Pediatr Radiol (1993) 23: 181–182

Pediatric Radiology

Congenital histiocytosis X

A. Vade[1], A. Hayani[2], K. L. Pierce[1]

[1] Department of Radiology, Loyola University Medical Center, Maywood, Illinois, USA
[2] Department of Pediatrics, Loyola University Medical Center, Maywood, Illinois, USA

Received: 24 December 1992/Accepted: 8 February 1993

Abstract. Congenital histiocytosis X involving multiple organs is a rare disease that causes rapid mortality in intrauterine and neonatal life. The diagnosis of histiocytosis X (Litterer-Siwe disease should be considered in a neonate with vesiculated crusting skin lesions. We present clinical, radiographic and histopathological findings in a neonate with congenital histiocytosis who died of respiratory failure due to diffuse infilteration of lungs with histiocytic cells.

Congenital histiocytosis X is a rare form of Langerhans cell histiocytosis [1, 2]. We report on an infant with congenital histiocytosis X who died within 10 days of birth due to diffuse infiltration of multiple organ systems with Langerhans histiocytic cells. To our knowledge, this is the first case of the radiographic illustration of progressive lung involvement in an infant with histiocytosis X.

Report

A 35-weeks gestation white female was born by normal spontaneous vaginal delivery to a 31-year-old G_1, P_0 mother who had a history of ulcerative colitis and vaginal lesions for 2 years. The infant presented with multiple vesiculated crusting skin lesions. The mother's vaginal lesion cultures were negative for herpes and vari-

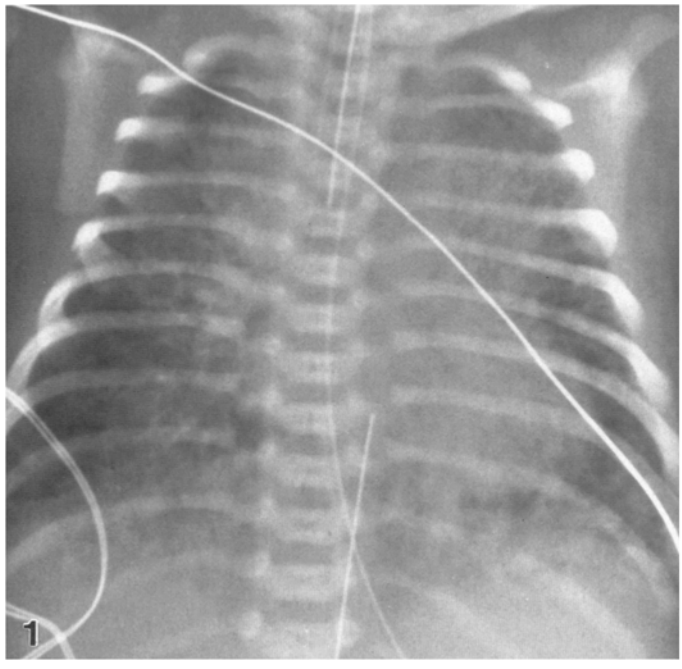

Fig. 1. AP view of the chest on birth day shows diffuse reticular – nodular infiltrates in both lungs

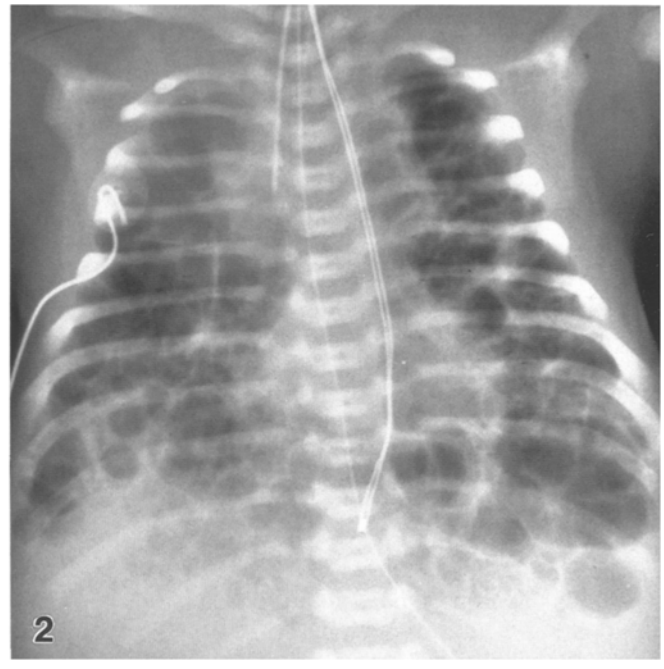

Fig. 2. AP view of the chest on 9th day after birth shows multiple cysts of varying sizes throughout both lung fields

Correspondence to: A. Vade, MD, Loyola University Medical Center, 2160 S. First Avenue, Maywood, IL 60153, USA

cella. The Apgar scores of the baby at birth were 5, 7 and 8. On physical examination the birth weight was 2.36 kg, pulse rate 152/min, respiratory rate 52/min, blood pressure 58 mm Hg/41 mm Hg, and temperature 37.5 °C. The liver and spleen were 5 cm and 2 cm below the chondrocostal margin respectively. Blood, urine, stool and skin lesion cultures were all negative. Evaluation for congenital infectious diseases such as cytomegalovirus, syphilis, herpes simplex virus, toxoplasma and hepatitis was negative. There was no evidence of IGM deficiency. By 24 h of age, the baby presented with severe respiratory acidosis. The infant was started on antibiotics (ampicillin, gentamicin and acyclovir) and improved on oxygen therapy. She remained clinically stable and by the fourth day, the original skin lesions were healing while new lesions were seen. By the fifth day, significant hepatosplenomegaly was noted. By the seventh day, lab results revealed leukopenia and thrombocytopenia. A chest radiograph at birth revealed diffuse reticular nodular infiltrates in both lungs (Fig. 1). On the 5th day scattered cystic lesions in both lungs were noted; and by the 9th day there was an increase in the size and number of cysts in both lungs (Fig. 2). Ultrasound of the abdomen on day 5 showed hepatosplenomegaly without focal lesions. The patient died on the ninth day from progressive respiratory deterioration associated with bilateral pneumothoraces and cardiorespiratory arrest.

Autopsy revealed pleomorphic histiocytic cells extensively infiltrating the papillary dermis, heart, lungs, thymus, liver, kidneys, bone marrow, pancreas, spleen and paratracheal lymph nodes. The histiocytic cells demonstrated S-100 positive, Vimentin positive, PNA positive and CD 68 negative immunohistochemical staining properties consistent with widely disseminated congenital histiocytosis X (Letterer-Siwe disease). Sections of both lungs revealed extensive histiocytic cell infiltrates in the alveolar and interstitial spaces as well as between the bronchial mucosa and cartilage. Multiple areas of lung tissue revealed nodular aggregates of histiocytic cells. Several nodules showed central hemorrhage and cystic degeneration. Areas of lungs uninvolved by the infiltrates demonstrated pulmonary interstitial emphysema characterized by disrupted alveolar walls and enlargement of alveolar spaces. Also present were areas of bronchopulmonary dysplasia characterized by interstitial edema and fibrosis with zones of atelectasis and bronchoepithelial hyperplasia. The alveoli in these areas demonstrated aggregates of fibrin.

Discussion

The spectrum of Langerhans cell histiocytosis (LCH) ranges from a disseminated life-threatening disease, previously known as Letterer-Siwe disease, to localized lytic bony lesions seen in eosinophilic granuloma [3]. A waxing and waning clinical course is frequently observed in Letterer-Siwe. Letterer-Siwe disease is most commonly seen in infants usually during the first and second years of life. The congenital form of the disease is uncommon [1, 2]. The congenital disease can be either rapidly fatal in intrauterine life[1] or within a few weeks of birth [2]. It can be selflimiting, (benign form) usually over a period of several months. However, spontaneous regression is a rare biologic event. Most of the benign congenital histiocytosis X reported in the literature demonstrated solitary skin involvement [4, 5].

Both benign and acute forms of this disease usually present with failure to thrive, fever and an extensive skin rash. This is often in combination with diffuse lymphadenopathy, hepatosplenomegaly and normochoronic anemia with neutropenia and thrombocytopenia. Our patient demonstrated pancytopenia most likely secondary to extensive involvement of bone marrow. Marked involvement of thymus probably led to an inadequate immune response.

The clinical presentation of acute congenital histiocytosis may also include bleeding per rectum or protein loosing enteropathy when the gastrointestinal tract is involved [6, 7]. These symptoms were not seen in our patient.

Pulmonary involvement with congenital histiocytosis has been described in the literature [2]. In our patient, the pulmonary infiltrates appeared initially as diffuse reticulonodular densities in the lungs. The necrotic and hemorrhagic degeneration of these nodular infiltrates associated with pulmonary emphysema subsequently gave a cystic appearance to the lungs.

A definitive diagnosis of LCH requires the findings of Birbeck granules in Langerhans cells by electron microscopy [8]. In our case, electron microscopic examination was negative for Birbeck granules. However, the examination was done on an inappropriately preserved specimen (with paraffin), and this may have contributed to the failure of demonstrating Birbeck granules. The massive multiorgan infiltration with S-100 and PNA positive histiocytes seen in our patient are most consistent with disseminated LCH (Letterer-Siwe disease).

Other histiocytic disorders in infants and neonates include familial erythrophagocytic lymphohistiocytosis (FEL), virus-associated hemophagocytic syndrome (VAHS), and X-linked lymphoproliferative syndrome (XLP) [3]. Association with immunodeficiency, hypertriglyceridemia, and viral infection have been reported in those syndromes [8]. Our patient did not have any relevant family history or documented viral infection, thus making the diagnosis of FEL, VAHS, or XLP unlikely.

References

1. Yu CP, Tseng HH, Tu YC (1990) Congenital Letterer-Siwe disease with intrauterine fetal death: a case report and review of the literature. Taiwan I Hsueh Hui Tsa Chih 89: 806–810
2. Kagalwala TY, Kallapur SG, Rathore AS, Bharucha BA, Irani SF, Sane Y, Parikh DA (1989) Congenital histiocytosis X. Indian Pediatr 26: 292–296
3. Chu T, D'Angio GJ, Favara B, Ladisch S, Nesbit M, Pritchard J (1987) Histiocytosis syndromes in children. Lancet: I: 208–209
4. Dehner LP, Bamford JT, McDonald EC (1983) Spontaneous regression of congenital cutaneous histiocytosis X: report of a case with discussion of nosology and pathogenesis. Pediatr Pathol 1: 99–106
5. Marsh WL Jr, Lew SW, Heath VC, Lightsey AL (1983) Congenital self-healing histiocytosis-X. Am J Pediatr Hematol Oncol 5: 227–233
6. Lee RG, Braziel RM, Stenzel P (1990) Gastrointestinal involvement in Langerhans' cell histiocytosis (histiocytosis X): diagnosis by rectal biopsy. Mod Pathol 3: 154–157
7. Tamura T, Umetsu M, Motoya H, Yokoyama S (1980) Congenital Letterer-Siwe disease associated with protein losing enteropathy. Eur J Pediatr 135: 77–80
8. McClain K, Gehrz R, Grierson H, Purtilo D, Filipovich A (1988) Virus-associated histiocytic proliferations in children. Am J Pediatr Hematol Oncol 10: 196–205