BOOP and COP

Pathological descriptions of rare lung diseases often precede their clinical recognition and classification. The confusion this can cause is well illustrated in the story of OB, COP, and BOOP, which came about in the following way.

In the first place pathologists described some characteristic patterns of response to insult in the lungs: bronchiolitis with or without obliteration was one and intra-alveolar inflammation and fibrosis was another. The former was described as a common feature in infections and was found with bronchitis and bronchiectasis but occasionally occurred in isolation. The latter pattern was usually seen in the context of organising infectious pneumonia, and occasionally the changes extended into the airways. Then three papers were published by clinicians and these pathological features became clinical diagnoses. The first two were essentially clinical descriptions of rare patterns of disease that were labelled according to the predominant histological abnormality. Geddes et al. described an airway disease and called it obliterative bronchiolitis (OB), while Davison et al. described an alveolar disease and called it cryptogenic organising pneumonia (COP). The third paper did not describe a clinical syndrome but started from the histology. Epler et al. looked through 2000 reports of open lung biopsies in Boston spanning 30 years and pulled out those that contained the words bronchiolitis obliterans, 94 in all. Fifty of these had no underlying cause and because the dominant pathological changes were in fact those of organising pneumonia they were described under the title of obliterative bronchiolitis organising pneumonia (BOOP). This histological pattern was essentially the same as that described by Davison in the paper on COP and had originally been described by Liebow and Carrington as bronchiolitis interstitial pneumonia.

Partly because the paper on BOOP appeared in the prestigious New England Journal of Medicine, partly because it still has the largest number of patients, and partly because BOOP is fun to pronounce, the name has stuck even though the first two letters refer to a minor and potentially misleading part of the disorder.

If all the patients in the three reports of OB, COP, and BOOP are considered together two quite different groups emerge. Patients in the first (OB) have small airway disease with normal alveoli and hypertransradiant lung fields without infiltrates and show little, if any, response to treatment. OB occurs in association with rheumatoid arthritis, in graft versus host disease in bone marrow transplantation, after viral infection, and as part of rejection in lung transplantation. Patients in the second group (BOOP) have an alveolar disease with granulation tissue that extends variably into the airways. These patients have infiltrates on the chest radiograph and, in general, a good response to corticosteroids. This second group, which accounts for the bulk of the patients of Epler et al., is commoner than the first, has been the subject of many recent papers, and is discussed in more detail below.

Pathology

The original description of COP emphasises buds of connective tissue in air spaces, indicating organisation of persistent exudate by fibroblasts and capillaries from the alveolar walls. Inflammatory cells that cluster in the centre of the buds include lymphocytes and plasma cells as well as a few neutrophils and eosinophils. The connective tissue extends into the alveolar ducts and occasionally into respiratory bronchioles. There is a minor amount of interstitial inflammation and fibrosis. The reported findings in COP are almost identical to those described as BOOP by Epler et al.

Subsequent reports have used these pathological features for diagnosis and so are largely repetitive. An interesting range of other features, however, has been mentioned. Cordier et al. in a review of 16 patients,
confirmed the predominantly alveolar distribution of the abnormalities. All patients showed some degree of interstitial inflammation and fibrosis but this was intense in only two patients. In three cases multinucleate giant cells were found. Miyagawei et al\(^8\) reported 11 patients with fleeting infiltrates on the chest radiograph and divided them into six with the above features but no eosinophils and five with eosinophils in the biopsy material. These latter patients had peripheral blood eosinophilia and fall clearly into a different clinical group of cases of pulmonary eosinophilia. Although the small airways were relatively unaffected in this eosinophilic group, pathologically the alveoli had many features in common with those of BOOP/COP, albeit with a greater predominance of eosinophils. In all of these reports the blood vessels were spared and there was no evidence of infecting microorganisms.

The pathological features of BOOP are essentially those of organising pneumonia and are therefore in no way specific. They may be found with viral and other organising infections, allergic alveolitis, irradiation pneumonitis, and drug reactions. In the idiopathic group overlap and diagnostic difficulty may also occur with Wegener's granulomatosis, and eosinophilic pneumonia when vasculitis and eosinophilia are the distinguishing characteristics.

**Clinical features**

The classical clinical presentation as described by Davison is of a subacute influenza-like illness, with cough, malaise, fever, and dyspnoea and with chest radiographic abnormalities and no response to antibiotics. Other reports have emphasised a wider spectrum of both symptoms and radiographic changes. These are summarised in Table 1.

Three points emerge from a comparison of the reports summarised in the table. The first is that the clinical spectrum cannot be completely defined when the condition requires histology for diagnosis. Transbronchial biopsy specimens are too small to be reliable and as only the more severe cases come to open lung biopsy the milder cases may remain undiagnosed. This is well brought out by Cordier's subgroup with localised disease that was removed to exclude neoplasia. If these patients had been given a short course of corticosteroids or possibly if they had been observed for a little longer the condition would have resolved and therefore never have been diagnosed. There may be many such patients and this clinical group remains undefined. The second issue is the range of radiographic abnormalities. Although peripheral fleeting shadows similar to pulmonary eosinophilia are characteristic it is now clear that localised disease may occur as well as diffuse changes. The localised and peripheral shadows are described as alveolar infiltrates whereas the diffuse changes have an interstitial appearance, and these changes appear more resistant to corticosteroid treatment. Whether these diffuse interstitial changes are the result of fibrosis from previous acute episodes is not clear, but this appears unlikely. A few shadows have cavitated and in a few patients pleural effusions have developed. The third point concerns the serological findings. Almost all patients have had a raised erythrocyte sedimentation rate and some have had autoantibodies. No reports have mentioned antineutrophil cytoplasmic antibodies.

**Aetiology and differential diagnosis**

There is some confusion about whether the label of BOOP should be used when the cause is known or whether it should be confined to cryptogenic cases, as suggested by the label COP. The above clinical, radiological, and pathological features have now been described in association with many different events (Table 2). The fact that the same pattern occurs as a result of infections, drugs, and connective tissue disorders confirms that BOOP is not a single clinicopathological entity but rather one way in which the lung mounts an inflammatory response to a range of different insults. The term BOOP is probably best restricted to those cases of unknown cause.

The idiopathic cases are likely to prove no more
BOOP and COP are essentially the same condition and represent one of many ways in which the lung may respond to an inflammatory stimulus. Some underlying causes of BOOP have been identified but in many cases no cause can be found. The clinical and radiological features are often those of a pneumonic illness that responds to corticosteroids rather than antibiotics, but as milder cases are being identified the clinical spectrum is widening. Most cases can be confidently diagnosed only by open lung biopsy, but bacteriological lavage and transbronchial biopsy followed by a trial of steroids may sometimes be considered.

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