

EDITORIAL

Transbronchial biopsy as a tool to evaluate small-airways disease in asthma. Pros

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Asthma is an inflammatory disease and although the existence of small airways disease has been described, a few decades ago, in asthma and chronic obstructive pulmonary disease (COPD), the possibility that small airway inflammation/remodelling is involved in the pathophysiology and clinical manifestations of these conditions has recently been re-emphasised [1–3]. Previous observations had shown small airways changes in asthma. Using surgically resected lung specimen of patients with asthma, HAMID *et al.* [1] observed an airway inflammatory process not only in large but also small airways, activated eosinophils being more numerous in peripheral airways. Small-airways disease has also been found in fatal asthma [4]. The inner-wall area of distal airways was found to be increased in patients who died of asthma or other causes; structural changes such as smooth-muscle thickening were observed in peripheral airways. There was an increased interest in exploring small-airways inflammation, with the development of new medications such as hydrofluoroalkanes-propelled beclomethasone (QVARTM, 3M Pharmaceuticals, St-Paul, MN, USA). This drug has an increased peripheral lung deposition that can help reduce peripheral-airway inflammation and induced-lung hyperinflation, but its effects on small airways remain to be explored further [5, 6].

Sophisticated imaging techniques have provided some information about small airways but cannot reveal the nature of the process involved [5]. Bronchoalveolar lavage (BAL) can help to characterise inflammatory events occurring in the peripheral airways [7, 8]. However, these may be different from those of the airway wall and BAL does not provide information on changes in airway structure. Endobronchial biopsies of lobar, segmental and subsegmental bronchi have been used in the last two decades to study the physiopathology of asthma and other diseases; this procedure can be carried out safely and is increasingly standardised [8]. However, it has been more difficult to analyse changes at the level of small airways and apart from looking at surgical specimens from asthmatic patients, which are rare, the possibility of obtaining transbronchial biopsies (TBB) for this purpose could be useful [9–11]. The main goal of such a procedure in the context of studies on asthma

pathophysiology is therefore to evaluate peripheral airways and lung parenchyma. The study by BALZAR *et al.* [11] shows that in addition to alveolar tissue, small airways can be sampled by TBB, allowing for the analysis of inflammation and tissue remodelling at this level in asthma. Small airways had higher cell counts than medium or large airways and the findings in TBB were similar to surgical samples available in three patients.

As indicated in the paper by BALZAR *et al.* [11], a limited number of small airways can be obtained for analysis. Out of 29 transbronchial biopsies, 45% had small airways [11]. However, this seems sufficient to gather the information expected. There may be differences in the density of inflammatory cells in the different parts of the lung, making it difficult to infer what is happening at the whole-lung level with only this number of specimens. The report from BALZAR *et al.* [11] indicated that the ratio of individual inflammatory cell types was similar among lung regions, except for an increase in the percentage of monocytes/macrophages in alveolar tissue. Nevertheless, more data should be obtained on the reproducibility of results before TBB is used in pharmacological or bronchoprovocation studies.

With regards to the ethical issues, such a procedure has the potential for significant side-effects and should be performed by experienced investigators with all the necessary precautions. Among the most feared effects are bleeding or pneumothorax induced by the procedure [12, 13]. Precautions to avoid or treat these potential problems, such as the use of fluoroscopy to direct the forceps, possibility of rapid chest-tube insertion, postprocedure radiograph and avoidance of drugs acting on coagulation, are mandatory. These procedures have however, been performed for a few decades under various conditions, mostly interstitial lung diseases, and a significant experience has been acquired with TBB. In experienced hands this technique has a good safety record [12–14]. As described by BALZAR *et al.* [11], in their hands, this procedure was safe and not associated with significant adverse events, even in severe asthmatics; in a series of ~100 bronchoscopies with TBB, there was a report of only one case of pneumothorax, which was treated conservatively.

To conclude, transbronchial biopsies may help to understand the contribution of peripheral airways to asthma pathophysiology. It also seems reasonable to consider using transbronchial biopsies for research,

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in experienced hands and for selected investigations where the benefits and the expected findings are considered to justify the procedure. Its potential clinical use in selected cases of asthma needs to be documented further. The safety record of transbronchial biopsies in asthma patients is good but should continue to be closely monitored. However, the type of data gathered is important to the understanding of the role of peripheral inflammation in patients with asthma, particularly when severe and refractory to steroid treatment.

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