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CASE REPORT

Swyer-James syndrome: bronchoalveolar lavage findings in two patients

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Swyer-James syndrome: bronchoalveolar lavage findings in two patients. F. Bernardi, S. Cazzato, V. Poletti, D. Tassinari, M. Burnaccini, M. Zompatori, E. Cacciari. ©ERS Journals Ltd 1995.

ABSTRACT: Swyer-James syndrome (SJS) is a rare constrictive bronchiolitis that appears to be the result of acute bronchiolitis in infancy or early childhood. In the present study the cytological and immunophenotypical profile of bronchoalveolar lavage (BAL) was studied in two patients with SJS who showed a different spectrum of clinical outcome.

The total BAL yield was markedly increased in the patient with chronic cough and acute episodes of dyspnoea but not in the patient with decreased exercise tolerance and longer duration of disease. In the two patients, the differential cell counts in percentage were characterized by a significant increase of neutrophils and a slight increase of lymphocytes. The analysis of lymphocyte subsets showed a significant increase of CD8+ cells (T-suppressor-cytotoxic) in both cases, resulting in a decreased CD4/CD8 ratio. In addition, an increase of cells bearing a B-phenotype (CD19+ cells) was noted in the fluid recovered from the patient with chronic cough and acute episodes of dyspnoea.

In conclusion, our data suggest that SJS is an active process with inflammatory characteristics. Further studies are needed to explain the mechanism leading to the expansion *in situ* of immunocompetent cells.

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It has been recognized that lower respiratory tract infections in early infancy may be associated with residual damage and chronic disease [1–3]. Swyer-James syndrome (SJS) [4] or MacLeod's syndrome [5] is a peculiar clinicopathological entity. It is a rare constrictive bronchiolitis with airflow obstruction, that appears to be the result of acute bronchiolitis characterized by the destruction of small airways with obliterative scarring [1, 3, 6, 7]. Several infections have been implicated in the cause of SJS, especially adenovirus, measles virus, respiratory syncytial virus, influenza virus and mycoplasma [1, 3, 8].

Clinically, it is a heterogeneous entity. In some cases, it is a chance discovery, often made on chest radiography. One group of patients characteristically have recurrent pulmonary infections or decreased exercise tolerance. In chest radiographs, classic findings include unilateral hyperlucency. Normal or slightly reduced lung volume on inspiration, severe air-trapping during expiration, and pulmonary oligoaemia are additional radiological abnormalities of the affected lung. Computed tomography reveals all of these changes better, often shows bilateral, patchy areas of involvement and bronchiectatic proximal bronchi, and helps in the differential diagnosis of hyperlucency [9–11].

Pathologists emphasize the fibrotic process in SJS, whereas the inflammatory component is generally not mentioned, but histopathological data are anecdotal. The present study was designed to evaluate the nature and degree of pulmonary involvement in SJS assessed by bronchoalveolar lavage (BAL). We undertook cellular examination and phenotypic characterization of lymphocytes recovered from BAL fluid.

Case reports

Case No. 1

An 18 year old boy was referred to our department because of decreased exercise tolerance and persistent crackles at the lung bases on chest auscultation. At the age of 11 months he had been admitted to another hospital for acute bronchiolitis with severe respiratory failure caused by an undetermined agent. After the episode of bronchiolitis, he had a history of recurrent pulmonary infections until the age of 5 yrs. During the next few years he suffered from a progressively decreased exercise tolerance, that had become the dominant clinical

Table 1. – Clinical characteristics of the patients with SJS

	Patient No. 1	Patient No. 2
Symptoms	Exertional dyspnoea	Repeated respiratory infections, cough, acute dyspnoea
Findings	Crackles	Crackles and wheezes
PFT % predicted		
FEV_1	61	48
FEV_1/VC	63	67
FEF_{25-75}	31	37
RV/TLC	203	130
$T_{LCO,SS}$	51	45
HR-CT	Bilateral hyperlucency	Bilateral hyperlucency

FEV_1: forced expiratory volume in one second; and VC: vital capacity; FEF_{25-75}: forced expiratory flow between 25–75% of the forced VC; RV: residual volume; TLC: total lung capacity; $T_{LCO,SS}$: carbon monoxide transfer capacity on the lung steady-state; HR-CT: high-resolution computed tomography.

symptom over the last 10 yrs. Pulmonary function tests revealed an obstructive pattern that was not reversible after a trial of bronchodilators and corticosteroid treatment, air-trapping, and a reduced carbon monoxide transfer capacity (table 1). Chest radiography showed hyperlucency of the right lung, with air-trapping on expiration. High-resolution computed tomographic (HR-CT) scan revealed patchy areas of density reduction in both lungs, with loss of normal anteroposterior attenuation gradient and marked air-trapping, confirmed during expiration HR-CT scans (fig. 1). Only the left upper lobe showed normal attenuation, although islands of normal tissue were present within hyperlucent regions. The lung vessels were thin and sparse in the affected regions. Bronchiectases were not found. Pulmonary arteries were seen bilaterally and the bronchial tree was patent.

Blood samples for routine laboratory tests were taken at the time of study. Total immunoglobulin IgG, IgM, IgA, and IgE values were within the normal range, erythrocyte sedimentation rate and C-reactive protein were normal. White blood counts and differential counts were within the normal range, and there were no abnormalities of blood T-cell subpopulations measured by monoclonal antibodies (MoAbs).

BAL was performed by instillation of 4×25 ml of saline solution into a lower right lobe segment. The lavage fluid analysis was carried out as described previously [12], and according to the European BAL Task Group [13]. The differential cell counts in percentage were characterized by a significant increase of neutrophils (15%) and a slight increase of lymphocytes (14%). Epithelial cells were less than 5% of total cells. The lymphocyte subsets evaluated by flow cytometry were characterized by a significantly increased percentage of CD8+ cells, resulting in a decreased CD4/CD8 ratio (table 2). Microbiological analysis performed on BAL fluid gave negative results.

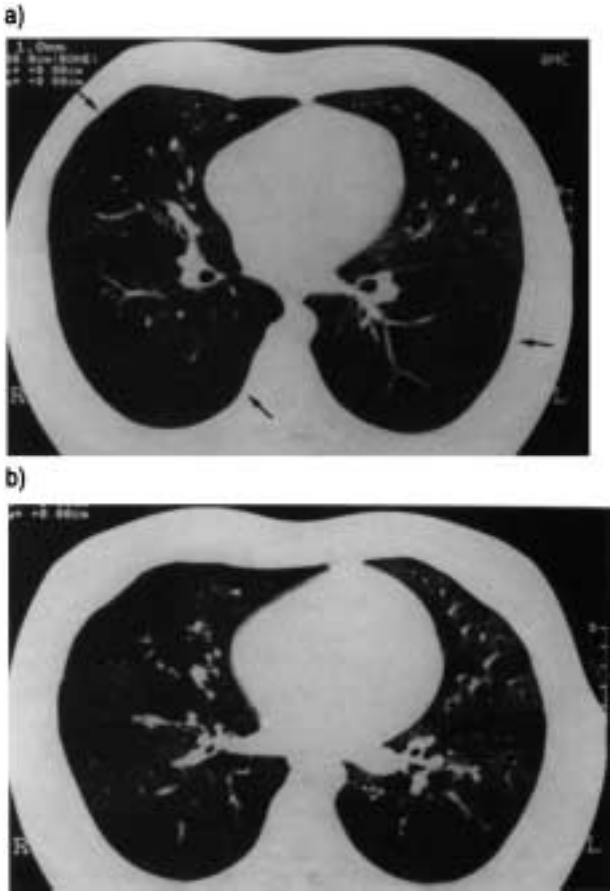

Fig. 1. – Patient No. 1. a) High-resolution computed tomography (HR-CT) scan during inspiration, showing bilateral diminished parenchymal attenuation (arrows) without normal anteroposterior gradient lung attenuation. Vessels in the hyperlucent regions are sparse and attenuated. b) HR-CT on expiration, showing marked air-trapping.

Table 2. – Differential cytology and lymphocyte subsets of BAL fluid

	Patient No. 1.	Patient No. 2
Fluid recovery ml *	39/100	40/75
Recovered cells$\times 10^4 \cdot ml^{-1}$	10	210
Differential count %		
Macrophages	70.5	31
Lymphocytes	14	15
Neutrophils	15	51
Eosinophils	0	3
Mast cells	0.5	0
Lymphocyte subpopulations % of total lymphocytes		
CD3+ (T cells)	89	73
CD4+ (T-helper)	28	21
CD8+ (T-suppressor/cytotoxic)	62	52
CD19+ (B-cells)	3	20
CD4/CD8 ratio	0.45	0.40
CD3+ HLA-DR+ (T-cells activated)	28	16

HLA-DR: class II molecules of the major histocompatibility complex. *: The first 25 ml aliquot recovered was discarded.

Case No. 2

An 8 year old girl was referred to us because of repeated pulmonary infections and dyspnoea, following a measles infection complicated by bronchopneumonia at the age of 13 months. During the last year before undergoing BAL, she was not affected by pneumonia but by coughing, without fever, and episodes of acute dyspnoea. Physical examination revealed crackles at both lung bases with bilateral expiratory wheezes. Pulmonary function tests revealed airway obstruction with a partial response to bronchodilators, air-trapping, and a reduced carbon monoxide transfer capacity (table 1). Chest radiographs showed hyperlucency of the right lung, with air-trapping during expiration. HR-CT scans revealed low attenuation areas in both lungs without the normal anteroposterior attenuation gradient, and greatly diminished peripheral lung circulation (fig. 2). HR-CT scans during expiration confirmed the severe air-trapping in the affected lung tissue. Minimal cylindrical bronchiectastic changes in the middle and both lower lobes were found. The pulmonary arteries were seen bilaterally and the bronchial tree was patent. As in case No. 1, routine laboratory blood tests performed at the time of BAL revealed normal values.

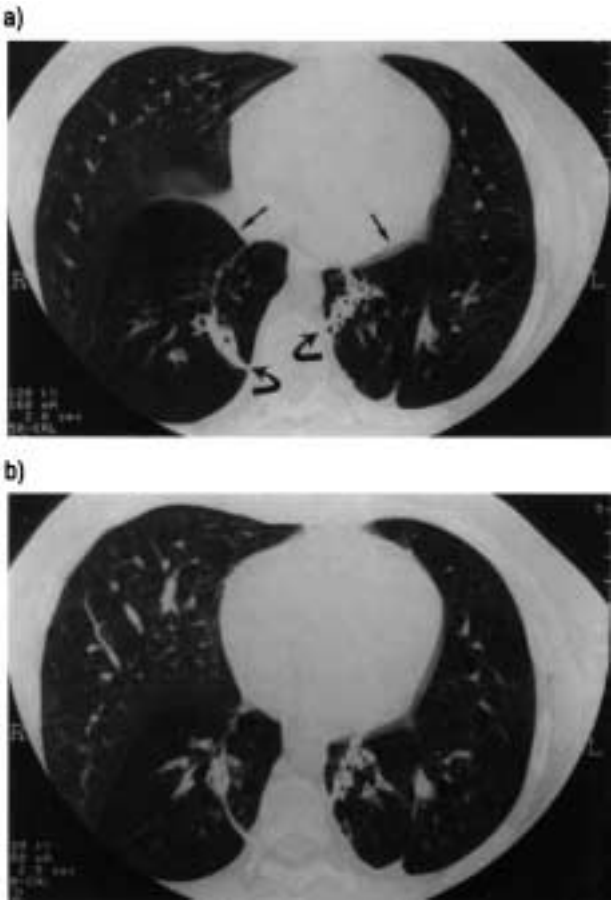

Fig. 2. – Patient No. 2. a) High-resolution computed tomography (HR-CT) scan during inspiration, showing bilateral lower lobes hyperlucency (straight arrows) with minimal cylindrical bronchiectasis (curved arrows). b) HR-CT scan during expiration, showing air-trapping in the lower lobes.

BAL was performed in a lower right segment, using 3×25 ml saline. The total number of cells recovered in BAL fluid was markedly increased (210×10^4cells·ml^{-1}) with a significant increase in percentage of neutrophils (51%), and a slight increase of lymphocytes (15%). Epithelial cells were less than 5% of total cells. The analysis of lymphocyte subsets (flow cytometry) from lavage showed a significant expansion of CD8+ cells, resulting in a decreased CD4/CD8 ratio. In addition, an increase of cells bearing a B-phenotype (CD19+) was found in the fluid recovered (table 2). All microbiological samples were negative.

Discussion

SJS syndrome, as originally described [4, 5], is characterized in radiographs by unilateral hyperlucency and air-trapping. In our two cases, HR-CT provided useful additional information, such as patchy bilateral regions of hyperlucency or bronchiectasis, in accordance with the experience of other authors [9, 11]. In both cases, HR-CT showed the typical findings of constrictive bronchiolitis: hyperlucent areas with diffuse oligoaemia and air-trapping during expiration. These findings are known in the literature as a mosaic "oligoaemia", and are easily distinguished from the ground glass- pattern of infiltrative lung disease. In ground-glass opacity, there is no air-trapping in the hyperlucent areas (which represent the normal lung) and the vessel calibre is the same in the opaque and lucent areas [14].

To our knowledge, there are no reports in the literature of BAL in SJS. This study evaluated the cytological and immunophenotypical profile of BAL fluid in our two patients with SJS, who showed a different spectrum of clinical course (table 1). Both patients had not been treated for three months prior to BAL. The data obtained from BAL in our patients are compared to normal subjects described previously [12], and reported by other authors [15–17]. In our two cases, BAL findings are representative of cells coming from centrilobular airways, as epithelial cells were less than 5% of total cells, and HR-CT scan excluded an infiltrative lung involvement. A significant increase of the BAL cellularity is present in patient No. 2, with chronic cough, acute episodes of dyspnoea and a recent history of repeated respiratory infections, but not in patient No. 1, who presented only restriction of exercise tolerance and longer duration of disease. In each patient, the cellular profile shows an evident neutrophil accumulation associated with a slight increase of lymphocytes. The increased percentage of neutrophil cells cannot be explained by concomitant bacterial infection. In fact, neither of the patients had pulmonary infiltrates or was suspected of having pulmonary infection, moreover microbiological samples obtained by BAL excluded this possibility. In addition, patient No. 2 had not been affected by pneumonia during the previous year.

In both cases, the inflammatory process in the distal airways is associated with an expansion of CD8+ cells. As a consequence, a decrease in the pulmonary CD4/CD8

ratio was observed in both patients. A similar BAL cell profile is reported in some lung disorders [18–23]. The considerable presence of B-cells (CD19+ cells) in the BAL fluid from patient No. 2 is interesting. In contrast, the lymphocyte subpopulations (evaluated by flow cytometry) in peripheral blood were normal in both patients. These findings suggest a hyperimmune reaction in the lung, that may play a role in the subsequent development of pulmonary impairment after the initial lung infection. In one case, a significant increase of lymphocytes with a polyclonal B phenotype may be related to a bronchus-associated lymphoid tissue hyperplasia. Cases of follicular bronchiolitis sustained by latent adenoviral infection have been reported [24].

In conclusion, in both patients BAL findings showed that the bronchoalveolar damage in SJS is an active process with inflammatory characteristics. In particular, the striking neutrophilia may play a pivotal role in sustaining peripheral airways damage and fibrotic remodelling. In the two patients, the difference between the total cells recovered from BAL may reflect a different stage or activity of the disease. However, it may be that the lungs of these patients respond to persistent (unknown) antigenic stimulus by activating its local immunological mechanism. Further studies are needed to confirm these data, and to explain the mechanism leading to the expansion of immunocompetent cells and the kind of mediators involved in the lung affected by this chronic disease.

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