42-Year-Old Man With Hemoptysis, Dyspnea, and Orthopnea

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A 42-year-old man was transferred to St. Mary's Hospital, Rochester, Minnesota, for evaluation of hemoptysis. He was born in Laos and immigrated to the United States at age 6 years. He had a history of mitral valve commissurotomy 25 years previously in the setting of rheumatic mitral stenosis (MS). He also had known esophageal varices from cirrhosis secondary to chronic hepatitis B. He had been in a normal state of health until 6 months before presentation, when he began experiencing increasing dyspnea on exertion. He also complained of progressively worsening nocturnal cough exacerbated by lying supine, forcing him to sleep in a recliner. The cough progressed to become productive of blood-tinged sputum. He denied having any syncopal episodes, fevers, chills, or night sweats. He was a lifelong nonsmoker and denied any intravenous drug use, recent travel, or history of incarceration.

1. Which *one* of the following is the *most likely* cause of hemoptysis in this patient?

a. Acute pulmonary embolism
b. Tuberculosis (TB)
c. Lung cancer
d. Esophageal varices
e. MS

Acute pulmonary embolism can cause distention of the pulmonary vessels, leading to rupture with resulting hemoptysis. The chronicity of this patient's dyspnea and lack of pleuritic chest pain make acute pulmonary embolism unlikely. Tuberculosis can cause hemoptysis resulting from caseous sloughing or endobronchial erosion. Hemoptysis may be sudden and massive in the case of pulmonary arterial erosion by an advancing tuberculous cavity (Rasmussen aneurysm). Despite having spent 6 years in Laos, our patient denied fever, night sweats, and other systemic findings seen with TB. Given the clinical history, TB would not be the most likely cause of hemoptysis in this patient. Malignancy must always be included in the differential diagnosis for hemoptysis, particularly in elderly smokers. The patient was 42 years old and had never smoked, making bronchogenic carcinoma an unlikely culprit. Prior upper endoscopy had demonstrated evidence of esophageal varices, which can cause hematemesis. However, they would not cause hemoptysis from bleeding into the tracheobronchial tree. Mitral stenosis has been reported to cause 5 different forms of hemoptysis: (1) "pulmonary apoplexy," ie, sudden, unexpected, profuse hemorrhage precipitated by exercise or pregnancy; (2) blood-stained sputum associated with dyspneic attacks due to acute pulmonary congestion; (3) pink, frothy sputum seen in pulmonary edema; (4) blood-streaked sputum associated with bronchitis; and (5) frank hemoptysis from pulmonary infarction.[1] The prevalence of hemoptysis in patients with MS was around 50% in earlier series among patients undergoing valvotomy or in cohorts from developing countries, which makes this the most likely answer.[1-3]

On arrival at our hospital, the patient was afebrile and had a blood pressure of 155/134 mm Hg, heart rate of 101 beats/min, arterial oxygen saturation of 94% while breathing room air, and respiratory rate of 18 breaths/min. Jugular venous pulsations were markedly elevated. Cardiac auscultation revealed a regular tachycardic rhythm. A grade 3/6 diastolic rumble was heard best at the apex, and a grade 2/6 systolic crescendo-decrescendo murmur was heard loudest at the right second intercostal space with radiation to the carotid arteries. There was no opening snap, S_3, or S_4. A left parasternal lift was palpable, suggestive of either right ventricular (RV) or left atrial (LA) enlargement. Pulmonary examination revealed stony dullness to percussion and significantly decreased breath sounds in the left lower lung base posteriorly.

Initial laboratory studies yielded the following results (normal reference ranges provided parenthetically for abnormal values): hemoglobin, 12.0 g/dL (13.5-17.5 g/dL); leukocyte count, 4.9 × 10^9/L; platelet count, 58 × 10^9/L (150-450 × 10^9/L); prothrombin time, 15.7 seconds (9.5-13.8 seconds); aspartate aminotransferase, 133 U/L (8-48 U/L); alanine aminotransferase, 68 U/L (7-55 U/L). (To convert hemoglobin value to g/L, multiply by 10.0; to convert aspartate and alanine aminotransferase values to μkat/L, multiply by 0.0167.)

2. Which *one* of the following electrocardiography (ECG) findings would you *most likely* see in this patient?

a. Biphasic P waves and tall R waves in V_1
b. Tall monophasic P wave in V_1 and right axis deviation
c. Left ventricular (LV) hypertrophy with repolarization abnormality
d. Irregular rate with no discernible P waves
e. Low voltage in limb leads with electrical alternans

Our patient has a history of MS treated with commissurotomy in the past. He presented with

See end of article for correct answers to questions.

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physical examination findings including RV lift and elevated jugular venous pulsations, suggesting secondary pulmonary hypertension as well as RV hypertrophy and dysfunction. Electrocardiographic evidence of LA enlargement is seen in up to 90% of patients with MS.[4] Biphasic P waves with prominent negative deflection in V_1 due to LA enlargement and tall R waves with right axis deviation suggesting RV hypertrophy can be seen on ECG in patients with MS because of pressure overload upstream of the mitral valve, which is why this is the correct answer. Monomorphic P waves in V_1 and right axis deviation are most suggestive of pulmonic valve stenosis. Left ventricular hypertrophy with repolarization abnormality may be seen in aortic stenosis or hypertrophic cardiomyopathy, but the left ventricle is not typically enlarged in MS. Although patients with MS often develop atrial arrhythmias, this patient's regular rhythm on auscultation makes atrial fibrillation unlikely. Blood pressure was elevated, and there were no muffled heart sounds to suggest pericardial effusion or tamponade, which may be associated with low voltage in limb leads and electrical alternans on ECG.

Electrocardiography was performed, demonstrating sinus tachycardia with normal axis. There were biphasic P waves and tall R waves in V_1 with no ST-segment or T-wave abnormalities.

Our patient was admitted to the hospital and placed in respiratory isolation until TB was ruled out. β-Blocker and loop diuretic therapy was initiated. Chest radiography revealed a moderate left-sided pleural effusion as well as left-sided retrocardiac infiltrates and mildly increased pulmonary vasculature. Thoracentesis of the left pleural effusion was performed for both therapeutic and diagnostic purposes. Culture and cytologic examination of the fluid showed no malignancy or infection. Our patient continued to complain of cough and hemoptysis while supine, which resolved by the third day of hospitalization. His heart failure was classified as New York Heart Association functional class III. Esophagogastroduodenoscopy revealed esophageal varices, portal hypertensive gastropathy, and superficial antral ulceration with duodenal bulb erosion.

3. Which *one* of the following is the *most common* cause of MS?

a. Congenital MS
b. Rheumatic fever
c. Exuberant vegetations associated with infective endocarditis
d. Ball-valve thrombus of the left atrium
e. Occlusive atrial myxoma

The most common cause of MS is rheumatic fever.[4] Of the stenotic mitral valves that are removed at the time of replacement, 99% have associated rheumatic changes.[4] Congenital MS, infective endocarditis–associated vegetations, LA thrombi, and atrial myxoma only rarely cause obstruction of LV inflow. Combined mitral and aortic stenosis in the same patient is almost exclusively secondary to rheumatic heart disease.[5]

Transthoracic and transesophageal echocardiography were performed, revealing severe rheumatic mitral valve stenosis with restricted mid-leaflet mobility resulting in "hockey stick" deformity with thickened calcified leaflet tips, commissural calcification, and moderate subvalvular thickening. The left atrium was severely enlarged, with no thrombus visualized in the LA appendage. The aortic valve also had thickened cusps, causing mild to moderate rheumatic aortic stenosis. Left ventricular ejection fraction was 65%.

4. On the basis of the echocardiographic findings, which *one* of the following would be the *best* course of action in this patient?

a. No additional therapy at this time. Follow up with outpatient echocardiography in 6 months
b. Continued medical management
c. Percutaneous mitral balloon valvotomy (PMBV)
d. Hemodynamic exercise test to assess dynamic change in mitral valve gradient
e. Mitral valve surgery

Echocardiography should be performed in asymptomatic patients with known MS at regular intervals (yearly for severe MS, every 1-2 years for moderate MS, and every 3-5 years for mild MS) to assess severity of valvular stenosis and also to assess pulmonary pressures.[6] Medical therapy may reduce symptoms, but because of the fixed nature of the obstruction, relief of obstruction is the preferred intervention in moderate to severe symptomatic MS. Percutaneous mitral balloon valvotomy is the initial treatment of choice in symptomatic patients with MS, provided the valve leaflets and subvalvular apparatus are not too thickened or calcified. However, our patient's severe valvular deformity and commissural calcification increase the risk of significant postprocedural mitral regurgitation with PMBV. The resting imaging study already demonstrates severe MS and secondary changes, and our patient is symptomatic. Therefore, in this setting, a hemodynamic exercise test does not add any incremental benefit in the evaluation. Thus, mitral valve surgery would be the treatment option of choice.

After detailed discussions between the hematology, hepatobiliary, cardiology, and cardiovascular surgery services, it was decided that the best treatment option for this patient would be to proceed with surgical replacement of his mitral and aortic

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valves using porcine and bovine bioprosthetic valves, respectively, to avoid the necessity of lifelong anticoagulation in the setting of coagulopathy and thrombocytopenia due to chronic liver disease. Three weeks later, the patient underwent bioprosthetic mitral and aortic valve replacement and exclusion of the LA appendage.

5. **In which *one* of the following patients with rheumatic MS and normal sinus rhythm would oral anticoagulation therapy be *most indicated*?**

   a. Older age (>75 years)
   b. History of embolic stroke
   c. Ejection fraction of 34%
   d. Moderate mitral regurgitation
   e. Coexisting severe rheumatic aortic stenosis

Older age is associated with increased risk of embolization in atrial fibrillation, but oral anticoagulation for patients with MS who have normal sinus rhythm is not recommended unless other indications are present. Oral anticoagulation therapy is indicated for MS in patients with atrial fibrillation, known LA thrombus, or prior embolic event (even in those with sinus rhythm).[6] Anticoagulation may also be considered in patients with severe MS and LA dimension greater than 55 mm on echocardiography.[6] Low ejection fraction, concurrent mitral valve regurgitation, and coexisting rheumatic aortic stenosis have not been associated with increased embolic risk in the setting of MS.

The decision regarding anticoagulation in our patient was complicated because of his coagulopathy, thrombocytopenia, and esophageal varices from cirrhotic portal hypertension and portal vein thrombosis detected postoperatively. Patients with liver cirrhosis are generally believed to be at high thromboembolic risk, whereas bleeding from esophageal varices is thought to be initiated by mechanical events. Our patient recovered well after surgery and was discharged home with a regimen of subcutaneous dalteparin. He continues to demonstrate improvement during routine follow-up visits in the outpatient setting.

DISCUSSION

Although now relatively rare in developed countries, MS remains prevalent in developing countries. Approximately 60% of individuals presenting with pure MS have a history of rheumatic fever.[1] A history of group A streptococcal pharyngitis is reported by two-thirds of patients presenting with acute rheumatic fever, and 0.3% to 3% of patients with untreated group A streptococcal pharyngitis develop rheumatic fever.[7] An autoimmune mechanism may be involved in which antigens in cardiac myocytes and valve tissue that resemble epitopes on bacterial surface are targeted.[8] In developed countries where the incidence of rheumatic fever is low, MS can be congenital or it can occur rarely with advanced mitral annular calcification.

Presenting symptoms in MS stem from impaired blood flow across the mitral valve and pressure overload in the pulmonary circulation. Patients may remain asymptomatic for years. While normal mitral valve area is 4.0 to 5.0 cm^2, a stenotic mitral valve narrows slowly by 0.1 to 0.3 cm^2 per year,[9] with symptoms apparent when valve area is less than 2.5 cm^2.[10] The most common presenting symptom in MS is dyspnea on exertion. Dyspnea in MS is caused by a decreased capacity to increase cardiac output during exertion or raised LA and pulmonary venous pressures leading to pulmonary edema. Elevated pulmonary pressures may lead to rupture of pulmonary vessels, causing hemoptysis. Hemoptysis in the setting of MS is rare in contemporary practice because of early intervention, and its presence suggests advanced disease. If large enough, the left atrium may compress the recurrent laryngeal nerve, leading to hoarseness (Ortner syndrome) or dysphagia. Left atrial enlargement also predisposes to both atrial fibrillation and LA appendage thrombus, increasing risk for embolism.

Diagnosis is made with history, clinical examination, chest radiography, ECG, and ancillary imaging.[5] An accentuated first heart sound and an opening snap due to abrupt restriction of complete opening of the mitral valve leaflets in early diastole may be heard. The murmur of MS is a low-pitched diastolic rumble best heard at the apex while the patient is lying in a left lateral decubitus position. It may be a short, mid diastolic, or late diastolic (presystolic) murmur. A short interval between the second heart sound and opening snap (S_2-OS interval), as well as a longer duration of the diastolic rumble, indicates more severe MS. In advanced disease, signs of pulmonary hypertension, such as a prominent P_2 and right parasternal heave, and an early diastolic murmur of pulmonary regurgitation (Graham Steell murmur) may be present.

Echocardiography may show signs of RV hypertrophy and LA enlargement, as described earlier in this article. Chest radiographs may reveal pulmonary congestion and enlargement of the pulmonary artery, right ventricle, and both atria.

Two-dimensional and Doppler echocardiographic evaluation is helpful in diagnosis and for evaluation of hemodynamic severity, concomitant valvular lesions, and valve morphology. Transesophageal echocardiography should be done in patients with MS to assess for LA appendage thrombus.[5] The severity of MS is determined using the mean transmitral pressure gradient and valve area estimated on

Doppler echocardiography, as well as pulmonary arterial pressure.

Medical management of MS includes loop diuretics with concomitant sodium restriction in patients with evidence of volume overload. β-Blockers decrease the heart rate and increase diastolic filling time, which can result in improvement in symptoms. Medical treatment can reduce symptoms but does not prevent progression of the disease. Systemic embolic events may develop in 10% to 20% patients with MS. Anticoagulation may be necessary to prevent systemic embolic events, particularly in patients with atrial fibrillation, prior embolic event (even in those with sinus rhythm), known LA thrombus,[5] and enlarged left atrium (>55 mm).[6]

Asymptomatic patients with mild MS (valve area >1.5 cm^2 and mean gradient <5 mm Hg) only require follow-up. Asymptomatic patients with moderate or severe stenosis (mitral valve area ≤1.5 cm^2) and moderate pulmonary hypertension (pulmonary artery systolic pressure >50 mm Hg) may be considered for PMBV. Symptomatic patients with moderate or severe MS are candidates for PMBV or surgery (mitral valve repair or replacement).[5] Percutaneous mitral balloon valvotomy can relieve obstruction and provide immediate relief, but it cannot be used if there is concomitant moderate or severe mitral regurgitation, the valve apparatus is too fibrotic or calcified, or there is an LA thrombus. Valve surgery is recommended in this setting.

Death from untreated MS is due to heart failure, pulmonary hypertension, thromboembolism, and endocarditis. Onset of symptoms usually heralds a rapid decline in cardiac function. Mitral stenosis is unique among valvular diseases in that intervention may be considered in asymptomatic patients with just moderate MS. As such, it is important that all physicians and health care providers remember that echocardiographic evidence of moderate MS should prompt further cardiology evaluation, even in the absence of symptoms, because early surgery or percutaneous intervention can delay or prevent atrial fibrillation, worsening of heart failure, and early morbidity and mortality.

Abbreviations and Acronyms: **ECG** = electrocardiography; **LA** = left atrial; **LV** = left ventricular; **MS** = mitral stenosis; **PMBV** = percutaneous mitral balloon valvotomy; **RV** = right ventricular; **TB** = tuberculosis

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CORRECT ANSWERS: 1. e, 2. a, 3. b, 4. e, 5. b

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