. 1C) showed persistent asymmetric lung opacities. Also seen were new septal lines, increased thickening of the right minor fissure, and increased perihilar haziness.

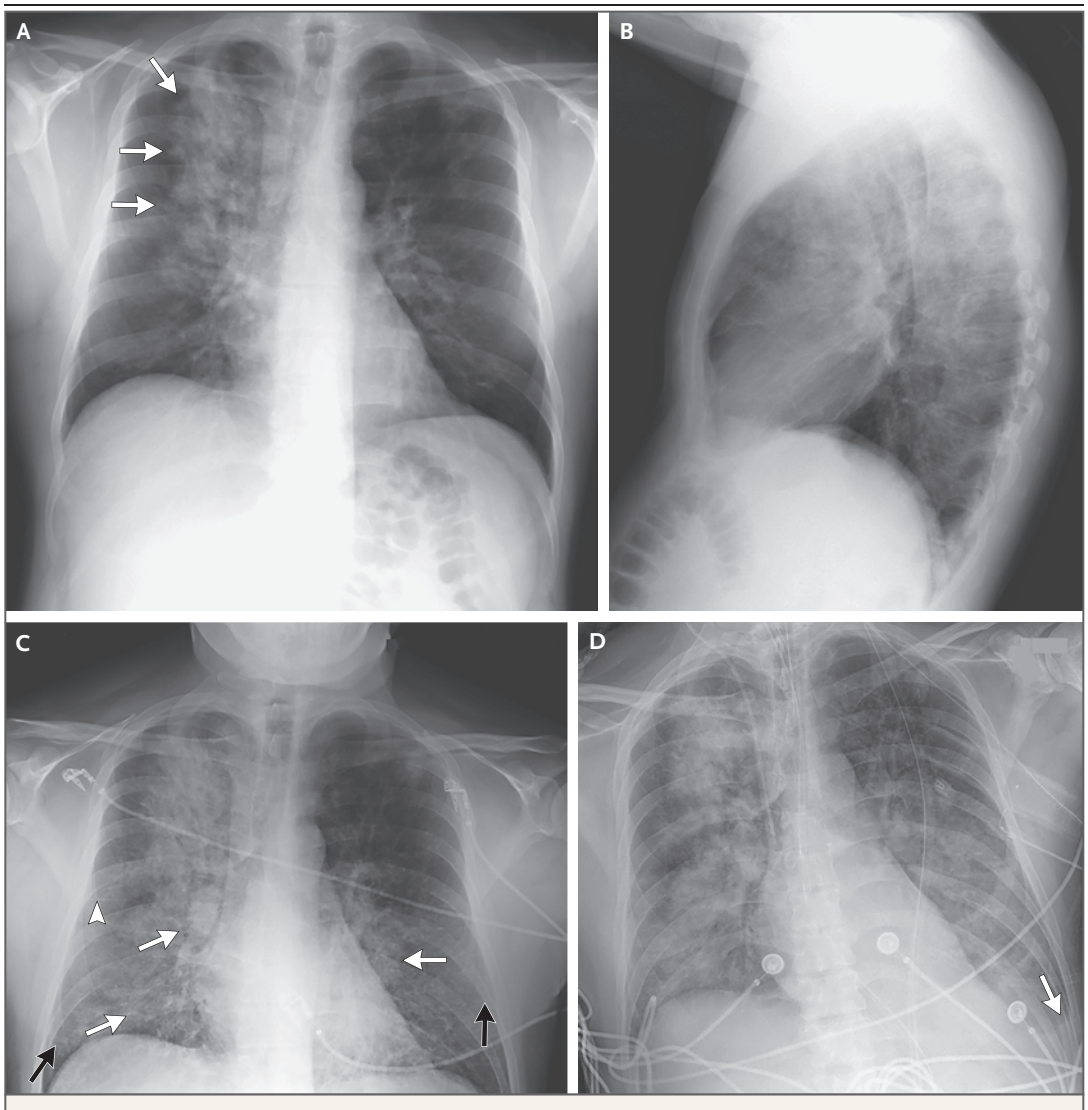


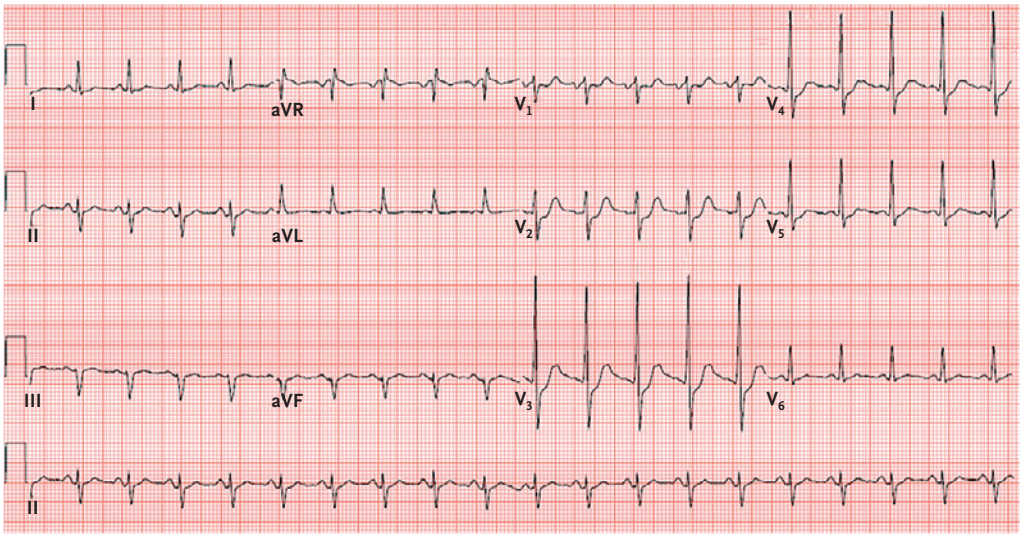
Figure 1. Chest Radiographs.

Initial upright posteroanterior and lateral chest radiographs obtained on presentation to the other hospital (Panels A and B, respectively) show markedly asymmetric lung opacities located predominantly in the central portion of the right upper lobe (Panel A, arrows). A semiupright anteroposterior portable chest radiograph obtained 5 hours after presentation to the other hospital (Panel C) shows persistent asymmetric lung opacities. Also shown are new septal lines (black arrows), increased thickening of the right minor fissure (arrowhead), and increased perihilar haziness (white arrows). An anteroposterior portable chest radiograph obtained on presentation to this hospital (Panel D) shows increased perivascular haziness diffusely, with a more widespread distribution of the previously seen opacities, which remain most dense in the right upper lobe. There is also new blunting of the left costophrenic angle (arrow). The endotracheal tube, nasogastric tube, esophageal temperature probe, and central venous catheter are in the appropriate positions.

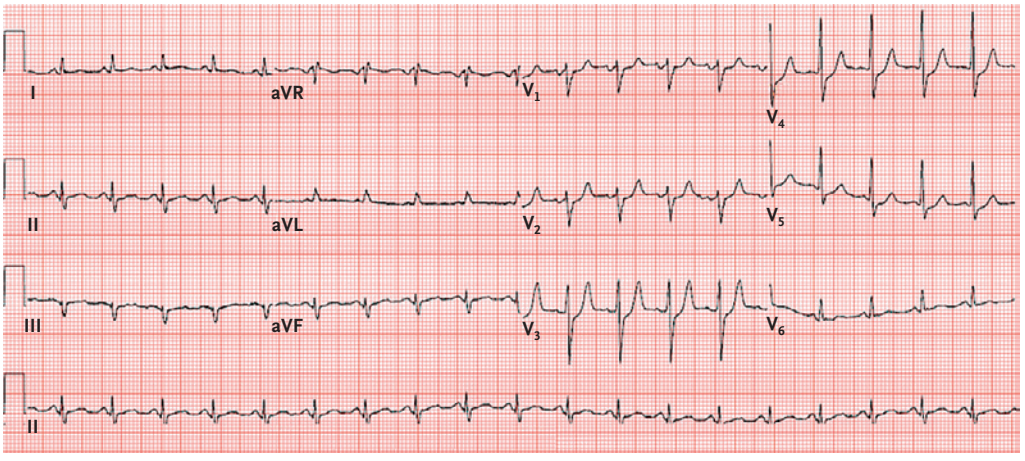
Dr. Martin: Eight hours after presentation to the other hospital, worsening shortness of breath developed, along with diaphoresis. On examination, the temperature was 37.7°C, the heart rate 146 beats per minute, the blood pressure 150/76 mm Hg, the respiratory rate 46 breaths per minute, and the oxygen saturation 88% while he was receiving oxygen through a nonrebreather face mask (F_{IO_2}, 1.0). Rapid antigen testing for influenza types A and B was negative.

A trial of noninvasive positive-pressure ventilation was performed, but respiratory distress

A On Presentation, Other Hospital



B 12 Hr after Presentation, Other Hospital



C On Presentation, This Hospital

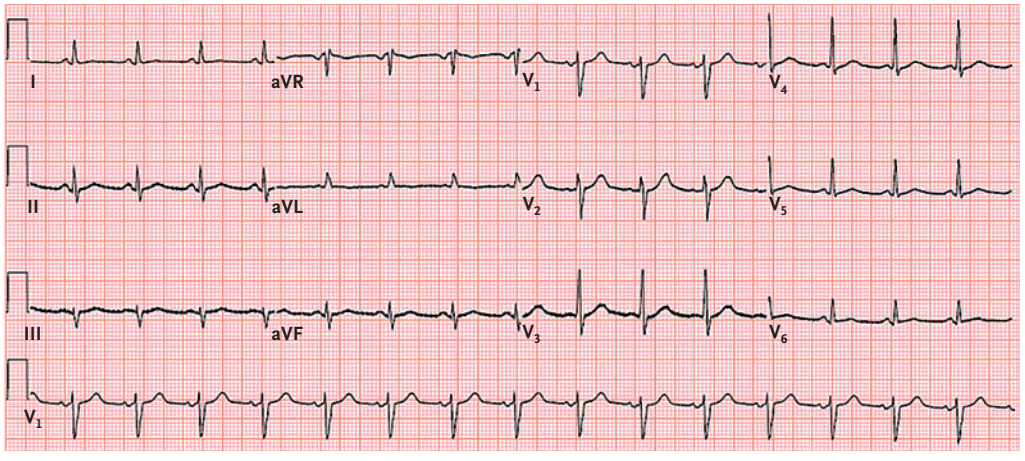


Figure 2 (facing page). Electrocardiograms.
An electrocardiogram obtained on presentation to the other hospital (Panel A) shows sinus tachycardia with left axis deviation, left atrial abnormality, early R-wave progression, and nonspecific ST-segment depressions in the anterior leads. A repeat electrocardiogram obtained 12 hours after presentation to the other hospital (Panel B) shows improvement in the ST-segment depressions in the anterior leads. An electrocardiogram obtained on presentation to this hospital (Panel C) shows normal sinus rhythm with resolution of the ST-segment depressions, without the development of any pathologic Q waves.

persisted. The trachea was intubated, and copious frothy secretions were noted. Mechanical pressure-control ventilation was initiated (inspiratory pressure, 15 cm of water; positive end-expiratory pressure [PEEP], 10 cm of water; F_{IO_2}, 1.0; respiratory rate, 14 breaths per minute; peak inspiratory pressure, 31 cm of water). Propofol was administered. Hypoxemia persisted despite the use of mechanical ventilation, deep suctioning, and recruitment maneuvers; paralysis with an infusion of cisatracurium was begun. Flexible bronchoscopy revealed a normal-appearing airway with pink frothy secretions, without purulent exudates or bleeding; bronchial washings and bronchoalveolar lavage (BAL) samples were obtained for microbiologic testing. A central venous catheter was placed in the right internal jugular vein; the central venous pressure was not recorded.

Dr. Malhotra: A repeat electrocardiogram (Fig. 2B) showed sinus tachycardia with left axis deviation and moderate improvement in the previously observed ST-segment depressions in the anterior leads.

Dr. Martin: Glucocorticoids and intravenous vancomycin, cefepime, levofloxacin, trimethoprim–sulfamethoxazole, and furosemide were administered. On serial arterial blood gas analyses performed over a 12-hour period, the patient had a pH as low as 7.11, a partial pressure of oxygen of 45 to 74 mm Hg, an oxygen saturation of 86 to 89% while he was receiving oxygen through a mechanical ventilator (F_{IO_2}, 1.0), and persistent tachycardia at a rate of 120 to 150 beats per minute. Early the following morning, he was transferred by ambulance to the ICU of this hospital.

On presentation to this hospital, additional information was obtained from the patient's partner. The patient had a history of hyperlipidemia, hypertension, benign prostatic hypertrophy, and hemorrhoids. He had undergone tonsillectomy but no other surgeries. His outpatient medications included atorvastatin, hydrochlorothiazide, inhaled fluticasone, and hydrocortisone rectal cream, but he had not been taking any medications regularly. He had no known allergies to medications. His father had died of a myocardial infarction at 61 years of age, and two paternal uncles had also died of coronary artery disease, one in the fifth decade and one in the sixth decade. He did not smoke tobacco, drink alcohol, or use illicit drugs. He had a long-term male partner but was not sexually active. He worked at a university. He had traveled to Washington, D.C., the week before presentation.

On examination, the temperature was 36.7°C, the heart rate 98 beats per minute, the blood pressure 116/77 mm Hg, and the oxygen saturation 93% while the patient was receiving oxygen through a mechanical ventilator (tidal volume, 420 ml; PEEP, 15 cm of water; F_{IO_2}, 1.0; respiratory rate, 28 breaths per minute; plateau pressure, 26 cm of water). The central venous pressure ranged from 12 to 15 cm of water. Auscultation of the chest revealed regular heart sounds, a systolic murmur (grade 3/6) that was best heard at the right upper sternal border, and scant rales and rhonchi bilaterally. The arms and legs were warm, without edema; faint areas of livedo reticularis were noted, but no rashes were seen. The remainder of the examination was normal.

Tests for *Legionella pneumophila* serogroup 1 and *Streptococcus pneumoniae* antigens in the urine were negative, as were polymerase-chain-reaction tests for influenza types A and B and respiratory syncytial virus in BAL samples. Tests for adenovirus and parainfluenza virus antigens in the sputum and human immunodeficiency virus p24 antigen and antibodies in the blood were negative. Gram's staining of the BAL samples revealed few neutrophils and no organisms. The C-reactive protein level was 333.0 mg per liter (reference range, <8.0); other laboratory test results are shown in Table 1.

Dr. Malhotra: An electrocardiogram (Fig. 2C) showed normal sinus rhythm with early R-wave progression and resolution of the previously observed ST-segment depressions.

Dr. Petranović: A portable chest radiograph (Fig. 1D) showed increased perivascular haziness diffusely, with a more widespread distribution of

the previously seen opacities, which remained most dense in the right upper lobe. There was also new blunting of the left costophrenic angle. The endotracheal tube, nasogastric tube, esophageal temperature probe, and central venous catheter were in the appropriate positions.

Dr. Martin: When the patient had arrived at this hospital, the ventilator mode had been switched to volume-controlled ventilation for lung protection, and the PEEP increased. The dose of cisatracurium was increased, and an intravenous hydromorphone infusion was started to optimize patient–ventilator synchrony. Four hours after arrival, the administration of inhaled nitric oxide was initiated. Eight hours after arrival, the F_{IO_2} was decreased from 1.0 to 0.4.

Diagnostic tests were performed.

DIFFERENTIAL DIAGNOSIS

Dr. Charles C. Hardin: This 52-year-old man presented with low-grade fever, hypoxemia, and a pulmonary infiltrate that was initially confined to the right upper lobe. In critical care, we frequently construct a differential diagnosis around the most life-threatening organ failure, which in this case is hypoxemia. Possible causes of hypoxemia include a low partial pressure of inspired oxygen (P_{IO_2}), diffusion limitation, hypoventilation, ventilation–perfusion mismatch, and shunt.[1]

Three of these causes of hypoxemia can be ruled out quickly in this patient. A low P_{IO_2} is typically observed at high altitude, and it would be observed at sea level only in an unusual set of circumstances. Diffusion limitation — failure of equilibration between the partial pressure of oxygen in the pulmonary end-capillary blood and the partial pressure of alveolar oxygen — occurs infrequently at rest. It typically occurs at high altitude and during high levels of exercise, as well as during low levels of exercise in patients with interstitial lung diseases.[2] Isolated hypoventilation results in hypoxemia with a normal alveolar–arterial gradient.[3] In this patient, the alveolar–arterial gradient is markedly elevated and the partial pressure of arterial carbon dioxide is low, findings that rule out hypoventilation as the cause of hypoxemia. We are therefore left with ventilation–perfusion mismatch and shunt, either alone or in combination, as possible causes of this patient's life-threatening illness.

The arterial oxygen content reflects the balance between air flow (ventilation) and blood flow (perfusion) into the alveolar air spaces. The ratio of these flows, known as the ventilation–perfusion ratio, is low when the balance is tipped toward perfusion and is high when the balance is tipped toward ventilation.[4] When the ventilation–perfusion ratio is low or high, ventilation–perfusion mismatch occurs. A low ratio can lead to arterial hypoxemia.

This patient initially had a response to supplemental oxygen. Such a response classically rules out the presence of a shunt,[5] but multiple mechanisms of hypoxemia may coexist.[6,7] The response to supplemental oxygen, however, indicates the presence of a low ventilation–perfusion ratio in at least some lung units, or areas of the lung, so we may construct our differential diagnosis on the basis of this finding.

Why does this patient have a low ventilation–perfusion ratio in some lung units? In the presence of a pulmonary infiltrate, we can infer that he has had a loss of alveolar stability and a subsequent decrease in ventilation. Loss of alveolar stability may occur when fluid enters the air spaces and disrupts the balance of forces at the air–liquid interface, which is facilitated by surfactant. This may result from increased permeability of the alveolar–capillary membrane (in noncardiogenic edema) or elevated pulmonary venous pressure (in cardiogenic edema). Depending on the severity of the disturbance, the end result is either a low ventilation–perfusion ratio or a fully developed intrapulmonary shunt, in which blood flows to a completely nonaerated lung unit.[5] Possible causes of a low ventilation–perfusion ratio in this patient include community-acquired pneumonia, acute respiratory distress syndrome (ARDS), pulmonary embolism, interstitial lung disease, pulmonary hemorrhage, and pulmonary edema from either heart failure or valve dysfunction, particularly mitral regurgitation.[8]

COMMUNITY-ACQUIRED PNEUMONIA

This patient presented with low-grade fever, an elevated C-reactive protein level, and a pulmonary infiltrate. However, a comprehensive infectious workup was performed and was negative. He could have pneumonia caused by an organism that is hard to identify or cannot be identified because of the rapid initiation of antibiotic therapy, but this

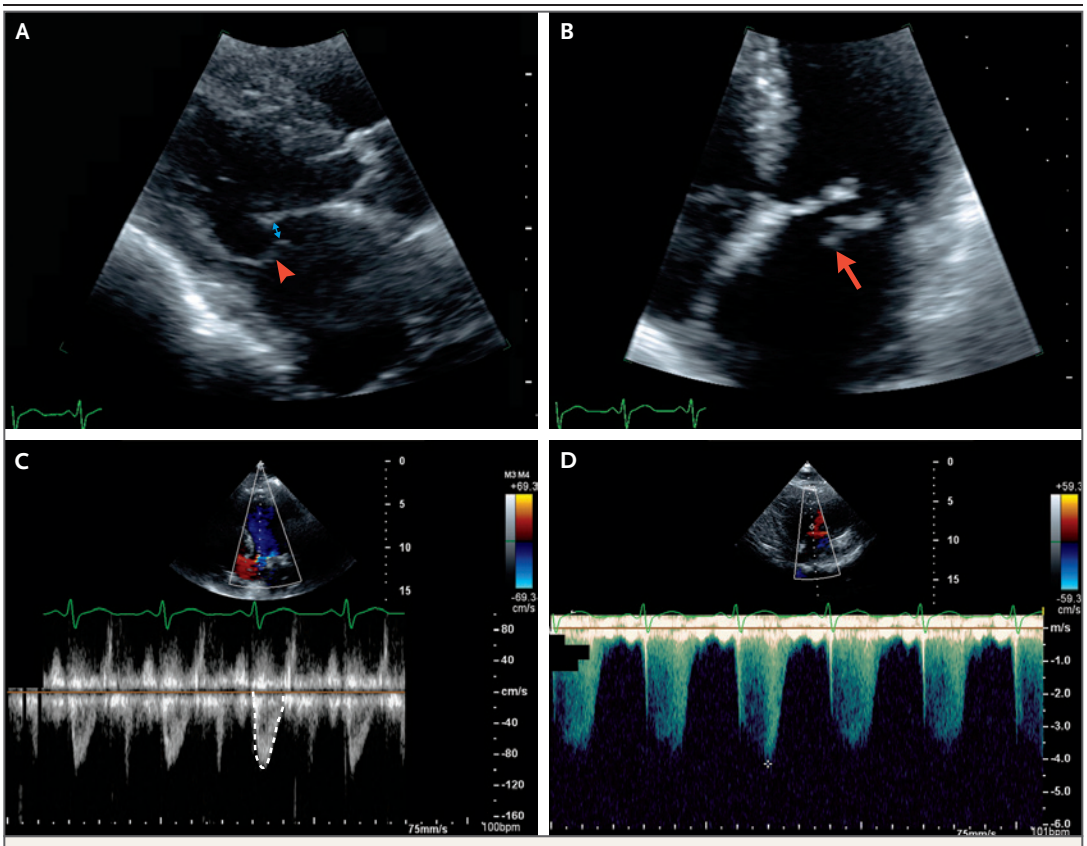


Figure 3. Transthoracic Echocardiogram.

A transthoracic echocardiogram was obtained on hospital day 2. The parasternal long-axis view (Panel A) shows a coaptation gap between the anterior and posterior mitral leaflets (double arrow) and a flail posterior mitral leaflet (arrowhead). The apical four-chamber view (Panel B) shows submitral chordae prolapsing into the left atrium (arrow) and rightward bowing of the interatrial septum. On spectral Doppler sampling (Panel C), the velocity time integral in the left ventricular outflow tract (dashed line) indicates a forward stroke volume of 37 ml (reference range, 60 to 120). Also on spectral Doppler sampling (Panel D), there is pulmonary hypertension with an estimated right ventricular systolic pressure of 79 mm Hg.

diagnosis is unlikely. Therefore, although pneumonia is possible, it is relegated to a low position in my differential diagnosis.

ACUTE RESPIRATORY DISTRESS SYNDROME

ARDS is a classic cause of noncardiogenic pulmonary edema.[9] Defining features of ARDS include an acute onset of illness, hypoxemia, and a bilateral infiltrate. In patients with ARDS, severe hypoxemia is most frequently associated with a concordant severe decrease in lung compliance and a widespread pulmonary infiltrate. We are told that after the ventilator mode was switched to volume-controlled ventilation, this patient had a plateau pressure of 26 cm of water and a PEEP of 15 cm of water. The driving pressure (the difference between the plateau pressure and the PEEP) of only 11 cm of water and the tidal volume of 420 ml suggest a disconnect between the severe hypoxemia and the moderate disturbance in lung compliance.

PULMONARY EMBOLISM

Pulmonary embolus can lead to a low ventilation–perfusion ratio, since the cardiac output is redirected from affected lung units. However, it does not commonly result in an infiltrate, and the infiltrate seen in this patient is not classic for a pulmonary infarct. In addition, there is no history suggestive of a prothrombotic state. Therefore, pulmonary embolus is unlikely in this case.

INTERSTITIAL LUNG DISEASE

Interstitial lung disease can be acute under some circumstances. Acute interstitial pneumonia, organizing pneumonia, and acute eosinophilic pneumonia can also mimic an acute infectious process. However, this patient has no specific imaging findings or history that would be consistent with interstitial lung disease, and the fact that the disease is acute also makes this diagnosis unlikely.

PULMONARY HEMORRHAGE

Patients with pulmonary hemorrhage can present with an infiltrate and hypoxemia. Pulmonary hemorrhage classically results from the various causes of pulmonary capillaritis, but coagulopathy can also lead to hemorrhage. The diagnosis is based on the progressive presence of blood in BAL fluid, which was not found in this patient; the absence of this finding rules out this diagnosis.

CARDIOGENIC PULMONARY EDEMA

Acute causes of cardiogenic pulmonary edema include acute coronary syndrome, acute heart failure, and acute valvular heart disease, specifically acute mitral regurgitation. Acute systolic dysfunction that results in an elevated pulmonary capillary wedge pressure (either ischemia or an acute exacerbation of chronic systolic dysfunction) is not consistent with the presence of a hyperdynamic left ventricle on bedside ultrasonographic examination. Hypertrophic obstructive cardiomyopathy would be consistent with the hyperdynamic left ventricle and can result in an elevated left ventricular end-diastolic pressure and systolic murmur. However, acute onset is rare and is more often associated with hypotension and hypoxemia than with isolated hypoxemia. Moreover, in patients with hypertrophic obstructive cardiomyopathy, hypoxemia is often associated with mitral regurgitation. Mitral stenosis and tachycardia can lead to pulmonary edema and hypoxemia but would typically be associated with a diastolic murmur.

Videos showing echocardiographic studies are available at NEJM.org

The diagnosis of acute mitral regurgitation may be supported by certain aspects of the history, such as the systolic murmur, which may be the murmur associated with regurgitant flow. The fact that the murmur was heard best at the right upper sternal border may reflect severe mitral regurgitation that is directed anteriorly, possibly toward the right upper pulmonary vein. Patients with acute mitral regurgitation can present with an asymmetric pulmonary infiltrate, which develops when an eccentric regurgitant jet leads to differential pressures in the pulmonary veins and disproportionate regional edema.[10] The hyperdynamic left ventricle on bedside ultrasonography is also consistent with acute mitral regurgitation. Finally, acute mitral regurgitation can be associated with severe hypoxemia, since the increase in volume results in a large increase in pressure in the relatively noncompliant left atrium. I suspect that acute mitral regurgitation is the most likely cause of this patient's pulmonary edema and hypoxemia. To confirm this diagnosis, I would obtain a formal transthoracic echocardiogram.

DR. CHARLES C. HARDIN'S DIAGNOSIS

Acute mitral regurgitation.

TRANSTHORACIC ECHOCARDIOGRAPHY

Dr. Sheila Klassen: A transthoracic echocardiogram obtained on hospital day 2 showed hyperdynamic left ventricular systolic function. A large portion of the posterior mitral leaflet was flail (Fig. 3A; and Video 1, available with the full text of this article at NEJM.org). Mobile linear echodensities that represented ruptured chordae were seen prolapsing into the left atrium (Fig. 3B). The mitral valve did not have a classic myxomatous appearance. There was anteriorly directed mitral regurgitation, which was severe according to both color Doppler assessment and quantitative measures. The image quality was not adequate to assess for flow reversal in the pulmonary veins; however, on color Doppler, flow was directed toward the right upper pulmonary vein (Video 2). The left atrium was dilated, and the interatrial septum was bowed rightward. The mean gradient across the mitral valve (measured at a heart rate of 100 beats per minute) was 6 mm Hg, indicating high transmitral flow. On spectral Doppler sampling, estimated velocities in the left ventricular outflow tract indicated a low forward stroke volume (Fig. 3C), a finding that reflects the severity of mitral regurgitation. There was pulmonary hypertension with an estimated right

ventricular systolic pressure of 79 mm Hg (Fig. 3D), as well as mild-to-moderate tricuspid regurgitation. Right ventricular systolic function was normal; there were no regional wall-motion abnormalities or vegetations on the cardiac valves, and there was no pericardial effusion.

DISCUSSION OF MANAGEMENT

Dr. Malhotra: In patients with acute mitral regurgitation, the regurgitant volume leads to an abrupt rise in left atrial pressure and a reduction in forward flow, commonly resulting in hypotension and shock. In patients with normal left atrial compliance, acute mitral regurgitation also leads to a dramatic rise in backward filling pressure in the pulmonary capillaries, which can result in severe pulmonary edema.

The focus of management of acute mitral regurgitation is to support the patient's hemodynamic and respiratory status. Medical stabilization with intravenous nitroprusside and inodilator therapy (dobutamine or milrinone) is often used as a bridge to corrective treatment. The advantage of inodilator agents is that they not only reduce systemic afterload but also increase contractility, which can potentially improve forward flow. Vasopressors are relatively contraindicated because of alpha-adrenergic–receptor agonism, which causes increased systemic afterload that may worsen the degree of regurgitation. If nitroprusside and inodilator therapy are insufficient to maintain adequate hemodynamic support, mechanical circulatory support would be considered. An intraaortic balloon pump reduces systemic afterload and also increases coronary perfusion, which can be beneficial in patients with ischemic mitral regurgitation.[11] Occasionally, other forms of mechanical circulatory support that provide greater flow, such as a percutaneous microaxial transaortic ventricular assist device or venoarterial extracorporeal membrane oxygenation, are used to maintain hemodynamic stability.

These therapies serve as a bridge to the corrective treatment of acute mitral regurgitation. The next step in the treatment of this patient is to determine the underlying cause of the acute mitral regurgitation. Some possibilities are ischemic mitral-valve disease, nonischemic mitral regurgitation due to myxomatous disease or endocarditis, and less commonly, rheumatic heart disease, trauma, or spontaneous rupture. The echocardiogram did not show evidence of myxomatous disease, endocarditis, or rheumatic heart disease. Acute chordal or papillary muscle rupture may be the cause in this patient.

In the case of acute ischemic mitral regurgitation, it is important to consider the blood supply to the mitral valve. Anterolateral papillary muscle rupture is an uncommon complication of myocardial infarction because the anterolateral papillary muscle has a dual blood supply from the left circumflex and left anterior descending arteries. Posteromedial papillary muscle rupture is more common because the posteromedial papillary muscle has a single blood supply from the posterior descending artery.[12] Emergency coronary revascularization is considered to be the treatment of choice for acute ischemic mitral regurgitation.[13-15]

In the absence of clinically significant epicardial coronary artery disease, acute mitral regurgitation can still result from ischemic causes in a condition known as myocardial infarction with nonobstructive coronary arteries (MINOCA)[16]; such causes include coronary artery vasospasm, acute coronary thromboembolic disease, microvascular disease, and stress cardiomyopathy. The spectrum of acute ischemic mitral-valve diseases ranges from full papillary muscle rupture to partial papillary muscle rupture or papillary muscle displacement without any rupture. The presence of any degree of rupture is an indication for rapid surgical intervention.

In this case, on the basis of the echocardiographic findings and the presence of hemodynamic instability, the patient was referred for emergency cardiac surgery. As part of the evaluation associated with that surgery, cardiac catheterization was performed.

ARTERIOGRAPHY

Dr. Nino Mihatov: Coronary arteriography was performed to determine whether coronary-artery bypass grafting would be needed during mitral-valve surgery and to elucidate the mechanism of papillary muscle rupture. Attention was first directed toward this patient's dominant right coronary artery, the vessel that gives rise to the posterior descending artery and supplies the posteromedial papillary muscle. There was no evidence of clinically significant obstructive cor-

onary artery disease in the right or left coronary arteries. After arteriography was performed, the patient underwent emergency mitral-valve surgery.

TRANSESOPHAGEAL ECHOCARDIOGRAPHY

Dr. Klassen: An intraoperative transesophageal echocardiogram that was obtained before the initiation of cardiopulmonary bypass again showed hyperdynamic left ventricular systolic function. A large portion of the P2 scallop and the lateral portion of the P3 scallop of the posterior mitral leaflet were flail (Video 3), causing the eccentric, anteriorly directed jet of mitral regurgitation. Ruptured chordae and a small segment of papillary muscle head were seen attached to the flail segments and prolapsing into the left atrium; these findings are consistent with posteromedial papillary muscle rupture. Intraoperative findings confirmed a ruptured papillary muscle supporting the P2 scallop of the posterior mitral leaflet. A triangular resection was performed to remove the flail segment, and the remainder of the leaflet was reapproximated to resemble normal anatomy. A complete annuloplasty ring was placed. On images obtained after cardiopulmonary bypass, the annuloplasty ring was well seated and there appeared to be trace residual mitral regurgitation (Video 4). The mean gradient across the repaired mitral valve (measured at a heart rate of 95 beats per minute) was 2 mm Hg.

PATHOLOGICAL DISCUSSION

Dr. Derek H. Oakley: The excision specimen of the mitral valve and papillary muscle was submitted for pathological evaluation. The specimen consisted of a 2.1-cm fragment of valve and attached papillary muscle, as well as a 1.0-cm fragment of valve leaflet. The resected fragment of mitral valve showed mild myxomatous degeneration. Hematoxylin and eosin staining revealed evidence of acute myocardial infarction of the papillary muscle that had occurred approximately 6 to 10 days earlier (Fig. 4). No specific cause of infarction was identified.

POSTOPERATIVE MANAGEMENT

Dr. Mihatov: A postoperative transthoracic echocardiogram showed preserved biventricular func-

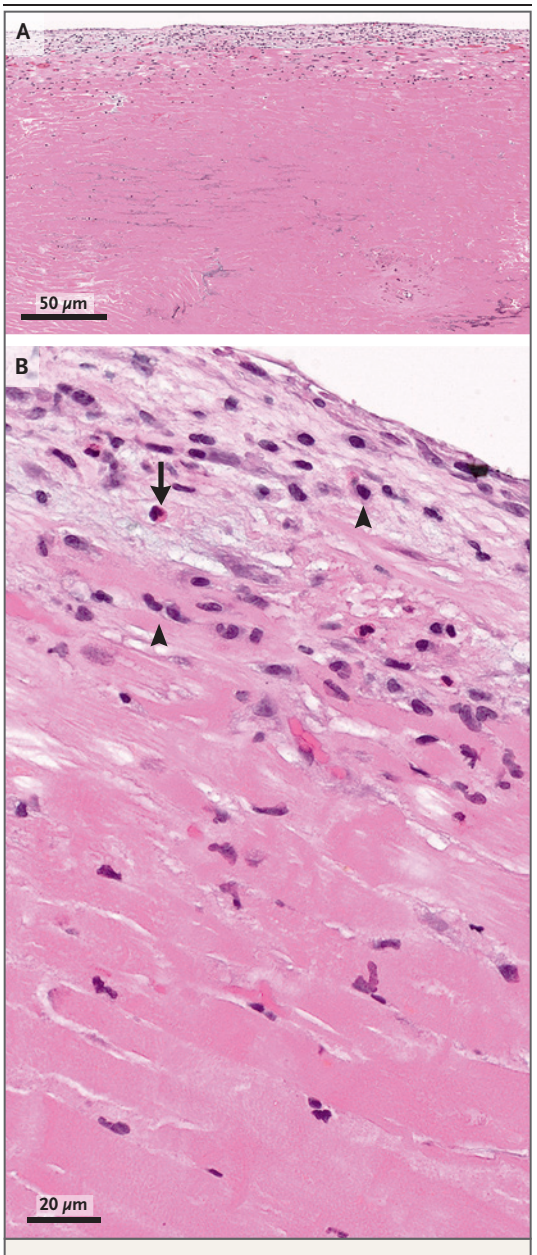


Figure 4. Excision Specimen.
Hematoxylin and eosin staining of the infarcted papillary muscle (Panel A) shows eosinophilia and loss of nuclear staining around the infarction. There is an inflammatory infiltrate arising from the ventricle and moving through the endocardial lining into underlying necrotic myocardium (top to bottom). There is superficial sparing of cardiomyocytes due to perfusion from the ventricular space. The absence of inflammation in the interior of the infarct is due to the absence of perfusion. At higher magnification (Panel B), there are necrotic cardiomyocytes and an inflammatory infiltrate composed predominantly of macrophages (arrowheads) with a few residual neutrophils (arrow).

tion and an appropriately placed annuloplasty ring. There was no evidence of a patent foramen ovale on spectral Doppler sampling or on studies obtained after the injection of agitated saline, both at rest and during a Valsalva maneuver. There was trace mitral regurgitation and a mean transvalvular gradient (measured at a heart rate of 93 beats per minute) of 4 mm Hg. After surgery, the patient had acute kidney injury but subsequently had complete recovery of renal function. All cultures remained negative. He was found to have a deep-vein thrombosis of the right common femoral vein, for which he was treated with warfarin (with a plan to continue treatment for 6 months). He was discharged on hospital day 19.

In anticipation of cardiac rehabilitation, the patient completed 10 minutes 30 seconds (an estimated 13 metabolic equivalents) of a standard exercise stress test in accordance with the Bruce protocol, attaining 88% of his maximum predicted heart rate. Nuclear perfusion imaging showed a fixed inferolateral perfusion defect that was suggestive of a small scar.

The patient was seen for a follow-up visit 1 month after discharge and had no residual symptoms. He returned to full-time work after successful completion of cardiac rehabilitation. He performed 30 minutes of aerobic exercise daily without symptoms, and he continued to do so 6 months after discharge.

FINAL DIAGNOSIS

Flail mitral valve due to acute myocardial infarction of the papillary muscle in the absence of obstructive coronary artery disease.

This case was presented at the Medical Case Conference.

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

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