Is bronchoalveolar lavage also an interstitial lavage?

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The ultrastructural anatomy of the lung identifies the alveolar wall covered by an epithelium facing the endoalveolar space and a basal membrane facing the interstitium. The interstitium is defined as the interalveolar septum formed mainly by connective tissue. Thus, from the anatomical point of view, it is important to distinguish the alveolar space from the interalveolar septum.

The term "alveolitis" has been used for over a century by pathologists to define the presence of an exudate, with few or several cells in the alveolar space. Alveolitis is defined "serous" if the exudate is formed by abundant serum,"fibrinous" if the exudate is rich of fibrin, and "haemorrhagic" if the exudate is rich of red globules. According to the presence of cells in the exudate, alveolitis is defined "purulent" when, in the alveolar exudate, granulocytes are predominant, while it is considered "desquamative" if macrophages are predominant. It should be stressed that lymphocytes have never been described by pathologists as predominant in the exudate in any kind of alveolitis.

The term used for the inflammation of the interstitium is "interstitial pneumonia". In 1964, Scadding proposed the term "fibrosing alveolitis" indicating an inflammatory modification of the alveolar walls evolving in interalveolar interstitial fibrosis, without the presence of an exudate in the alveolar lumen (1). The term "fibrosing alveolitis" resulted ambigous and prompted Liebow in 1975 to define the same condition as "usual interstitial pneumonia" (2).

Today, the term alveolitis is used in a broader fashion referring to the presence of inflammatory cells in the bronchoalveolar lavage (BAL) fluid. BAL is a precious invasive technique that allows the study of the inflammatory events of the lung. BAL recruits from specific areas of the lung any kind of inflammatory cells in fibrosing diseases. In 1981, the increased number of lymphocytes found in BAL prompted Hunninghake et al. to believe that this was dependent from an increased number of lymphocytes in the alveolar space (3): this event was and still is named "lymphocytic alveolitis". Thus, BAL is now considered by the literature as reflecting the presence of cells found always in the endoalveolar space, whether some uncertainties have been raised about the variability of the fluid recovered during the lavage (4).

We know that lymphocytes have never been found in the alveolar space in the exudate of different alveolitides as the only or prevalent cell population. Thus, the main problem that may be addressed is from where are recruited the many lymphocytes detected in the BAL fluid in sarcoidosis, in other lung granulomatoses and in connective tissue diseases.

Particularly in sarcoidosis, BAL is now a fundamental tool to achieve the diagnosis. Pathological findings show that interalveolar septa are enlarged and occupied by confluent granulomas while the alveolar spaces are empty (Fig. 1). At the periphery of every septal nodule, below the basal membrane of the alveolar epithelium, large agglomerate of lymphocytes are found (Fig. 2). In sarcoidosis, the presence of many lymphocytes in the BAL fluid may induce to suggest that the fluid opens the gaps between the alveolar epithelial cells, and cleans the subepithelial lymphocytes that are sucked away with the lavage fluid. Thus, in sarcoidosis the increase of lymphocytes in the BAL fluid may not reflect a real alveolitis but an interstitial granulomatous inflammation.

In idiopathic pulmonary fibrosis and in pulmonary fibrosis secondary to connective tissue diseases, as scleroderma, granulocytes are predominant in the BAL fluid. Hunninghake et al. referred to this as "granulocytic alveolitis" (3). The pathological features of these fibroses do not present a purulent alveolitis but interstitial inflammation leading to fibrosis with atelectasic alveoli free of exudate. The presence in some alveoli of inflammatory cells (macrophages, eosinophils, lymphocytes, neutrophils) without exudate might indicate a desquamation in the alveolar space of interstitial cells through a damage of the lining of alveolar epithelial cells and basal membrane (regressive or degenerative sufference of the alveolar structure). Also during pulmonary fi-

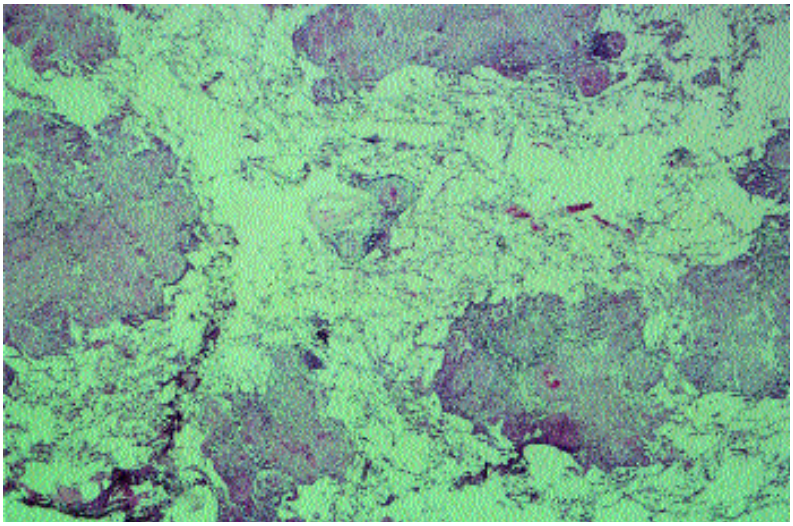

Fig. 1. Pulmonary sarcoidosis: several nodules of sarcoidosis composed of multiple granulomas are evident in the alveolar septa. No cells are present in the alveoli. (E&O, x40)

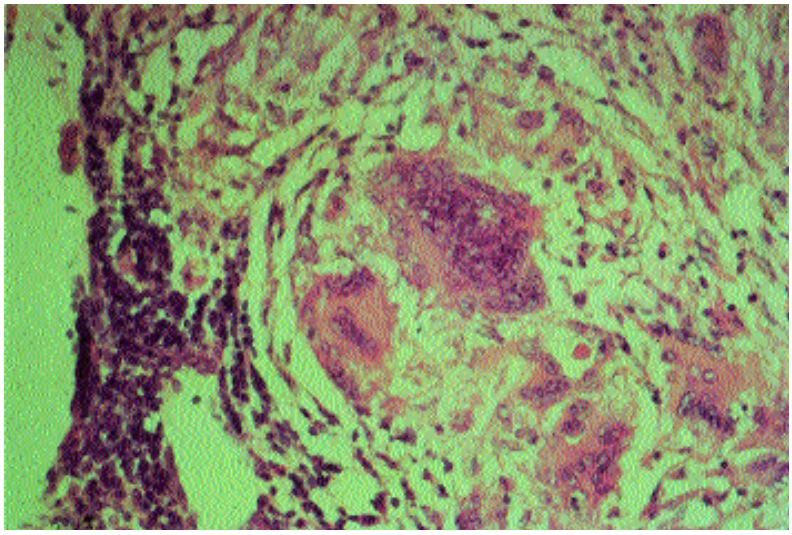

Fig. 2. Pulmonary sarcoidosis: in the interstitial septa a granuloma is lining the alveolar space. In the granuloma, epitelioid and giant cells are detectable and in the periphery, close to the alveoli free of cells, many lymphocytes are visible (E&O, x250)

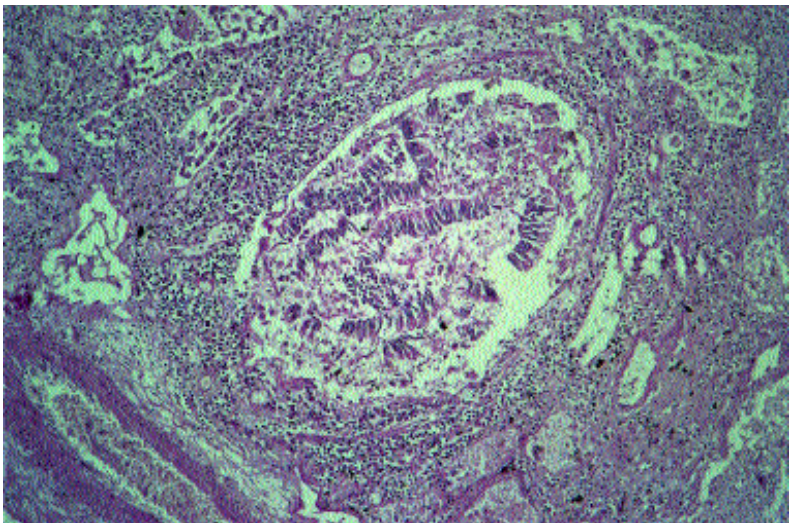

Fig. 3. Advanced systemic sclerosis of the lung:in the parenchymal fibrotic tissue the bronchiolar wall is infiltrated by neutrophils. The lumen is filled with desquamated epithelial cells. (E&O, x100)

broses, cells present in the BAL may reflect the inflammation of the interstitium.

In honeycombing, the detection of granulocytes in the lavage may not reflect an alveolar or interstitial inflammation but the purulent inflammation of the walls of the terminal and respiratory bronchioles (Fig. 3), that are dilating and evolving in the bronchiolar emphysema of honeycombing (5, 6).

The interpretation of BAL as being limited to the alveolar space triggers obviously some questions as which is the structure where the disease develops, which is the structure that is the source of the chemoattractants recruiting PMN, and why should these cells move to the alveolar space. No answer may satisfy today these questions and it is clear that the term alveolitis complicates the understanding of the disease pathogenesis.

In conclusion, in sarcoidosis and other granulomatous diseases of the lung as well as in pulmonary fibroses, the cell count in the BAL might reflect more likely the cellular infiltrates of the interstitium than that present in the alveoli. The term BAL may induce to construct, in different pathologies, an artifactual alveolitis and an inappropriate terminology. Given the pivotal importance of BAL in detecting the cell population in the lung, the term BAL might be enriched by the term bronchoalveolar-interstitial lavage. This is a clear-cut terminology might be more adherent to the the pathologic findings of different fibrosing lung diseases.

References

1. SCADDINGJG: Fibrosing alveolitis. *Br J Med* 1964; 2: 686-92.
2. LIEBOW AA: Definition and classification of interstitial pneumonia in human pathology. *Progr Resp Res* 1975; 8: 1-12
3. HUNNINGHAKE GW, GADEK JC, WEINBERG S *et al.*: Characterisation of the inflammatory and immune effector cellss in the lung parenchyma of patients with interstitial lung disease. *Am Rev Resp Dis* 1981; 123: 407-13
4. BAUGHAM RP: The uncertainties of bronchoalveolar lavage. *Eur Resp J* 1997; 10: 1940-2.
5. HEPPLESTON AG: The pathology of honeycomb lung. *Thorax* 1956; 11: 77-84.
6. PIMENTEL JC: Tridimensional photographic reconstruction in a study of the pathogenesis of honeycomb lung. *Thorax* 1967; 22: 444-9.