CASE REPORT

Value of bronchoalveolar lavage in lipidoses with pulmonary involvement

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Value of bronchoalveolar lavage in lipidoses with pulmonary involvement. L. Tabak, D. Yılmazbayhan, Z. Kılıçaslan, C. Taşçioğlu, M. Ağan. ©ERS Journals Ltd 1994.

ABSTRACT: Adult lipid storage disorders with pulmonary involvement are rare and usually diagnosed at autopsy. We report a patient with splenomegaly and reticulonodular pattern on lung computed tomography.

Bronchoalveolar lavage was performed and revealed the presence of lipid-containing foamy cells, with the demonstration of both periodic acid-Schiff (PAS) and scharlach red stain positive vacuoles in the cytoplasm of alveolar macrophages. The same cells were found in bone marrow biopsy.

As in other rare disorders, bronchoalveolar lavage may be of diagnostic value in lipid storage disorders with pulmonary involvement.

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Lipid storage disorders, such as Gaucher's disease and Niemann-Pick disease, are inherited diseases in which deposits of certain lipids occur in various organs as a result of specific enzyme deficiencies [1, 2]. These disorders are quite rare and most are transmitted in an autosomal recessive fashion.

The adult variants of the lipidoses are characterized by their benign course with little involvement of the central nervous system, whilst the infantile forms progress rapidly, with a complex pattern of visceral and neurological involvement, until death occurs. Although many visceral organs and the central nervous system have been extensively studied in lipidoses, comparatively little attention has been paid to the lungs. Interestingly, the limited references to pulmonary changes have dealt largely with autopsy or roentgenographic findings in children [3].

Actually, pulmonary involvement and symptoms are not unusual in the infantile forms of lipidoses, but they are rare in the adult forms [4]. In this paper, we suggest bronchoalveolar lavage (BAL) as a diagnostic tool for the evaluation of pulmonary involvement in lipidoses.

Case report

A 27 year old Caucasian male was admitted to the hospital because of abdominal pain. The patient had been in good health until seven months earlier when he began to experience abdominal pain accompanied with intermittent fatigue. A month before entry, the abdominal pain became considerably worse and he consulted a physician. Spleen enlargement was detected on physical examination and he was referred to our hospital for eval-

uation. The patient was a farmer. He had been born to healthy, unrelated parents after a normal pregnancy and delivery; and was the third of five children. One of the patient's elder sisters was known to be insane. There was no history of chills, sweats, anorexia, chest pain, orthopnea, haemoptysis, gastroesophageal reflux, weight loss, diarrhoea, recent travel, exposure to infected persons or animals, use of alcohol or tobacco, administration of blood products, use of illicit drugs or exposure to toxic chemicals.

On physical examination, the patient was thin and appeared weak. No rash, splinter haemorrhages or lymphadenopathy were found. The physical examination of head, neck, lungs and heart was normal. A slightly tender spleen with a blunt edge was palpated 10 cm below the left costal margin; the liver was not palpated. There was no abdominal mass, ascitic fluid or collateral venous circulation. The extremities and genitalia were normal. Neurological examination was negative.

Routine laboratory investigations revealed a decreased haemoglobin, $12.0 \text{ g}\cdot\text{l}^{-1}$, a decreased total white cell count of $2.1 \times 10^9\cdot\text{l}^{-1}$ with normal differential count and a decreased platelet count of $38 \times 10^9\cdot\text{l}^{-1}$. Sedimentation rate was $125 \text{ mm}\cdot\text{h}^{-1}$. Routine blood chemistry and urinalysis were normal, except for an elevation in serum acid phosphatase and angiotensin-converting enzyme levels. An electrocardiogram was normal. An ultrasonographic examination of the abdomen showed the enlarged spleen, dilated portal vein and collateral circulation at the hilus of spleen. The tests for hepatitis B surface antigen (HBsAg), hepatitis B core antigen (HBcAg), anti-HBcAg, anti-delta and anti-hepatitis C virus were all negative. The serological tests for *Brucella* sp. and *Salmonella* sp. were also negative.

A diagnosis of non-cirrhotic presinusoidal portal hypertension was suspected but oesophagogastrosocopy disclosed no varices or ulcers.

Chest radiography disclosed thin reticulonodular opacities, which were more prominent in the lower regions and locally confluent to ground-glass opacities. Upper lung fields were affected to a lesser extent. High-resolution computed tomography of the lung disclosed diffuse interstitial infiltration, thickening of the interlobular septa, extensive subpleural fibrosis, subpleural and peribronchial thickening and marked nodular thickening of broncho-vascular bundles. Lymphangitis carcinomatosa, fibrosing alveolitis or lymphocytic interstitial pneumonia was suspected. The pulmonary function test results were: forced vital capacity (FVC) 4.44 l (96% pred), forced expiratory volume in one second (FEV₁) 3.69 l (94% pred) and diffusing capacity of the lungs for carbon monoxide (DLCO) 96% pred. Arterial blood gases in room air were normal (arterial carbon dioxide tension (Paco₂) 38 mmHg (5 kPa), arterial oxygen tension (Pao₂) 90 mmHg (12 kPa)).

In order to establish the suspected diagnosis of interstitial pneumonia, BAL was performed. One hundred millilitres 0.9% sterile saline, in five 20 ml aliquots, were instilled into the middle lobe using a flexible bronchoscope. The fluid was retrieved by gentle suction, filtered immediately through gauze and placed on ice. The percentage of instilled fluid recovered was 68% and gross appearance was clear. The cells were separated from the lavage fluid by low speed centrifugation (800 ×g for 10 min). The bronchoalveolar cells were counted and a trypan blue exclusion test for cell viability was performed. The total number of cells recovered was 16.2×10⁶ and the cell viability was 89%. Differential counts were made from smears stained with May-Grünwald Giemsa stain, by counting 800 cells.

The BAL contained 84% macrophages with foamy cytoplasm, 13% lymphocytes and 3% neutrophils. Macrophages were distended with foamy cytoplasm and rather small, uniform, often eccentric nuclei. The cells were sometimes multinucleated (fig. 1). They were intensely periodic acid-Schiff positive and had red granules stained by scharlach red in their cytoplasm, resembling Gaucher's cells.

Transbronchial biopsy of the left lower lobe disclosed a distorted alveolar pattern and alveolar spaces containing foamy cells with distended cytoplasm and eccentric nuclei.

The initial diagnosis was a lipid storage disease. X-ray films of humerus and femur demonstrated expansion of the medullary cavity and thinning of the cortex (Erlenmeyer flask deformity). Detailed ophthalmic examination and fluorescein angiography of the fundus were normal and no retinal spots were detected. Bone marrow aspiration disclosed a normocellular bone marrow with a normal ratio of white and red cells. Biopsy of bone marrow revealed normocellular bone marrow containing foamy cells (fig. 2).

Symptomatic therapy was prescribed. Splenectomy was not considered because the patient did not bleed despite thrombocytopenia. The patient is currently receiving supportive therapy at home and his capacity for physical activity is limited.

Fig. 1. – Foamy cells in bronchoalveolar lavage (BAL). The cytoplasm reveals fine vacuoles and granular component. (May-Grünwald Giemsa stain, magnification ×500).

Fig. 2. – Bone marrow infiltration by foamy cells. Note the eccentric nuclei and granular cytoplasm. (Haematoxylin and eosin stain, magnification ×500).

Discussion

This paper presents the BAL findings in a patient with a lipid storage disorder with pulmonary involvement. The clinical course and histological findings, whilst atypical, are compatible with either type I (adult) Gaucher's disease or type E Niemann-Pick disease. In the adult form of Gaucher's disease, the excess cerebroside accumulates in the spleen, liver, lymph nodes and bone marrow. Pulmonary involvement has been reported in all types of Gaucher's disease [4, 5]. Niemann-Pick disease is caused by abnormal metabolism and storage of the diaminophospholipid sphingomyelin. Patients with type E Niemann-Pick disease show a generalized organ involvement, including the lungs, with questionable sphingomyelinase deficiency. The organ distribution of lipids in our case is consistent with either Gaucher's or Niemann-Pick disease.

The skeletal manifestations, such as Erlenmeyer's flask deformity, are seen in all lipidoses, which is not surprising in view of their identical pathogenesis. The presence of epiphyseal osteonecrosis or well-circumscribed radiolucent lesions could facilitate the radiographic diagnosis of Gaucher's disease, but is not pathognomic.

The cytological and histochemical findings are of more value in differentiating between Gaucher's and Niemann-Pick disease. In our case, the finely vacuolated cytoplasm of the macrophages is consistent with Niemann-Pick disease, whilst the granular cytoplasm is more compatible with Gaucher's disease. The similarities of clinical, chemical and morphological features between Gaucher's disease and Niemann-Pick disease are so great that demonstration of the enzymatic defect is necessary, which is unavailable in this country. However, whether this case is Gaucher's disease or Niemann-Pick disease, it is evident from the findings that a lipid storage disorder was present.

The aim of this paper was not to assess the definite diagnosis but to draw attention to the value of BAL in the diagnosis of pulmonary involvement in lipidoses. Whilst patients with lipidoses do have an increased incidence of pulmonary infections [6], BAL may be of value in excluding the involvement of lungs by the primary process. With the exception of a unique case reported by MERKLEN *et al.* [7] in 1933, in which Gaucher's cells were found on sputum examination, pulmonary involvement in lipidoses has, so far, usually been diagnosed radiologically or at autopsy. There is only one previous report in which BAL revealed characteristic signs of a lipid storage disorder, a case of Hermansky-Pudlak syndrome [8], which is characterized by ceroid accumulation.

In conclusion, as in a number of other rare disorders, such as histiocytosis-X, pulmonary haemorrhage, pulmonary alveolar proteinosis and eosinophilic pneumonitis [9], BAL may be of diagnostic value in lipidoses with pulmonary involvement.

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