Pulmonary Langerhans cell histiocytosis presenting as skin lesion in a young child exposed to chronic passive smoking: A case report

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ABSTRACT

Pulmonary Langerhans cell histiocytosis (PLCH) is a rare disease in childhood. We report a case of a 3-year-old boy who was exposed to chronic passive smoking in family presented with PLCH with isolated skin involvement. The boy presented with a history of recurrent respiratory tract infections requiring intensive care unit admissions for severe respiratory distress. The chest X-ray showed bilateral honeycombing of lungs, which was further confirmed by chest computed tomography showing diffused bilateral multiple cystic lesions with ground-glass haziness of lung parenchyma. Skin biopsy from suspected cutaneous lesions confirmed the diagnosis by positive S-100 and CD-1a. After initiating intensive chemotherapy, the patient showed significant improvement. Based on our experience, it can be suggested that knowledge of such condition with high clinical suspicion and simple skin biopsy can be a valuable modality in diagnosing PLCH in cases without putting the other internal organs at risk.

Key words: *CD-1a, Cutaneous Langerhans cell histiocytosis, Pulmonary Langerhans cell histiocytosis, S-100*

Langerhans's cell histiocytosis (LCH) is a rare disorder characterized by proliferation and activation of mononuclear phagocyte system, which may infiltrate single or multiple organs. It is common in infants and young children. The incidence of LCH is quite low and accounts for about 4–5 cases/million children. Signs and symptoms of LCH are non-specific and clinical presentation is highly variable which ranges from isolated, self-resolving skin, and bone lesions to life-threatening multisystem disease. The characteristic radiographic finding is considered as the most valuable clue for diagnosis. Lung involvement is a well-known complication of multisystem LCH, both in children and in adult. Isolated lung involvement has been found more in adults than in children, specifically, with a history of chronic cigarette smoking. Whether passive smoking can lead to isolated pulmonary LCH (PLCH) in children is not known. Here, we report a case in a very young boy with PLCH involving only skin with long history of passive smoking.

CASE REPORT

A 3-year-old developmentally normal male child presented to the emergency with chief complaint of cough and difficulty in breathing for 15 days. According to the mother, the illness started at the age of 7 months which necessitated intensive care unit admission for a week and was treated for necrotizing pneumonia. The patient was not on any regular medication at admission including bronchodilator. Since then, there were multiple episodes of recurrent respiratory tract infections, hospitalization, and ventilation and the patient was on anti-tubercular therapy for 6 months, 1 year before this visit, based on chest computed tomography (CT), showing evidence of tuberculosis (documents not available).

He had associated chest pain with cough and hurried breathing, but no history of feeding difficulties, cyanosis, palpitation, or history suggestive of paroxysmal nocturnal dyspnea or swelling of body. In between the episodes, the child was normal but for the past 5 months, the patient had rapid breathing, which was present even at rest. He was the first birth order child, a product of non-consanguineous marriage with uneventful birth history, immunized as per national immunization schedule, with non-contributory family history (younger 1½-year-old female healthy sibling), except that father was a chronic cigarette smoker.

On examination, the patient was afebrile, with a respiratory rate – 44/min regular, SpO_2 of 82% at room air, and 94% with high flow oxygen through nasal prongs (3 L/min). The patient was severely underweight with 8 kg weight and 80 cm height (<3 Z score). On respiratory system examination, he had severe intercostal and subcostal retractions, decreased chest expansion, and air entry bilaterally with coarse crepitation all over the lung fields.

The patient was given respiratory support with continuous positive airway pressure (5 mm of H_2O) and IV antibiotics were started. On day 2 of admission, the patient was put on mechanical ventilation in view of worsening of respiratory distress. The chest X-ray was

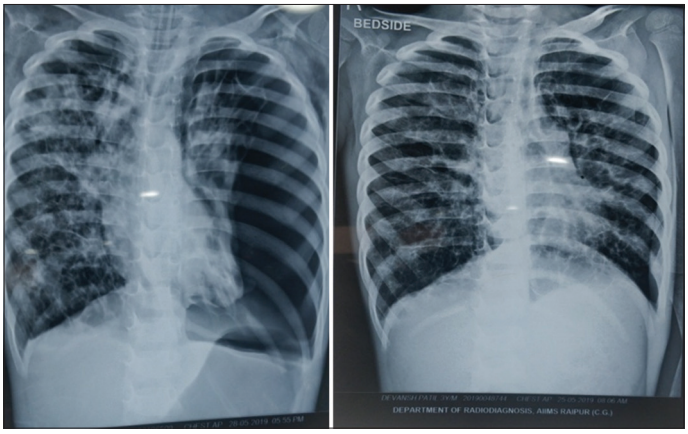

Figure 1: X-ray chest showing diffuse honeycombing of lungs and pneumothorax on left side

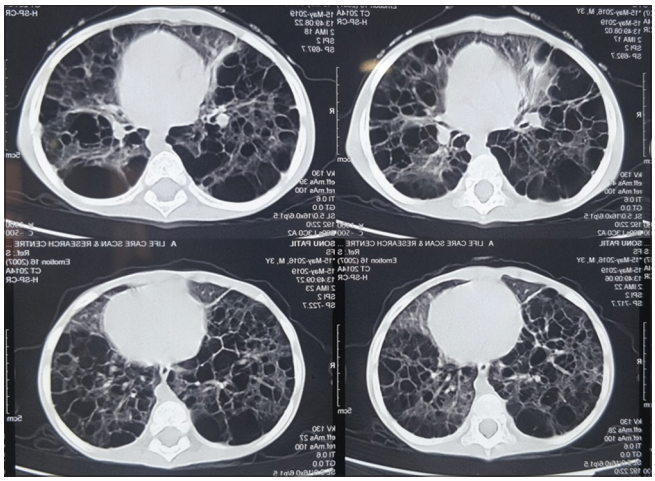

Figure 2: High-resolution computed tomography of chest showing diffuse cystic changes in bilateral lungs

suggestive of heterogeneous opacities in bilateral lung fields with multiple cystic cavities (Fig. 1), and the CT scan was suggestive of multiple cystic lesions throughout the lung fields causing extensive architectural distortion of the lungs (Fig. 2) highly suggestive of LCH-like changes, which was the first clue to the diagnosis.

Skin biopsy was done from small petechial like spots along with scaly seborrhea like plaques behind the ears and back to rule out skin involvement (Fig. 3). The patient developed left-sided spontaneous pneumothorax twice during the hospital stay for which implantable cardioverter-defibrillator was put and pleurodesis was done with bleomycin to prevent recurrent pneumothorax. The lung biopsy was planned but postponed, waiting for skin biopsy report. The skin biopsy was suggestive of infiltration of abnormal cell which comprised round to plasmacytoid cells with abundant eosinophilic cytoplasm and nuclear grooves into the papillary dermis of skin, diagnostic of LCH. Immunohistochemistry showed diffuse cytoplasmic S-100 and membranous CD-1a positivity (Fig. 4).

X-ray skull and complete radiographic survey were normal. The child also had polyuria and polydipsia and urine osmolality was normal. Ultrasonography abdomen was essentially normal. Bone marrow examination was unremarkable. The patient was started on intensive chemotherapy with prednisolone, etoposide,

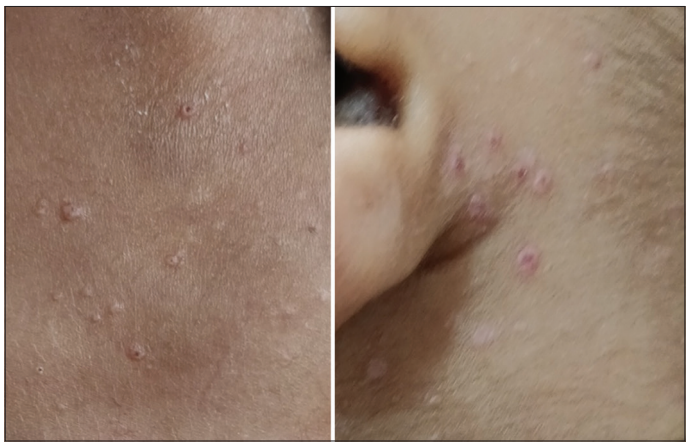

Figure 3: Papular, umbilicated with some healed hypopigmented lesions of cutaneous Langerhans cell histiocytosis on anterior chest and near ear lobule

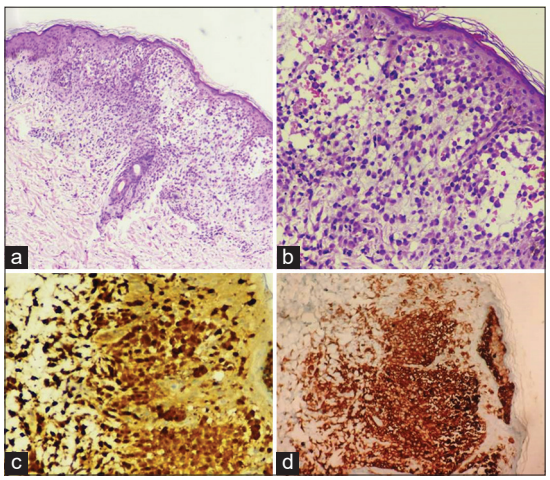

Figure 4: The histopathology and immunohistochemistry images showing (a) a tumor infiltrating into the papillary dermis of skin, low power (HE ×40), (b) high-power image showing tumor comprises round to plasmacytoid cells with abundant eosinophilic cytoplasm and nuclear grooves (HE ×100), (c) S-100 stain showing diffuse nuclear and cytoplasmic positivity in tumor cells (IHC ×100), (d) CD1a stain displaying diffuse intense membranous positivity in tumor cells

and vinblastine. After giving one cycle of etoposide, 21st day, it was stopped after review from expert and possibility of future second malignancy. The patient gradually improved and was off ventilator and showed good response to treatment. Repeat X-ray showed good response to chemotherapy with significant decrease in cystic lesions. The patient was planned for 1–2 years of chemotherapy based on positron emission tomography scan follow-up.

DISCUSSION

The hallmark of LCH is the accumulation of Langerhans cell-like dendrites in one or more tissues or organs. The most common site of involvement is bone and skin, but virtually any organ or system can be involved (bone, skin, lymph node, lung, and central nervous system). It is one of the rare diseases with an estimated incidence of 2.6–8.9 cases per million per year in children under 15 years of age [1]. The peak age at diagnosis is 2 years, but it

can present anytime from birth to adulthood. Isolated PLCH in adults is closely associated with cigarette smoking, which usually resolves with cessation of smoking [2]. Cigarette smoking has not been linked to LCH in children. Although it is difficult to prove causative association between LCH and smoking in children, only one case each in infant and adolescent has been reported so far in literature, suggesting a causal relationship [3].

Multisystemic LCH predominantly occurs in children, and pulmonary involvement is seen in 20–50% of cases [4,5]. The clinical manifestations of LCH are protean. The patient may present with localized pain, soft tissue and skin involvement, lymphadenopathy, organomegaly, cytopenia, and diabetes insipidus. PLCH usually presents with chronic cough, fever, dyspnea, tachypnea, chest pain, and pneumothorax. Recurrent pneumothorax is a real concern with fatal tension pneumothorax as reported by Catalina *et al*. [6]. Involvement of two or more organ systems is referred to as multisystem LCH (MS-LCH). In about half of MS-LCH cases, risk organs, i.e., liver, spleen, and hematopoietic systems are affected [4,5]. In our case, only lungs and skin were involved. There were no specific clinical features, physical examination findings, or routine laboratory tests which were suggestive of the diagnosis of LCH.

Radiologic finding plays an important role in the diagnosis of LCH, as they can be the first clue [7]. In our case, reticulonodular pattern on chest X-ray and multiple cystic lesions in bilateral lung fields in high-resolution CT gave us the first clue to the diagnosis. LCH lesions at all sites share common histopathologic features as accumulation of large neoplastic Langerhans cell with dense pink cytoplasm and distinctive cleaved nuclei admixed with inflammatory cells. In all sites, the neoplastic Langerhans cell expresses the LC markers CD1a and Langerin as well as S100 protein and fascin, as discussed by Vassallo *et al*. [8]. In our case, we preceded with biopsy of the most accessible site, i.e., the skin, because of its less invasive nature and lower risk of complications in comparison to lung biopsy, which came positive for LCH. In suspected LCH cases, complete evaluation for disease extent is indicated.

The classic radiological finding like cystic area formation diffusely in bilateral lungs is highly suggestive of PLCH, as reported by Bano *et al*. [7]. The author has witnessed and published a similar case which helped in making an early diagnosis [9-12]. To complete the evaluation and assessment of other systems, we did complete skeletal survey, bone scan, ultrasound abdomen, and bone marrow biopsy which all came unremarkable. Children with MS-LCH are at an increased risk of morbidity and mortality, and hence, an aggressive treatment is justified. In our case, we started with intensive chemotherapy with prednisolone, etoposide, and vinblastine and other chronic diseases, within 1 week of admission after excluding infections such as tuberculosis and cystic fibrosis. The skin biopsy was done and the patient was put on LCH protocol for 10 days after admission. This was in accordance with the protocol reported by Allen *et al*. [13]. The patient was discharged after 4 weeks when steroid was put on tapering mode and oxygen was removed. The patient improved and was followed up for the first 6 months with good response and asked to continue medication and follow-up as per protocol.

The children who did not respond promptly to vinblastine and prednisolone had an unfavorable prognosis with survival rate of only 10–34%. The children with refractory LCH can be treated with allogeneic hematopoietic stem cell transplantation with guarded prognosis [14]. Some children experience reactivation after initial improvement; therefore, close follow-up with complete physical examination and growth monitoring is necessary. An increase in erythrocyte sedimentation rate and platelet counts can be of help to identify disease reactivation.

CONCLUSION

Chronic passive smoking may predispose children with pulmonary LCH which should be verified with adequate sample size. In our case, diagnosis was delayed as the patient reported late with diffuse pulmonary involvement. More invasive procedures like lung biopsy can be deferred as biopsy from other accessible sites such as skin can still give definite clues for the diagnosis of LCH.

REFERENCES

1. Maurizio A. Langerhans cell histiocytosis in children: From the bench to bedside for an updated therapy. Br J Haematol 2016;173:663-70.
2. Aydin GB, Kibar E, Han U, Kale Y, Aslan A, Kose G. Pulmonary Langerhans cell histiocytosis in an infant: Can passive smoking accelerate the disease progress? Pediatr Pulmonol 2007;42:565-7.
3. Çıtak EÇ, Ak E, Sağcan F, Balcı Y, Bozdoğan-Arpacı R, Kuyucu N. Primary pulmonary Langerhans cell histiocytosis associated with smoking in an adolescent boy. Turk J Pediatr 2017;59:586-9.
4. Drutz JE. Histiocytosis. Pediatr Rev 2011;32:218-9.
5. Windebank K, Nanduri V. Langerhans cell histiocytosis. Arch Dis Child 2009;94:904-8.
6. Catalina MV, Isabel D, Gema RV. Tension pneumothorax as an unusual cause of isolated pulmonary histiocytosis in paediatrics. Arch Bronconeumol 2011;47:213-7.
7. Bano S, Chaudhary V, Narula MK, Anand R, Venkatesan B, Mandal S, *et al*. Pulmonary Langerhans cell histiocytosis in children: A spectrum of radiologic findings. Eur J Radiol 2014;83:47-56.
8. Vassallo R, Ryu JH, Colby TV, Hartman T, Limper AH. Pulmonary Langerhans'-cell histiocytosis. N Engl J Med 2000;342:1969-78.
9. Kanik-Yuksek S, Ozkaya-Parlakay A, Gulhan B, Ozyoruk D, Karakus E, Cinel G, *et al*. A rare diagnosis in children: Isolated pulmonary Langerhans cell histiocytosis. Clin Respir J 2018;12:355-6.
10. Adams EP, Sauceda D, Oliver J, Cecalupo A. Isolated pulmonary Langerhans cell histiocytosis in a 17-year-old male. J Pediatr Hematol Oncol 2007;29:121-4.
11. Jang H, Kim YH, Kim KW, Sohn MH, Lyu CJ. Isolated pulmonary Langerhans cell histiocytosis in a 10-month-old infant. Allergy Asthma Respir Dis 2018;6:179-83.
12. Verma S, Jondhale S, Bansal D, Radotra B, Singhi S. Iodopovidone pleurodesis for isolated pulmonary Langerhan's cell histiocytosis in a two year old child. Indian J Pediatr 2014;81:715-8.
13. Allen CE, Ladisch S, McClain KL. How I treat Langerhans cell histiocytosis. Blood 2015;126:26-35.
14. Narula G, Pradhan ND, Arora B, Banavali S. Treatment of Langerhans cell histiocytosis with a modified risk-adapted protocol-experience from a tertiary cancer institute in India. Pediatr Blood Cancer 2018;65:e27028.

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