of pulmonary hemorrhage after thrombolytic therapy that was confirmed pathologically. Our patient had no underlying predisposing factors for pulmonary hemorrhage apart from heart failure. We conclude that pulmonary hemorrhage is a rare but important complication of thrombolytic therapy. Underlying pulmonary disease, pulmonary artery catheterization, or pulmonary edema may predispose to this event. Pulmonary hemorrhage should be considered in the differential diagnosis of new infiltrates on chest radiography or falling hemoglobin levels in patients who received thrombolytic therapy. Awareness of the possibility of such a side effect, early recognition, and treatment may prevent significant morbidity and mortality.

REFERENCES
3 Didier L, Rosendorff A. Pulmonary hemorrhage following intravenous streptokinase for acute myocardial infarction. Int J Cardiol 1990; 20:387-90

Granulomatous Pneumonitis Following Intravesical BCG*

What Therapy Is Needed?

Gregory F. LeMense, M.D.; and Charlie Strange, M.D., F.C.C.P.

A 68-year-old man developed fever, cough, and dyspnea after intravesical bacillus Calmette-Guerin (BCG). Chest radiograph revealed diffuse reticulonodular infiltrates with caseating granulomas on transbronchial biopsy specimen. Cultures were negative and the patient’s condition improved with corticosteroids. The mechanism for BCG-induced granulomatous inflammation is poorly understood. Optimal therapy includes corticosteroids. (Chest 1994; 106:1624-26)

*From the Division of Pulmonary and Critical Care Medicine, Medical University of South Carolina, Charleston.
Reprint requests: Dr. LeMense, 812 CSB, 171 Ashley Avenue, Charleston, SC 29425

Intravesical bacillus Calmette-Guerin (BCG) has been used in the treatment of superficial bladder cancer since 1976. While the incidence of local side effects such as cystitis and hematuria is high, the incidence of systemic side effects from intravesical BCG is less than 1 percent. In the majority of cases, systemic toxicity manifests by granulomatous inflammation involving multiple organs, which is culture negative and shows no organisms on mycobacterial stains.

Because the pathogenesis of systemic granulomas remains unclear, treatment remains controversial. Although some cases may regress without therapy, antituberculous chemotherapies with or without corticosteroids have been used in the majority of reported cases. We report a case of granulomatous pneumonitis following intravesical BCG that improved slightly with no therapy, and improved markedly after corticosteroid therapy alone.

CASE REPORT

A 68-year-old man was diagnosed as having recurrent grade 2 transitional cell cancer of the bladder in August 1992. He was begun on a regimen of weekly intravesical BCG therapy. After the fourth BCG treatment, he noted the onset of low-grade fevers, headache, dyspnea, and cough productive of scant sputum. After the sixth BCG treatment, repeated cystoscopy with biopsy specimen showed multiple caseating granulomas with no organisms seen on special stains and negative cultures. Chest radiography revealed diffuse reticulonodular infiltrates (Fig 1). Pulmonary function tests showed mild restriction (FEV₁ = 1.77 L, 73 percent predicted; FVC = 2.22 L, 74 percent predicted) with a marked decrease in diffusion (Dco = 5.71 ml/min/mm Hg, 23 percent

FIGURE 1. Chest radiograph at initial presentation showing bibasilar nodular interstitial infiltrates. Chest radiograph when starting corticosteroid therapy was unchanged.
predicted). History was significant for a positive tuberculin test in 1984, treated with 12 months of isoniazid prophylaxis.

Bronchoscopy with transbrachial biopsies and bronchoalveolar lavage was performed. Biopsy specimens revealed caseating granulomas with negative acid-fast bacilli (AFB) and fungal stains and negative cultures. Bronchoalveolar lavage had $4.4 \times 10^5$ WBC per milliliter with a differential cell count of 58 lymphocytes, 93 monocytes, 4 neutrophils, and 5 eosinophils.

The patient was followed up closely without therapy. Six weeks later, cough and sputum had improved (FEV$_1$ = 2.14 L, 88 percent predicted; FVC = 2.89 L, 96 percent predicted). Dyspnea, decreased diffusion, and abnormal chest radiograph persisted. Prednisone therapy (40 mg/d) was begun, with complete resolution of the patient's dyspnea and improvement in the radiograph after 3 weeks of therapy (Fig 2). The Deo remained low. Glucose intolerance developed after 3 weeks of corticosteroid therapy, and the patient was quickly weaned. Pulmonary function testing 6 weeks after corticosteroid therapy showed improvement in diffusion (Deo = 11.87 ml/m/mm Hg, 48 percent predicted). The patient remains well 6 months after discontinuation of corticosteroid therapy.

**DISCUSSION**

Pulmonary manifestations of intravesical BCG present radiographically as diffuse reticulonodular infiltrates with transbrachial biopsy specimens revealing caseating or noncaseating granulomas in some cases. Pathogenesis of these lesions remains unclear because organisms have been cultured from lung tissue in only one case. Sputum cultures have been positive in only two cases, with one of these cases occurring after BCG vaccination. A single case with acid-fast organisms on transbrachial biopsy specimen was recently reported, but cultures of the biopsy were negative. Bronchoalveolar lavage is characterized by a T4 lymphocytosis, which is also seen with active pulmonary tuberculosis. However, reports of improvement with just corticosteroid therapy and lack of recurrence after therapy suggest an immunologic lung injury is responsible for the lesions.

While culture-positive BCG mycobacteremia does occur, the incidence is very low. Described patients are critically ill with high fever, shaking chills, hypotension, disseminated intravascular coagulation, and respiratory failure. With the paucity of proven cases of BCG mycobacteremia, it appears the predominant mechanism is a hypersensitivity reaction characterized by fever, malaise, rash, arthralgias, pneumonitis, or hepatitis. The increased incidence of side effects with successive BCG treatments and the fact that all of the case reports of pneumonitis occurred after at least three BCG instillations support this contention. The hypersensitivity theory is further supported by beneficial effects of corticosteroids on morbidity and mortality after intraperitoneal BCG injection in mice, as well as case reports of two patients with total resolution of symptoms after receiving just corticosteroid therapy. Whether this patient's previous tuberculosis exposure increased the risk of hypersensitivity to BCG remains unknown.

The heterogeneity of recommended therapeutic options is highlighted in a recent series of three patients who received no treatment, corticosteroids alone, and corticosteroids with brief triple-drug antituberculous chemotherapy, respectively. Our patient convincingly demonstrated that corticosteroids can speed the time to resolution of granuloma.

An interesting facet of the case was the very low Deo that was the last abnormality to improve. The persistent diffusion abnormality is similar to that described with miliary tuberculosis, suggesting the underlying abnormality of interstitial granulomatous inflammation from hematogenous spread of antigen is similar. The improvement in diffusion after corticosteroid therapy seen in this patient has also been reported in miliary tuberculosis following treatment with antituberculous therapy and corticosteroids.

In summary, this case suggests that treatment for BCG-induced granulomatous pneumonitis should include corticosteroids in addition to removal of the antigen. Antituberculous therapy is not necessary once active infection is excluded.

**REFERENCES**

8. Orme IM, Anderson P, Boom WH. T cell response to myco-

**FIGURE 2.** Chest radiograph after 3 weeks of corticosteroid therapy.

Unsuspected Infrahepatic Interruption of Inferior Vena Cava Associated With Floppy Mitral Valve, Mitral Valve Prolapse, and Severe Mitral Regurgitation*

Antonio Dellavalle, M.D.; Flavio Ribichini, M.D.; and Giuseppe Steffenino, M.D.

We describe a case of unsuspected infrahepatic interruption of the inferior vena cava with hemiazygous continuation in a 67-year-old man presenting with chest pain and evidence of mitral regurgitation. He had no persistent superior vena cava, with the hemiazygous draining directly into the right superior vena cava. Polysplenia and severe mitral prolapse were also present: the latter may represent more than an incidental finding in this condition. This malformation may deserve consideration in adults undergoing femoral right heart catheterization. Chest radiographic studies are the basic clue to the diagnosis. (Chest 1994; 106:1228-1229)

IVC = inferior vena cava; SVC = superior vena cava

In patients with congenital heart disease, the infrahepatic interruption of the inferior vena cava (IVC) has a reported prevalence between 0.6% and 2.9 percent.2 This condition may be associated with anomalous position of the heart and viscera in the typical polysplenia sequence.3 Concomitant left atrial isomerism and complex cyanotic cardiovascular defects are also described in the literature. Anomalies of pulmonary venous return, pulmonary atresia, atroventricular canal, cor biloculare, common atrium, transposition of the great ateries, patent ductus arteriosus, and combinations of the above are most often encountered.1,5 Infrahepatic interruption

*From the Laboratorio di Emodinamica, Divisione di Cardiologia, Ospedale Santa Croce, Cuneo, Italy.

Manuscript received August 12, 1993; revision accepted November 4.

of the IVC is a very rare finding in adults with otherwise normal hearts. We report a case with hemiazygous continuation in a male adult with severe mitral regurgitation.

CASE REPORT

A 67-year-old man was admitted to the hospital for a chest pain of 10 min at rest with ECG changes of uncertain significance. His family history was not remarkable: his mother and father had both died after age 70 years and the cause was not known, one sister had died at age 35 years soon after the birth of her first son, and a second one was still alive and healthy about 20 years after moving to a remote country. The patient was well until 7 years earlier, when moderate shortness of breath appeared. At that time a diagnosis was made of paroxysmal atrial fibrillation, moderate mitral regurgitation, and mild arterial hypertension. Symptoms had improved with oral digoxin and nifedipine.

At the time of hospital admission, the patient was in no distress, and his chest pain had spontaneously subsided. His arterial blood pressure was 170/95 mm Hg. A hyperkinetic left cardiac impulse, a soft first heart sound, and a grade 5 holosystolic murmur at the apex were apparent on physical examination, results of which were otherwise unremarkable. The posteroanterior chest radiograph showed only mild atrial enlargement and a cardiothoracic ratio of 0.42. The ECG showed regular sinus rhythm at 70 beats/min, and signs of left ventricular hypertrophy with overload. Depression of the ST segment was more marked than on previous tracings and T waves were deeply inverted throughout the precordial leads.

The patient had no symptoms during his hospital stay. An echocardiogram showed a slightly enlarged left ventricular chamber (end diastolic diameter = 55 mm/m2) with normal systolic function, an enlarged left atrium (56 mm), and a marked prolapse of the posterior mitral leaflet. The former appeared grossly thickened, normally inserted, and with no sign of chordal rupture. The color-Doppler examination showed a severe mitral regurgitation. The other chambers were normal, as was the tricuspid valve. A stress test was not performed because of baseline ST segment and T-wave abnormalities.

Right and left heart catheterization through the femoral route was performed to evaluate the valvular abnormality and exclude the presence of significant coronary disease, with a view toward possible surgical repair. During the right heart study, the course of the catheter in the upper abdominal tract and through the diaphragm was seen to point to the left of the spine and posteriorly, with a marked curve to the right and anteriorly at the level of the eighth thoracic vertebra, to reach the normally positioned superior vena cava (SVC), the right atrium, and ventricle (Fig 1). The diagnosis of infrahepatic interruption of the IVC was made. Caval angiography showed an enlarged hemiazygous vein continuing the suprapenal segment of the IVC and emptying into the SVC through a dilated segment of the azygos vein (Fig 2).

Cardiac angiography and oximetric runs excluded the presence of other lesions, and pulmonary pressures were normal. The left ventricle had a normal end-diastolic volume (87 ml/m2) with an ejection fraction of 65 percent, and a grade 4 mitral regurgitation. The coronary arteries were normal. A complete chest radiographic study was obtained. No IVC shadow was apparent in the lateral projection. In the left anterior oblique projection (Fig 3), the anomalous shadow of the hemiazygous vein appeared to be superimposed on the ascending aorta. A supplemental cardiac ultrasound study was performed. In the subcostal views, a significant obstruction was seen in the great vein approaching the right atrium from below: the latter showed a direct connection with the hepatic veins. An ultrasound study of the abdomen showed

Downloaded From: http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21703/ on 06/21/2017