Bronchiolitis Obliterans Associated with Polyarteritis Nodosa*

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Bronchiolitis obliterans with organizing pneumonia (BOOP) has not previously been described in association with polyarteritis nodosa (PAN). This report describes a patient in whom fulminant systemic PAN followed subacute onset of BOOP, with associated pulmonary arteritis.


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\text{BOOP} = \text{bronchiolitis obliterans with organizing pneumonia;}
\text{PAN} = \text{polyarteritis nodosa}
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Bronchiolitis obliterans with organizing pneumonia (BOOP) is usually not associated with any apparent cause of underlying disorder, although some cases occur after inhalation of noxious gases, recent infection, or one of the connective tissue disorders.\(^1\) It has not previously been described in association with polyarteritis nodosa (PAN). This report describes a patient who presented with a systemic illness and BOOP and whose underlying PAN did not become manifest until some months after the onset of his pulmonary disease. This report adds PAN to the list of associated disease processes to consider in a patient presenting with BOOP.

CASE REPORT

A 71-year-old nonsmoking retired carpenter presented with a four-week history of fever, sweating, anorexia, malaise, weight loss (3.2 kg), dry cough, and muscle aches without chest pain, hemoptysis, or previous pulmonary disease. He was febrile (38°C) with signs collapse/consolidation in the left upper zone only plus paninflammatory crackles at both bases.

A chest roentgenogram revealed patchy left upper zone consolidation.

The white cell count was 15,600/cu mm (80 percent neutrophils with left shift; no eosinophilia). The hemoglobin level was 11.1 g/L (normal, 13 to 18 g/L); erythrocyte sedimentation rate, 90 mm/h; platelet count, 832,000/cu mm. The serum albumin concentration was 29 g/L (normal, 35 to 45 g/L); alkaline phosphatase, 287 U/L (normal, 35 to 135 U/L); aspartate aminotransferase, 43 U/L (normal, 6 to 42 U/L); creatinine, 87 μmol/L (normal, <120 μmol/L); urea nitrogen, 6.1 mmol/L (normal, 3 to 8 mmol/L); electrolytes, normal. Urine microscopic findings were normal. Levels of serum immunglobulins G, M, A, and E were all within normal limits, and the antinuclear factor and rheumatoid factors were both normal. Hepatitis B serologic testing was negative.

The patient was treated with systemic antibiotics (erythromycin, clindamycin, and cefotaxime) but remained well. All investigations for infective agents were negative, specifically, sputum examination (including examination for acid-fast bacilli) and serologic testing for respiratory viruses (influenza A and B; adenovirus; parainfluenza 1, 2, 3, 4).

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Figure 1. Bronchoscopic views of the left main bronchus, showing (left) tumor extension, obscuring the carina and the orifice of the left lower lobe bronchus before HDR brachytherapy and the local situation thereafter. Following HDR (right), radical pneumonectomy could be performed.

cm intraluminal tumor length axis; specific activity iridium:192 10 Ci; 10 Gy at 1 cm from the source axis) in two sessions two weeks apart. The total duration of each bronchoscopic session was less than 15 min. On bronchoscopic evaluation four weeks after HDR, there was a significant reduction of the tumor mass (Fig 1). Biopsies and aspirates of the main carina and the proximal part of the mucosa of the left main bronchus were negative. A left pneumonectomy was carried out. The resected margin and all mediastinal lymph nodes were free of tumor (T2N0M0). No tumor recurrence has been assessed after a follow-up of 43 months.

DISCUSSION

Our case documents that HDR is effective in reducing mucosal tumor infiltration. The HDR treatment prior to surgery permitted less extensive surgical resection avoiding resection of the main carina. The approach to use HDR to improve resectability in NSCLC seems especially appropriate in cases of intraluminal mucosal tumor infiltration. It may enable a less extensive surgical approach. The feasibility of this approach could be valuable in surgical candidates with limited pulmonary function.
II, and III; respiratory syncytial virus; cytomegalovirus; varicella) as well as for psittacosis, Q fever, Mycoplasma, and Legionella (all performed on two separate occasions) plus Toxoplasma, Leptospira, and Brucella.

The patient remained unwell, and the cough persisted. A chest roentgenogram showed progression of the left upper zone changes, with infiltration of the right middle and upper zones. Bronchoscopy revealed no endobronchial lesion, and bronchial washings, brushings, and biopsy revealed no infective organisms. Bronchoalveolar lavage was markedly abnormal with elevated neutrophil proportions (50 percent; normal, <4 percent) with some elevation in eosinophil and lymphocyte proportions (2 percent and 17 percent, respectively [normal, respectively] <1 percent and <16 percent).

Open lung biopsy of the right upper lobe was performed four weeks after admission. Biopsy of the right upper lobe showed severe patchy alteration of lung architecture by loose intra-alveolar fibroblastic tissue and associated nonspecific chronic interstitial inflammation. Many bronchioles contained polypoid projections of fibroblastic and inflammatory tissue, and the numbers of identifiable bronchioles were reduced (Fig 1). Small, thick-walled muscular vessels were present within damaged lung tissue. One medium-sized artery demonstrated fibrinoid necrosis of the wall and infiltration by lymphocytes, histiocytes, and neutrophils (Fig 2). This vessel was considered to be a pulmonary artery, rather than a bronchial artery, because of its large size in relation to the adjacent bronchiolar structure; the vessel was similar in size to other pulmonary arteries in nearby lung, whereas identifiable bronchial arteries were of smaller diameter.

Postoperatively, the patient's renal function deteriorated, the creatinine level rising to 355 \( \mu \text{mol/L} \). Urinalysis demonstrated hematuria, proteinuria, and occasional hyaline and granular casts. A renal biopsy was performed. One segmental area of glomerular fibrinoid change was evident, together with a mild focal and segmental increase in glomerular mesangial cellularity, and patchy interstitial infiltration. A large arcuate artery showed severe fibrinoid necrosis of the wall. Ultrastructurally, there were no electron-dense deposits.

Despite treatment with systemic methylprednisolone and cyclophosphamide, the patient developed ARDS one week postoperatively and died in respiratory and renal failure.

At autopsy, the lungs exhibited alveolar exudation of neutrophils and macrophages and foci of hemorrhage and necrosis. Areas of fibrosis and organizing pneumonia were also present, although changes of bronchiolitis were difficult to find. No vasculitis could be identified in multiple lung sections, and no organisms were seen with special stains.

The kidneys had mottled external surfaces with hemorrhagic and infarcted areas with aneurysmally dilated blood vessels. Multiple foci of segmental or circumferential fibrinoid necrosis were observed microscopically in medium-sized arteries (Fig 3), as well as patchy interstitial hemorrhage and numerous foci of ischemic necrosis. Vasculitis was confirmed microscopically in the testes, deltoid muscle, tongue, sciatic nerve, prostate gland, and adrenal glands. Fibrinous pericarditis was noted.

**Discussion**

The features of a systemic illness associated with patchy pulmonary consolidation, after exclusion of pulmonary infection, and the open-lung biopsy findings confirmed a diagnosis of BOOP. This condition has a distinctive histologic pattern of subacute lung reaction to injury characterized by patchy lung involvement, intra-alveolar fibroblastic tissue, polypoid projections of fibroblastic and inflammatory tissue within bronchioles, bronchiolar destruction and disappearance, and a variable degree of interstitial inflammation and fibrosis. In most cases, there is no known precipitating event. The cryptogenic form of BOOP usually presents clinically as a severe subacute illness over several months with dyspnea, fever, and patchy or interstitial bilateral lung shadowing. Diagnosis is usually made at open-lung biopsy. Recognition of the pattern histologically and distinction from other fibrosing lung processes, in particular usual interstitial pneumonitis, is important, since most cases of
cryptogenic BOOP will respond to corticosteroid therapy and often resolve completely. Some patients suffer progressive lung impairment and death.

High-dose corticosteroids and cyclophosphamide failed to prevent progression of this patient's pulmonary or renal disease, suggesting that despite the subacute onset of his condition, the disease process in both organs accelerated rapidly at the end of his clinical course.

The sequence of histologic changes was that of BOOP followed by the development of florid PAN of the classic type, apart from one focus of necrotizing vasculitis in a medium-sized pulmonary artery. Although the lung exhibited one focus of necrotizing vasculitis, further vasculitis was not evident in lung at autopsy despite florid vasculitis elsewhere.

The pathogenetic processes underlying the various forms of bronchiolitis obliterans are unknown. It has been suggested that, when associated with connective tissue diseases, heart-lung transplantation, and perhaps viral infection, the disease represents an autoimmune process whereby the host immune system responds to airway epithelial cell class II antigen expression induced by gamma interferon.14,15 Spontaneous gamma interferon production by cells obtained at bronchoalveolar lavage was measured in this patient as part of another study and was very high (390 units/10^{10} cells in 24 h [normal individuals release \leq 10 units/10^{10} cells in 24 h]).14,15 This finding is consistent with the above hypothesis.

The failure to respond to treatment is a little unusual for BOOP; although death from progressive disease has been well described.14 This patient clearly had a very aggressive form of the disease.

This report describes an association between BOOP and PAN, which suggests that similar pathogenetic mechanisms may be present in some patients with these disorders. Also, since BOOP can clearly precede the clinical manifestations of PAN, awareness of these facts may lead to careful monitoring for PAN and therefore to earlier therapy.

**REFERENCES**


**Bilateral Proximal Pulmonary Artery Aneurysms Simulating Hilar Adenopathy**

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Proximal pulmonary artery aneurysms (PAAs) are rare. Most are associated with secondary pulmonary hypertension or a variety of rare systemic disorders. An asymptomatic adult patient presented with bilateral hilar enlargement on a routine chest roentgenogram. Computed tomography of the chest revealed 5 cm bilateral proximal PAAs with a normal pulmonary trunk. The clinician should consider proximal PAA in the differential diagnosis of hilar enlargement.

(CHEST 1992; 102:311-13)

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<th>DC0/VA = specific diffusing capacity; PAA = pulmonary artery aneurysm; PT = pulmonary arterial trunk</th>
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Bilateral hilar enlargement is a relatively frequent roentgenographic pattern. In almost all cases, bilateral hilar enlargement is due to enlarged hilar lymph nodes or hilar vessels. Bilateral hilar adenopathy is typically seen with either benign granulomatous disease (sarcoid and infection) or malignant disease. Vascular causes for bilateral hilar enlargement are far less common. The majority of proximal PAAs, those involving the pulmonary trunk and/or major divisions, are associated with pulmonary hypertension, either primary or secondary to a number of cardiopulmonary disorders.2,11 Isolated proximal PAAs in the absence of predisposing conditions are particularly unusual.4, Also, all

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