Tanaffos (2002) 1(3), 57-61

Infantile Histiocytosis X: Case Report

Mohammad Reza Boloorsaz [1], Abbas Mir-Afsharieh [2], Kian Khodadad [3], Makan Sadr [1]

[1]Department of Pediatrics, [2]Department of Clinical Anatomical Pathology, [3]Oncology Unit, NRITLD, Shaheed Beheshti University of Medical Sciences and Health Services, TEHRAN-IRAN

ABSTRACT

Langerhans cell histiocytosis (LCH) is a disease of unknown etiology that presents in three forms: Letterer- Siwe disease, Hand-Schuller-Christian disease, and Eosinophilic Granuloma. It is a multifocal disease that usually affects several organs and unifocal forms are rare. Pulmonary involvement occurs in approximately 40% of cases and almost always in young adults. Lungs are rarely affected in infant patients. This report presents a 15-month-old male infant that was admitted for cyanosis and respiratory distress. Diagnostic work up revealed a primary pulmonary histiocytosis and the treatment made a significant improvement of signs and symptoms by the time of discharge.

(Tanaffos 2002; 1(3): 57-61)

INTRODUCTION

Langerhans cell histiocytosis (LCH), previously known as histiocytosis X, is caused by infiltration of histiocytes in various tissues. Any of the tissues that contain monocytic phagocytes are prone to this disease.

Infiltration of Langerhans cells in the skin, osteaclasts in bones, Kupffer cells in the liver, microglia in the brain, and alveolar macrophages in the lungs are observed in histiocytosis. Involvement of kidney, adrenal gland, bladder, and testis has not been reported (1).

The disease may occur at the time of birth up to the old age with a peak between 1 and 3 years. Males are more sensitive. The incidence is 1.2 per 200000 infants per year (2). It usually affects multiple organs and presents as each of the three clinicopathologic entities which are as follows(3):

- Letterer- Siwe disease: This progressive disseminated form usually affects Infants younger than 6 months old. The skin, liver, spleen, lymph nodes, bone marrow, and lungs are involved. Clinical features include fever, generalized seborrheic or hemorrhagic eruptions, icterus, hepatosplenomegaly, and lymphadenopathy. Pulmonary involvement is usually evident on chest radiographs, rarely producing symptoms, and may regress with time.

Some infants developed dry cough, cyanosis, and tachypnea, so that FTT (Failure to Thrive) ensues as a result of increased respiratory effort.

- Hand- Schuller- Christian disease: This form affects the children older than the age of 6 months old; isolated or multiple bones are usually involved along with other organs. Lung involvement was

Correspondence to: Sadr M
Tel.:+98-21-2803549; fax:+98-21-2803549
E-mail address: makansadr@nritld.ac.ir

observed in the majority of cases studied at autopsy. The signs and symptoms of pulmonary involvement are cough, tachypnea, cyanosis, clubbing, and hemoptysis. Pneumothorax is another presentation of the disease. Pulmonary involvement may be asymptomatic or progressive that ends up in pulmonary failure and corpulmonale.

- Eosinophilic granuloma: Pulmonary involvement is a common finding observed in 1/3 of infants with disseminated LCH. However, primary pulmonary LCH is rare in children under the age of 15 years old and the course of progression or regression of the lesions is very insidious. Chest x-ray, even in the absence of clinical findings, reveals diffuse nodular lesions, reticulonodular lesions, or signs of interstitial pathologies. A diagnostic hallmark for LCH is the presence of tennis-racket granules called Birbeck's granules in the cytoplasm of histiocytes within the lesion. Therefore, the detection of CD1a, expressed by immunohistochemical techniques, aids the diagnosis. This article presents a case of LCH with isolated lung involvement.

CLINICAL SUMMARY

A 15-month-old male infant was referred to Massih Daneshvari hospital for cyanosis and respiratory distress. In a 6-month period, he had progressive cough and dyspnea. Physical exam revealed the signs of FTT due to increased respiratory effort (wt =8kg), as well as tachypnea (RR=40/min), tachycardia (PR= 130/min), fever, and coarse crackles in both lungs. All laboratory tests included blood indices, liver function tests, and urine analysis were normal. Smear and culture of gastric lavage were negative for B.K as well as PPD test. Chest x-ray revealed diffuse infiltrative lesions in both lungs (Fig.1) which appeared as nodular densities in chest CT-scan (Fig.2). The skull x-ray showed no signs of bone lesions.

Open lung biopsy was performed for histopathologic evaluation. Macroscopically, there were small nodules within a background of normal pulmonary tissue. Microscopcally, it was diagnosed as LCH (Fig.3). The patient was treated by prednisolone 2mg/kg for 4 weeks then tapered within 8 weeks along with vincristine 1.5 mg/m^2 once every 1 to 2 weeks and trimethoprim-sulfamethoxazole with usual dosage (4).

Following the treatment he began to improve and after 2 weeks both clinical respiratory exams and chest x-ray showed significant improvement (Fig.4).

Fig 1. Chest-x ray during active period of disease

Fig 2. Thoracic CT-scan shows nodular densities

Fig 3.Pathologic confirmation of disease

Fig 4. Chest-x ray revealed significant improvement after treatment

DISCUSSION

Histiocytosis often affects the lungs both clinically and subclinically. Primary pulmonary LCH is characteristic of young adults and middle-age patients (aged 20-40 years old, mean age of 32 years old). Smoking is a known risk factor for the development of pulmonary LCH in adults. To our knowledge, only 2 cases of isolated pulmonary LCH in infancy have been reported (1,7). The reason is, that despite the fact that lungs are affected in 40% of multifocal LCH, other organs show signs of involvement as well; therefore, very rarely the lungs are the only affected sites in LCH of infancy (5,6). Moreover, the incidence of pneumothorax, pleural effusion, and diabetes insipidus is lower in affected infants and children comparing with adult patients.

In early LCH, chest X-ray reveals diffuse, symmetric linear and nodular opacities in the interstitial tissue of the upper and middle parts of the lungs. No differences were identified in the chest radiographic findings of patients with primary or generalized pulmonary LCH.

Radiologic differential diagnosis includes sarcoidosis, allergic alveolitis, idiopathic pulmonary fibrosis, and lymphangioleiomyomatosis. In spirometry, LCH displays a mixed restrictive-obstructive pattern. Early in the course of the disease, interstitial and alveolar infiltration disturb gas exchange. Later on, cystic changes, bullous formation, and pneumothorax may ensue. With progression of the disease, pulmonary fibrosis increases the dead space volumes, which in turn causes V/Q mismatch and finally leads to hypoxemia.

Pathologic findings in LCH have been recently reviewed. Light microscopy revealed symmetric nodules with fibrotic center and cellular periphery. Early on, accumulation of Langerhans cells is observed along with variable numbers of eosinophils. Langerhans cells are characterized by indented nucleus and abundant eosinophilic cytoplasm. In end-stage lesions, stellate scans surrounded by air spaces are developed mainly due to airway dilation. Immunohistochemically, Langenhans cells react with antibodies to S-100 protein and CD1a. The hallmark of LCH is Bribeck's granule determined by microscopy.

LCH could be confirmed via transbronchial biopsy in 15-20% of the patients; however, open lung biopsy (as performed for our patient) is our last choice. Furthermore, the presence of CD1a cells (≥5%) in the BAL sample could establish the diagnosis.

Pulmonary hypertension is an uncommon but serious manifestation of LCH (7) and it is suggested that LCH could be considered as a reason of pulmonary hypertension.

REFERENCES

1. Ha SY, Helms P, Fletcher M, et al. Lung involvement in Langerhans' cell histiocytosis: prevalence, clinical features, and outcome. ***Pediatrics*** 1992; 89(3): 466-9.
2. Hentre JI, Elinder G, Soder O, et al. Incidence in Sweden and clinical features of familial hemophagocytic lymphohistiocytosis. ***Acta Paediatr Scand*** 1991; 8(4): 428-35.
3. King TE Jr, Crausman RS. Pulmonary histiocytosis X. In: Fishman AP, Elias JA, Fishman JA, et al, editors. ***Fishman's pulmonary disease and disorders***. Mc-Graw Hill; US: 1998.p.1163-7.
4. Viana MB, Oliveria BM, Silva CM, et al. Etoposide in treatment of six children with Langerhans cell histiocytosis. ***Med Pediater Oncol*** 1991; 19(4): 289-94.
5. Smets A, Mortele K, de Praeter G, et al. Pulmonary and mediastinal lesions in children with Langerhans cell histiocytosis. ***Pediatr Radiol*** 1997; 27(11): 873-6.
6. Soler P, Tazi A, Hance AJ. Pulmonary Langerhans cell granulomatosis. ***Curr Opin Pulm Med*** 1995;1(5): 406-16.
7. Fartoukh M, Humbert M, Capron F, et al. Severe pulmonary hypertension in histiocytosis X. ***Am J Respir Crit Care Med*** 2000;161(1):216-23.