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Bronchoalveolar Lavage in Children With Chronic Diffuse Parenchymal Lung Disease

Roberto Ronchetti, MD,[1]* Fabio Midulla, MD,[1] Thomas Sandstrom, MD,[2] Lief Bjermer, MD,[3] Jerzy Zebrak,[4] Jacek Pawlik, MD,[4] Maria Pia Villa,[1] and Alberto Villani, MD[1]

Summary. The aim of the present study was to compare cellular and noncellular components of bronchoalveolar lavage fluid (BAL) in a group of children with a diagnosis of chronic diffuse parenchymal lung disease (cDPLD) and a group of children without parenchymal lung disease undergoing BAL for various clinical indications (control group). We evaluated cellular and noncellular components (total proteins, albumin, hyaluronic acid, and fibronectin) in BAL fluid from 14 children (7 boys and 7 girls; mean age 9.2 years, range 5 months to 18.4 years) fulfilling the clinical and radiological diagnosis of chronic cDPLD, and in 19 controls without evidence of lung disease. The 14 patients were assigned to two study groups: *early-stage* cDPLD (6 patients; age range 5 months to 5.2 years; duration of illness, 5–7 months) and *long-standing* cDPLD (8 patients; age range 9.6–18.4 years; duration of illness, 1.2–17.6 years).

Ninety-three percent of the patients with cDPLD had at least two BAL constituents outside normal limits, with high numbers of cells, including all types of alveolar cells, but especially lymphocytes and foamy macrophages. These findings indicate a mixed, predominantly lymphocytic alveolitis. Our patients also had a significant increase in two noncellular BAL components, namely fibronectin and hyaluronic acid. BAL samples from children with *long-standing* cDPLD contained increased numbers of lymphocytes, whereas samples from children with *early-stage* cDPLD contained increased percentages and numbers of foamy macrophages and increased concentrations of fibronectin, hyaluronic acid, and albumin.

In conclusion, we clearly identified an abnormal BAL profile in our group of cDPLD patients. Moreover, BAL findings differentiated younger cDPLD patients in the *early stages* of their illness from old patients with *long-standing* disease. **Pediatr Pulmonol. 1999;27:395–402.**

Key words: bronchoalveolar lavage; cytology; cytokines; children; interstitial lung disease.

INTRODUCTION

Several recent reports have described children who present with chronic respiratory disorders characterized by respiratory symptoms lasting at least 6 months, ranging in severity, and having dry velcro crackles, abnormal arterial oxygen tension on exertion or at rest, dyspnea, and bilateral diffuse interstitial infiltrates on chest radiographs.[1–4] In this paper we have classified these conditions under the term "chronic diffuse parenchymal lung disease" (cDPLD). The above-mentioned signs and symptoms will usually suffice to suggest a provisional diagnosis, yet, despite being easily obtainable, they lack sensitivity and are not necessarily diagnostic or predictive of the future course of the disease. In children with progressive or severe clinical symptoms, the procedure of choice to obtain a more specific diagnosis is an open lung biopsy.[5] However, this is an invasive procedure that is not easily repeatable. Diagnostic measures to guide initial therapy and clinical follow-up are needed in cDPLD children, in whom little is known about the natural history of the disease, and the procedures with prognostic value remain largely undefined. The diagnostic usefulness of open lung biopsy in cDPLD remains incompletely evaluated.[6–8] While BAL is the main diagnostic procedure for defining the infective etiology in immunocompromised patients and in pulmonary he-

[1]Second Department of Pediatrics, University of Rome "La Sapienza," Rome, Italy.

[2]Department of Lung Medicine, University Hospital of Umeå, Umeå, Sweden.

[3]Department of Lung Medicine, University Hospital of Trondheim, Trondheim, Norway.

[4]Pediatric Faculty, National Institute of Tuberculosis and Lung Disease, Rabka, Poland.

*Correspondence to: Professor Roberto Ronchetti, II Cattedra di Clinica Pediatrica Universita' di Roma "La Sapienza," Viale Regina Elena 324, 00161 Rome, Italy.

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TABLE 1—Clinical Features in Children With Chronic Diffuse Parenchymal Lung Disease

	Gender	Age (years/months)	Duration of disease (years/months)	Signs and symptoms	X-ray findings[1]	Associated conditions
Early-stage cDPLD						
1	F	0/5	0/5	hypoxemia	GG	Alveolar proteinosis
2	M	1/1	0/6	hypoxemia	GG	Postnatal CMV and chlamydia trachomatis infection
3	M	1/2	0/7	hypoxemia	GG	Perinatal CMV infection
4	M	2/6	0/6	hypoxemia	RN	Bronchiolitis obliterans organizing pneumonia; Epstein-Barr virus antibodies
5	F	4/8	1/2	hypoxemia	L	Systemic lupus erythematosus
6	M	5/2	0/6	crackles	RN	Follicular bronchiolitis and food allergy
Long-standing cDPLD						
7	F	9/6	7/2	crackles	RN	
8	F	11/0	2/0	crackles	RN	
9	F	11/8	3/0	crackles	RN	
10	M	15/1	6/0	crackles	N	Extrinsic allergic alveolitis
11	F	15/3	9/0	clubbing	L	Extrinsic allergic alveolitis
12	M	15/8	6/0	clubbing	L	
13	M	17/6	17/6	clubbing	RN	
14	F	18/4	9/0	clubbing	RN	
Mean ± SD		9.2 ± 6.6	4.6 ± 5.0			

[1]L, linear; N, nodular; RN, reticulo-nodular; GG, ground-glass.

mosiderosis,[9,10] a recent study concluded that BAL had a relatively low diagnostic yield in children with cDPLD.[11] The description of the cellular and noncellular BAL profile in these diseases could help the clinician in the initial approach to these patients and in their follow-up.

In this study we compared the cellular and noncellular components of BAL fluid recovered from children with a clinical, functional, and radiologic diagnosis of cDPLD and from a group of control children. We also assessed whether BAL differed between young cDPLD patients, usually in the *early stages* of their illness, and older patients with more *long-standing* disease.

MATERIALS AND METHODS

We studied 14 children (7 boys and 7 girls; mean age 9.2 years, median age 12.3 years; range 5 months to 18.4 years) fulfilling the clinical and radiological definition of cDPLD,[12] and a group of 19 control children, all of whom were undergoing a diagnostic workup for other conditions, but also had a fiber-optic bronchoscopy and BAL (Table 1).

Abbreviations

BAL	Bronchoalveolar lavage
BOOP	Bronchiolitis obliterans organizing pneumonia
cDPLD	Chronic diffuse parenchymal lung disease
CMV	Cytomegalovirus
ILD	Interstitial lung disease

Patients

Children in the cDPLD group were consecutive children observed in the Second Pediatric Department, University of Rome "La Sapienza," Rome, Italy between June 1, 1992 and June 1, 1993, and in the National Institute of Tuberculosis and Lung Disease-Pediatric Faculty, Rabka, Poland between June 1, 1992 and September 1, 1992 for clinical evaluation; they fulfilled clinical and radiological diagnostic criteria for cDPLD. cDPLD was defined as chronic respiratory symptoms and diffuse bilateral pulmonary infiltrates on chest X-ray.[13,14] Chronic respiratory symptoms were defined as symptoms lasting for at least 6 months or from neonatal age on and ranging in severity and having from diffuse bilateral crackles with cough, dyspnea and hypoxemia.[1] Two independent radiologists assessed diffuse bilateral pulmonary infiltrates in postero-anterior and lateral chest roentgenograms according to McLoud et al.[15] Accordingly, 7 patients had a reticulonodular pattern, 3 had a linear pattern, and 3 had a ground-glass appearance; only one child had an obvious nodular pattern (Table 1). All children underwent BAL on entry. No patient had obvious immunological deficiencies, an abnormal birth history, bronchopulmonary dysplasia, or cystic fibrosis. During the early months of their illness, all of them had received several courses of corticosteroid treatment for an uncertain duration. One patient with alveolar proteinosis (seen at age 5 months) died at 8 months despite repeated alveolar lavages. A second patient (age 5.2 years on entry) with cDPLD and severe food allergy had a thoracoscopic-guided lung biopsy which demonstrated the presence of

follicular bronchiolitis.[16] In a third patient (initially aged 2.6 years), in whom Epstein-Barr virus blood antibodies were demonstrated, thoracoscopic lung biopsy revealed a histological pattern of bronchiolitis obliterans organizing pneumonia (BOOP). One child, aged 13 months on entry, had cytomegalovirus (CMV) in BAL fluids and high IgM and IgG serum antibodies for CMV. Chlamydia trachomatis was isolated from nasal and conjunctival swabs. A diagnosis of postneonatal CMV and chlamydia infection was made, and foscarnet and erythromycin treatment was instituted. The child regained normoxemia and normal lung function in 5 months. Another child, aged 14 months on entry, also had CMV in BAL fluid and persistently high IgG antibodies in serum. Gancyclovir treatment stabilized his clinical condition within 2 months despite hypoxemia, which persisted for 2 years after hospital discharge. The diagnosis was perinatal CMV infection. Neither child with CMV infection underwent lung biopsy. In 2 additional patients (aged 6 and 9 years) a diagnosis of extrinsic allergic alveolitis had been made several years before the study. In another child (aged 4.8 years) a diagnosis of systemic lupus erythematosus was made according to clinical and immunoserological findings. The remaining 6 patients had cDPLD of unknown cause. Except for the child with alveolar proteinosis, who could not be studied, all patients underwent lung function tests. The 3 patients under 3 years of age had a time constant on expiration following Hering-Breuer reflex-induced apnea of less than 63% of predicted, supporting a restrictive pattern of lung pathophysiology. Lung function tests in the 10 other children revealed markedly reduced functional residual capacities (in 6 cases, less than 70% of predicted value) or reduced diffusion capacity ($D_{L,CO}$) (in 5 cases, less than 85% of predicted value); thus, these 10 patients had at least one of the two functional abnormalities. Clinical examination showed that all patients had one or more of the following symptoms: dyspnea on effort or at rest, clubbing, dry cough or bilateral dry crackles (Table 1). At the time of the BAL procedure only one patient was receiving prednisone, begun because of relapsing respiratory symptoms.

For further analysis, patients were assigned to two groups. The first group (*early-stage* cDPLD) consisted of 6 young patients with a recent onset of illness (less than 12 months duration; age range, 5 months to 5.2 years; median age, 1.8 years; duration of illness, 5 months to 14 months). The second group (*long-standing* cDPLD) consisted of 8 older patients with chronic illness (more than 12 months duration; age range, 9.6–18.4 years; median age, 9 years; duration of illness, 2.0–17.6 years). Five of the 6 patients in the *early-stage* group, but none in those in the *long-standing* group, were hypoxemic in room air when first seen (Table 1).

Control Group

The control group consisted of 19 children who were admitted to the Pediatric Department of Rome (13 boys and 6 girls; mean age, 3.1 ± 1.1 years; median age, 1.4 years; range, 2 months to 14.4 years) and who underwent fiberoptic bronchoscopy for various clinical indications, i.e., persistent stridor, 10 cases; to ensure complete recovery 2 months after removal of a foreign body, 4 cases; to evaluate chronic cough unresponsive to medications, 3 cases; to monitor the progression of left lobar emphysema associated with mild stenosis of the lingular bronchus 2 years after initial diagnosis, 1 case; and to monitor stenosis of the left main stem bronchus 1 year after initial diagnosis, 1 case. These children were defined as not having parenchymal lung disease according to the following criteria: normal bronchial mucosa on inspection, sterile BAL culture, and normal sedimentation rate and white blood cell count. The results of the BAL fluid analysis in this control group have been published elsewhere.[17]

Bronchoalveolar Lavage and Lavage Fluid Analysis

Identical procedures were used for fiberoptic bronchoscopy and BAL in Italy and in Poland.[17] The procedure had the approval of the Institutional Review Boards of both institutions, and informed parental consent was obtained. Before fiberoptic bronchoscopy, subjects received topical lidocaine anesthesia of the upper airways and sedation with meperidine 1–2 mg/kg iv. A Pentax FB10H fiberoptic bronchoscope (external diameter 3.5 mm) was used in children younger than 6 years, and a Pentax FB15H bronchoscope (external diameter 4.9 mm) was used in children older than 6 years. During fiberoptic bronchoscopy, children were breathing spontaneously, and supplemental oxygen was administered through a nasal catheter. Children were monitored during the procedure for heart rate and oxygen saturation (Ohmeda pulse oxymeter). BAL fluids were obtained from the right middle lobe or lingula. Two 10 mL aliquots (in children under 6 years) or two 20 mL aliquots (in children over 6 years) of prewarmed sterile saline were instilled via the suction channel into each lobe. Each aliquot was immediately suctioned back into the same syringe and subsequently stored in ice. The first aliquot was used for viral and microbiological studies, the second aliquot for cellular and noncellular analysis. Differential cell counts were determined by two independent observers on May-Grünwald-Giemsa-stained cytospin preparations (10^5 cells/0.5 mL, 90 g, Shadon-Elliot) on at least 200 cells, obtained from uncentrifuged BAL fluid.[19] The percentage of "foamy" macrophages was also determined (Fig. 1). The same investigators (F.M. and A.V.)

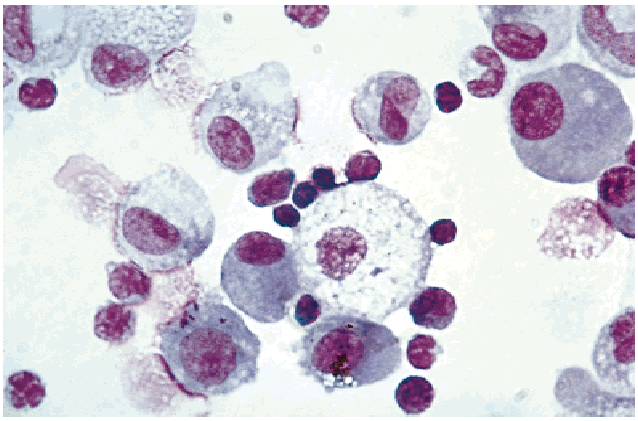

Fig. 1. BAL cytology in a patient with early-stage cDPLD, showing a "foamy" macrophage (original magnification, ×1250).

conducted all the cellular studies and used identical criteria. BAL fluids were stored at −70°C and analyzed for noncellular components. The total amount of protein in BAL was determined using the Bio-Rad protein assay (BioRad Laboratories, Munich, Germany), based on the principle of protein binding to Comassi brilliant blue.[18] The intra-assay coefficient of variation was 2.7%, the inter-assay coefficient was 4%, and the detection limit was 12 mg/L. Albumin was measured with the nephelometric method (Beckman assay protein system, Beckman Instruments Inc., Brea, CA). The total intra-assay and inter-assay coefficients of variation were below 3.3% and the detection limit was 6 mg/L. Fibronectin was measured with a double-sandwich enzyme-linked immunosorbent assay (ELISA) as described previously.[19] The intra-assay and inter-assay variation was <7%, and the detection limit was 10 μg/L. Hyaluronic acid was measured in duplicate samples by means of a radioimmunoassay (Pharmacia Diagnostic, Uppsala, Sweden), as previously described.[20] The detection limit was 1 μg/L. Variability of the measurements was <10%.

Statistical Analysis

Data are reported as means and standard errors of the mean. Differences between groups were determined with the Mann-Whitney U-test for two independent samples. A *P*-value less than or equal to 0.05 was considered statistically significant.

RESULTS

Chronic Diffuse Parenchymal Lung Disease (Patients vs. Controls)

Thirteen (93%) of the 14 patients studied had at least two BAL constituents outside of the normal limits (Fig. 2). A significantly higher percentage of the BAL fluid instilled ($p = 0.0001$) was recovered in cDPLD patients than in the controls (Table 2). Children with cDPLD had significantly higher BAL cellularity than controls ($p = 0.0002$), macrophages being the predominant cell type. In 9 patients, but in none of the controls, at least some of the alveolar macrophages had a "foamy appearance" (Fig. 1). The percentage of foamy alveolar macrophages ranged from more than 90% (in the patient with alveolar proteinosis) to about 5% (in the patient with biopsy-proven follicular bronchiolitis). In 6 patients younger than 5 years, some macrophages had a foamy appearance, whereas in all 4 patients younger than 3 years, more than 15% of the macrophages had a foamy appearance. BAL fluid also contained foamy macrophages in 3 of the remaining 8 patients older than 5 years: one was the only patient who underwent BAL while receiving corticosteroid treatment during relapse of severe respiratory symptoms (breathlessness); the second patient was the only one older than 5 years who had increased amounts of hyaluronic acid; the third patient was the only one in our study who had a nodular chest X-ray.

Differential cell counts showed that 11 of the 14 patients had increased fractions of lymphocytes (20–74%), and 9 patients had increased numbers (range, 566,000–953,000 per mL^3; Table 2). The mean percentage of neutrophils was within normal limits, but 8 patients had high neutrophil counts. Similarly, 8 patients had high eosinophil counts, but most patients (11/14) had normal percentages.

BAL samples from 7 patients contained abnormally high amounts of total proteins. Fluid from 7 patients had high amounts of fibronectin and high hyaluronic acid in 5 patients.

Early-Stage cDPLD vs. Long-Standing cDPLD Patients

The mean values of several of the BAL variables measured differed significantly in the two subgroups of patients (Fig. 2). In particular, patients with *early-stage* cDPLD had significantly higher concentrations of fibronectin and hyaluronic acid than patients with *long-standing* disease. Albumin also differed in the two groups, being elevated in 4 of the 6 patients with *early-stage* cDPLD and in none of the 7 patients with *long-standing* cDPLD. Patients with *early-stage* cDPLD had higher percentages and counts of foamy macrophages, but lower percentages and counts of lymphocytes than patients with *long-standing* disease. The 4 patients who were younger than 3 years were hypoxic in room air when they underwent BAL; all had >15% foamy macrophages (Fig. 1) and markedly elevated amounts of fibronectin in BAL samples. Three of these patients, had ground-glass appearance on X-ray, and elevated hyaluronic acid.

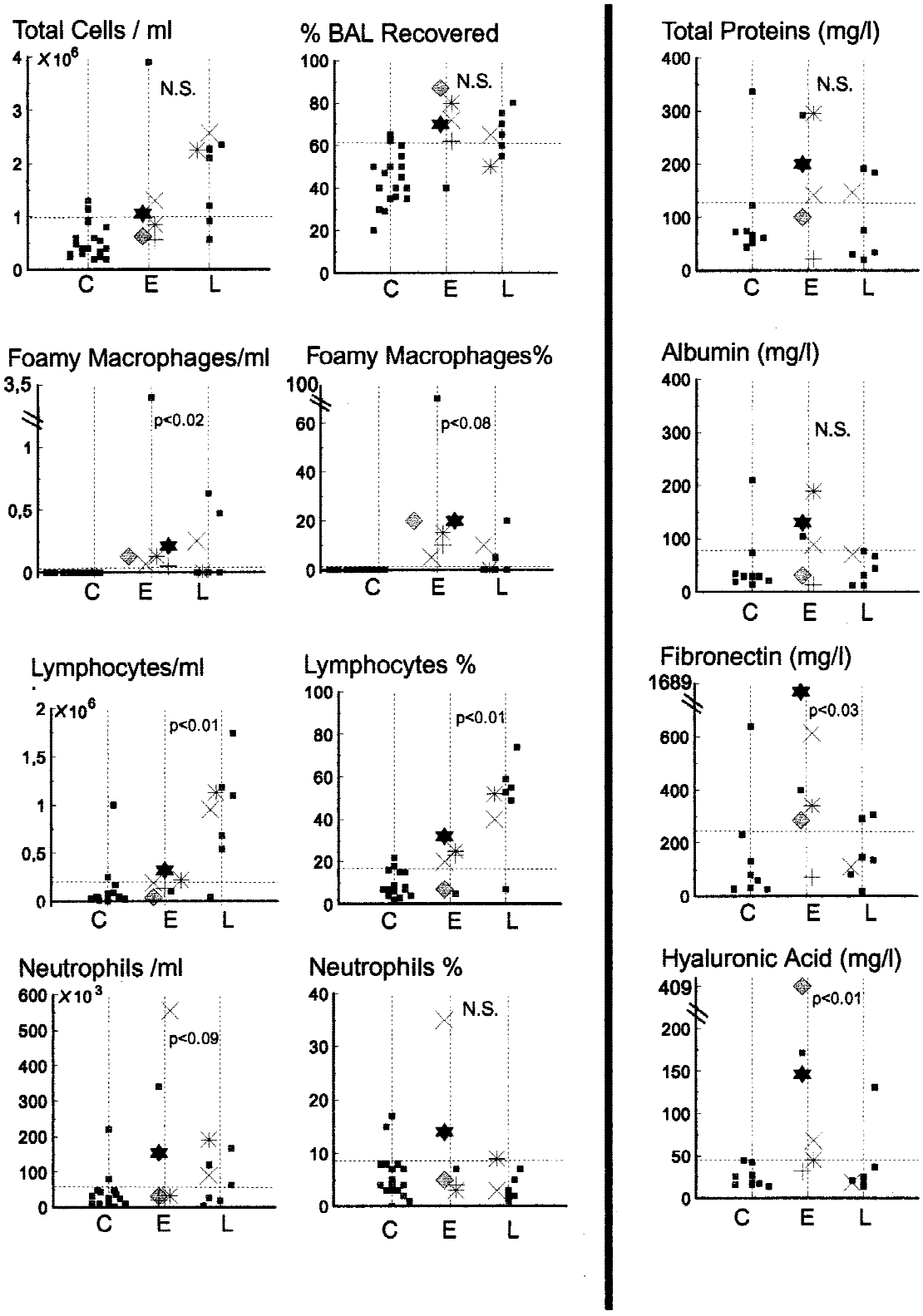

Fig. 2. BAL cell differentials and noncellular constituents in control and cDPLD children; 90% of the observations in the control group come below the dashed line. C, control children; E, *early-stage* cDPLD (▪, alveolar proteinosis; ✻, perinatal CMV infection and Chlamydia trachomatis infection; ◆, postneonatal CMV infection; ★, bronchiolitis obliterans organizing pneumonia; ×, follicular bronchiolitis and food allergy; ┼, systemic lupus erythematosus); L, *long-standing* cDPLD (✳, ×, extrinsic allergic alveolitis; ▪, unknown etiology). Statistical significance between E and L subgroups is indicated.

TABLE 2—BAL Findings in Controls and in Children With Chronic Diffuse Parenchymal Lung Disease

	Controls (n = 19)	cDPLD (n = 14)	*P*
% BAL recovery	44.2 ± 2.7	66.5 ± 3.4	0.0001
Cells/mL ($\times 10^3$)	540 ± 700	1615 ± 262	0.0002
Differential cell counts			
Macrophages			
%	86.4 ± 1.7	56.1 ± 5.9	0.0003
$\times 10^3$/mL	460 ± 200	892 ± 212	0.009
Cases with >5% of foamy macrophages	0/19	9/14	
Foamy macrophages			
%	0	13.9 ± 6.2	0.0001
$\times 10^3$/mL)	0	349 ± 246	0.0001
Lymphocytes			
%	8.8 ± 1.3	35.8 ± 5.9	0.0004
$\times 10^3$/mL	50 ± 10	596 ± 143	0.0001
Neutrophils			
%	5.1 ± 1.0	7.1 ± 2.3	0.6
$\times 10^3$/mL	30 ± 10	130 ± 41	0.007
Eosinophils			
%	0.2 ± 0.1	0.9 ± 0.2	0.0008
$\times 10^3$/mL	0.7 ± 0.2	11.6 ± 3.9	0.0001
Noncellular constituents	n = 9	n = 13	
Total proteins (mg/L)	98.8 ± 30	133.3 ± 27	0.4
Albumin (mg/L)	51.1 ± 21	66.9 ± 14.4	0.3
Fibronectin (μg/L)	139 ± 67	345.9 ± 121	0.02
Hyaluronic acid (μg/L)	24.7 ± 4	87 ± 31	0.03

DISCUSSION

In this report we compared cellular and noncellular BAL components of children without parenchymal lung disease undergoing fiber-optic bronchoscopy with children who fulfilled the clinical and radiological criteria for a diagnosis of cDPLD. Our findings show the presence of BAL abnormalities in pediatric patients with *early-stage* and *long-lasting* cDPLD; 13 (93%) of the 14 patients had at least two BAL constituents outside normal limits. Hence the examination of BAL fluid in children with chronic respiratory symptoms and bilateral infiltrates seems a procedure capable of providing information regarding the abnormal, self-perpetuating pathophysiologic processes existing in the lung parenchyma of these patients. It is also a relatively simple method for monitoring the clinical course of disease and the response to therapy. These BAL abnormalities are certainly not specific for cDPLD patients, who do not represent a recognized disease entity. Yet, BAL analysis repeated over time probably contributes as much to these patient's management as do X-ray images or lung function tests.

Our is a pilot study, designed to delineate BAL abnormalities in patients with a rare pathological condition associated with a heterogeneous group of diseases with different etiologies. Although several patients selected by the criteria above could also be labelled as cases of interstitial lung diseases (ILD),[21] we prefer to reserve the term ILD for biopsy-proven (usually more severe) cases of chronic diffuse parenchymal lung disease. Applying the relatively new tool of BAL only to our biopsy-proven cases would limit the interpretation of our findings, and there is a need to increase our ability to apply BAL findings to children with clinically less severe forms of chronic respiratory diseases with diffuse pulmonary infiltrates. A multicentric study with a sufficiently larger number of cases including more severe, biopsy-proven cases and milder forms in whom biopsy was not considered would be of interest. One reason such a multicenter study has not been done is the difficulty in defining cDPLD and the lack of standardized BAL procedures.

In our study, the percentage of BAL fluid recovered was higher in cDPLD patients than in control patients. The finding is particularly evident in *early-stage* cDPLD patients. Presumably, it is due to the reduced collapsability of the system during suction maneuvers secondary to the low compliance of lung parenchyma in patients with cDPLD.

Compared with samples from controls, BAL samples from children with cDPLD had higher numbers of cells/mL: this increase involved all types of alveolar cells, including macrophages (normal and foamy), lymphocytes, neutrophils, and eosinophils. These findings indicate a mixed, predominantly lymphocytic alveolitis. The presence of alveolitis might be less well-defined if cell populations were expressed in percentages rather than in

absolute numbers per mL of BAL fluid recovered. For example, our study patients had lower macrophage percentages than controls, but significantly higher absolute numbers. Lymphocytic alveolitis, the outstanding finding in our patients with cDPLD, was previously reported in adult patients with extrinsic allergic alveolitis,[22] idiopathic pulmonary fibrosis,[23] sarcoidosis,[24] and measles pneumonia.[25] Yet, the precise role of lymphocytes in the alveoli remains unclear. Recent evidence shows that in fibrosing alveolitis, most lymphocytes express several activation markers, including interleukin 2 receptors (CD25), human leukocyte antigen DR (HLA-DR),[26] and the phenotype of memory T cells (CD45RO).[27] These findings indicate the presence of cells under continuous stimulation, with an enhanced response to recall antigens present within the lung and able to perpetuate the inflammatory response.

Foamy macrophages have been described in adult patients with active forms of BOOP, extrinsic allergic alveolitis, and to a lesser extent, in chronic eosinophilic pneumonia.[28] In children, foamy macrophages have been noted "frequently" as an intraalveolar component of the exudate[4] in histologic preparations from desquamative interstitial pneumonia, and in some patients with chronic pneumonitis of infancy; in one of these cases, foamy macrophages predominated.[29] These cells probably represent macrophages that are degrading fibrin bundles intracellularly.[30] Previous observations and our findings confirm foamy macrophages as markers of the active stages of cDPLD.

Further confirmation of alveolitis in our patients comes from the significant increase in two noncellular BAL components, namely, hyaluronic acid and fibronectin. Hyaluronic acid is the major glucosamine of perivascular and peribronchial interstitium, is produced mainly by activated fibroblasts, and is an expression of enhanced local synthesis of connective tissue components.[31] Hyaluronic acid is considered a marker of disease activity in adult idiopathic pulmonary fibrosis and is increased in patients with farmer's lung and in patients who have had radiation therapy for breast cancer.[19,32,33] In adult sarcoidosis, hyaluronic acid is markedly increased and correlates inversely with lung function.[34] We are not aware of hyaluronic acid measurements in lung diseases of childhood: in our study its increase strongly indicated early-stage or relapsing forms of chronic ILD.

Fibronectin is a glycoprotein which has multiple biologic functions in embryogenesis, tissue repair, and cell migration. It also interacts with numerous microorganisms. In the lung it is present during the reparative phase after acute lung injury or in inflammation. It is synthesized along with multiple extracellular matrix components in the developing lung.[35,36] In adults, increased fibronectin production has been found in interstitial pulmonary fibrosis, acute interstitial pneumonia, BOOP, and the organizing phase of the adult respiratory distress syndrome.

The patients described in this paper represent our most recent clinical experience. They belong to two distinct age subpopulations. Although both subgroups satisfied the criteria of long-standing severe respiratory impairment and typical bilateral radiological interstitial infiltrates, the 8 children with long-standing chronic pulmonary disease were older and had less severe symptoms and belong to a population of children with a milder form of cDPLD. The divergent BAL findings in the two subgroups therefore need to be interpreted with caution. BAL fluids from children with *long-standing* cDPLD contained significantly higher percentages and numbers of lymphocytes, whereas fluid from children with *early-stage* disease contained increased percentages and numbers of foamy macrophages and increased concentrations of hyaluronic acid and fibronectin. Albumin was abnormally high in 4 of the 6 children with *early-stage* cDPLD, but was absent in the 8 with *long-standing* cDPLD. Finally, 3 patients with early-stage cDPLD had onset of respiratory symptoms under age 2 years; chest X-ray films showed a ground-glass appearance; none of the other patients we studied had this radiological findings.

In conclusion, we identified an abnormal BAL profile in our patients defined as having cDPLD (chronic respiratory symptoms and typical bilateral radiological infiltrates). Their cellular and noncellular BAL abnormalities demonstrated an active lymphocytic alveolitis. Most of our patients with *early-stage* cDPLD had elevated concentrations of hyaluronic acid and fibronectin, whereas patients with *long-standing* cDPLD had normal concentrations of these mediators. This finding shows that the analysis of noncellular BAL components differentiates the pathophysiologic processes of patients with cellular alveolitis. Children under age 3 years typically had ground-glass chest X-ray film appearances, large numbers of foamy macrophages, and elevated amounts of hyaluronic acid, fibronectin, and albumin.

We are well aware that the numbers in our group are limited and that all our results in this rare pediatric illness need confirmation. If confirmed, the differences we noted in BAL cellular and noncellular components could be useful in defining the clinical phases during the follow-up of children with chronic diffuse parenchymal lung disease.

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