ALVEOLITIS IN OCCUPATIONAL LUNG DISEASES (OLD)

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INTRODUCTION

The prevalence of inhalatory pulmonary diseases, caused by many occupational and environmental exposures to organic and inorganic substances, remains a problem that may be underestimated because, in many instances, the disease has an insidious character and the host lung response protect and smoulder the clinical picture.

Although many primary industries, such as granite sheds and asbestos mines, improved control measures, the exposure remains in secondary and tertiary manufacturing trades, which use those products.

The correct diagnosis can be missed and to avoid it the physician must use all his sense of purpose and curiosity in the study of the suspect OLD patient. It is also expected that a better knowledge of the OLD mechanisms constitute the foundation for the understanding and diagnosis of these diseases.

The bronchoalveolar lavage (BAL) seems to fulfil this goal as it is now well known that the study of BAL fluid closely mimics the events happening in the interstitial space.[4,8,9,12]

Confirming this in Extrinsic Allergic Alveolitis, it is generally accepted that the study of BALF discloses an alveolitis although it is not completely established if and how there is a correlation between the gravity of disease and the intensity of the alveolitis found. However it is considered that the increased number of effector cells found in BALF of these patients, is the local expression of the basic immunologic mechanisms of the disease, evolving to the formation of granulomas and, lately, contributing to fibrosis.[4,11,16]

Regarding the interstitial lung diseases caused by inorganic dusts, only recently has the occurrence of an alveolitis been accepted,[2,3,4,13,14] and Begin et al., even found that the alveolitis in subsets of silica exposed workers, with distinct clinical stages of disease, was found to have distinct biological characteristics.[2]

In this study we tried to evaluate the existence or not, and the type of alveolitis found in a group of 48 patients with occupational lung disease confirmed by the usual criteria. We also compared the patients with occupational history of exposition to organic dust (Group I) with the patients exposed in work environment to mineral dust (Group II). Finally we tried to correlate the findings with clinical manifestations and evolution.

MATERIAL AND METHODS

Patients

We studied 48 patients, being 28 males and 20 females. The average age was 42 ± 13 years old, ranging from 73 to 28 years old.

Twenty-four patients had smoking habits. None of the patients had history of other concomitant pulmonary disease.

All patients were referred to the Outpatient Clinic of Occupational Diseases because of respiratory complaints and 10 (21%) had also systemic complaints—fever, weight loss and asthenia.

Thirty of the patients were exposed to mineral dusts (63%): silica (8 patients), iron (7 patients), cement (1 patient), asbestos (1 patient) and the other 13 patients to various other mineral dusts.

Eighteen patients were exposed to organic dusts (37%), mainly pigeon dregs (10 pt), wood (4 pt), cork (2 pt), wool (1 pt) and flour (1 pt).

All patients were submitted to a standard posteroanterior and lateral X-ray, read by 3 observers, according to ILO classification (10) and to a functional respiratory study by body plethysmography.

In all patients broncbofibreoscopy was performed followed by bronchoalveolar lavage, being the effluent fluid recovered.

Fourteen patients, during diagnosis procedures, were submitted to a transbronchial lung biopsy.

After the diagnostic assessment in all patients with an alveolitis disclosed by BAL a treatment with corticosteroids was prescribed (Prednisone—1 mg/Kg of body weight).

Methods

Bronchoalveolar Lavage:

Briefly the BAL was performed with 200 ml saline serum, warmed up to 37°C, instillated by syringe in 4 alliquots of 50 cc, through a wedge broncbofibreoscopy in a subsegment of the medium lobe followed a few seconds after by recovery of the lavage effluent proceeded by gentle syringe suction.

After remotion of mucus, cells were counted in a hemocytometer and cytocentriphuge smears were prepared and stained by May—Grunwald-Giemsa method for identification of the cellular populations.

The cellular pellet was obtained by centrifugation—500 G at 4°C during 20 minutes—washed three times with PBS balanced solution and resuspended in PBS solution at the final concentration of 5×10^6 cells/ml.

T-Lymphocytes

The T-lymphocytes and its subpopulations were characterized by indirect immunofluorescence after banding to specific monoclonal antibodies (Ortho—OKT_3, OKT_4 and OKT_8) following procedures previously described.[7,14]

Statistical Analysis

The results are expressed as the mean ± SD. The data were tested by the Student's test for differences between groups—and by Chi-Square test when appropriate.[1]

RESULTS

The cellular analysis of BALF stated increased number of cells with a significative difference in Group I, as compared to controls (Table I), 67% of Group I and 40% of Group II patients fulfilled the criteria for an alveolus defined by a number of cells per ml of BALF superior to that of controls average + SD.

The alveolitis in both groups is mainly due to a significative increase of lymphocytes: 35.7 ± 21.6% (Group I) and 28.0 ± 15.0 (Group II). There was also a slight but not significative increase in the PMN cells. The percentage decrease on macrophages is not accompanied by a diminishing of the absolute number of these cells; on the contrary a slight increase was found.

The observation of cytocentrifuge smears frequently proved foamy macrophage, the existence of Spontaneous Rosetts Macrophage-Lymphocyte and a number of giant cells above 3% on average.

Regarding the T-lymphocytary populations we found an increase in the number of T cells in both groups being significative in Group I. The analysis of the T-lymphocyte subsets proved a predominance of the T supressor cells in the groups of patients leading to an inversion of T helper/T supressor ratio. So in 16 pt (88%) of the Group I and in 26 patients (86%) of the Group II the T_h/T_s ratio was below 1 (Table II).

The incidence of a lymphocytary alveolitis was significantly higher in patients of Group I than in those of Group II: 67% and 40% respectively—$p<0.02$—(Table III).

In the patients with systemic symptoms the BAL disclose an alveolitis in 60% of them and a normal pattern in others 40%—$p<0.02$—(Table IV).

Among the 14 patients in which lung biopsy was performed alveolitis was found in the BAL of 9 patients. From these 9 patients 8 (88%/) showed granulomas or lymphoplasmocytary infiltration of the alveolar septa (Table V). From the 5 patients without alveolitis in BAL only one presented granulomas in the lung biopsy (20%). The difference between the two groups is significative for a $p<0.02$.

Besides aggressive dust evication of all patients we submitted the 24 patients with alveolitis to corticotherapy (Prednisone 1mg/Kg of body weight). Only 53% of this group of patients improved clinically and functionally, compared

Table I
Differential Cell Count—Bronchoalveolar Lavage

	GROUP I	GROUP II	CONTROLS
nº cells/ml	$46.6 \pm 39.5 \times 10^4$ *	$36.3 \pm 36.0 \times 10^4$	$17.4 \pm 4.3 \times 10^4$
Macrophages	*** 56.1±21.8 %	*** 67.0±18.4 %	90.8±2.2
Lymphocytes	** 35.7±21.6 %	*** 28.0±15.0 %	8.0±1.6
P M N	5.4±6.4	3.2±5.9	1.1±0.9

* S $p<0.05$ ** S $p<0.01$ *** S $p<0.001$

Table II
Lymphocytary Subpopulations—Bronchoalveolar Lavage

	GROUP I	GROUP II	CONTROLS
T_3	83.9±6.5 % ***	75.2±11.3 N.S.	70.1±3.3
T_4	32.7±12.4 *	28.2±6.3 ***	42.0±2.1
T_8	50.8±13.7 ***	43.4±10.8 ***	26.5±1.9
T_4/T_8	0.7±0.3	0.8±0.7	1.4±0.3

S * $p < 0.05$ S *** $p < 0.001$

Table III
Patients with Lymphocitary Alveolitis

	GROUP I	GROUP II
Lymphocitary Alveolitis	12 pts (67%)	12 pt (40%)
	→ p < 0,01 ←	
T_4 / T_8 Inversion	26 pts (86%)	16 pt (88%)
	N.S.	

Table IV
Clinic and Alveolitis

	SYSTEMIC SYMPTOMS	
Alveolitis	60%	↓
Without Alveolitis	40%	p < 0,02 ↑

Table V
Lung Biopsy and Alveolitis

	Granuloma or Lymphoplasmocitary Infiltration	Other Pathological Findings	TOTAL
Alveolitis	8 pt (88%)	1 pt (11%)	9
Normal BALF	1 pt (20%)	4 pt (80%)	5

$\chi^2 = 6.57$ S ** $p < 0.02$

Table VI
Treatment and Alveolitis

	ALVEOLITIS	NORMAL BALF	TOTAL
Clinical Improvement	13 pt (53%)	20 pt (83%)	33
No response or worsening	11 pt (46%)	4 pt (17%)	15
TOTAL	24	24	48

$\chi^2 = 4,76$ S ** $p < 0.05$

to 83% of the patients without alveolitis in BAL—$p<0.02$—(Table VI).

DISCUSSION

Being an heterogeneous population it is difficult, in a certain way, to take conclusions from the results. Anyway it becomes evident that an important number of OLD patients presents an alveolitis which has the same characteristics: it is an lymphocytary alveolitis. This suggests that at least some of the pathogenic pathways are similar in spite of the nature of the inhaled noxious dust. Besides, a great number of patients show an inversion of the T helper/T supressor ratio, that could indirectly demonstrate an activation of the immunologic local mechanisms of defense in almost all the studied patients.

It is easy to accept the immunologic via to the patients exposed to organic dust, but more difficult for those exposed to inorganic materials. Taking into consideration the findings that the number of macrophages is also increased besides the above referred morphologic modifications (foamy cells, rosetts lymphocytes—macrophage and numerous giant cells), we could think that the alveolar macrophages are activated. This activation can be provoked either by immunologic and no immunologic stimulation and leads to the realization of mediators like IL_1 able to activate the T-lymphocyte.[5,6]

Once again we found a good correlation between the histological data and the study of BALF proving the interest of this technique in the study of the interstitial lung diseases.[9,12,15]

The fact that only 53% of the patients that presented an alveolitis in BALF improved, in despite of being under corticotherapy, is in striking contrast with the improving of 83% of the patients without alveolitis in which the only therapeutic measure was the withdrawal of the causing dust. So the BALF study has some predictive value and the existence of an alveolitis signifies, in our opinion, not only an involvement of the lung interstitium but also expresses the existence of amplification and perpetuation mechanisms centered in the activated alveolar macrophage and T-Lymphocyte.[5,6]

In this study we found a marked increase in the T supressor cells. This is also reported by others and is common to almost all occupational lung diseases with some exceptions such as the case of berylliosis and asbestosis.[3,4,11,14] This fact can contribute to the differential diagnosis and real meaning of this immunologic abnormality is not well established; perhaps

it signifies one attempt to brake the local immunologic processes.

In conclusion, we think that BAL is a good method to the study and comprehension of the occupational lung diseases. It contributes to the stagging and understanding of the pathogenic mechanisms.

The study of the cellularity is, although insufficient, being crucial, the study of the lymphocytary populations and the quantification of various chemical mediators released by the different cells involved in the pathogenesis of these diseases.

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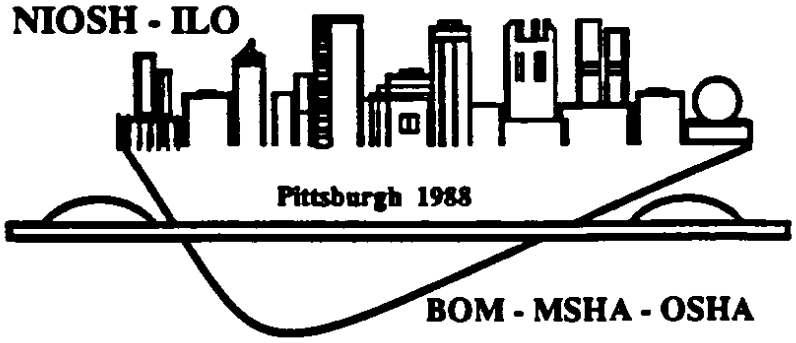

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