clinical problems in cardiopulmonary disease

Hemoptysis, Hepatopulmonary Syndrome, and Respiratory Failure*

Clinical Conference on Management Dilemmas

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Key words: arteriovenous malformation; bronchial artery embolization; double-lumen endotracheal tube; hemoptysis; hepatic nodular regenerative hyperplasia; hepatopulmonary syndrome; hereditary hemorrhagic telangiectasia; independent lung ventilation; spider angiomas; telangiectases

Abbreviations: AVM=arteriovenous malformation; ITP=idiopathic thrombocytopenic purpura; PVR=pulmonary vascular resistance

Pulmonary clinicians are often faced with management problems for which there are no answers at hand, either because there is no literature that definitely gives answers or because the circumstances surrounding the clinical cases are unusual enough to prevent the application of existing scientific knowledge. When faced with these problems, clinicians are forced to make decisions based on a logical extension of their scientific knowledge into uncharted clinical waters. They are forced to make judgments based on the conviction of their speculations and the prior experiences of others and of themselves.

This case conference addresses difficult management problems without singularly correct decisions; its object is *not* necessarily to seek consensus. Defining the exact issues, formulating rationales for decision making, and committing to the decisions themselves are all equally important in this presentation. This is a real case in which the decisions were made by the "Treating Pulmonologist" without input from the other participants. The "Responses of Pulmonary Experts" are given only with the knowledge of the case presentation up to the moment at which each expert gives his or her decision and without the knowledge of any of the other opinions rendered. The last "Commentary" is given only with the knowledge of the full case presentation and the "Follow-up by the Treating Pulmonologist" but without the knowledge of any of the other opinions rendered. The "Commentary" is the last opinion in the sequence of this presentation, but it is not necessarily offered as the definitive solution to the problems posed in the case. The reader is the ultimate arbiter in this presentation of decision-making alternatives.

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Case Presentation

A 13-year-old Hispanic man presented with hematemesis, thrombocytopenia, splenomegaly, and liver function abnormalities. His bleeding was secondary to esophageal varices, and liver biopsy specimen was consistent with nodular regenerative hyperplasia. A bone marrow biopsy specimen showed increased megakaryocytes. Thrombocytopenia was believed to be secondary to hypersplenism or idiopathic thrombocytopenic purpura (ITP), and he was treated with high-dose steroids. At age 17 years, he had a splenectomy for refractory thrombocytopenia but still required steroids to maintain his platelet count at 80,000/mm^3.

At age 18 years, he returned with hematemasis and was noted to be hypoxemic. His room air arterial blood gas values were pH of 7.47, P_{CO_2} of 36 mm Hg, P_{O_2} of 55 mm Hg, with an O_2 saturation of 91%. Bronchoscopy was unremarkable, and bleeding was believed to be due to esophageal varices. An HIV test was negative.

At age 20 years, he had progressive dyspnea, severe bone pain, and clubbing. Radiographs of the tibia and ulna revealed hyper-

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trophic osteoarthropathy. Arterial blood gas values on room air were pH of 7.50, P_{CO_2} of 24 mm Hg, and P_{O_2} of 44 mm Hg. Pulmonary function tests were performed (Table 1). A CT scan of the chest showed a peripheral wedge-shaped infiltrate in the right lower lobe. Lung ventilation/perfusion scan was read as low probability for pulmonary embolism, but there was excessive uptake of the lung perfusion scan tracer (^{99m}technetium macroaggregated albumin) in the kidneys, thyroid gland, and brain. An echocardiogram was normal and a cardiac catheterization failed to demonstrate an intracardiac shunt. Cardiac output and right- and left-sided pressures were "normal." A pulmonary angiogram was read officially as "unremarkable," but one radiologist thought there was "increased vasculature." Antinuclear antibody test was positive with a speckled pattern; VDRL, rheumatoid factor, and HIV test were negative, and complement levels were normal. A diagnosis of intrapulmonary microshunts secondary to cirrhosis (*ie,* "hepatopulmonary syndrome") was entertained. The patient was given antibiotics for a right lower lobe pneumonia and his condition improved.

He was readmitted to the hospital at age 25 years with severe abdominal pain. CT scan of the abdomen was consistent with small-bowel ischemia and mesenteric vein thrombosis. An antithrombin III level was mildly reduced at 15 mg/dL (normal, 22 to 33). He was treated conservatively with hydration and recovered uneventfully. Room air arterial blood gas values were pH of 7.46, P_{CO_2} of 25 mm Hg, and P_{O_2} of 55 mm Hg, with an O_2 saturation of 91%.

Two months later, on July 6, 1991, he presented to one of us (J.S.) with several episodes of gross hemoptysis, almost one cup of dark red blood each time. He stated that his bleeding was coming from the right side of his chest. He was receiving no medications. Vital signs were normal, and he appeared comfortable but had cyanosis of the lips and nailbeds. There were multiple telangiectases on the oral mucosa, which had not been noticed before, and rales at the right lung base. Stool was guaiac positive. Findings from the rest of the examination were unremarkable. Room air arterial blood gas values were pH of 7.42, P_{CO_2} of 31 mm Hg, and P_{O_2} of 58 mm Hg with an O_2 saturation of 91%. WBC count was 5,500/mm^3 (66% lymphocytes), hemoglobin was 16 g/dL, hematocrit was 47%, and platelet count was 82,000. Serum lactate dehydrogenase value was 311 U/L (normal range, 60 to 200 U/L) but results of other blood chemistry studies were unremarkable. Prothrombin time and partial thromboplastin time were normal. He was admitted to hospital (chest radiograph on admission is seen in Fig 1). Bronchoscopy revealed diffuse telangiectases throughout the endobronchial mucosa without active bleeding.

On July 9, the patient had several episodes of gross hemoptysis with hypoxemia. He was transferred to the ICU and transfused with packed RBCs and platelets. Treatment with IV methylprednisolone, 40 mg q12h, and γ-globulin was started for ITP, and he was electively intubated. Chest radiograph had a left upper lobe alveolar infiltrate, so the right main bronchus was selectively intubated. Bronchoscopy was again performed. The right lower lobe airways were soiled with blood, but there was no active bleeding. The endotracheal tube was slowly pulled back under direct bronchoscopic visualization until a rush of fresh blood poured from the right upper lobe bronchus. Topical epinephrine controlled the bleeding. Endobronchially, the left lung was soiled but had no active bleeding. The left main bronchus was then selectively intubated and the patient placed in the right lateral decubitus position and sedated.

Table 1—*Pulmonary Function Tests*

Parameter*	Measured	% Predicted
FVC, L	3.49	53
FEV_1, L/s	1.97	55
$FEF_{25-75\%}$, L/s	2.00	38
FEV_1,%	76	
Dco, mL/min/mm Hg	5.0	11

*$FEF_{25-75\%}$ = forced expiratory flow rate between 25% and 75% of the FVC; Dco = diffusion of carbon monoxide.

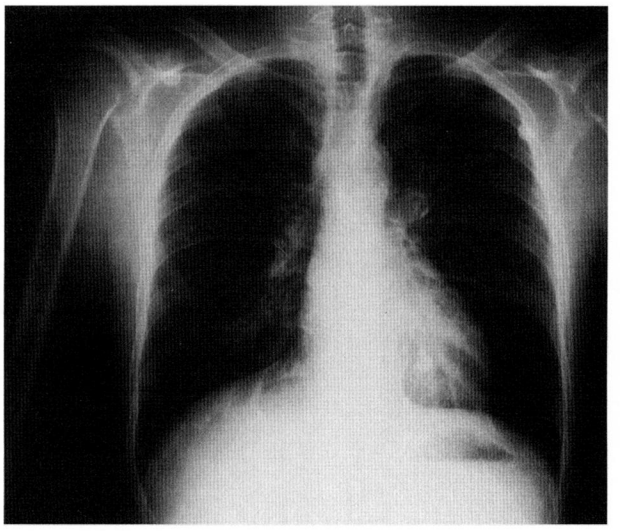

FIGURE 1. Chest radiograph on July 6, 1991 at time of hospital admission for massive hemoptysis. Unchanged from May 11, 1991 with mild accentuation of interstitial shadows.

An emergency bronchial angiogram was performed (Fig 2). The right upper lobe bronchial artery appeared markedly hypertrophied with anastomosis to a branch of the pulmonary artery. An arteriovenous malformation (AVM) associated with this anastomosis was seen to be extravasating blood. No vertebral arteries were seen to anastomose with the bronchial arteries, thus reducing the procedural risks of embolization, *ie,* paralysis or cord ischemia/infarction. The hypertrophied bronchial artery was occluded with a 4-mm endovascular metallic coil. On July 10, chest radiograph showed atelectasis of the entire right lung (Fig 3). On July 11, the patient remained in stable condition on one-lung ventilation but required a fraction of inspired oxygen of 100% to maintain an O_2 saturation of 88%.

Responses of the Pulmonary Experts

Robert M. Smith, MD, FCCP, San Diego

This individual carries a diagnosis of hepatopulmonary syndrome apparently believed to be due to cryptogenic cirrhosis, but there is well-preserved hepatic function and no information to support the presence of elevated portal pressures. The patient now has massive pulmonary hemorrhage and multiple mucosal telangiectases. These lesions are not fully described, and I would want to know if they are "spider" nevi. Neither hemoptysis nor oral telangiectases are characteristic of hepatopulmonary syndrome, which may suggest an alternate diagnosis such as hereditary hemorrhagic telangiectasia.[1] The

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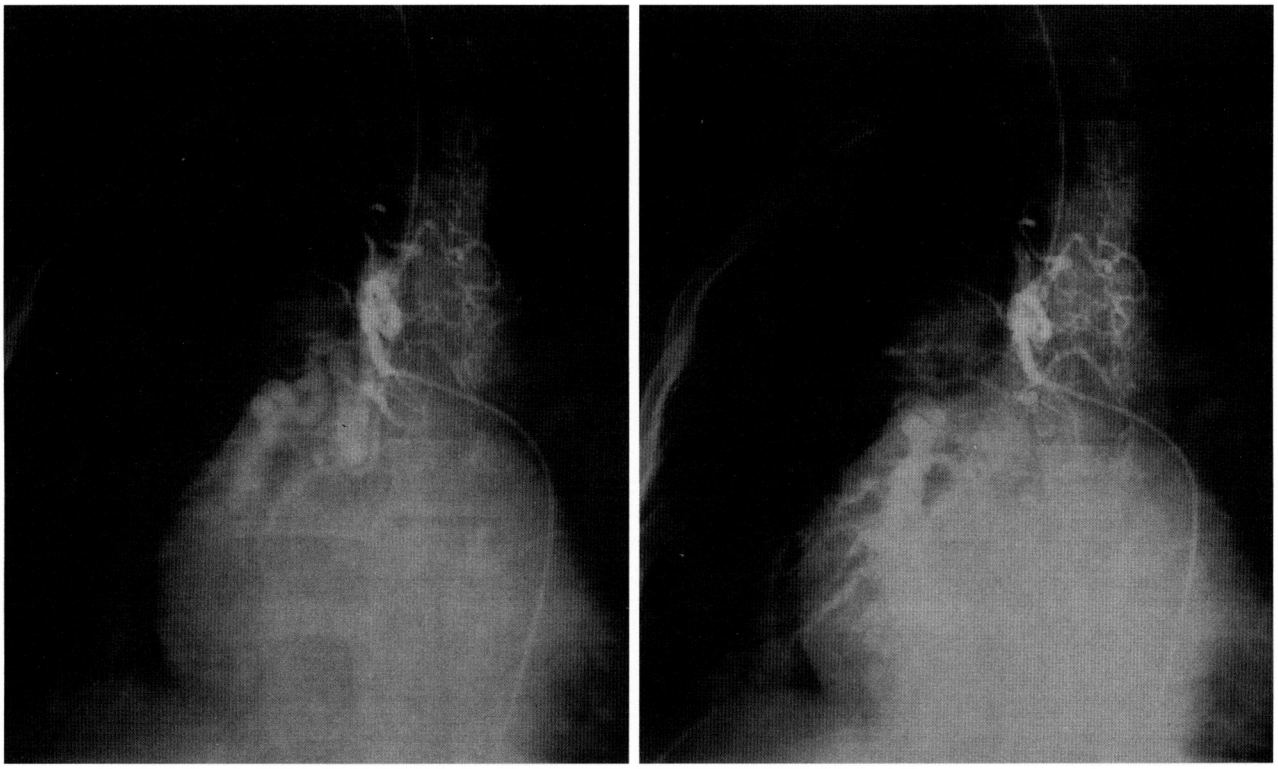

FIGURE 2. *Left* and *right*: bronchial artery angiogram on July 9, 1991 revealing an anastomotic plexus of vessels in the right lung field and upper mediastinum (see text for further detail).

appearance of the mucosal telangiectases may distinguish between the conditions. The site associated with the current episode of life-threatening hemoptysis appears to be in the right upper lobe. In contrast to the arterio-*venous* communications seen in hepatopulmonary syndrome or hereditary telangiectasia, the angiogram shows a large systemic-pulmonary artery communication. This lesion is more often seen in chronic inflammation (*eg*, bronchiectasis) or bronchopulmonary sequestration, although to my knowledge, there is no historical information to support either of these possibilities. The communication appears to be localized to the right upper lobe, but a careful review of the angiogram is warranted. The systemic-pulmonary artery communication is likely to have been controlled temporarily by embolization.

The most immediate problem is the need to improve gas exchange and reduce the risk of oxygen toxicity. With the left mainstem bronchus selectively intubated after embolization of the right upper lobe shunt, I would start by placing the patient in the left lateral decubitus position. This may have limited efficacy depending on the extent of intrapulmonary shunting related to the hepatopulmonary syndrome or hereditary telangiectasia. The patient has complete right lung atelectasis due to endotracheal tube placement in the left mainstem bronchus. Although blood clots on the right side might limit the ability to recruit the right lung, the right mainstem bronchus appears patent on the radiograph. I would attempt to withdraw the endotracheal tube into the trachea over a bronchoscope and inspect the right side for continued bleeding. I would anticipate that the embolization procedure had controlled the bleeding, at least temporarily. If continuing bleeding is seen from the right upper lobe bronchus, consideration may be given to occluding the bleeding airway with a balloon, provided the rate of hemorrhage allows visualization of the site and does not preclude the ability to work in the airway. Use of a rigid scope would be difficult at best. Additionally, continuing bleeding from the right upper lobe should prompt consideration of right upper lobectomy. This heroic procedure should be considered if careful inspection of the angiogram (or a further study) does not show other systemic-pulmonary artery communications.

Finally, if the patient survives, consideration should be given to attempts at long-term control of the underlying hypoxemia. Hypoxemia associated with large pulmonary AVMs, whether due to hepatopulmonary syndrome or hereditary telangiectasia, may be controlled by embolization of the feeding branch of the pulmonary artery.[1] For this reason, I

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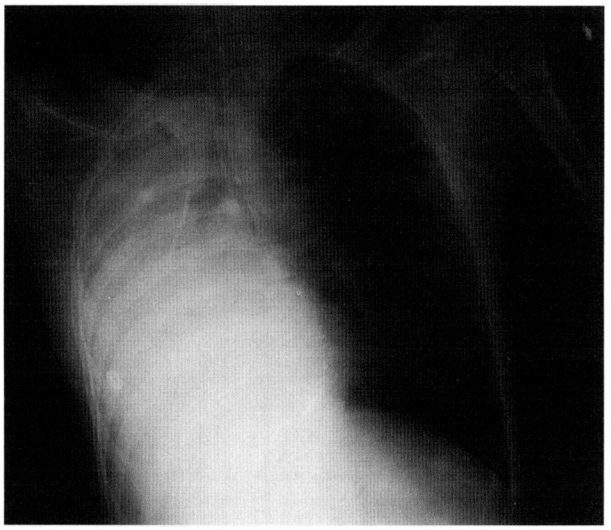

FIGURE 3. Chest radiograph on July 10, 1991 showing atelectasis of the right lung and an abrupt cutoff of the silhouette of the right main bronchus. The left main bronchus is selectively intubated. An endovascular coil is seen in the mediastinum, superimposed on the shadow of the endotracheal tube in the left main bronchus. A central venous catheter is in the superior vena cava.

would perform a pulmonary angiogram and embolize any discrete lesions. Unfortunately, hepatopulmonary syndrome may be associated with the diffuse microscopic arteriovenous communications thought to be present 5 years earlier in this patient. These "microshunts" have a better PaO_2 response to breathing 100% oxygen, but are not amenable to direct embolization.[1] However, certain authors have suggested that reduction of portal venous pressures may improve the hypoxemia.[2] Therefore, if the pulmonary angiogram does not show discrete AVMs, I would measure hepatic venous wedge pressure to establish the degree of portal venous hypertension[3] and would consider transjugular intrahepatic portosystemic shunting or portocaval shunting procedures if portal hypertension were present.

E. James Britt, MD, FCCP, Baltimore

No situation can compare with massive hemoptysis for the difficulties of management and decision making—given the risk of asphyxia when a patent airway cannot be maintained. In this case scenario, much difficult decision making has already taken place. Bronchoscopy was successfully completed under trying circumstances and seems to have convincingly localized bleeding to the right upper lobe. Emergency bronchial arteriography found the anatomic connection in the form of a hypertrophied bronchial artery anastomosing with a pulmonary artery. While this connection of itself (using simple plumbing analogies) would only serve to increase blood flow through the lung and possibly raise pulmonary artery pressure, the presenter mentioned an arteriovenous component of the process, hence the "shunt." Embolization of the bronchial artery seems prudent as a way to decrease blood flow and pressure through the abnormal connection. At the time of the bronchial arteriogram, the right lung was still expanded. On the next day, it appeared atelectatic. It is possible that some of the atelectasis was due to obstruction from clot, suggesting continued bleeding. Atelectasis in the right lung may have also served to substantially reduce blood flow to the right lung, further enhancing the ability to terminate the hemoptysis.

At this stage, I would now plan to pull back the endotracheal tube from the left mainstem bronchus and attempt to visualize the right lung through the bronchoscope. If the lung is atelectatic, then I leave the endotracheal tube in the trachea and let the right lung reinflate. Blood flow would return to the lung. If the embolization was successful, then we would have 1 to 2 months of stability to explore options. Alternatively, massive hemoptysis could recur, and we would again have to collapse the right lung. If the lung is occluded and atelectatic secondary to clot, then I would leave well enough alone and rely on the miracle of the macrophages to clear the clot over time. I would not attempt to dislodge or remove the clot. Oxygenation is temporarily borderline adequate. Anecdotal reports of the use of estrogens and vasopressin (Pitressin) under difficult bleeding circumstances exist and might be considered here as adjuncts to therapy.

The patient should be considered for elective right upper lobectomy. Repeated studies will be required, such as with MRI or repeated angiography, to determine if other abnormal vascular connections exist. Mechanical lung function is borderline adequate. There is some further risk to repeated angiography with contrast. I have seen contrast-induced hyperemia or vasodilation in the chest (experienced by patients as a "warm feeling") reactivate hemoptysis from inflammatory lesions. Emergency right upper lobectomy seems a heroic but possible option. Lastly, I would consider this patient for lung transplantation. At the time of this writing, a variety of patients with complex conditions are considered. In 1991, options may have been more restrictive. There are numerous obstacles to overcome. Stability would be required for a period of time to give careful consideration to this option. The chronic liver disease is a major obstacle. However, the patient has not exhibited hepatic insufficiency. A trial of transplant medications, *eg*, azathioprine or cyclosporine, prior to placing the patient on the transplant list, might predict his ability to tolerate the medical

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regimen. The hematologic disorder (ITP vs hypersplenism) needs clarification as well. Nevertheless, lung transplantation should be addressed given the patient's age.

Follow-up by the Treating Pulmonary Consultant
Jeff Schnader, MD, FCCP, Dayton, Ohio

This patient presented to me with liver disease, vascular anomalies, chronic respiratory failure manifesting as hypoxemia, and massive hemoptysis resulting in acute respiratory failure. Liver disease was his first diagnosed problem (along with ITP), and may have been the underlying cause of all his other problems. Liver disease is known to be associated with a number of vascular abnormalities, including spider angiomata of the systemic circulation, hepatopulmonary syndrome (intrapulmonary microshunts secondary to cirrhosis also called "lung spiders"), sluggishness of hypoxic pulmonary vasoconstriction, pulmonary plexigenic vasculopathy that is pathologically identical to primary pulmonary hypertension, and esophageal varices and related hypertrophy of the collateral circulation (*eg*, caput medusae).[4] Although there is a differential diagnosis for telangiectases, including connective tissue and congenital disease, I believe that, in the current patient, the vascular abnormalities were most likely related to the liver disease. Specifically, the telangiectases of the mucous membranes (lung and oral) were likely communications between arterioles and venules.[5] The vascular malformation in the lung was specifically described as a connection between a bronchial artery (being injected) and a pulmonary vascular structure that the radiologist interpreted to be a pulmonary artery. Whether this vascular malformation was a collateralization of the hypertensive portal circulation akin to the patient's esophageal varices, a hypertrophy of the vasa vasorum (bronchial arteriolar feeders to the walls of the pulmonary arteries), or even an angiogenesis-type lesion is unclear;[6,7] but because it crossed from the systemic to the pulmonary circulation, it appeared less likely that it was a simple spider angioma. Finally, the fact that perfusion scan tracer was injected into the pulmonary circulation and ended up in brain, kidney, and thyroid could not be explained by a vascular malformation with blood flow from the bronchial artery to the pulmonary circulation, and this implied the presence of another type of shunt. Prior right heart catheterization had not revealed pulmonary hypertension, so I did not suspect a patent foramen ovale or intracardiac shunt; rather, I suspected hepatopulmonary syndrome was also present in this patient. Hepatopulmonary syndrome would explain the perfusion scan abnormalities and the severe hypoxemia that he exhibited as it is known to cause chronic hypoxemic respiratory failure.[4,8]

I did not suspect that pulmonary thromboemboli were involved in this patient's hemoptysis or other problems despite the history of superior mesenteric artery thrombosis and low antithrombin III levels, and this is why I did not administer heparin and did not request a pulmonary angiogram. My worry was that the multiple vascular abnormalities might be related to an abnormal and bleeding vascular communication associated with a bronchial artery, as was found. Other possibilities for the hemoptysis included the telangiectases that I had seen at bronchoscopy and that may cause occasional bleeding in Osler-Weber-Rendu disease (hereditary telangiectasis), a similar condition.[1]

In summary, I believed that the chain of events was that the liver caused vascular malformations, which caused first chronic hypoxemia and then acute bleeding. The bleeding and the collapse of the right lung both contributed to the acute respiratory decompensation requiring mechanical ventilation. My belief was that further management options should address control of further bleeding, reinflation of the right lung, maintenance of adequate ventilation to the left lung, and prevention of soiling of the left with blood from the right. I did not consider lobectomy to be a suitable option since the patient's diffusion of carbon monoxide was only 11% of predicted (Table 1) and the bleeding was controlled at this point. My decision was to isolate the right lung with a double-lumen endotracheal tube and use simultaneous independent lung ventilation to accomplish all of these goals.

After 48 h of left lung unilateral ventilation, the right lung had become tightly atelectatic and stiff. With blood in the alveoli, it would require high pressures to open the lung to ventilation. Bilateral lung ventilation would probably result in the normally compliant left lung overdistending with excessive risk of barotrauma, and the stiff right lung not ventilating at all. Independent lung ventilation facilitated by use of a double-lumen endotracheal tube would obviate both of these problems and simultaneously control the right-sided airway and protect the left.

Hospital Course: A bronchoscope was passed via the endotracheal tube and then both scope and tube were slowly withdrawn into the trachea to assess the airway. There was no active bleeding, but there was concern that bleeding would recur. A double-lumen (Broncho-Cath; Mallinckrodt Medical; St. Louis, Mo) endotracheal tube was placed with the distal cuff in the left main bronchus. The patient was paralyzed and sedated. Independent lung ventilation was begun using two ventilators, one for each lung.

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Initially, the right lung had a peak inspiratory pressure >100 cm H_2O with tidal volume set at the minimum value on the ventilator of 100 mL. As ventilator tubing has a compliance of between 3 and 4 mL/cm H_2O, much of the tidal volume was probably going into the expansion of the tubing so that calculated compliance of the right lung was undoubtedly <1 mL/cm H_2O and possibly as low as 0.2 mL/cm H_2O. The low compliance confirmed that without the independent lung ventilation, it may have been impossible to reinflate the right lung. Gradually, compliance rose to 3 mL/cm H_2O at a tidal volume of 200 mL, and then, after 3 h, to 12 mL/cm H_2O with a tidal volume of 300 mL (see chest radiograph, Fig 4).

On July 12, a covering physician noted that a small amount of fresh blood was suctioned from the right lung. Repeated angiography failed to reveal the source. Later that day, the patient became hypothermic and hypotensive, with bilateral patchy pulmonary infiltrates. He was treated for sepsis and presumed ARDS with broad-spectrum antibiotics and IV crystalloid volume repletion. A chest radiograph from July 13 is seen in Figure 5. After this radiograph, a pulmonary artery catheter was placed (Table 2) and did not reveal pulmonary hypertension. The pulmonary vascular resistance (PVR) was abnormally low, consistent with intrapulmonary shunting, *ie,* hepatopulmonary syndrome. There was no pneumothorax on the postprocedure radiograph, but several hours later, the airway pressures began to rise on the right and an apical pneumothorax was diagnosed clinically and radiographically. A chest tube was placed. Electromechanical dissociation ensued and resuscitation attempts failed.

Necropsy Findings: Autopsy reconfirmed the primary diagnosis of nodular regenerative hyperplasia of the liver with "multiple fibrin thrombi in veins of the portal triads and central veins" and superior mesenteric vein "organizing mural thrombus." The right and left pleural cavities contained 100 and 50 mL of bloody fluid, respectively. The pericardial sac contained 550 mL of bloody fluid. "The cause of death was a massive right intrapulmonary hemorrhage and confluent bronchopneumonia. There was extensive intra-alveolar, intrabronchiolar and intrabronchial hemorrhage in the right middle and lower lobes. There was marked congestion in all lobes of both lungs and widely scattered areas of severe bronchopneumonia with pulmonary edema and hyaline membrane formation. There was no evidence of thromboemboli in the medium or large pulmonary arteries, but the walls of the pulmonary arteries were thickened. There was distention and arterialization of the peribronchial pulmonary veins, many with recent thrombi or fresh fibrin." Neither telangiectases nor AVMs were mentioned in the autopsy report. Esophageal varices were seen. A patent foramen ovale was noted.

It may be that the patent foramen ovale exhibited some blood flow from right to left during life. However, with such a low PVR and central venous pressure during life and without pulmonary hypertension (Table 2), one would not suspect enough right-to-left shunting through the patent foramen to account for either the baseline hypoxemia or the perfusion scan lighting up the systemic organs, as it did. It is interesting that neither telangiectases nor AVMs were seen at autopsy in view of the fact that, during life, telangiectases were seen on oral examination and at bronchoscopy, an AVM was documented at angiography, and arterialization of the pulmonary veins (seen at autopsy) was present. Most likely, the reduction of arterial pressure after arrest of the circulation to a mean circulatory pressure of 7 mm Hg[9] depressurized and emptied these vascular malformations to the point of their becoming unnoticeable.

COMMENTARY

Mark Kelley, MD, FCCP, Philadelphia

The beginning of the terminal events in this patient began at the age of 25 years when he had a spontaneous mesenteric vein thrombosis with a low antithrombin III level. This event suggested a hypercoaguable state that may have explained the finding of thrombosis in his pulmonary veins at autopsy. Two months later, he presented with massive hemoptysis raising a number of diagnostic possibilities, well discussed by Dr. Schnader.

Pulmonary vascular abnormalities and hemoptysis have been described with liver disease. There have been case reports of varices in the pulmonary circulation in association with portal hypertension. In one report, these varices were located in the trachea and originated from the esophageal circulation after esophageal sclerotherapy.[10] Such an observation was not made in this case. Portal hypertension promotes collateral channels between the pulmonary veins and the venous circulation of the esophagus, or even the colon. When these vascular channels open, they can result in the appearance of a mass-like structure within the lung. In one case report, the vascular complex disappeared after liver transplantation.[11,12]

In this patient, the injection of the bronchial circulation demonstrated a vascular plexus within the right lung. Blood seemed to be leaking from this complex, thereby explaining the hemoptysis.

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These angiographic findings suggested not just a connection, but a very large vascular channel extending directly from the bronchial artery to the pulmonary vasculature. At autopsy, there was "arterialization" of the pulmonary veins, but there was no vascular abnormality noted by the pathologist in the lung at autopsy. How can we pull these findings together? The most common way such vascular findings are explained is on the basis of a focal inflammatory process, *eg*, bronchiectasis, pulmonary sequestration, or more rarely neoplasm, which can create capillary connections from the bronchial artery to the pulmonary artery. However, these processes were not borne out at autopsy. In this case, the inciting event was mesenteric vein thrombosis which leads me to suspect a less common clinical sequence of events: an abrupt increase in portal pressure (from liver disease and mesenteric thrombosis) created intrapulmonary varices with localized pulmonary venous hypertension. Consequently, the bronchial artery circulation may have been redirected away from the pulmonary veins and toward the lower resistance circuit of the pulmonary artery. This would have promoted local "systemic arterialization" of the pulmonary artery. The fact that the portal-pulmonary connection was not visualized at autopsy does not seem inconsistent as the involved vessels shrunk in size when the blood they contained, during life, drained into lower pressured vascular structures after death.

The accuracy (or inaccuracy) of my speculation does not change the therapy in this patient. The therapeutic maneuvers used in this patient were appropriate and consisted of isolating the right lung to prevent hemorrhage into the left lung, occlusion of the bleeding bronchial artery, and independent lung ventilation of each lung. However, given all his other problems, this man's clinical outcome was predictably grim. The mortality of massive hemoptysis, even in the modern era, may be as high as 20%.[13] In addition, this patient had ARDS and severe liver disease and was highly susceptible to infection, the ultimate cause of his death. Even when his hemoptysis abated, his predicted mortality from the combination of respiratory and liver failure exceeded 70%. These events pushed this unfortunate man off the tightrope he had carefully walked for so many years.

FIGURE 4. Chest radiograph on July 11, 1991 showing atelectasis of the right lower lobe but a fully aerated right upper lobe. A double-lumen endotracheal tube is inserted with the distal cuff inflated in the left main bronchus. The endovascular coil is again seen in the mediastinum. A central venous catheter is in the superior vena cava.

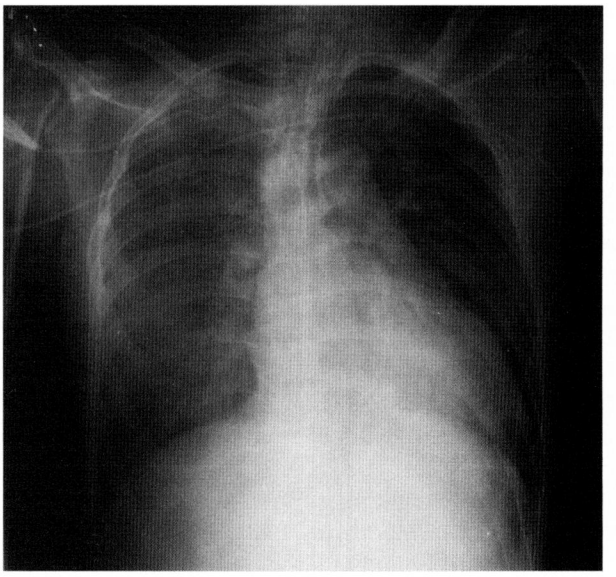

FIGURE 5. Chest radiograph on July 12, 1991 reveals bilateral, diffuse hazy shadows consistent with pulmonary edema or ARDS. There is consolidation behind the heart with air bronchograms in the left lower lobe. A double-lumen endotracheal tube is inserted with the distal cuff inflated in the left main bronchus. The endovascular coil is again seen in the mediastinum. A central venous catheter is in the superior vena cava.

Table 2—*Pulmonary Artery Catheter Measurements*

Parameter	Measurement
CVP, mm Hg	3
Pulmonary artery, mm Hg	20/3
PCWP, mm Hg	3
Cardiac output, L/min	8.9
SVR, dyne · s · cm^{-5}	719
PVR, dyne · s · cm^{-5}	51

*CVP = central venous pressure; PCWP = pulmonary capillary wedge pressure; SVR = systemic vascular resistance.

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Commentary on the Hepatopulmonary Syndrome in This Case

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This patient demonstrated all the features of the hepatopulmonary syndrome. The hepatopulmonary syndrome is the occurrence of hypoxemia and shunting in the presence of chronic liver disease and absence of causative cardiac and pulmonary factors. The hypoxemia may improve with recumbency (orthodeoxia) and the "shunting" may be overcome by oxygen. Spider angiomata, clubbing, and osteoarthropathy can be found. Often these patients have angiomata on the skin and pleura and extensive vascular hyperplasia, especially in areas affected by portal hypertension such as the mediastinum. The responsible intrinsic vasodilators, angiogenic factors, and other mediators have not been well identified. It is unclear whether there is faulty catabolism or enhanced anabolism in the liver or altered sensitivity to these agents in the vasculature. The increased portal pressure also may lead to pulmonary vascular changes.[2] The confirming diagnostic test, a radionuclide lung scan or bubble echocardiogram, shows that large particles bypass lung capillaries.[8] In an animal model of cirrhosis, the mean diameter of the lung capillaries is modestly increased.[14] This dilatation may allow erythrocytes to pass through the lung without being fully oxygenated, perhaps because of a change in the diffusion distance, deformation of RBCs, or transit time through the alveoli. The capillary dilatation may be extreme enough to be angiomatoid,[15] but this is by no means the whole story. Shunting may occur from the portal vein to the pulmonary veins.[12] Blood from the bronchial circulation may bypass the lungs to enter the pulmonary circulation at precapillary, capillary, or postcapillary sites,[16] and the regulation of the pulmonary vascular tone is abnormal in liver disease.[17]

This patient had nodular regenerative hyperplasia of the liver, which is a cause of noncirrhotic portal hypertension but an uncommon cause of the hepatopulmonary syndrome. The lung scan and bronchial arteriogram of this patient showed that he had multiple shunting sites. The bronchial arteriogram showed direct bronchial blood flow into the pulmonary arteries. This is brought about by enlargement of the vasa vasorum of the pulmonary artery. These small bronchial vessels appear to empty directly into the pulmonary arteries,[16] and under certain conditions (usually an obstructed pulmonary artery), they undergo hypertrophy into the large size shown in Figure 2. Finding no telangiectasia or AVM in this patient at postmortem is not surprising because the vasculature collapses. Light microscopy of patients with cirrhosis generally shows no lung capillary abnormality, but casting this patient's bronchial and pulmonary vessels (and examining them with scanning electron microscopy) should have shown abundant vascular changes. The autopsy finding of more pulmonary venous than arterial changes is interesting because nodular regenerative hyperplasia and pulmonary veno-occlusive disease can be associated with toxic agents.[18] I wonder if the venous muscular hypertrophy and thrombosis indicated pulmonary vascular disease beyond what would be expected with merely increased flow and shunting; however, significant venous occlusion should have resulted in elevated PVR, which was not present in this patient. The best hope for this patient may have been a liver transplantation.[1]

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