Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 1s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Uncommon Oral Manifestations and Growth Failure in A Pediatric Multisystem Langerhans Cell Histiocytosis: A Case Report

Dr. Kavya Janardhan[1], Dr. Azmathulla Khan[2], Dr. Mithila Das Mazumder[3], Dr. Manjushree Pushpa[4], Dr. SL Akhila Swaraj[5], Dr. Santoshkumar S Asangi[*6]

[1]Post Graduate-3 , Department of Paediatrics, Vydehi Institute of Medical Sciences and Research Centre,Bangalore-560066, Email ID: Kavyareddy378@gmail.com

[2]Post Graduate-2, Department of Paediatrics, Vydehi Institute of Medical Sciences and Research Centre, Bangalore-560066, Email ID: azmathk97@gmail.com

[3]Associate Professor, Department of Paediatrics, Vydehi Institute of Medical Sciences and Research Centre, Bangalore-560066, Email ID: mithila5435@vimsmail.com

[4]Senior Resident, Department of Paediatrics, Vydehi Institute of Medical Sciences and Research Centre, Bangalore-560066, Emai ID: manjushreepushpa@gmail.com

[5]Post Graduate-2, Department of Paediatrics, Vydehi Institute of Medical Sciences and Research Centre, Bangalore-560066, Email ID: akhila.swaraj@gmail.com

[*6]Corresponding Author

Senior Resident,

Department of Medical Oncology, Vydehi Institute of Medical Sciences and Research Centre,Bangalore-560066, Email ID: asangisantosh@gmail.com

Cite this paper as: Dr. Kavya Janardhan, Dr. Azmathulla Khan, Dr. Mithila Das Mazumder, Dr. Manjushree Pushpa, Dr.SL Akhila Swaraj, Dr. Santoshkumar S Asangi, (2025) Uncommon Oral Manifestations and Growth Failure in A Pediatric Multisystem Langerhans Cell Histiocytosis: A Case Report. *Journal of Neonatal Surgery*, 14 (1s), 1006-1009.

ABSTRACT

Langerhans cell histiocytosis (LCH) is a rare condition characterized by the clonal proliferation of Langerhans cells, leading to varying degrees of organ dysfunction. This report presents a challenging case of multisystem LCH in a 1-year-8-month-old female, exhibiting symptoms like gingival hypertrophy, cutaneous lesions, and failure to thrive. Diagnosis was confirmed by histopathology and immunohistochemistry, which revealed CD1a-positive Langerhans cells. The patient underwent chemotherapy, achieving significant clinical improvement. This report emphasizes the need for vigilance when evaluating pediatric patients with nonspecific symptoms and the importance of a multidisciplinary approach in diagnosing and managing this rare disorder.

Keywords: *Gingival hypertrophy, failure to thrive, Langerhans cell histiocytosis*

1. INTRODUCTION

Langerhans cell histiocytosis (LCH) is a hematological disorder marked by abnormal proliferation of immature myeloid dendritic cells derived from bone marrow. These Langerhans cells infiltrate various organs, including the skin, bone, and lymph nodes (1). The incidence of LCH is about 5-9 cases per million annually in children under 15 years and 1 per million in individuals older than 15 years (2). Despite ongoing research, its etiology remains elusive, with potential environmental, infectious, immunologic, and genetic factors implicated.

Oral involvement often represents the first manifestation of LCH. However, initial symptoms are typically nonspecific, leading to frequent misdiagnoses and delayed treatment. Diagnosis combines clinical and radiological findings with histopathological evidence of histiocyte infiltration, displaying ultrastructural or immunophenotypic features characteristic of Langerhans cells (2). Emerging treatments include monoclonal antibody therapy targeting CD1a and gene transfer into hematopoietic progenitor cells (3).

Here, we present a case of multisystemic LCH in a child presenting with gum hypertrophy, seborrhoeic dermatitis, and failure to thrive. A thorough evaluation confirmed the diagnosis of multisystemic LCH.

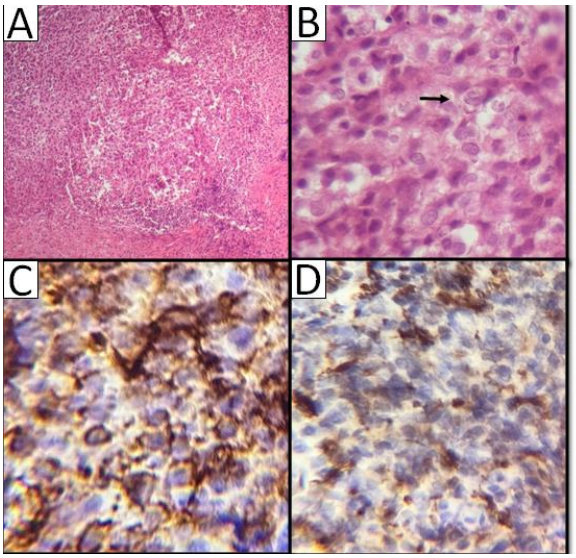
2. CASE REPORT

A 1-year-8-month-old female, the third child of a non-consanguineous marriage, presented with low-grade fever predominantly at night for one month, accompanied by left ear discharge, gum hypertrophy, mobile teeth, severe halitosis, excessive drooling, and feeding refusal for one week. Symptoms had been recurrent since 11 months of age, alongside poor weight gain, prompting repeated hospital visits and antibiotic treatments. The mother also reported scaly scalp lesions in the past. Developmental delays in gross motor and language milestones were noted.

On examination, the child appeared toxic, with height and weight below the third percentile and a mid-upper arm circumference (MUAC) of 11 cm. Cervical lymphadenopathy was evident, with the largest nodes measuring 2.5×1.5 cm (right, level II) and 2×1.5 cm (left, level II). No organomegaly was present. Primary differential diagnoses included primary immunodeficiency disorders.

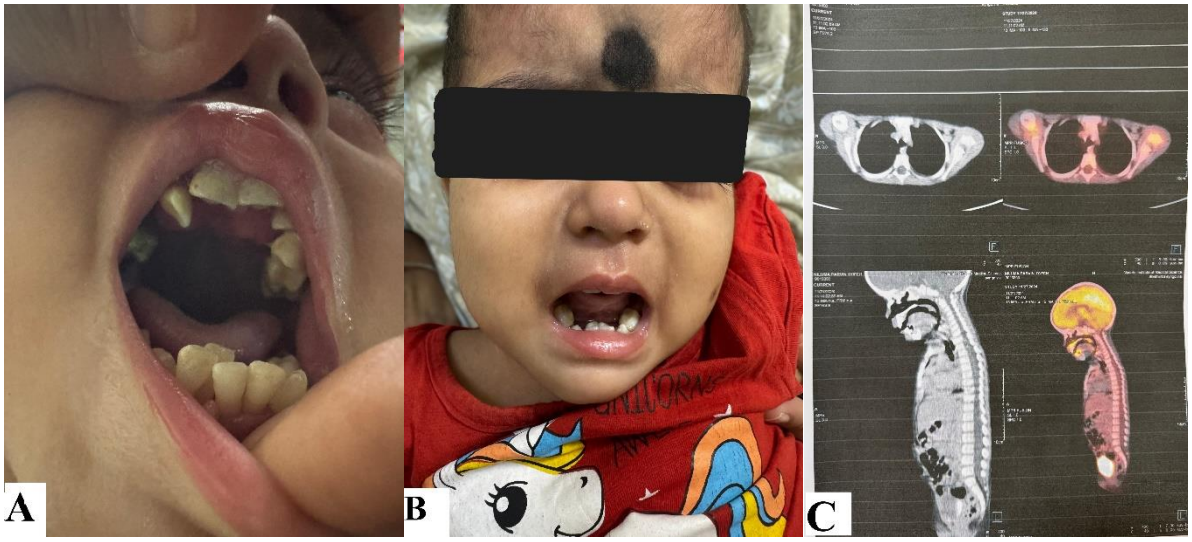
Investigations revealed hemoglobin at 9.7 g/dL, with a peripheral smear showing moderate microcytic hypochromic anemia. Total leukocyte count was 11,400 per mm³, platelets 428,000 per mm³, ESR 44 mm/hr, and CRP 8.3 mg/dL. Coagulation profiles were normal. A chest X-ray showed absence of the thymus shadow. FNAC of cervical lymph nodes was inconclusive, and ear discharge culture grew Pseudomonas, treated with IV antibiotics based on sensitivity testing. Immunoglobulin levels and flow cytometry of T, B, and NK cells were normal.

Biopsy of the gingiva performed by dental specialists revealed hyperparakeratinized stratified squamous epithelium and fibrovascular stroma containing histiocytes with reniform nuclei, nuclear grooves, eosinophils, and multinucleated giant cells. Immunohistochemistry confirmed CD1a and CD68 positivity, establishing the diagnosis of LCH.



A. H&E(10x): Sheets of histiocytes admixed with eosinophils and multinucleated giant cells.
B. H&E(40x): Histiocytes show reniform nuclei, prominent nuclear grooves.
C. IHC------(40x): Membranous staining in tumor cells
D. IHC------(40x): Golgi dot like membranous staining in tumor cells

PET CT Showed - Diffuse hypermetabolic bulky lymphoid tissue in bilateral tonsillar fossa and retropharyngeal region of nasopharynx, thickened upper and lower gingival mucosa, Low-grade hypermetabolic mucosal thickening in bilateral maxillary sinuses, Hypermetabolic bilateral level IB, bilateral level II, bilateral level Ill cervical lymph nodes and Low grade hypermetabolic lytic lesion in left occipital bone. Having Skeletal, Skin and lymph node involvement, the child was diagnosed as a case of Multisystemic LCH with low risk. Chemotherapy was planned with initial induction therapy with Continuous oral prednisone (PRED) 40mg/m2 daily in three divided doses for 4 weeks, tapering over a period of 2 weeks (20mg/m2 at week 5, 10mg/m2 at week 6) and Vinblastine (VBL) 6mg/m2/dose i.v. bolus on day 1 of weeks 1, 2, 3, 4, 5, 6.



A: Gum Hypertrophy, B: Mobile teeth, C:PET CT

3. DISCUSSION

Formerly known as histiocytosis X, the term Langerhans cell histiocytosis (LCH), is a clinically diverse malignancy characterised by inflammatory lesions with infiltrating CD1a+/CD 207+ pathologic Dendritic cells. The annual incidence of LCH in children younger than 15 years of age is around 5 to 9/million and 1/million in patients older than 15 years of age (2). It is usually encountered in children between 1 and 15 years of age with a peak incidence between 2 and 4 years of age, with male predilection twice that of female(4).

Langerhans cells are dendritic mononuclear cells which are generally found in the epidermis, mucosa, lymph nodes, and bone marrow. They generally present antigens to T- lymphocytes; however, literature review of

LCH indicates that Langerhans cell histiocytes proliferate monoclonally, resulting in the destruction of hard and soft tissues(5). In LC from LCH lesions, constitutive activity of the mutant BRAF V600E protein is predicted to bypass the requirement for mitogen induced activation of RAF by RAS. This may lead to dysregulated signaling through the MEK-ERK pathway and thereby favor the survival and proliferation of lesional LCH cells.

LCH can be classified as Unifocal LCH: Often involves bones (eosinophilic granuloma), presenting as lytic lesions; Multifocal Unisystem LCH: Multiple areas within one system, typically bone or skin; Multisystem LCH: Involves two or more systems, with risk organs being the liver, spleen, and bone marrow, which denote a higher risk group. Specific Manifestations include Pulmonary LCH: Predominantly in adults, linked to smoking, showing nodules or cysts on imaging; Endocrine System: Diabetes insipidus from hypothalamic-pituitary involvement is common; Gastrointestinal: Rare but can lead to significant morbidity.

The clinical features are highly variable and can involve any organs except kidney and gonads. Children demonstrate multisystem involvement with initial general clinical presentation includes skin rash, cradle cap, otitis media, fever, organomegaly, anemia, pain and pathological fracture of involved bone, and diabetes insipidus(6). In our case the child presented with oral manifestations which is the most common presenting feature according to Greenberg et al(7). It includes nonspecific multiple presentations such as gingival hypertrophy, oral ulceration, mobility of teeth with alveolar expansion, jaw pain, facial swelling, and mental nerve anesthesia. The child also had history of recurrent otitis media and seborrhoric dermatitis which was resistant to treatment.

The radiological features of Langerhans Cell Histiocytosis (LCH) are attributed to bone destruction caused by the infiltration of Langerhans cells, a pattern consistent across all three forms of the disease. This osteolytic process can affect any bone, but in the head and neck region, it most commonly involves the posterior mandible. In the disseminated form of LCH, multiple areas of bone destruction occur, varying in size, often leading to cortical perforation and pathological fractures. Involvement of the superficial alveolar bone presents as a characteristic scooped-out appearance, with teeth floating, displacement, periodontitis, and early tooth loss. Occasionally, mucosal lesions may develop as gingival masses if the disease extends beyond the bone.

As there are no pathognomonic clinical and radiographic features of LCH, the diagnosis of LCH is based on histopathological examination. Microscopic examination shows an inflammatory pattern consisting of eosinophils, neutrophils, lymphocytes, and macrophages in addition to the LCs. LCH cells are generally large, round to oval in shape, with a coffee-bean nuclear groove, and without the branching that characterizes inflammatory CD1a1 dendritic cells. LCH express the histiocyte

markers CD1a, S100, and CD207 (langerin) and contain Birbeck granules. Birbeck granules are intracytoplasmic rod-shaped organelles with central striation that can be demonstrated on electron microscopy.

The treatment of multifocal Langerhans cell histiocytosis (LCH) typically involves a combination of surgical excision, chemotherapy, and/or radiation therapy, depending on the extent and location of the disease. In addition to many therapeutic combinations, new therapeutic strategies are represented by monoclonal CD-1a-antibody-therapy and gene transfer into haemopoietic progenitor cells(3). In our case, only chemotherapy was pursued as the treatment option. Prognosis is poor in younger patients or those multifocal disease. Therefore, early diagnosis and treatment is important for control and better prognosis of disease. Due to the multifocal nature of LCH and its potential for delayed recurrence or progression, long-term follow-up is essential. This ongoing monitoring is necessary to assess the disease's course, detect any potential relapses, and manage any long-term effects of treatment.

This case study shows a great degree of clinical suspicion is needed to diagnose such cases and also the need for multidisciplinary approach for the management of such cases.

REFERENCES

[1] Altay MA, Sindel A, Özalp Ö, et al. Langerhans cell histiocytosis: a diagnostic challenge in the oral cavity. Case Rep Pathol.2017;2017:1- 6.

[2] Emile JF, Abla O, Fraitag S, Horne A, Haroche J, Donadieu J, Requena-Caballero L, Jordan MB, Abdel-Wahab O, Allen CE, Charlotte F, Diamond EL, Egeler RM, Fischer A, Herrera JG, Henter JI, Janku F, Merad M, Picarsic J, Rodriguez-Galindo C, Rollins BJ, Tazi A, Vassallo R, Weiss LM; Histiocyte Society. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. Blood. 2016 Jun 2;127(22):2672-81. doi: 10.1182/blood-2016-01-690636. Epub 2016 Mar 10. PMID: 26966089; PMCID: PMC5161007.

[3] Brenner M. Current status of gene transfer into hamatopoietic progenitor cells: application to langerhans cell histiocytosis. Br J Cancer suppl.1994;23:S56-7

[4] Yashoda-Devi B, Rakesh N, Agarwal M. Langerhans cell histiocytosis with oral manifestations: A rare and unusual case report. J Clin Exp Dent 2012;4:e252-5.

[5] Rao DG, Trivedi MV, Havale R, Shrutha SP. A rare and unusual case report of Langerhans cell histiocytosis. J Oral MaxillofacPathol. 2017;21(1):140- 144. doi:10.4103/jomfp.JOMFP

[6] Tesluk EW, Szutkowski Z, Kawecki A. Langerhans cell histiocytosis of bone – A case report and review of literature. J Onco 2003;53:161-4.

[7] Greenberger JS, Crocker AC, Vawter G, Jaffe N, Cassady JR. Results of treatment of 127 patients with systemic histiocytosis. Medicine (Baltimore) 1981;60:311-38

[8] Kumar YP, Agrawal J, Mohanlakshmi J, Kumar PS. Langerhans cell histiocytosis revisited: Case report wit review. Contemp Clin Dent 2015;6:432-6.

[9] Badalian-Very G, Vergilio JA, Degar BA, MacConaill LE, Brandner B, Calicchio ML, Kuo FC, Ligon AH, Stevenson KE, Kehoe SM, Garraway LA, Hahn WC, Meyerson M, Fleming MD, Rollins BJ. Recurrent BRAF mutations in Langerhans cell histiocytosis. Blood 2010; 116: 1919-1923.

[10] Berres ML, Merad M, Allen CE. Progress in understanding the pathogenesis of Langerhans cell histiocytosis: back to Histiocytosis X? Br J Haematol 2015; 169: 3-13.