Place of Bronchoscopy in the Diagnostics and Follow-up of Patients with Idiopathic Pulmonary Hemosiderosis

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Abstract

The idiopathic pulmonary hemosiderosis is a rare, life-threatening condition observed mainly in children and characterized by recurrent episodes of diffuse alveolar hemorrhages. The disease is characterized by the triad of hemoptysis, alveolar infiltrates in chest radiography, and iron-deficiency anemia. The recurrent episodes of alveolar hemorrhage can lead to chronic iron-deficiency anemia and irreversible pulmonary fibrosis; therefore, early diagnosis and treatment are crucial to the outcome of the disease.

Keywords
bronchoalveolar lavage, flexible bronchoscopy, hemosiderin-laden macrophages, pulmonary hemosiderosis

INTRODUCTION

Pulmonary hemosiderosis is an accumulation of hemosiderin in the lungs as a result of a diffuse alveolar hemorrhage which may be due to a primary pulmonary process or a secondary condition (cardiovascular disease, infectious disease, vasculitis syndrome, hemorrhagic diathesis, etc.). After excluding other causes for alveolar hemorrhage, the pulmonary hemosiderosis is considered to be idiopathic.

The estimated incidence of idiopathic pulmonary hemosiderosis (IPH) ranges from 0.24 to 1.23 per 1 000 000/year. In 80% of the cases it occurs during the first decade of life, most often before the age of 7. Only about 500 IPH cases have been described in the medical literature. There is no data in the available medical literature on the frequency and average age of onset of the disease in Bulgaria.

The etiology and pathogenesis of the disease are still questionable. Immune mechanisms have been suggested.

The rare incidence of IPH, as well as the different clinical image, makes it difficult to make a diagnosis. Chest radiography and high-resolution computer tomography (HRCT) are an integral part of the diagnosis and the follow-up of patients with IPH, bronchoscopy should be performed in order to confirm the diagnosis.

Although there is no established etiologic treatment for IPH, corticosteroids and immunosuppressants are used empirically, individually or in combination.

On the occasion of a clinically diagnosed case of IPH (proven by the presence of hemosiderin-laden alveolar macrophages by bronchoalveolar lavage) and passed in clinical remission with corticosteroid treatment, we discuss the importance of early recognition of IPH and the place of bronchoalveolar lavage (BAL) in the diagnosis and follow-up of patients.
CASE REPORT

A child at the age of 2 years and 8 months, with iron-deficiency anemia diagnosed at the age of one. Several hemotransfusions and therapy with iron preparation were performed, but without effect.

The child was hospitalized in our clinic after a single episode of hemoptysis, cough, subfebrile temperature, fatigue, and paleness. It was assumed that the case was related to respiratory failure in the course of influenza hemorrhagic pneumonia. There were no deviations in the remaining somatic and neurological status.

Based on the results of the routine laboratory tests, severe microcytic hypochromic anemia with low serum iron was diagnosed: hemoglobin 58 g/l, erythrocyte 3.4×10¹²/l, hematocrit 0.24 l/l, MCV 63.9 fl, leukocytes 10.7×10⁹/l, platelets 439×10⁹/l, serum iron 4.5 μmol/L, and total iron-binding capacity (TIBC) 55.7 μmol/L. There was no evidence of coagulation disorders and hemoglobinopathies and no deviations in the other biochemical parameters.

Chest radiography showed diffuse alveolar infiltrates (Fig. 1A). Because of the triad of hemoptysis, anemia, and X-ray data of pulmonary infiltrates, the possibility of pulmonary hemosiderosis was discussed, fibrobronchoscopy was performed: hemosiderin-laden macrophages were detected through BAL (Figs 2A, 2B).

Other causes of pulmonary hemosiderosis such as ANCA-associated vasculitis in the small vessels, celiac disease, Goodpasture syndrome, and allergy to cow’s milk protein (Heiner syndrome) were excluded.

We assumed that the case was related to IPH and corticosteroid therapy was initiated at 2 mg/kg per day. The antibiotic therapy – ceftriaxone 70 mg/kg/day – was discontinued and the symptoms of respiratory failure were con-

Figure 1. A. Chest radiography – shows diffuse alveolar infiltrates (before initiation of treatment); B. Chest radiography – reverse dynamics of the infiltrative changes (15 days after initiation of corticosteroid treatment, 2 mg/kg).

Figure 2. A. Bronchoalveolar lavage (BAL) with H&E staining – hemosiderin-laden alveolar macrophage, which is identifiable by light microscopy as golden-yellow to brown, granular pigment. Surrounded by normal ciliated columnar bronchial epithelia cells and few erythrocytes; B. Bronchoalveolar lavage (BAL) with Perl’s Prussian blue reaction which stained in blue hemosiderin-laden alveolar macrophage.
trolled within 48 hours. After 4 weeks, the dose of corticosteroids was reduced to 1 mg/kg per day. Reverse dynamics of the physical and X-ray pulmonary changes was reported (Fig. 1B). It was decided that the child did not need control fibrobronchoscopy with BAL. The patient is subject to follow-up.

DISCUSSION

Early diagnosis of IPH is a challenge, especially in children, as the disease does not always debut with the classical triad. The most common symptoms are anemia and dyspnoea due to pulmonary infiltrates. Hemoptysis is less common in infancy as small children often swallow their phlegm. In this case, the disease started with severe iron-deficiency anemia 19 months before the appearance of the typical clinical triad of the IPH and was diagnosed through establishment of hemosiderin-laden macrophages by BAL.

A gold standard for diagnosis of IPH is still the pulmonary biopsy, but after the widespread introduction of bronchoscopy in the pediatric practice, BAL has become the method of choice for diagnosis of the disease. Pulmonary biopsy is a risky manipulation, especially in unstable patients with respiratory failure, and can be performed only in cases where other non-invasive or less invasive methods have not contributed to the diagnosis.

Transbronchial lung biopsy has a lower diagnostic value and is not recommended for routine clarification of alveolar hemorrhage.

In 1970, BAL was introduced as a diagnostic method of alveolar hemorrhage and is now used to prove the disease and to exclude other underlying diseases.

Bronchoscopy is a safe procedure with minimal and rare complications and it is recommended for all patients with suspected alveolar hemorrhage regardless of the severity of the disease. The aim is to exclude bleeding of bronchial origin, to search for infectious agents and to confirm alveolar hemorrhage by proving hemosiderin-laden macrophages through BAL. It has been established that hemosiderophages accumulate in the alveoli within 50 hours after acute alveolar hemorrhage. They may be present in a small amount also in healthy individuals, smokers and patient with pneumonia. The presence of more than 20-30% of hemosiderophages in BAL suggests pulmonary hemosiderosis. Hemosiderin-laden macrophages can also be found in stomach fluids and sputum, but the sensitivity of the latter is only 30% compared to BAL the sensitivity of which is 92%.

It is important to note that the reverse dynamics of the imaging changes in chest radiography and HRCT does not always correlate with a successful remission of the disease. It is necessary to observe the patients by conducting regular bronchoscopies with BAL for detection of hemosiderophages, as well as HRCT for monitoring of pulmonary parenchymal changes. The number of hemosiderophages in BAL several months after the hemorrhagic episode can be used as a marker for detection of remission of the disease and assessment of the effect of the applied treatment.

Systemic glucocorticoids are the primary treatment for IPH. Their therapeutic dose varies from 0.5 mg/kg per day to 2 mg/kg per day during acute bleeding episodes.

Corticosteroids are considered effective in the treatment of the acute phase of alveolar hemorrhage. They show a reduction in morbidity and mortality during acute episodes of alveolar hemorrhage and slow the progression to pulmonary fibrosis.

Recurrences of IPH are known to be common during the process of reducing or withdrawing therapy. Long-term low-dose glucocorticoid therapy or in combination with other immunosuppressive agents such as hydroxychloroquine and azathioprine may help reduce relapses. Most patients receive this therapy for about 2 years after the acute phase of the disease at maintenance doses of 10 to 15 mg per day.

Regarding our patient, in the acute phase of the disease, the child was treated with methylprednisolone at a dose of 2 mg/kg with a gradual reduction of the dose to 1 mg/kg, after which we switched to oral treatment with dehydrocortison to 1 mg/kg. Reverse dynamics of clinical and imaging changes are reported. Subsequently, treatment with low doses of 10 mg dehydrocortison was performed on a variable regimen. No exacerbation of the disease was observed for a period of 6 months. Follow-up of the patient continues.

The follow-up of patients after an acute episode of IPH requires periodic assessment of growth, oxygen saturation, pulmonary and renal function, and hemography and chest radiography. If recurrence is suspected, bronchoscopy with BAL is performed for detection of hemosiderophages.

The long-term prognosis is different, but most patients have episodes of disease exacerbation despite continued therapy. The average life expectancy of about 2.5 years was reported in 1960, and in the last few years immunosuppressive therapy has been successful. Saeed et al. reported a 5-year survival rate in 86% of patients taking corticosteroids with or without immunosuppressive agents.

CONCLUSIONS

Every case of a child with persistent severe iron-deficiency anemia, especially if it is combined with respiratory symptoms, should be considered to be related to pulmonary hemosiderosis. The method of choice for diagnosis and monitoring of the effect of the treatment is bronchoscopy with BAL.

REFERENCES