nephritis with IgG and C3 deposits in the mesangium. There was no
evidence of vasculitis. Aortic arch angiogram revealed complete
occlusion of the right innominate artery at its origin and stenosis of
the left subclavian and carotid arteries with poststenotic dilation.

The patient was given prednisone, 100 mg daily, for six weeks with
a fall in the ESR to 50 mm hr. However, there was no improvement in
chest roentgenogram or pulmonary function. New transient
ischemic attacks prompted bypass surgery resulting in relief of her
neurologic symptoms. A biopsy of the artery provided insufficient
material to confirm Takayasu's arteritis. There was no evidence of
thrombosis. An open lung biopsy showed characteristic changes of
usual interstitial pneumonitis. The alveolar septa were irregularly
thickened due to interstitial fibrosis and lymphocytic infiltrates.
Some areas revealed severe fibrosis approaching "honey-combing"
with air spaces lined by bronchiolar epithelial cells and type 2
pneumocytes (Fig 1b).

Over the next 15 months, the patient was treated with prednisone
and azathioprine. However, the patient developed increasing dysp-
nea and loss of lung function. Her vital capacity fell to 1.70 L. Right
heart catheterization revealed a pulmonary artery pressure at rest of
47/12 mm Hg which rose to 100/17 mm Hg with exercising to fatigue.
Her pulmonary artery occlusion pressure ranged from 2 to 6 mm Hg.
A pulmonary angiogram was normal.

DISCUSSION

The diagnosis of Takayasu's arteritis is dependent on recog-
nizing symptoms of ischemia and the finding of bruits and decreased or
absent pulses. Confirmation by arteriography which shows varying degrees of aortic and arterial narrowing or
obstruction, and may include aneurysms.4 This patient with
hypertension, a left carotid bruit, and a pulseless upper extremity had a diagnostic arteriogram with total occlusion of
the innominate artery and stenosis of the subclavian and carotid arteries. Systemic lupus erythematosus has been
reported to rarely mimic Takayasu's arteritis.6 In these
cases, there is evidence of arterial thrombosis with subse-
cquent deficit in pulses. However, the present patient had no
evidence for active lupus erythematosus. Specifically, she
had a negative antinuclear antibody, normal complement
levels, and a negative assay for circulating immune com-
plexes.

Dyspnea is quite common in patients with Takayasu's arte-
ritis.6,7 Usually, this is attributed to cardiovascular abnormali-
ities. It is felt that pulmonary manifestations of Takayasu's
arteritis are usually due to pulmonary artery involvement. In
one series of patients undergoing pulmonary angiography, 13
of 26 cases had abnormalities.8 This case demonstrated widespread
lung fibrosis with no evidence of arteritis in the lung
biopsy or pulmonary angiogram. The positive gallium scan
and the abnormal BAL findings are consistent with active
alveolitis.8 However, the biopsy demonstrated only fibrosis.
An increased percentage of neutrophils and the presence of
eosinophils in the BAL fluid can be seen in interstitial fibrosis
associated with collagen vascular disease. Pulmonary symp-
toms have also been reported in patients with giant cell
arteritis, a disease similar to Takayasu's arteritis.9

The finding of both renal and pulmonary involvement in
this case suggests a systemic vasculitis. Renal involvement in
Takayasu's arteritis is usually related to stenosis of renal
arteries. Recently, there have been reports of Takayasu's arte-
ritis associated with glomerulonephritis.10 In three of four
cases, immunoglobulin and complement were demonstrated in
the mesangial and glomerular capillary loops, as seen in
this patient.

The cause of the patient's pulmonary and renal symptoms
are unclear. The etiology of Takayasu's arteritis is entirely un-
known; therefore, an immune complex mediated disease not
detected by our assay is possible. Another possibility could
be that the arteritis came first. The renal and pulmonary
disease resulted from immune complex mediated disease.
The immune complexes could have been generated by either
the primary antigen or material released from damaged
arteries.

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Pulmonary Tuberculosis and Bronchocentric Granulomatosis*

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Bronchocentric granulomatosis (BG) is an uncommon in-
flammatory lesion of unknown etiology defined on mor-
phologic grounds by the presence of necrotizing granu-

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lomata centered on bronchi and bronchioles. We report the
typical pathologic features of BG in a patient with tuber-
culosus. Mycobacterial and other types of infection should
be excluded by appropriate stains and in all patients
with BG on lung biopsy, especially those who are non-
asthmatic.

Bronchocentric granulomatosis, a pathologic entity of
unknown etiology first described by Liebow,1 is charac-
terized by necrotizing granulomata centered on bronchi. In
asthmatic patients, BG is a well-documented manifesta-
tion of allergic bronchopulmonary aspergillosis which generally
has a favorable prognosis. It is therefore important to distin-
guish it from the more serious types of granulomatosis,
even those of infectious etiology.2,3 We report the typical
pathologic features of BG in a patient with tuberculosis.

CASE REPORT

A 24-year-old previously healthy Yemenite immigrant was admit-
ted to the hospital with a three-month history of epigastric pain. On
the day of admission, he vomited bright red blood and experienced
fever and night sweats. The results of the initial physical examination
and chest roentgenogram were normal. The hemoglobin level was
10.2 g/100. The white blood cell and differential counts were normal.
Intermediate-strength PPD skin test produced 20 mm of induration
at 48 hours. Upper gastrointestinal tract barium study demonstrated
narrowing of the pyloric channel and three linear intraluminal filling
defects in the distal small bowel, typical of ascariasis. An umbilicated
antral ulcer was visualized with gastroscopy. No parasites were seen.
The patient was treated with antacids and no further episodes of
hematemesis occurred.

On the seventh hospital day, the patient became febrile to 102.8°F. A
chest roentgenographic examination demonstrated a fluffy infil-
trate in the left mid-lung field. The next day, a course of therapy with
piperazine was initiated. Two days later, an additional infiltrate
developed in the right lung field. The patient remained febrile.
Repeated blood cultures and sputum smears stained with Gram's and
Ziehl-Neelsen stains gave negative results. Multiple sputum and
gastric aspirates were cultured for mycobacteria. The white blood
cell count remained normal, but a monocytosis of 12 percent was
observed. Treatment with isoniazid, ethambutal, and pyridoxine was
initiated on day 10 because of persistent fever, pulmonary infiltrates,
and a positive PPD test result. The patient became afebrile within six
days. The right pulmonary infiltrate cleared, but the left lung
infiltrate persisted. Stool examination for ova and parasites was
negative. Serologic tests for toxoplasmosis, echinococcosis, and
amebiasis were nonreactive. An open lung biopsy was performed on
the 23rd hospital day to examine the persistent left pulmonary
infiltrate (Fig 1).

Pathologic Findings

Multiple large, discrete, round inflammatory lesions were obser-
ved on microscopic examination of the open lung biopsy spec-
imen. Each of these lesions consisted of a central necrotic zone
containing numerous polymorphonuclear leukocytes surrounded by
a zone of epithelioid cells and occasional scattered giant cells. At the
periphery of these granulomas was a zone of granulation tissue
containing numerous plasma cells and eosinophiles, and small
numbers of macrophages and lymphocytes. Some of these lesions
obviously involved bronchioles and were centered on them (Fig 2).
In others, the presence of elastic tissue remnants in the center of the
lesion, or the presence of a small pulmonary artery at the periphery,
provided indirect evidence of bronchocentric localization. In some of
the lesions, bronchocentric localization could not be definitely

Figure 1. Chest roentgenogram showing left lung field infiltrate
prior to open lung biopsy.

established. No bacteria, fungi, or acid-fast bacilli were identified by
staining or culture of the lung biopsy specimen. Step sections of the
bacteria blocks were examined in order to attempt to identify parasites,
but none was found. None of the bronchioles or bronchi examined
showed mucoid impaction.

Clinical Follow-up

The patient was discharged on the 31st hospital day, and continued
on antituberculosis therapy. A culture of sputum collected on the
ninth hospital day grew Mycobacterium tuberculosis. The patient
remained asymptomatic and gained 18 pounds within one month of
discharge. His chest film appeared normal.

DISCUSSION

Bronchocentric granulomatosis in asthmatic patients is a
well-documented manifestation of allergic bronchopulmonary
aspergillosis.2,3 However, there is a second, more hetero-

Figure 2. Bronchocentric necrotizing granuloma. The granuloma is
present at left. A bronchiole entering from the right exhibits
extensive destruction within the granuloma. (Verhoeff-van Gieson
stain, original magnification X 25).
genuous group of patients with BG. These patients are not asthmatic, have little or no blood or tissue eosinophilia, and usually do not have mucoid impaction or noninvasive fungi in the airways. The pathogenesis of BG in this second group is largely unknown, and multiple etiologic agents are likely. Our case falls into this second group.

We believe that the bronchocentric granulomas in our patient are a manifestation of infection with *Mycobacterium tuberculosis*. This conclusion is supported by the positive sputum culture for *M tuberculosis* and the clinical and radiographic improvement which followed antituberculosis chemotherapy. Failure to demonstrate mycobacteria in the lung biopsy specimen may be accounted for by the thirteen days of antituberculosis chemotherapy the patient received prior to the lung biopsy. Pathologic findings in our patient's lung biopsy are characteristic of the lesions of BG described by Liebow, and are unlike typical tuberculous granulomas. Our patient had roentgenographic evidence of a roundworm infestation. However, no worms were identified in multiple post-treatment stool specimens, by endoscopy, or in the lung biopsy specimen. Pulmonary infection with Ascaris and *Toxocara* species can produce granulomatous lesions in the lungs, but peripheral eosinophilia and demonstration of larvae in lung tissue would be expected. Therefore, we do not believe that the bronchocentric granulomatous lesions in our patient were the result of parasitic infiltration of the lungs.

The pathologic pattern of BG in the nonasthmatic patient has been associated with fungal and mycobacterial infection, but not with culture-proven tuberculosis. Ulbright and Katzenstein reported that 14 of 86 resected solitary pulmonary granulomas demonstrated the pathologic pattern of BG. Acid-fast bacilli were seen on the Ziehl-Neelsen stain in eight of the 14 specimens with BG, but detailed culture results were not reported. Duncan-Myers and Katzenstein reported four additional nonasthmatic patients with pathologic features of BG who were eventually proven to have infection. Rare acid-fast bacilli were demonstrated on stain in two, one of which grew *M intracellulare* on culture. Two additional case reports describe patients with BG on lung biopsy and atypical mycobacteria cultured from sputum or lung biopsy.

In conclusion, we report a patient with BG which we believe is a manifestation of tuberculosis. BG is most commonly one of the histologic manifestations of allergic bronchopulmonary aspergillosis. Other agents, including infectious agents, almost certainly can produce the same pathologic pattern. It is important to consider tuberculosis and other infections whenever BG is diagnosed on lung biopsy, particularly if the patient is nonasthmatic. Corticosteroids and cytotoxic drugs have been used in the treatment of some patients with BG, and failure to consider and diagnose an infectious etiology for BG could result in further dissemination of infection.

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Pulmonary Hypertension, Hemolytic Anemia, and Renal Failure

**A Mitomycin-Associated Syndrome**

James T. McCarthy, M.D.; and Bruce A. Staats, M.D.

After treatment with mitomycin C, a patient developed pulmonary hypertension with interstitial infiltrates, microangiopathic hemolytic anemia, systemic hypertension, and renal failure with the nephrotic syndrome. Open lung biopsy documented intracapillary fibrin thrombi in the pulmonary vasculature. Renal biopsy documented glomerular and arteriolar changes that were most consistent with a thrombotic-thrombocytopenic-like process. Treatment with corticosteroids, fresh-frozen plasma, and total plasma exchange was ineffective. The patient died six months after the onset. When mitomycin-C therapy is given, the clinician should be aware of the pulmonary, renal, and microangiopathic changes that can be associated with such therapy.

Mitomycin C (MMC) is an alkylating agent commonly used in the chemotherapy of gastrointestinal cancer, breast cancer, and other solid tumors. In this case report, we detail the course of a patient who became dyspneic while being treated with MMC. She rapidly developed pulmonary and systemic hypertension, interstitial pulmonary infiltrates, microangiopathic hemolytic anemia, and azotemia with the nephrotic syndrome. We believe this distinct syndrome can be attributed to MMC therapy.

**Case Report**

A 46-year-old white woman was initially seen by us in early June 1984. In July 1983, a localized grade 2 adenocarcinoma of the colon, infiltrating to the serosal surface but without nodal metastases, was resected. There was no known evidence of pulmonary or renal disease at this time, although the patient was a current smoker of 20 cigarettes daily.

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