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Nodular fibrosis of the lung in diabetes mellitus

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Abstract The target organs in diabetes mellitus include the kidneys, the eyes and the small vessels. In these organs some specific histopathological changes have been described but there are few reports of histopathoogical changes in the lung in diabetic patients. Several reports describe abnormal pulmonary function in diabetic patients and consider these abnormalities to be due to histopahtological changes found in the pulmonary vessels. We have studied the histopathological changes in the diabetic lung comparing the findings in the autopsies of 61 diabetic and 50 non-diabetic patients. Statistically significant differences in the incidence of chronic obstructive lung disease and pulmonary haemorrhage exist. There are no differences in the incidence of fibrosis of the alveolar walls or intimal and medial thickening of small vessels, changes associated with diabetes according to the literature. We have found a specific type of nodular fibrosis not previously reported which we believe to be typical of diabetes.

Key words Diabetes mellitus · Pulmonary function · Nudular fibrosis

Introduction

Diabetes mellitus is one of the most frequent metabolic diseases and is associated with lesions in several target organs, mainly the kidneys and the small vessels. The lung has not been classically considered a target organ and therefore little is known about pulmonary changes in the disease. Some authors have reported abnormalities in pulmonary function [4, 7], mainly a reduction in the diffusing capacity, vital capacity, total lung capacity and residual volume, and have considered that these abnormalities might be due to the changes in the pulmonary vessels seen in the autopsies of diabetic patients. Our objective was to study the changes in the lung in diabetic patients and to compare them with those of a sex- and age-matched group of non-diabetic patients.

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Materials and methods

We collected 111 autopsies, 61 diabetic and 50 non-diabetic, and studied the histopathological changes in the lungs. Both groups were homogeneous in terms of age and sex. In each group 55% were men and the median age was 70 years. The autopsies were performed over a 5-year period in our department. We studied formalin-fixed, paraffin-embedded tissue stained with haematoxylin and eosin and, when necessary, Wilder's reticulin, Ziehl Neelsen, Grocott's hexamine-silver, Masson's trichrome and periodic acid-Schiff. We compared the histopathological changes seen in the lungs of these two groups of patients and studied the statistical significance of the differences with the χ^2 test.

Results

The results of our study are summarized in Table 1. We found statistically significant differences between our groups only in the incidence of chronic obstructive lung disease and pulmonary haemorrhage (both more frequent in the non-diabetic group, $P<0.05$). We found no statistically significant differences in the incidence of either intimal and medial thickening of the small pulmonary vessels or fibrosis of the alveolar walls, although these are the changes described in the literature. Nevertheless, when we studied the fibrosis we noticed that diabetic patients showed a fairly specific type that we have called nodular fibrosis (Figs. 1, 2). This nodular deposition of collagen located in the middle of the alveolar walls was present in all the 29 diabetic patients who had fibrosis and we did not find it in any other patients.

On reviewing the literature, we found several reports of a high incidence and severity of pulmonary infections in diabetics [5]. We also noticed a higher incidence of bronchopneumonia in diabetic patients in our cases but the difference was not significant. Boucot and Cooper [3] reported a higher incidence of tuberculosis in diabetic adults, mainly over 65 years [6], but we found no differences between the groups, possibly because of the

Table 1 Histopathological findings in the autopsies of diabetic (group A, n=61) and non-diabetic patients (group B, n=50)

	Group A (diabetics)		Group B (non-diabetics)		
	Total	Percentage	Total	Percentage	χ^2
Acute inflammatory diseases (bronchopneumonia)	26	42.62%	17	34%	0,862 (P>0.3)
Chronic obstructive lung disease	23	37.7%	29	58%	4,545 (P<0.03)
Active tuberculosis	3	4.9%	1	2%	0,095 (P>0.3)
Fungal infections	1	1.63%	0	0%	0,01 (P>0.3)
Arteriosclerosis	21	34.42%	13	26%	0,918 (P>0.3)
Thickening of media and intima of small vessels	32	52.45%	29	58%	0,341 (P>0.3)
Pulmonary thrombo-embolism	8	13.11%	5	10%	0,258 (P>0.3)
Microthrombosis	11	18.03%	12	24%	0,596 (P>0.3)
Pulmonary haemorrhages	4	6.55%	13	26%	8,009 (P=0.005)
Fibrosis of the alveolar walls	27	44.26%	17	34%	1,209 (P=0.283)
Pleural thickening	22	36.06%	16	32%	0,202 (P=0.317)

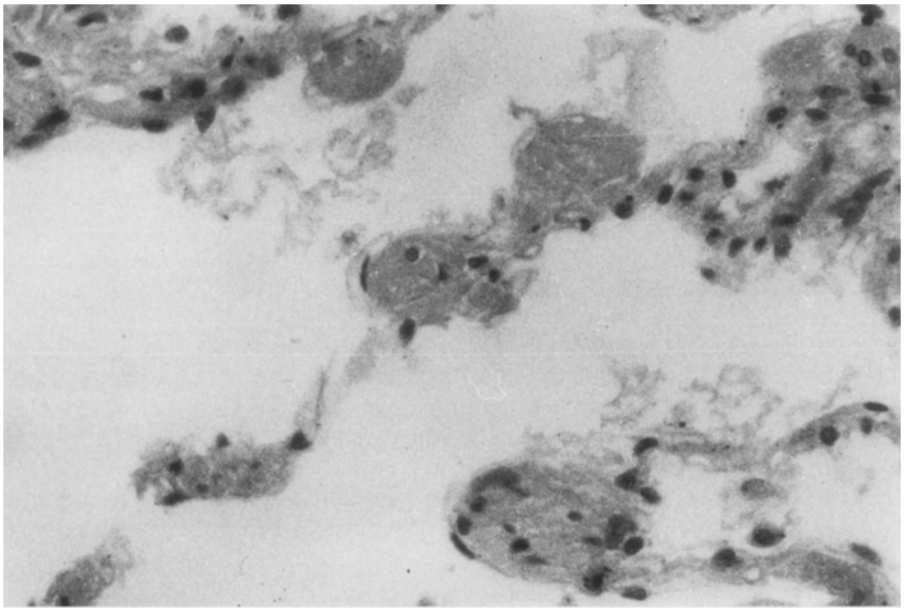

Fig. 1 Nodular fibrosis in the alveolar walls of a diabetic [Haematoxylin and eosin (H&E), ×200]

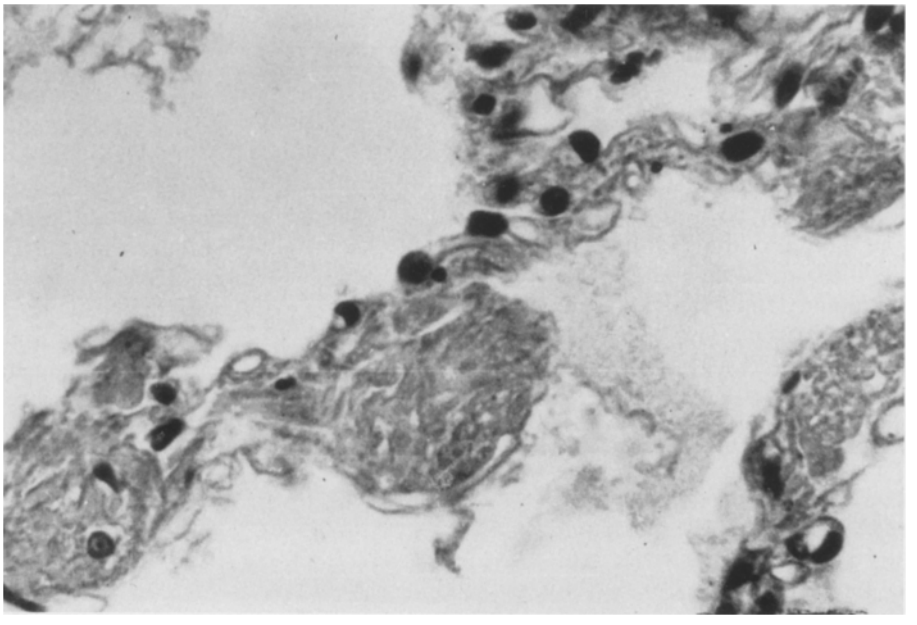

Fig. 2 High power view of the fibrotic nodule in the alveolar wall (H&E, ×450)

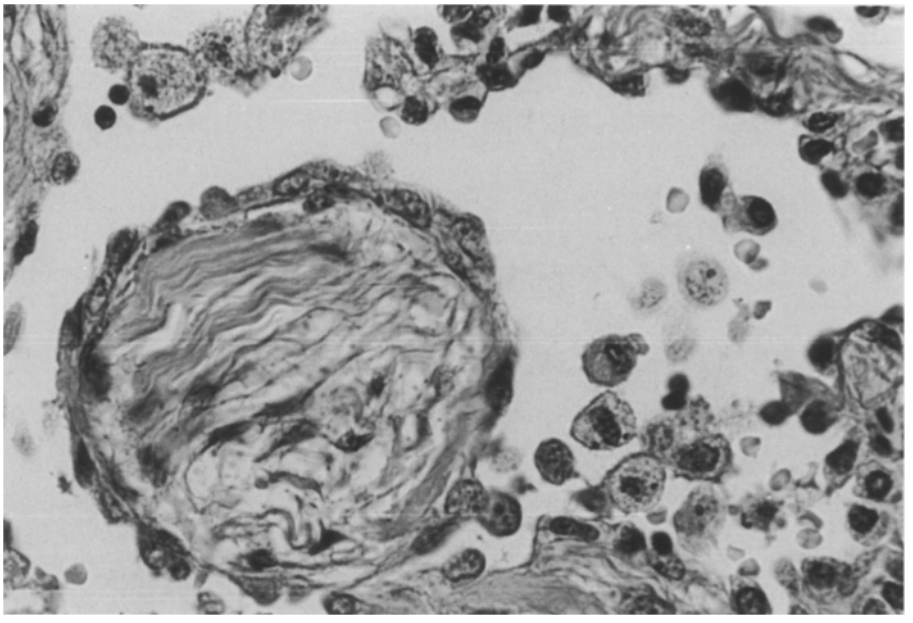

Fig. 3 Masson's body in bronchiolitis obliterans organizing pneumonia (H&E, ×450)

high incidence of tuberculosis in our country, mainly in the elderly. Most authors agree that diabetes and other chronic immunosuppressive diseases are predisposing factors for fungal infections, mainly aspergillosis [11]. We encountered only one case of aspergillosis in a diabetic patient with acute lymphoblastic leukaemia.

Systemic arteriosclerosis is more frequent and severe in diabetes and Bierman [2] reported an increased incidence of pulmonary arteriosclerosis in diabetics under 40 years (75% vs 5% in non-diabetics). Some experimental models with streptozotocin-induced diabetes [10] confirmed this increased incidence of pulmonary arteriosclerosis. In our groups, the incidence was slightly higher in the diabetic group but the difference was not statistically significant.

In our groups we have seen no cases of the pulmonary perivascular xanthogranulomatosis described by Bennington [1] and Reinila [9] in diabetics.

Discussion

The commonest histopathological change described in the diabetic lung is thickening of the media and the intima of small vessels [4, 7] which may explain the abnormalities in pulmonary function observed in these patients. Like Schnaff et al. [8] we have seen an increased amount of collagen in the alveolar walls, in the main airways and in the walls of the great vessels. This fact seems to be due a non-enzymatic glycosylation-induced alteration of lung connective tissue, which could explain the abnormalities in lung function described in these patients.

In diabetics we have found a special type of fibrosis, a nodular deposition of collagen in the interstitium of the alveolar walls, which was not found in any of the autopsies of non-diabetic patients. This lesion is easily distinguished from the Masson's bodies found in bronchiolitis obliterans (Fig. 3) and from the diffuse thickening of the alveolar walls present in several other lung diseases. We think that this nodular interstitial fibrosis can be considered specific for the diabetic lung, as we have seen it in no other patients. It may result from abnormalities in the turn-over of collagen. The microangiopathy and the fibrosis, including the specific nodular fibrosis we describe in this report, can account for the abnormalities in pulmonary function described by several authors and imply that the lung is another important target organ in diabetes.

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