**Title Page**

Langerhans cell histiocytosis presenting with Diabetes insipidus in a 2 years old child: A Case Report

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**INTRODUCTION**

Langerhans cell histiocytosis (LCH) is a neoplastic disorder characterized by the proliferation of early myeloid cells within the bone marrow. This condition is often caused by a clonal mutation in the RAS/MAP Kinase signaling pathway. Although LCH is relatively uncommon in children, it involves the clonal expansion of Langerhans cells, which are identifiable by the expression of CD1a, Langerin, and other markers, and the presence of Birbeck granules, as seen through electron microscopy [1,2].

In this report, we describe a child with disseminated LCH who presented with failure to thrive, diabetes insipidus, osteolytic bone lesions, and an extensive cutaneous eruption.

**CASE HISTORY/EXAMINATION**

A 2-year-old boy was admitted to the pediatrics ward at Black Lion Hospital due to failure to thrive. He presented in a cachectic state with a mid-upper arm circumference (MUAC) of 11 cm and a weight-for-height measurement below -3 standard deviations on the WHO Z-score. The child appeared mildly lethargic. Over the past year, he had experienced progressive weight loss, which was accompanied by vomiting, polyuria, and polydipsia. During this time, he also developed an extensive skin eruption on his scalp.

Upon examination, multiple erythematous papules with purulent discharge were observed throughout the scalp, extending to involve the left eye. Additionally, hypopigmented macules and papules were noted on the chest. No respiratory distress, lymphadenopathy, or hepatosplenomegaly was detected.

**METHODS**

**DIFFERENTIAL DIAGNOSIS**

The most important differential diagnoses that were considered for this patient are inborn errors of metabolism and leukemias.

**INVESTIGATIONS**

Investigations revealed moderate microcytic anemia suggestive of iron deficiency anemia on the complete blood count (CBC). Urinalysis showed a specific gravity between 1.001 and 1.004, indicating diabetes insipidus (DI). Serum electrolyte levels indicated a sodium level of 150 milliequivalents per liter, which was elevated and consistent with central diabetes insipidus (CDI). A skull X-ray showed diffuse, different-sized lytic punched-out lesions involving the entire skull, the skull base, the maxilla, and the mandible. A brain CT scan revealed multiple diffusely lytic lesions in the skull vault, thickening of the pituitary stalk, and global brain atrophy. Histopathological examination showed hypercellular discohesive Langerhans cells that were singly scattered, featured abundant eosinophilic cytoplasm, and had characteristic retiform convoluted nuclei with distinct longitudinal grooves.

**TREATMENT**

After The patient was diagnosed with Langerhans Cell Histiocytosis (LCH) with multi-organ involvement. A chemotherapy protocol consisting of 6 weeks of prednisone and intravenous vinblastine was initiated, followed by 12 months of maintenance therapy with mercaptopurine, methotrexate, intravenous pulses of vinblastine, and oral prednisolone. Due to the patient's poor nutritional state, he was started on F75 during his admission. For the CDI-induced polyuria, which was approximately 10–14 ml per kg per hour, he was managed with oral hydration, while no specific medication was initiated.

**OUTCOME AND FOLLOW-UP**

The patient was hospitalized for 2 months to complete his induction chemotherapy and was discharged with an appointment to continue his chemotherapy regimen as an outpatient.

**DISCUSSION**

Langerhans cell histiocytosis (LCH) is a disease characterized by the clonal expansion of myeloid precursors that differentiate into CD1a+/CD207+ cells in lesions. It can present at any age with varying degrees of systemic involvement. Although the cure rates for LCH are high, patients may experience severe long-term neurological or endocrine complications that can significantly affect their quality of life [3].

Historically, there was considerable confusion regarding the classification of histiocytosis due to incomplete understanding of its origin. However, with the development of immunohistochemical staining techniques, the Histiocyte Society proposed a reclassification system based on the predominant cell type found in the infiltrate. This initial classification included: Langerhans histiocytosis (Class I), non-Langerhans cell histiocytosis (Class II), and malignant histiocytosis (Class III). As more information became available, a revised classification schema was developed, which encompasses dendritic cell disorders, macrophage-related disorders, and malignant histiocytic disorders [4].

In our patient, there was multifocal bone disease, including a CNS risk lesion, indicating multisystem LCH. Multisystem LCH, historically known as Hand-Schüller-Christian disease, was classically described by a triad of symptoms: lytic bone lesions, exophthalmos, and diabetes insipidus. It most commonly occurs in younger children. Symptoms include bone lesions and exophthalmos, which results from a tumor mass affecting the orbital cavity, particularly the roof and lateral walls of the orbital bones. This orbital involvement can lead to vision loss or strabismus due to the impact on the optic nerve or orbital muscles, respectively [5]. The most frequently affected sites in the skeleton are the flat bones of the skull, ribs, pelvis, and scapulae. The skull may show extensive, irregularly shaped, lytic lesions. Long bones and lumbosacral vertebrae can also be involved, typically affecting the anterior portion of the vertebral body. Oral involvement often impacts the gums and palate, leading to the characteristic appearance of a "floating tooth" on dental radiographs. Large areas of the mandible may be involved, resulting in bone loss and diminished height of the mandibular rami. Chronic otitis media, due to involvement of the mastoid and petrous portions of the temporal bone, along with otitis externa, is commonly observed [6].

In our patient, central diabetes insipidus (CDI) was indicative of CNS involvement, confirming his LCH as multisystemic. The presence of CDI and pituitary thickening suggests involvement of the hypothalamic-pituitary axis. Our patient was fortunate that LCH was diagnosed soon after the detection of CDI; in some cases, LCH can be diagnosed years after CDI manifests.

The treatment of LCH depends on the pathogenesis of the disease, the patient's age, and the extent of lesion dissemination. Multisystemic disease necessitates systemic chemotherapy. Common agents used in various combination regimens across several cycles include corticosteroids, vinblastine, etoposide, cytarabine, 6-mercaptopurine, methotrexate, 2-chlorodeoxyadenosine, cyclosporine, thalidomide, among others. A combination of vincristine and prednisone appears to reduce the risk of recurrence [7-9].

Prognostic criteria for LCH include (1) age—children under 2 years typically have disseminated disease and a poorer prognosis; (2) the number of sites involved—multisystem disease correlates with a worse prognosis; and (3) organ dysfunction, which, if present, also leads to a poor prognosis. In our patient, the age and multisystem involvement were considered poor prognostic factors. Consequently, he was started on a chemotherapy protocol that consisted of 6 weeks of prednisone and intravenous vinblastine, followed by 12 months of maintenance therapy with mercaptopurine, methotrexate, intravenous vinblastine pulses, and oral prednisolone [7-10].

The reason for reporting this case of a 2-year-old child is that it represents a rare and unusual presentation of LCH, particularly with the occurrence of diabetes insipidus and cutaneous lesions on the scalp. LCH should be considered in the differential diagnosis, as early treatment may prevent permanent damage to the hypothalamic-pituitary axis.

**List of abbreviations**

**LCH:** Langerhans Cell Histiocytosis

**CNS:** Central Nervous System

**CDI:** Central Diabetes Insipidus

**CBC:** Complete Blood Count

**Author Contributions**

**Kidus Geabriel Yohannes:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Validation, Visualization, Writing - original draft.

**Nibretu Bekele Kassa:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision.

**Zerubabel Girma Tesso:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing - original draft.

**Abubeker Mahammud Digga: Conceptualization,** Data curation, Formal analysis, Investigation, Supervision.

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**Consent for publication**

After the patient recovered, the parents were informed about the case report, and written informed consent was obtained for the publication of clinical details and images from the patient's parents.

**Conflicts of Interest**

The authors declare no conflicts of interest.

**Data Availability Statement**

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

**Ethics approval and consent to participate**

Ethical approval is held to be unnecessary by Tikur Anbessa hospital Institutional Review Board as this is a single rare case encountered during clinical practice. Informed written consent to participate was obtained from parent of the patient.

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**REFERENCE**

1. Cara V, Samuel B, Bhupendra C.Langerhans Cell Histiocytosis.NIH,2024 APR 18:56(4); PMC-Pub Med.

2. Dhanu G, Mala V, Raghavendra H, Shrutha S. A rare and unusual case report of Langerhans cell histiocytosis. J Oral Maxillofac Pathol. 2017 Jan-Apr;21(1):140–144. doi: [10.4103/jomfp.JOMFP\_10\_17](https://doi.org/10.4103/jomfp.JOMFP_10_17).

3. Daniel N , Ian G. A case of multisystem Langerhans cell histiocytosis presenting as central diabetes insipidus. J Community Hosp Intern Med Perspect. 2019 Dec 14;9(6):515–517. doi: [10.1080/20009666.2019.1698231](https://doi.org/10.1080/20009666.2019.1698231).

4. Satter, Elizabeth K, Whitney A. Langerhans Cell Histiocytosis: A case report and summary of the current recommendations of the Histiocyte Society. Dermatology Online Journal Volume 2008 Jan;14(3);  <http://dx.doi.org/10.5070/D317b778j6>.

5. Grois N, Fahrner B, Arceci RJ, et al. Central nervous system disease in Langerhans cell histiocytosis. J Pediatr. 2010;156(6):873–881.e871.

6.Aakash M, Sandesh G, Sanjeev K, Aman M, Sandip K, Nibesh p, Ashim G. Incidental finding of Langerhans cell histiocytosis of temporoparietal bone - A case report. International Journal of Surgery Case Reports.2021 Aug;85; <https://doi.org/10.1016/j.ijscr.2021.106179>.

7. Aki S, Masayuki K, Nozomi Y, Miho O, Eigo S, Toyotaka K, Kazuaki Y, Yasunori O, Tatsuo I, Hitoshi O, Yasuo M, Emiko S, Tadakazu K, Seiya I, Yasuhito N, Kinuko M, Arinobu T. Clinical and prognostic features of Langerhans cell histiocytosis. Cancer Sci. 2023 Jun 26;114(9):3687–3697. doi: 10.1111/cas.15879.

8. Onyiriuka AN, Iduoriyekumwen NJ. Central diabetes insipidus due to Langerhans’ cell histiocytosis in an adolecent nigerian girl. Sri Lanka Journal of Diabetes Endocrinology and Metabolism [Internet]. 2017 Feb 26;7(1):21. Available from: <https://doi.org/10.4038/sjdem.v7i1.7322>

9. Lestari DM, Rini NEA. Central diabetes insipidus in Langerhans cell histiocytosis: a case report. Bioscientia Medicina Journal of Biomedicine and Translational Research [Internet]. 2023 Apr 5;7(2):3108–11. Available from: https://doi.org/10.37275/bsm.v7i2.776

10. Wu, H. T., Chen, B. H., Sheen, J. M., Chang, T. T., & Ko, S. C. (1999). Diabetes insipidus in Langerhans' cell histiocytosis: report of a case. *The Kaohsiung journal of medical sciences*, *15*(5), 302–306.

**IMAGES**

Fig 1 A Fig B

