# Congenital Self-Healing Langerhans Cell Histiocytosis with Pulmonary Involvement : Spontaneous Regression

AMORNSRI CHUNHARAS, M.D.*,
WASUTHIDA PABUNRUANG, M.D.*,
SURADEJ HONGENG, M.D.*

**Abstract**

Congenital self-healing Langerhans cell histiocytosis (CSHLCH) is a rare condition which may present at birth or during the neonatal period. It is usually characterized by eruption of multiple, discrete and red-brown papules and nodules which may increase in size and number during the first few weeks of life with spontaneous regression. Systemic signs are usually absent except for occasional mild hepatomegaly. The authors report a case of CSHLCH associated with multiple lung cysts with spontaneous regression. A healthy full term male infant presented at birth with numerous diffuse discrete dark-red papules sized 0.2-1.0 cm scattered on the eyelids, temporal areas of the scalp, neck, palms and soles. Histologic findings were mixed inflammatory infiltration of numerous histiocytes. Immunochemistry findings were S-100 and CD1a positive consistent with CSHLCH. Hepatomegaly and multiple lung cysts were detected at 1 month old. Since he was healthy, no medication was given except for close monitoring. At 2 months of age, hepatomegaly was resolved but the liver had sclerosing change. Skin lesions regressed completely at the age of 4 months. Lung cysts were markedly improved at 7 months old and completely resolved at 1 year old. Spontaneous regression in CSHLCH with lung involvement has never been reported in Thailand.

**Key word** : Congenital Self-Healing Histiocytosis, Langerhans Cell Histiocytosis, Lung Cyst

**CHUNHARAS A, PABUNRUANG W, HONGENG S**
**J Med Assoc Thai 2002; 85 (Suppl 4): S1309-S1313**

Congenital self-healing Langerhans cell histiocytosis (CSHLCH) or previously called congenital self-healing histiocytosis is the rarest form of Langerhans cell histiocytosis. The term histiocytosis-X has been replaced by Langerhans cell histiocytosis[1]. Hashimoto and Pritzker first described this disease in 1973[2]. It is a benign disorder, which is diagnosed at birth[3,4]. The skin is the predominant

* Department of Pediatrics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand.

organ involved and lesions may be widespread and discrete dark-red papules. Hence, the skin lesions make the baby look like a "blueberry muffin". Pulmonary involvement of this disease is usually reported in older children and adults(5). Treatment for this condition in previous reports mostly required chemotherapy(5). To our knowledge, this is the first case report of spontaneous regression of lung cysts in CSHLCH in Thailand.

## CASE REPORT

A 1-month-old Thai male infant was referred to our hospital with a history of multiple dark-red granulomatous-like papules, hepatomegaly and multiple lung cysts. He was a full-term healthy newborn. His skin lesions appeared at birth. Physical examinations revealed discrete dark-red papules sized 0.2-1.0 cm scattered on his eyelids, temporal areas of the scalp, neck, palms and soles (Fig. 1). Biopsy of the skin lesions obtained at one-week old revealed diffuse infiltration of mainly two types of neoplastic cells. One cell type was a large cell with eosinophilic cytoplasm and eccentrically located histiocytic-like nuclei. Anisonucleosis and presence of nucleoli in some cells with groove-like structure were noted. Binucleated and multinucleated cells scattered among diffuse large cells with a moderate number of eosinophils were observed. Some neoplastic cells contained PAS positive material in cytoplasm. Immunoperoxidase staining was positive for S-100 protein and CD1a. The above histological findings were consistent with CSHLCH. One month later, he developed hepatomegaly. Chest X-ray showed multiple thin wall cysts in both lungs (Fig. 2). Skull X-ray was normal. Complete blood count (CBC) revealed a hematocrit of 29.6 per cent, white blood cell count of 17,600/μl, neutrophil 60 per cent, lymphocyte 38 per cent, eosinophil 1 per cent, atypical lymphocyte 1 per cent and platelet counts of 492,000/μl. Serum immunoglobulin (Ig) determination revealed normal IgG, IgM and IgA levels. Urinary examination, blood urea nitrogen, creatinine and liver profile were normal. Serum lactic dehydrogenase (LDH) level was 657 U/L (normal 180-430 U/L) and alkaline phosphatase was 207 U/L (normal 145-420 U/L). Serologic studies for rubella, cytomegalovirus, herpes simplex and HIV were negative. Bone marrow aspiration revealed normocellular marrow showing unremarkable trilineage hematopoiesis with mild eosinophilia. Since he was healthy, he was closely observed with no medical intervention. Ultrasonography of the liver at two months old showed normal size with mild sclerosing change seen around the portal veins. At 4 months of age, all of the skin lesions had regressed leaving only atrophic scars. Chest X-ray showed marked improvement of the cystic lesions in both lung fields at 7 months old (Fig. 3). There was nearly complete regression at one year old (Fig. 4). He has been followed-up for 2 and a half years and remains in good condition.

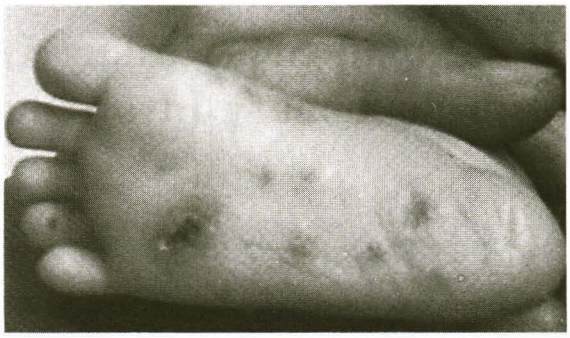

**Fig. 1. Dark-red granulomatous like papules on the right sole.**

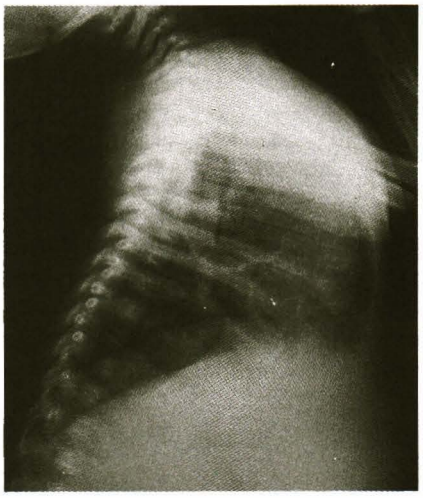

**Fig. 2. Chest X-ray shows multiple lung cysts at 1 month old.**

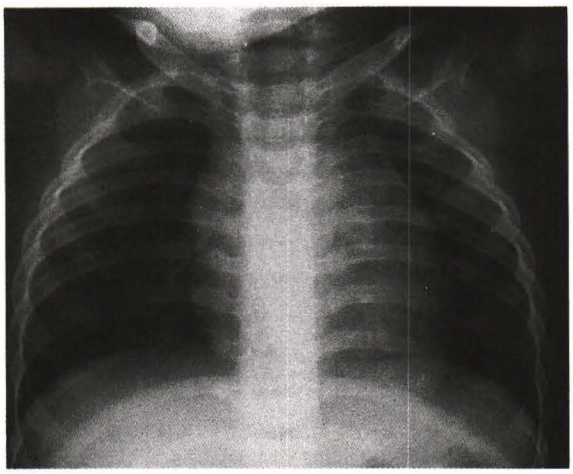

**Fig. 3. Chest X-ray shows marked improvement of multiple lung cysts at 7 months old.**

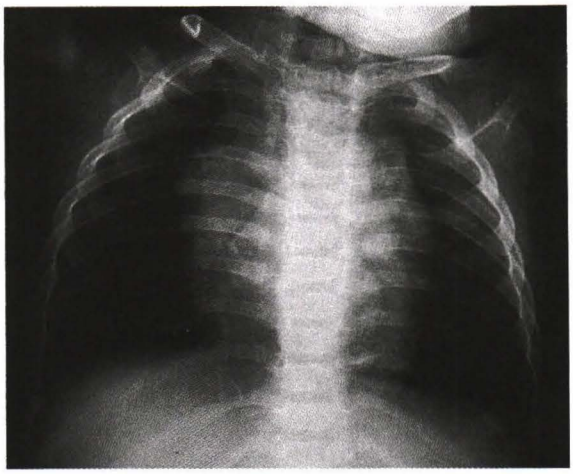

**Fig. 4. Chest X-ray shows total improvement of multiple lung cysts at 1 year old.**

## DISCUSSION

CSHLCH is a benign disorder diagnosed at birth. The skin is the predominant organ involved and will be resolved within a few months[4, 6-10]. There are six characteristic features of CSHLCH: 1) congenital symptomless papulonodules, 2) self-healing within a few months without recurrence, 3) no or mild systemic symptoms, 4) histopathology showing large mononuclear cells and multinucleated giant cells with ground-glass or foamy cytoplasm in the dermis and epidermis, 5) electron microscopy showing Birbeck granules and dense bodies (some with myelin-like lamination) and 6) immunoperoxidase staining positive for T6, HLA-DR and S-100[11,12]. Histology is usually a dense infiltration of large histiocytes in the middle and lower dermis. The histiocytes have kidney-shaped nuclei with irregular contours and abundant eosinophilic ground-glass cytoplasm with a variable number of PAS-positive granules. Multinucleated cells are invariably present. There are also lymphocytes and eosinophils. The tumor cells usually express CD1 and S100 positive. Electron microscopic evaluation demonstrates Birbeck granules or laminates dense bodies inside in 10-30 per cent of the histiocytes. The coexistence of laminated dense bodies with Birbeck granules has been proposed as a specific marker for this disease[9,13]. CSHLCH has a benign course with spontaneous regression of skin lesions and resolution of the visceral involvements such as liver, bone, heart, lungs and central nervous system[14]. This disease can progressively involve bone marrow and visceral organs [5,15]. Micronodular infiltration or cystic lesions in the lung with or without pneumothorax have mostly been reported in older children and adults[5,15]. There has been a reported case of a 15-year-old boy with diabetes insipidus and pulmonary involvement. He had 4 episodes of pneumothorax[16]. It is also important to carefully examine to detect other systemic involvement. Appropriate investigations include complete blood count, serum chemistry, liver function test, and skull, chest, and long bone roentgenography as well as abdominal ultrasonography.

The reported patient had many positive findings compatible with the diagnosis of CSHLCH which subsequently was confirmed by skin biopsy. At the present time, there is no definite recommendation for the treatment of systemic involvement of this condition and particularly chemotherapy which is quite toxic in young infants. Therefore, the patient was closely observed without medical intervention. He has been followed-up with serial CBC and monitored hepatic size by ultrasonography which showed normal size at 2 months old. Serial chest X-rays were

obtained and showed nearly complete regression at 1 year old. The disease usually has a favorable prognosis. However, long-term follow-up is required because pneumothorax has been reported in adult patients[8]. Moreover, relapsing of skin lesions and visceral involvements have been reported in older children and adults[14,17].

## SUMMARY

To the best of the authors' knowledge, this is the first case report of CSHLCH with multiple lung cysts with spontaneous regression in Thailand. Medical intervention is not required for systemic involvement in CSHLCH. Long-term follow-up for detecting complications and relapse is recommended.

(Received for publication on September 23, 2002)

## REFERENCES

1. Writing Group of the Histiocyte Society. Histiocytosis syndromes in children. Lancet 1987; I: 208-9.
2. Hashimoto K PM. Electron microscopic study of reticulocytoma. An unusual case of congenital, self-healing histiocytosis. Arch dermatol 1973; 107: 263-70.
3. Chun SI, Song MS. Congenital self-healing reticulohistiocytosis: Report of a case of the solitary type and review of the literature. Yonsei Med J 1992; 33: 194-8.
4. Schaumburg-Lever G, Rechowicz E, Fehrenbacher B, Moller H, Nau P. Congenital self-healing reticulohistiocytosis: A benign Langerhans cell disease. J Cutan Pathol 1994; 21: 59-66.
5. Ha SY HP, Fletcher M, Broadbent V, Pritchard J. Lung involvement in Langerhans' cell histiocytosis: Prevalence, clinical features, and outcome. Pediatrics 1992; 89: 466-9.
6. Jang KA, Ahn SJ, Choi JH, Sung KJ, Moon KC, Koh JK. Histiocytic disorders with spontaneous regression in infancy. Pediatr Dermatol 2000; 17: 364-8.
7. Shy SW, Lee WH, Chang YC, Wu W. A solitary congenital self-healing histiocytosis. Report of a case and review of the literature. Pathol Res Pract 1996; 192: 869-74.
8. Chevrel J, Barba G, Legrain-Lifermann V, et al. Self-healing Hashimoto-Pritzker histiocytosis. Arch Pediatr 2000; 7: 629-32.
9. Larralde M, Rositto A, Giardelli M, Gatti CF, Santos Munoz A. Congenital self-healing histiocytosis (Hashimoto-Pritzker). Int J Dermatol 1999; 38: 693-6.
10. Marsh WL Jr LS, Heath VC, Lightsey AL. Congenital self-healing histiocytosis-X. Am J Pediatr Hematol Oncol 1983; 5: 227-33.
11. Berger TG. LT, Headington JT. A solitary variant of congenital self-healing reticulohistiocytosis: Solitary Hashimoto-Pritzker disease. Pediatric Dermatology 1986; 3: 231-5.
12. Hashimoto K, Kagetsu N, Taniguchi Y, Weintraub R, Chapman-Winokur RL, Kasiborski A. Immunohistochemistry and electron microscopy in Langerhans cell histiocytosis confined to the skin. J Am Acad Dermatol 1991; 25: 1044-53.
13. Weedom D. Cutaneous infiltrates. In: Weedom D. The skin. London: Churchill Livingstone, 1992: 995-1050.
14. Longaker MA, Frieden IJ, LeBoit PE, Sherertz EF. Congenital "self-healing" Langerhans cell histiocytosis: The need for long-term follow-up. J Am Acad Dermatol 1994; 31: 910-6.
15. Nondahl SR, Finlay JL, Farrell PM, Warner TF, Hong R. A case report and literature review of "primary" pulmonary histiocytosis X of childhood. Med Pediatr Oncol 1986; 14: 57-62.
16. Okten A MH, Erduran E, Aslan Y, Gumele HR, Ozoran Y. Langerhans cell histiocytosis associated with recurrent pneumothorax: A case report. Turk J Pediatr 1996; 38: 125-30.
17. Whitehead B, Michaels M, Sahni R, Strobel S, Harper JI. Congenital self-healing Langerhans cell histiocytosis with persistent cellular immunological abnormalities. Br J Dermatol 1990; 122: 563-8.

# รายงานผู้ป่วย Congenital Self-Healing Langerhans Cell Histiocytosis ที่มีความผิดปกติในปอด

*อมรศรี ชุณหรัศมิ์, พ.บ.*,*
*วสุธิดา ปะบุญเรือง, พ.บ.*, สุรเดช หงส์อิง, พ.บ.**

โรค congenital self-healing Langerhans cell histiocytosis (CSHLCH) เป็นโรคในกลุ่ม Langerhans cell histocytosis ที่พบน้อยที่สุด ผู้เขียนรายงานผู้ป่วยเด็กทารกแรกเกิดเพศชายที่มาด้วยตุ่มที่ผิวหนัง ตรวจร่างกายพบ dark-red papules ขนาด 0.2-1.0 เซนติเมตร กระจายที่ขมับทั้งสองข้าง, หนังตา, ศีรษะ, คอ, ฝ่ามือ และฝ่าเท้า เมื่ออายุ 1 เดือน พบมีตับโต, เอ็กซ์เรย์ปอดพบว่ามีความผิดปกติในปอดทั้งสองข้าง ลักษณะเป็นถุงลมใหญ่ ผลการตัดชิ้นเนื้อส่งตรวจทางพยาธิวิทยาและ immumoperoxidase stain พบว่ามี histiocyte ซึ่งย้อมติดสี S-100 protein และ CD1a ซึ่งเข้าได้กับโรค CSHLCH เนื่องจากผู้ป่วยแข็งแรงและไม่มีอาการผิดปกติใด ๆ จึงไม่ได้ให้การรักษาด้วยยาเคมีบำบัด แต่ติดตามผู้ป่วยต่อไปอย่างใกล้ชิด พบว่า ตับยุบลงขนาดเท่าปกติเมื่ออายุได้ 2 เดือน ความผิดปกติทางผิวหนังหายหมดภายใน 4 เดือน เหลือแต่เพียงรอยแผลเป็นผลเอ็กซ์เรย์ปอดเป็นระยะ ๆ พบว่าความผิดปกติในปอดดีขึ้นชัดเจนเมื่ออายุ 7 เดือน และหายจนปกติเมื่ออายุประมาณ 1 ปี ขณะนี้ผู้ป่วยอายุ 2 ปีครึ่ง แข็งแรงและตรวจไม่พบความผิดปกติอย่างอื่น รายงานนี้เป็นรายงานโรค CSHLCH ที่มีความผิดปกติของปอดที่หายเองโดยไม่ต้องให้การรักษาด้วยยาเคมีบำบัด อย่างไรก็ตามยังคงต้องติดตามดูแลผู้ป่วยอย่างใกล้ชิดต่อไป

**คำสำคัญ** : ฮีสติโอไซโตซีสแต่กำเนิดที่หายเอง, แลงเกอร์ฮานเซลล์, ฮีสติโอไซโตซีส, ถุงลมในปอด

**อมรศรี ชุณหรัศมิ์, วสุธิดา ปะบุญเรือง, สุรเดช หงส์อิง**
**จดหมายเหตุทางแพทย์ ฯ 2545; 45 (ฉบับพิเศษ 4): S1309-S1313**

* ภาควิชากุมารเวชศาสตร์, คณะแพทยศาสตร์ โรงพยาบาลรามาธิบดี, มหาวิทยาลัยมหิดล, กรุงเทพ ฯ 10400