LEADING ARTICLE

BOOP – BRONCHIOLITIS OBLITERANS ORGANIZING PNEUMONIA

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TERMINOLOGY

Bronchiolitis obliterans is a lesion describing the widespread inflammation and fibrotic obstruction of small airways[1]. Grinblat et al in 1981 recognized an "organizing pneumonia-like process" in two well-studied cases of infiltrative lung disease[2] and in 1983 a paper from Turner Warwick's group published a report on eight patients with what they termed "cryptogenic organizing pneumonitis"[3] who responded dramatically to prednisolone.

It was in 1985 that Epler with Colby & Carrington among others, reported on 50 patients with idiopathic Bronchiolitis Obliterans Organizing Pneumonia (BOOP)[4] and placed in perspective this disorder among the spectrum of interstitial fibrotic lung diseases. They coined this term BOOP with a distinct clinical, radiological, histological picture, and stressed again its steroid-responsiveness.

SPECTRUM

Lung fibrosis is usually irreversible. Sub-classification of the various lung diseases characterized by pulmonary fibrosis is difficult, controversial and often confusing. Terminology used has not been consistent and that group labelled as "cryptogenic fibrosing alveolitis", "idiopathic pulmonary fibrosis" or "usual interstitial pneumonia (UIP)" typically have a progressive, untreatable, relentless course to death. BOOP is characterized by fibrosis of the small airways and alveoli and had been misclassified as one of the above until the good clinical and prognostic outcome with steroids was stressed[4] and the disease is now accepted as a clinicopathological entity distinct from usual interstitial pneumonia[4,5].

Bronchiolitis obliterans results when injury to small conducting airways is repaired by proliferation of granulation tissue and is a reaction to diverse insults. It may or may not be associated with alveolar scarring which follows intra-alveolar inflammation and organization. Organizing pneumonia had been described in the preantibotic era following failure of resolution of lobar pneumonia[6,7].

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A proposed clinical classification of bronchiolitis obliterans[4] is as follows:

1. Toxic fume bronchiolitis obliterans
2. Post infectious bronchiolitis obliterans
3. Bronchiolitis obliterans associated with connective tissue disease
4. Localized lesion with bronchiolitis obliterans eg. distal to obstruction or bronchiectasis
5. Idiopathic BOOP

IMPORTANCE OF BOOP

BOOP forms a distinct part of the spectrum of infiltrative lung diseases. It is possible to differentiate BOOP from UIP and idiopathic pulmonary fibrosis on clinical grounds on the basis of an atypically brief history and an unusual radiograph. With a proper open lung biopsy, the pathologist can also note its distinctive histology. Thus the diagnosis can be quite firm.

BOOP is treatable and reversible. With high dose prednisolone, complete clinical and physiologic recovery occurred in 65% of cases[4] although two died from progressive disease.

HISTORY

There are only two paragraphs in Harrison's Textbook of Medicine[1] on bronchiolitis obliterans, a disease more familiar to paediatricians than adult physicians as it was thought to occur in those who had suffered severe viral infection in childhood eg. parainfluenza.

BOOP is not a new lesion but the idiopathic form of the disorder had not been recognized as a distinctive subset in the spectrum of infiltrative lung disease until 1985[4]. Prior to this, its histological features were considered a part of general bronchiolitis obliterans, or organizing diffuse alveolar damage, or idiopathic pulmonary fibrosis.

Organizing pneumonia is inflammatory intra-alveolar exudate followed by organization and could be caused by rheumatic lung[8], renal failure[9], congestive heart failure[10], hexamethonium[11] and busulphan[12].

Thus both bronchiolitis obliterans and organizing pneumonia as separate, distinct entities have existed but it is only 5 years ago that their coexistence has been associated with a benign course and dramatic therapeutic response.

CLINICAL

From Epler's analysis of 50 patients with BOOP[4], a characteristic clinical picture evolved. Most had a history suggesting a slowly resolving viral pneumonia spanning

weeks or a few months. Men and women were affected equally, usually in the fifth and sixth decades. Persistent and nonproductive cough was a common presenting symptom, as was mild dyspnoea on exertion .The onset of illness with malaise, fever, fatigue and cough (emphasis on nonproductive and persistent) suggested a flu-like syndrome. Many had symptoms less than two months although less than 20% had over a year of symptoms.

Crackles were present and wheeze usually absent despite the "obstructive" nature of the disease. About 25% of subjects had no abnormal physical findings. None had clubbing. In the British series of cases with organizing pneumonitis[3] as distinct from fibrosing alveolitis, clubbing was present in only one of 8 patients in the former but in two thirds of patients with the latter.

RADIOGRAPHY

Radiographs show an unusual pattern of bilateral patchy densities with a ground glass appearance which sometimes begins as focal lesions and progress bilaterally over time. This was recognized as typical for the disease[4]. Cavities, effusions and hyperinflation are uncommon.

In a paper contrasting radiographic manifestations of BOOP with UIP, Chandler et al[13] showed that patients with BOOP have chest radiographs showing alveolar opacities without lung volume loss whereas the other group has bilateral diffuse interstitial opacities with occasional honeycomb changes and loss of lung volume in most cases. However there was no direct correlation between X-ray patterns and histology.

The characteristic finding in BOOP not present in UIP or small airway disease[14] is patchy air-space consolidation[15]. Rarely is the chest X-ray in BOOP normal.

PULMONARY FUNCTION TESTS

BOOP presents with a restrictive pattern on testing (reduced volumes, impaired diffusion and preserved flow rates FEV_1/FVC). In this respect it is similar to cases with UIP and although histologically there is bronchiolitis and extensive plugging of small airways there is no obstructive pattern on testing[15]. There is little correlation between histopathology and lung function testing. Hypoxemia is present in arterial blood gas. The restrictive pattern with reduced DL_{co} suggests interstitial lung disease.

HISTOPATHOLOGY

Transbronchial lung biopsy is not recommended because of the small specimens and patchy nature of the disease. The distinctive histologic features are - the remarkable temporal uniformity of granulation tissue plugs, their even spacing across the lung section on scanning power, the patchy distribution of the reaction and the general preservation of background architecture[4]. Granulation tissue plugs are within the lumens of small airways, often extending into alveolar ducts. The distinguishing histological feature of organizing pneumonia is the presence of small buds of connective tissue ('bourgeons conjunctifs') in air spaces and this indicates organization of a persistent exudate by fibroblasts and capillaries from the alveolar walls[3]. On using a pathologic scoring system to assess changes in the membranous and respiratory bronchioles, the inflammatory process is more severe in these bronchioles in BOOP than in UIP and small disease[15]. Further, the organization of the inflammatory process with loose connective tissue deposition in the air spaces differentiates BOOP from UIP.

WHEN TO SUSPECT BOOP

A patient in middle age with a longer than expected flu-like illness presenting with a persistent nonproductive cough should be suspected of having BOOP. Cigarette smoking history is relevant as there may be an added obstructive element to the patient's symptomatology. The long-lasting flu-like illness reminds one of an atypical pneumonia process and it is in this setting that investigations should proceed. Unlike the patient with a typical pneumonia, crackles tend to be the predominant chest finding. Clubbing is notable for its absence.

The other causes of bronchiolitis obliterans as given earlier should be excluded clinically and by investigations.

WHAT TO DO

A chest radiograph is essential to show the patchy air space consolidation which tends to be bilateral and progressive over time. Pulmonary function testing will reveal a non-specific restrictive pattern of defect which combined with an impaired DL_{co} leads one to infer an interstitial lung disease. Sputum cultures for bacteria including mycobacterium tuberculosis and blood cultures for the usual pathogens should be sterile. Serology results should include the aetiological agents of atypical pneumonia viz. coxiella burnetii, chlamydia psittaci, mycoplasma pneumoniae and common respiratory viruses and legionella.

There should be no eosinophilia and antibodies to common probable agents of type III immune injury should be absent.

An open lung biopsy is recommended if thought justified.

HOW TO TREAT

Prednisolone is the treatment of choice with 1 mg/kg body weight dose given daily for one to three months. After improvement, the dose is tapered and eventually kept at a lower dose of 10 to 20 mg every other day. The duration of treatment should be one year. Too rapid tapering of steroids can lead to rebound.

Immunosuppressives have not been shown to be useful.

In this issue of the Journal is the first report of a local case. BOOP is in Singapore. The 70 year old male patient responded well to treatment emphasizing the importance of a diagnosis secured though an open lung biopsy. A prolonged follow-up is necessary as steroid dosage judiciously tailored to the parameters of the disease and patient's well-being is mandatory.

REFERENCES

1. Harrison's Principles of Internal Medicine. 11th edition. McGraw Hill International Edition, 1987 : 1094-5.
2. Grinblat J, Mechlis S, Lewitus Z. Organizing pneumonia-like process : an unusual observation in steroid responsive

cases with features of chronic interstitial pneumonia. Chest 1981; 80 : 259-63.
3. Davison AG, Head BE, McAllister WAC, Turner-Warwick MEH. Cryptogenic Organizing Pneumonitis. Q J Med 1983; 52: 382-94.
4. Epler GR, Colby TV, McLord TC, Carrington CB, Gaensler EA. Bronchiolitis Obliterans Organizing Pneumonia. N Engl J Med 1985; 312: 152-8.
5. Katzenstein A, Myers JL, Prophet D, Corley LS, Shin MS. Bronchiolitis obliterans and unusual interstitial pneumonia : a comparative clinicopathological study. Am J Surg Pathol 1986; 10 :373-81.
6. Milne LS. Chronic pneumonia (including a discussion of two cases of syphilis of the lung). Am J Med Sci 1911; 142: 408-38.
7. Floyd R. Organization of pneumonic exudates. Am J Med Sci 1922; 163: 527-48.
8. Neuberge KT, Geever EF, Rutledge EK. Rheumatic pneumonia. Arch Pathol 19444; 37: 1-15.
9. Auerbach SH, Mins OM, Goodpasture EW. Pulmonary fibrosis secondary to pneumonia. Am J Pathol 1952; 28: 69-87.
10. Heard BE, Steiner RE, Herdan A, Gleason D. Oedema and fibrosis of the lungs in left ventricular failure. Br J Radiol 1968; 41:1611-71.
11. Heard BE. Fibrous healing of old introgenic pulmonary oedema (Hexamethonium lungs). J Pathol Bact 1962; 83 : 159-64.
12. Heard BE, Cooke A. Busulphan lung. Thorax 1968;23 ;187-93.
13. Chandler PW, Shin MS, Friedman SE, Myers JL, Katzenstein AL. Radiographic manifestations of Bronchiolitis Obliterans with Organizing Pneumonia vs Usual Interstitial Pneumonia. Am J Radiol 1986: 14447 : 899-906.
14. Macklem PT, Thurlbeck WM, Fraser RG. Chronic obstructive disease of small airways. Ann Intern Med 1971; 74 : 167-77.
15. Guerry-Force ML, Muller NL, Wright JL et al. A comparison of Bronchiolitis Obliterans with Organizing Pneumonia, Usual Interstitial Pneumonia and Small Airway Disease. Am Rev Respir Dis 1987; 135 : 705-12.