Obliterative Small Airway Diseases in Rheumatoid Arthritis

Although rheumatoid arthritis (RA) is characterized by erosive destructive polyarthritis, it is essentially a systemic disease involving many organ systems. Among them, respiratory involvement is frequent including pleuritis, interstitial pneumonitis/fibrosis, and bronchiolitis; the latter two can be life threatening. Obliterative bronchiolopathies in the general population are classified into 3 categories: bronchiolitis obliterans (BO), obliterative bronchiolitis, OB), diffuse panbronchiolitis (DPB), and bronchiolitis obliterans organizing pneumonia (BOOP), and all 3 have been reported to be complicated with RA (1). In addition, some drugs, in particular, disease-modifying antirheumatic drugs (DMARDs), may induce bronchiolopathy.

The most frequent disease that can be diagnosed is interstitial disease because of its fibrotic sequela left in several per cent of RA patients, followed, maybe for its transient nature, by pleurisy, and then BOOP; pure BO and DPB are rare. When studying the occurrence of small airway diseases in collagen vascular diseases, we found only a few cases; under several % of patients could be picked up as cases with any of the obliterative bronchiolopathy.

In BOOP, the pathological changes extend over from bronchiole to alveoli and to interalveolar septa (2). Bronchioles are narrowed or completely obliterated by proliferative bronchiolitis, and alveolar channel and distal alveoli are filled with intraluminal exudate containing mucopolisaccharide and macrophages and fibroblast resulting in organizing or organized pneumonia. The clinical scenario includes preceding flu-like symptoms with or without fever, cough, and dyspnea, and rales. The onset is usually subacute; an acute onset can occur, too. Chest radiograph, although not sufficiently characteristic, shows common findings of patchy acinar infiltrates with uneven distribution, and increased density of bronchovascular bundle with air-bronchogram. Pulmonary function test shows restrictive volume loss, diffusion disturbance, and mild to severe hypoxemia. In the Japanese population, most cases with BOOP are idiopathic, and about 12% were complicated with collagen vascular diseases (3). RA and Sjögren’s syndrome are most frequently seen among the diseases which could be complicated with BOOP (4–7). In contrast the conventional dose of steroid is generally effective in idiopathic BOOP, BOOP that is complicated with collagen vascular diseases sometimes progresses severely, requiring steroid pulse therapy or immunosuppressive drugs.

In cases in which an adverse reaction is caused in the lung by DMARD, we found a good therapeutic response, and chest radiograph and lung biopsy showed findings very similar to BOOP (8). In its early stage, a rapid and fairly good recovery may occur only after the discontinuation of the drug. We also found that serum immunoglobulin decreased concurrently with the development of DMARD-induced lung injury, and re-increased with the recovery from the injury (8).

Pure BO is rare, but at least when it progresses over some extent, it appears as a fairly severe disease with constrictive narrowing and obliteration of bronchiole with slight chance of recovery. Chest radiograph shows only overinfiltration and hyperlucency without any infiltrative shadows. Dyspnea with and without cough, and with scarce sputum, if any, develops subacutely and a weak high pitch wheeze or ‘squeak’ may be audible. We treated a patient with insidious progression with vasculitis other than RA (9). Lung function test showed an obstructive pattern especially in the small airways, but diffusion capacity was maintained in the early stage. Lung transplant might be the only possibility left (10), but obstructive bronchiolopathy is reported to develop in the transplanted lung; the limitation of adaptable diseases other than systemic ones is another problem. DMARDs, especially D-penicillamin, have been sometimes focused to be a cause, but this has not yet been confirmed and there is no report in Wilson’s disease. As chrysotherapy, sulfasalazine or thiopronin is also postulated as a possible cause (11–13), and DMARDs are just common drugs prescribed to many RA patients, BO might occur as a part of RA itself. Histocompatibility background for RA with BO is reported to be a significantly increased prevalence of HLA-B40 and DR4 (13, 14).

DPB has been reported primarily in Japan. Several Japanese cases with DPB were reported to also have RA. The clinicopathological characteristics are mentioned in the case report in this issue (15).

See also p 338.

As both diseases have been suggested to be correlated with HLA-DR4 and B54 in the Japanese population, some authors have proposed the possible occurrence of DPB as a feature of RA itself (14). However, as DPB is quite rare in the rheumatology clinic, and the morbidity of DPB in the general population is now decreasing, it might be difficult to clarify whether this association is significant.

In summary, obliterator small airway involvement in collagen vascular diseases must be taken into account, especially when focusing on RA, for the early prevention of the progres-
sion of rheumatoid lung disease and drug-induced disease.

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References