

Orbital Langerhans Cell Histiocytosis in Young Pediatric Patients: Two Case Reports and Literature Review

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Objective: Langerhans cell histiocytosis (LCH) is a rare neoplastic proliferative disorder and there are relatively few studies on the treatment of pediatric patients in early childhood with orbital LCH.

Materials and Methods: This case report describes the treatment experiences of two pediatric patients with LCH who presented with similar clinical characteristics. They each had temporal orbital lesions, but the severity of their symptoms varied. Both patients underwent subtotal tumor resection. Postoperatively, only Patient 1 received low-dose chemotherapy and corticosteroid therapy.

Results: During the six-year follow-up period, Patient 1 exhibited no recurrence, whereas Patient 2 who developed recurrent systemic symptoms including cranial and cutaneous manifestations was subsequently treated with chemotherapy and hormonal therapy in the pediatrics department.

Conclusion: Based on our case observations and literature review, we realize that the early and accurate diagnosis of pediatric focal orbital LCH remains challenging. Meanwhile, the combination of surgery and chemotherapy yields satisfactory outcomes in young pediatric patients with orbital LCH, with a low recurrence rate.

Keywords: Langerhans cell histiocytosis, LCH, children, orbit, treatment, diagnosis

Introduction

Langerhans Cell Histiocytosis (LCH) is a rare condition, affecting approximately 4–9 children per a million under the age of 15,^{1,2} and is more common in children around the age of 3 years, with a high rate of recurrence.^{3–5} The pathology of LCH centers on the overgrowth of immature dendritic cells, which infiltrate various body systems, including bones, marrow, skin, CNS, lungs, liver, spleen, and lymph nodes, leading to a spectrum of clinical presentations.^{6–8} LCH is categorized by the extent of organ involvement into single-system and multi-system diseases, each with distinct treatment approaches.^{9,10} Unifocal LCH is often misdiagnosed when multisystem lesions presents with isolated lesions.¹¹ The scope of the disease, age factors and early treatment response are important prognostic factors.¹² The most frequently affected sites are the skull (80%) and skin (33%),^{9,13} with orbital lesions seen in 20% of bone-damaging LCH case.¹⁴ Orbital LCH can lead to significant ophthalmic symptoms such as soft tissue masses, pain, exophthalmos, and limited ocular mobility, seriously impacting children's ocular development and risking craniocerebral damage.¹³ The differential diagnosis includes orbital cellulitis, inflammatory pseudotumor, orbital bone tumors, and rhabdomyosarcoma.¹⁵ The rarity of LCH and the unique aspects of pediatric care mean that research on orbital LCH in children is insufficient and controversial, resulting in delayed or inappropriate treatment, and sometimes permanent disability.¹⁶ This case report

details the treatment and follow-up process of two male patients aged 3 years with orbital LCH from the same area. Herein, by summarizing recent literature on similar cases, an inductive analysis is made on the disease characteristics and key points of attention for pediatric patients with orbital LCH.

Case Presentation

Patient I

A 3-year-old boy presented with a two-month history of right eye swelling that progressively worsened, accompanied by pain. There was no relevant family medical history. On specialist examination, the right upper eyelid appeared red and swollen, with a palpable mass on the temporal aspect (soft, smooth, non-tender, ill-defined, and minimally mobile). There was associated mild proptosis with inferomedial deviation and severe ptosis. Conjunctival congestion was mild, and the pupillary light reflex was normal. Visual acuity and intraocular pressure were within normal limits (Figure 1A).

Laboratory tests revealed a leukocyte count of $11.23 \times 10^9/L$ with eosinophils at 10.6% and lymphocytes at 53.2%. Coagulation profiles, liver and renal functions, blood glucose, and urine analyses were unremarkable. No systemic abnormalities were found in the skin, lungs, brain, or other tissues. Computed tomography (CT) scan of the cranium and orbit indicated osteolytic lesions of the right supraorbital wall and zygomatic prominence, with an associated soft tissue mass (Figure 1B). Magnetic resonance imaging (MRI) showed a right superolateral orbital soft tissue mass involving the lacrimal gland and multiple enlarged lymph nodes in the right submandibular and neck regions (Figure 1C–F).

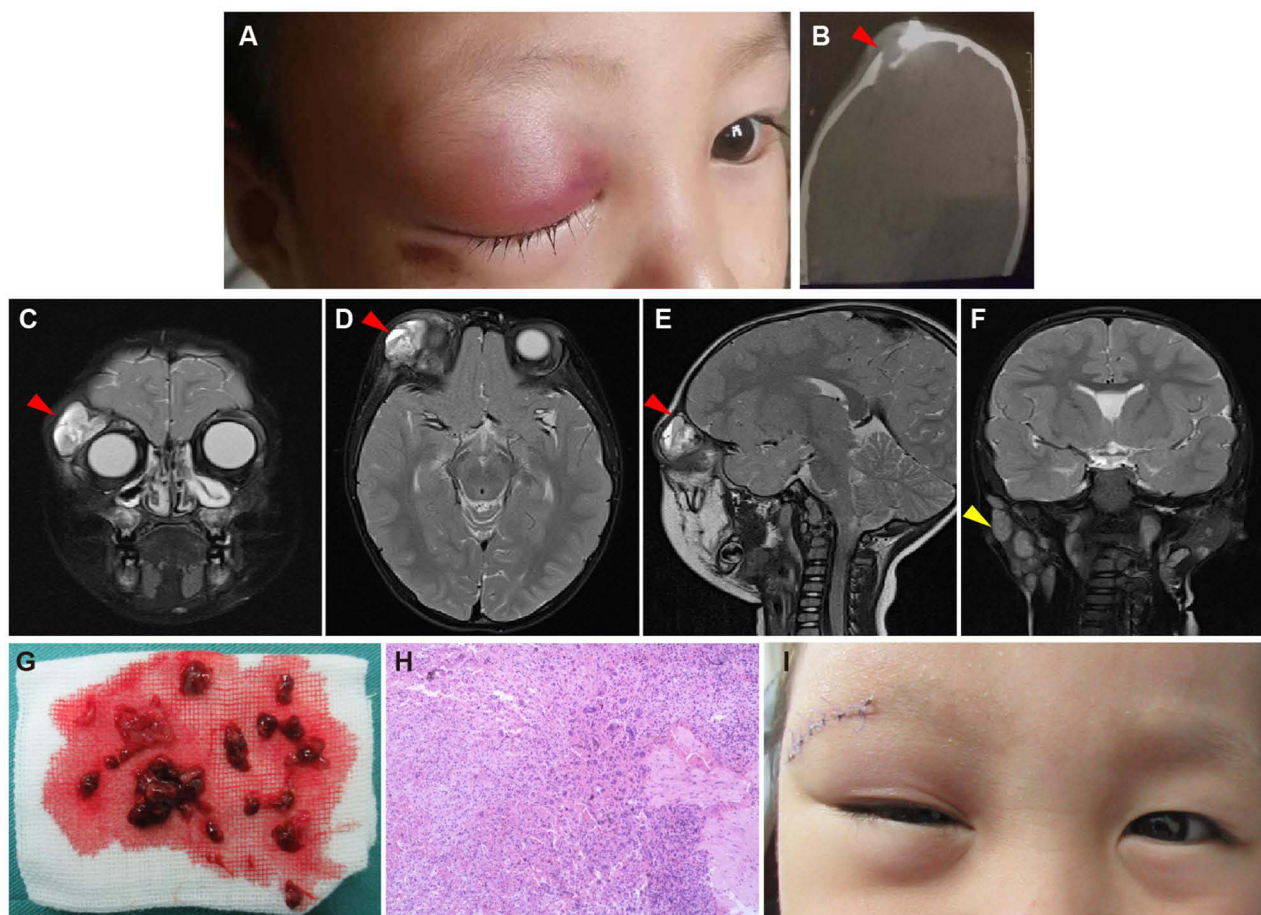


Figure 1 The pre-treatment and post-treatment data of patient I. (A) Swelling and redness of the right upper eyelid with severe ptosis. (B–F) are CT scan and MRI images of patient I respectively. Red arrows show patient I's right orbital mass and adjacent orbital bone lesions, and the yellow arrow in figure (F) shows enlarged lymph node. (G and H) present the partial orbital masse and its corresponding histopathological image, respectively. (I) is the postoperative recovery photo of patient I.

After careful review of the indications for surgical intervention, the patient underwent right anterior orbital exploration and subtotal tumor resection under general anesthesia. Postoperatively, the resected tissue was sent for pathological examination, which confirmed LCH (CD207+, CD1a+) (Figure 1G and H). The patient recovered well from surgery (Figure 1I). Given the child's pronounced symptoms, large mass, and lymph node involvement, we administered chemotherapy and steroid therapy (vincristine + prednisone) for nearly a year after the initial month. The patient remained recurrence-free during a six-year follow-up.

Patient 2

A 3-year-old boy presented with a left upper eyelid bulge for over two months and occasional left-sided pain, with no family history of note. On specialist examination, there was mild ptosis of the left upper eyelid and a caraway bean-sized swelling in the superolateral orbit (soft, ill-defined, immobile, non-tender, without skin redness or swelling). The left globe was not visibly deviated, and extraocular movements were full (Figure 2A). Visual acuity was 0.8, intraocular pressure measured 15 mm Hg, and funduscopic examination was incomplete. Blood work revealed a white blood cell count of $11.91 \times 10^9/L$ with lymphocytes at $7.92 \times 10^9/L$, constituting 66.5% of the total. Other tests, including coagulation profiles, liver and renal functions, blood glucose, and urine analysis, were unremarkable. Systemic examination showed no significant abnormalities in the skin, lungs, or other tissues. A CT scan revealed soft tissue density in the supratemporal left orbit and osteolytic lesions at the frontal bone on the temporal side (Figure 2B–D).

The patient underwent left eye anterior orbital exploration and subtotal tumor resection under general anesthesia. Pathological examination confirmed LCH (Langerin+, CD1a+) (Figure 2E and F). Postoperatively, the patient received tobramycin and dexamethasone eye ointment (5 mg once daily) and ibuprofen suspension (3mL twice daily), recovered well, and had no significant complications (Figure 2G–J). However, over a six-year follow-up, the patient experienced two recurrences starting the second-year post-surgery, underwent repeated chemotherapy, and currently maintains a stable condition.

Literature Review

We conducted a narrative review of pediatric cases involving orbital lesions of Langerhans Cell Histiocytosis (LCH) within the same age bracket of 1 to 6 years, spanning the past two decades. The diagnostic criteria for LCH are based on the 2022 international expert consensus.¹⁷ According to this criterion, there were 28 pediatric patients screened through PubMed and Embase databases (Table 1). The average age at diagnosis was 3.1 years, with a male preponderance at 68%. The majority of the cases presented with monocular involvement, and all exhibited osteolytic changes affecting the orbital bones. The initial clinical presentations were diverse, with eyelid swelling observed in 22 cases, proptosis in 8 cases, and restricted ocular motility in 3 cases. Diagnosis was established through a synergistic approach combining pathological findings with clinical manifestations.

The treatment regimens were categorized into three distinct groups: a combination of surgical intervention and chemotherapy was administered in 20 cases, chemotherapy alone in 5 cases, and surgical resection in 3 cases. The patients were followed up over an average period of 48.8 months, during which two recurrences were noted—both in patients who had initially received surgery plus chemotherapy and recurred nearly five years post-treatment. While precise data on the recurrence rate for children with orbital LCH treated surgically are lacking, it is noteworthy that the reactivation rate for single-system unifocal LCH after initial treatment has been reported to be as high as 17.4%,²³ which compares with the significantly lower recurrence rate of early surgery combined with chemotherapy.

Discussion

In ophthalmic clinical practice, achieving accurate diagnosis and implementing effective therapeutic interventions for pediatric orbital LCH pose significant challenges. The difficulty of the former lies in the fact that LCH is a very rare disease, which is prone to affect multiple systems throughout the body, and young pediatric patients generally have a low degree of cooperation during the physical examination process. Fortunately, pathological results can be an important basis for the final diagnosis of this disease.¹⁷ The difficulty of the latter is that there are few studies on this disease at present, and the therapeutic effect varies greatly. Therefore, the treatment of orbital LCH is still controversial.^{4,12} Some

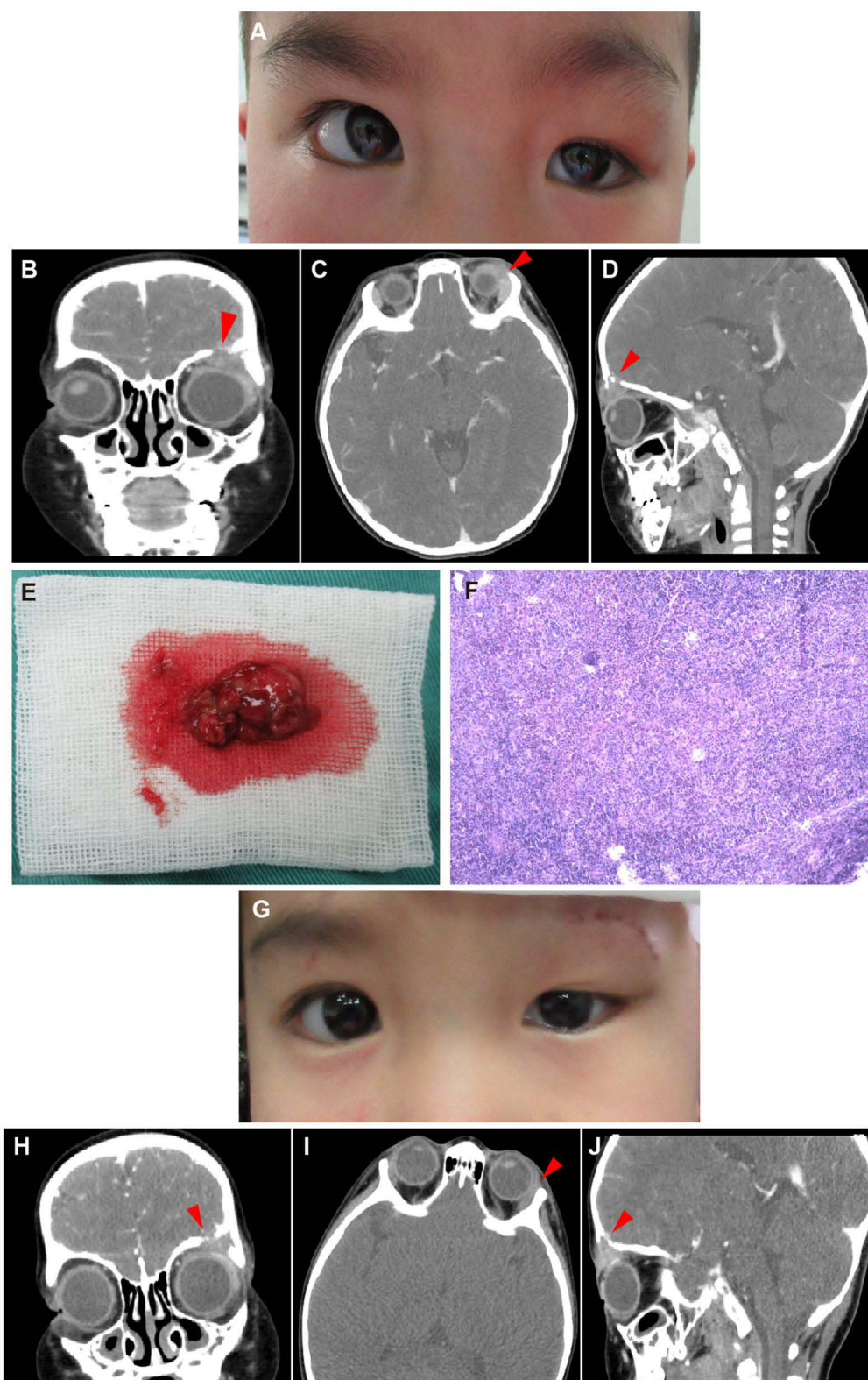


Figure 2 The pre-treatment and post-treatment data of patient 2. (A) Patient 2 showing swelling of the lateral half of upper eyelid and superolateral periorbital area. (B–D) are left orbital masses and adjacent orbital bone lesions of patient 2. (E and F) present images of the partial orbital masse and the pathological results of resected masse. (G) is the postoperative recovery photo of patient 2. (H–J) On CT scans, small amount of inflammatory tissue is found and the healing of orbital bone is observed. The red arrow shows the lesion of patient 2's left eye.

Table 1 A Literature Review of Cases of Young Pediatric Patients with Orbital Langerhans Cell Histiocytosis (LCH)

Study	No. of Cases	Mean Age (Years)	Presenting Complaint	Lesion Location	Management	Mean Follow-Up	Recurrence
Mayuresh Naik, ¹⁸ 2018	1	2	Painless progressive lump	Right infratemporal periorbital	CT(VB)+ST	2 years	Nil
Tariq Alzahem, ¹⁹ 2023	3	2.9	Upper eyelid swelling, displacement of the eyeball, drooping eyelid	Periorbital superior temporal	SSE+CT (VB)+ ST	46.5 months	Nil
Kirithi Koka, ¹² 2020	3	3.6	Upper eyelid swelling, Proptosis	Parietal orbit, supratemporal periorbital	CT (VB)+ ST	34 months	Nil
Hayyam Kiratli, ²⁰ 2013	8	2.7	Upper eyelid swelling, Proptosis	Parietal orbit, supratemporal, infratemporal	SSE + CT (VB)	48.9 months	1 case
Neda Esmaili, ¹³ 2016	4	2.1	Upper eyelid swelling, erythema, Proptosis	Parietal orbit	SSE+CT (VB)+ ST	5 years	1 case (Relapse in the fifth year)
Martina C. Herwig, ²¹ 2013	1	3	Upper eyelid swelling	Parietal orbit	CT (etoposide)	11 years	Nil
A. Kaan Gündüz, ²² 2018	1	3.3	Upper eyelid swelling	Parietal orbit	SSE+CT (VB)+ ST	2 years	Nil

Abbreviations: SSE, Surgical subtotal excision; CT, Chemotherapy; VB, Vinblastine; ST, Oral steroids.

research has indicated that children presenting with unifocal orbital LCH may be managed similarly to those with unifocal LCH in other tissues. This approach advocates for a more conservative treatment strategy, which involves surgical subtotal resection of the tumor, complemented by local injection of corticosteroids.^{24,25} In the case of multi-systemic orbital LCH, particularly when it involves organs with significant risk, a consensus among scholars leans towards a more comprehensive treatment approach. This typically involves a combination of surgical intervention to address the orbital lesions, alongside chemotherapy to target the systemic aspects of the disease. This dual approach aims to effectively manage both the local and systemic manifestations of LCH, ensuring a more holistic treatment strategy for affected children.^{12,26} However, it is worth noting that LCH disease is prone to affect multiple systems, and the diagnosis of single-focal orbital LCH in children often requires special attention. In recent years, there has been a paradigm shift in the management of orbital LCH, particularly following its reclassification as an inflammatory medullary tumor.²¹ This new understanding has prompted an increasing number of studies to contemplate the surgical and chemotherapeutic regimen as a standard treatment option for all types of orbital LCH lesions. The evolving perception of LCH as an inflammatory myeloid tumor has led to a reevaluation of the therapeutic strategies, with a growing emphasis on the potential benefits of combining surgical intervention with chemotherapy. This integrated approach is believed to offer a more effective means of addressing the complex inflammatory and neoplastic characteristics of orbital LCH, thereby optimizing outcomes for affected patients.¹⁷

The two pediatric patients discussed in this article were both 3 years old, aligning with the peak age of onset for LCH. By integrating the patients' medical histories, clinical presentations, imaging studies, and pathological assessments, a definitive diagnosis of LCH was established. Both children presented with localized periorbital masses and evidence of orbital osteolytic lesions. However, upon thorough evaluation, no additional systemic involvement was detected, except for patient 1, who also had involvement of nearby lymph nodes. Tailored treatment approaches were adopted for each child based on their specific condition. Both underwent subtotal resection of the mass, but patient 1 received adjuvant therapy with steroids and vincristine for one-year post-surgery. At the 6-year follow-up, patient 1 maintained stable disease with no significant recurrence. Regrettably, despite patient 2 having a unifocal lesion, the disease recurred shortly after surgery, with a total of two recurrences observed. This observation draws our attention to the possible significant role of early chemotherapy in children with orbital LCH, particularly those with unifocal lesions. It underscores the need for a more comprehensive approach that takes into account the potential for recurrence, even in cases that initially appear to be localized.

1. Age Considerations. While some studies have suggested varying treatment strategies for LCH based on the focality of lesions—differentiating between unifocal and multifocal presentations—they have not paid sufficient attention to crucial factors such as age differences.²⁷ It is essential to recognize that pediatric patients constitute the majority of LCH cases, and there is a correlation between earlier onset and both a higher recurrence rate and a poorer prognosis.²⁸ This

correlation underscores the importance of considering appropriate treatment options for pediatric patients with unifocal LCH, as their age may significantly impact both the treatment approach and the anticipated outcomes.

2. **Orbital LCH Lesions and Their Risks.** Orbital LCH lesions inherently carry a high risk due to the ill-defined tumor margins, which complicates complete surgical excision. Although current evidence does not suggest that LCH with localized cranial involvement is prone to transformation into high-risk Central Nervous System (CNS)-LCH,^{13,29} the proximity of orbital LCH to the cranial brain poses a risk of meningeal breach and potential impact on vital intracranial structures.^{13,30,31} Furthermore, the majority of orbital masses are poorly demarcated, complicating attempts at complete surgical resection. Taking into account the collective expertise from multiple disciplines, including oncology and hematology, it seems prudent to administer postoperative chemotherapy. This integrated approach aims to mitigate the risks associated with incomplete resection and the potential for disease progression or transformation.³²

3. Based on a review of recent literature regarding diseases of a similar nature, the overall effectiveness of combining surgery with chemotherapy in children with orbital LCH lesions is relatively positive, and the recurrence rate is low (Table 1). In our case report, the benefits of early implementation of a combined surgical and chemotherapeutic approach for such patients are also underscored. Recent studies have demonstrated that the combination of surgery and chemotherapy yields satisfactory outcomes in children with orbital LCH, with a notably low recurrence rate as presented in Table 1. Our case report further emphasizes the advantages of promptly employing a multimodal treatment strategy that includes both surgery and chemotherapy for pediatric patients with this condition.

4. Due to the limited compliance often exhibited by young pediatric patients, conducting comprehensive and systematic examinations can be troublesome, underscoring the importance of prompt and appropriate treatment. LCH, being a rare disease, is difficult to diagnose routinely, with diagnosis primarily relying on the collective assessment of pathological findings and clinical signs.¹⁵ Consequently, most ophthalmologists are prone to misdiagnosing or overlooking the condition.³³ Furthermore, children may not readily recognize early multisystem symptoms and are less capable of enduring the extensive systemic examinations that adults can tolerate, further elevating the risk of misdiagnosis. Therefore, the diagnosis of isolated orbital lesions requires careful consideration and a high index of suspicion.

Based on the analysis presented, we suggest that the early adoption of surgery combined with chemotherapy in children with orbital LCH may be considered as an important intervention, regardless of the unifocal or part of a multi-systemic lesions, provided there are no overt contraindications and the child's physical condition permits such treatment. The following recommendations are offered: 1. In clinical practice, ophthalmologists should actively consider the possibility of orbital LCH lesions and differentiate them from conditions like cellulitis promptly, especially when encountering pediatric patients with periorbital mass and evidence of osteolytic changes in the orbital bones. 2. Upon diagnosing a child with orbital LCH, it is imperative to conduct a thorough examination of multiple organ systems, including but not limited to other bones, skin, hematopoietic system, lymph nodes, ears, lungs, central nervous system, liver, and spleen. Involvement of high-risk organs (eg, CNS, liver, spleen, bone marrow) may portend a poor prognosis,³⁴ necessitating more aggressive treatment strategies and vigilant follow-up. 3. Pediatric patients may experience their common chemotherapy-related complication compared to adults, which can raise concerns for ophthalmologists.^{35,36} Engaging multidisciplinary teams, including oncologists and hematologists, can aid in treatment and mitigate the risks associated with therapy. 4. The literature reviewed in this paper often lacks detailed clinical treatment data. Additionally, variations in surgical approaches and chemotherapy protocols across different studies may contribute to differing treatment outcomes. It is encouraged that more ophthalmic clinicians report the treatment details of such cases and contribute to the research and statistical understanding of these patient populations. 5. The perception of LCH has evolved from a reactive proliferation of Langerhans cells to that of inflammatory myeloid tumors, and from immune disorders to malignant tumors.^{37,38} Consequently, new insights into treatment strategies are continuously emerging. With 60% of LCH patients exhibiting BRAF oncogene mutations³⁹ targeted therapies against BRAF-V600E mutations and MAPK pathway activation are also areas of intense research.^{40,41} Furthermore, hematopoietic stem cell transplantation is a potential treatment option for patients with high-risk organ involvement.⁴²

Multidisciplinary familiarity with LCH is critical for ophthalmologists and practitioners, as it affects multiple systems within the body, including some vital organs, making it prone to missed and delayed diagnoses.

Conclusions

The LCH presentation with orbital bone involvement is an exceedingly rare condition, and there is a paucity of definitive evidence to guide early diagnosis and treatment in the population of young children. Through our case observations and literature review, we advise a thorough systemic examination for young children with focal orbital LCH to rule out multi-system lesions. In addition, we also recommend the combined treatment of surgery and chemotherapy for young children with orbital LCH and provide close follow-up.

Abbreviations

LCH, Langerhans cell histiocytosis; CT, Computed tomography; MRI, Magnetic resonance imaging; MAPK, Mitogen-activated protein kinase.

Data Sharing Statement

Data and materials supporting the results reported in the manuscript are available upon reasonable request. Readers can contact the corresponding author, Xi Zhang: Department of Ophthalmology, The General Hospital of Western Theater Command, zhangxizx@yeah.net.

Ethics Approval and Consent to Participate

Institutional approval was obtained from the Ethics Committee of Army Medical Center (Daping Hospital) for the publication of the case details without identifiable information.

Consent for Publication

Written informed consents were obtained from the parents for publication of this Case Report and accompanying images. A copy of the written consent is available for review by the editors of this journal.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

References

1. McCullough WP, Pollock AN. Langerhans cell histiocytosis presenting as chronic otitis externa. *Pediatr Emerg Care*. 2017;33(1):67–69. doi:10.1097/PEC.0000000000001012
2. Zinn DJ, Chakraborty R, Allen CE. Langerhans cell histiocytosis: emerging insights and clinical implications. *Oncology*. 2016;30(2):122–32, 139.
3. El Demellawy D, Young JL, Nanassy JD, et al. Langerhans cell histiocytosis: a comprehensive review. *Pathology*. 2015;47(4):294–301. doi:10.1097/PAT.0000000000000256
4. Rodriguez-Galindo C, Allen CE. Langerhans cell histiocytosis. *Blood*. 2020;135(16):1319–1331. doi:10.1182/blood.2019000934
5. Tran G, Huynh TN, Paller AS. Langerhans cell histiocytosis: a neoplastic disorder driven by Ras-ERK pathway mutations. *J Am Acad Dermatol*. 2018;78(3):579–590.e4. doi:10.1016/j.jaad.2017.09.022

6. Papo M, Cohen-Aubart F, Trefond L, et al. Systemic histiocytosis (Langerhans Cell Histiocytosis, Erdheim-Chester disease, Destombes-Rosai-Dorfman disease): from oncogenic mutations to inflammatory disorders. *Curr Oncol Rep*. 2019;21(7):62. doi:10.1007/s11912-019-0810-6
7. Papadopoulou M, Panagopoulou P, Papadopoulou A, et al. The multiple faces of Langerhans cell histiocytosis in childhood: a gentle reminder. *Mol Clin Oncol*. 2018;8(3):489–492. doi:10.3892/mco.2017.1539
8. Donadieu J, Heritier S. [Child Langerhans cell histiocytosis]. *Presse Med*. 2017;46(1):85–95. doi:10.1016/j.lpm.2016.09.013
9. Krooks J, Minkov M, Weatherall AG. Langerhans cell histiocytosis in children: history, classification, pathobiology, clinical manifestations, and prognosis. *J Am Acad Dermatol*. 2018;78(6):1035–1044. doi:10.1016/j.jaad.2017.05.059
10. Haupt R, Minkov M, Astigarraga I, et al. Langerhans cell histiocytosis (LCH): guidelines for diagnosis, clinical work-up, and treatment for patients till the age of 18 years. *Pediatr Blood Cancer*. 2013;60(2):175–184. doi:10.1002/pbc.24367
11. Bezdjian A, Alarfaj AA, Varma N, et al. Isolated Langerhans Cell Histiocytosis bone lesion in pediatric patients: systematic review and treatment algorithm. *Otolaryngol Head Neck Surg*. 2015;153(5):751–757. doi:10.1177/0194599815598969
12. Koka K, Alam M, Subramanian N, et al. Clinical spectrum and management outcomes of Langerhans cell histiocytosis of the orbit. *Indian J Ophthalmol*. 2020;68(8):1604–1608. doi:10.4103/ijo.IJO_1375_19
13. Esmaili N, Harris GJ. Langerhans cell histiocytosis of the orbit: spectrum of disease and risk of central nervous system sequelae in unifocal cases. *Ophthalmic Plast Reconstr Surg*. 2016;32(1):28–34. doi:10.1097/IOP.0000000000000402
14. Lisicic-Konakovic M, Lokvančić-Bekto A, Kulašević A, et al. Langerhans Cell histiocytosis in a three-year-old girl in bosnia and herzegovina. *Acta Med Acad*. 2021;50(2):340–343. doi:10.5644/ama2006-124.351
15. Wu C, Li K, Hei Y, et al. MR imaging features of orbital Langerhans cell histiocytosis. *BMC Ophthalmol*. 2019;19(1):263. doi:10.1186/s12886-019-1269-9
16. Laurencikas E, Gavhed D, Stålemark H, et al. Incidence and pattern of radiological central nervous system Langerhans cell histiocytosis in children: a population based study. *Pediatr Blood Cancer*. 2011;56(2):250–257. doi:10.1002/pbc.22791
17. Goyal G, Tazi A, Go RS, et al. International expert consensus recommendations for the diagnosis and treatment of Langerhans cell histiocytosis in adults. *Blood*. 2022;139(17):2601–2621. doi:10.1182/blood.2021014343
18. Naik M, Mehta A, Mehrotra N, et al. Isolated Langerhans Cell Histiocytosis of orbit: a case report and review of the literature. *Case Rep Ophthalmol Med*. 2018;2018:1529281. doi:10.1155/2018/1529281
19. Alzahem T, Alkatan HM, Maktabi AM, et al. Ophthalmic histiocytic lesions (diseases of the L group): a multicenter clinicopathological study of 18 cases and review of literature. *Eur J Ophthalmol*. 2023;33(1):556–566. doi:10.1177/11206721221113431
20. Kiratli H, Tarlan B, Soylemezoglu F. Langerhans cell histiocytosis of the orbit. *Eur J Ophthalmol*. 2013;23(4):578–583. doi:10.5301/ejo.5000244
21. Herwig MC, Wojno T, Zhang Q, et al. Langerhans cell histiocytosis of the orbit: five clinicopathologic cases and review of the literature. *Surv Ophthalmol*. 2013;58(4):330–340. doi:10.1016/j.survophthal.2012.09.004
22. Gunduz AK, Temel E. Histiocytic lesions of the orbit: a study of 9 cases. *Saudi J Ophthalmol*. 2018;32(1):40–44. doi:10.1016/j.sjopt.2018.03.004
23. Pollono D, Rey G, Latella A, et al. Reactivation and risk of sequelae in Langerhans cell histiocytosis. *Pediatr Blood Cancer*. 2007;48(7):696–699. doi:10.1002/pbc.21145
24. Gardner H, Minkov M, Grois N, et al. Therapy prolongation improves outcome in multisystem Langerhans cell histiocytosis. *Blood*. 2013;121(25):5006–5014. doi:10.1182/blood-2012-09-455774
25. Harris GJ. Langerhans cell histiocytosis of the orbit: a need for interdisciplinary dialogue. *Am J Ophthalmol*. 2006;141(2):374–378. doi:10.1016/j.ajo.2005.08.029
26. Slama T, Mader L, Žarković M, et al. Chronic health conditions after childhood Langerhans cell histiocytosis: results from the Swiss childhood cancer survivor study. *J Cancer Surviv*. 2024.
27. Shetty SB, Mehta C. Langerhans cell histiocytosis of the orbit. *Indian J Ophthalmol*. 2001;49(4):267–268.
28. Heritier S, Barkaoui M-A, Miron J, et al. Incidence and risk factors for clinical neurodegenerative Langerhans cell histiocytosis: a longitudinal cohort study. *Br J Haematol*. 2018;183(4):608–617. doi:10.1111/bjh.15577
29. Margo CE, Goldman DR. Langerhans cell histiocytosis. *Surv Ophthalmol*. 2008;53(4):332–358. doi:10.1016/j.survophthal.2008.04.007
30. Grois N, Pötschger U, Prosch H, et al. Risk factors for diabetes insipidus in langerhans cell histiocytosis. *Pediatr Blood Cancer*. 2006;46(2):228–233. doi:10.1002/pbc.20425
31. Maccheron LJ, McNab AA, Elder J, et al. Ocular adnexal Langerhans cell histiocytosis clinical features and management. *Orbit*. 2006;25(3):169–177. doi:10.1080/01676830600669486
32. Lakatos K, Sterlich K, Pötschger U, et al. Langerhans cell histiocytosis of the orbit: spectrum of clinical and imaging findings. *J Pediatr*. 2021;230:174–181.e1. doi:10.1016/j.jpeds.2020.10.056
33. Stefanato CM, Andersen WK, Calonje E, et al. Langerhans cell histiocytosis in the elderly: a report of three cases. *J Am Acad Dermatol*. 1998;39(2 Pt 2):375–378. doi:10.1016/S0190-9622(98)70395-0
34. Krooks J, Minkov M, Weatherall AG. Langerhans cell histiocytosis in children: diagnosis, differential diagnosis, treatment, sequelae, and standardized follow-up. *J Am Acad Dermatol*. 2018;78(6):1047–1056. doi:10.1016/j.jaad.2017.05.060
35. Yildirim UM, Tekkesin F, Koc BS, et al. Acute complications observed during intensive chemotherapy in pediatric patients with acute lymphoblastic leukemia: single-center experience. *North Clin Istanb*. 2023;10(4):458–469. doi:10.14744/nci.2022.47600
36. Franzon J, Berry NM, Ullah S, et al. Heart failure following blood cancer therapy in pediatric and adult populations. *Asia Pac J Clin Oncol*. 2018;14(3):224–230. doi:10.1111/ajco.12782
37. Kobayashi M, Tojo A. Langerhans cell histiocytosis in adults: advances in pathophysiology and treatment. *Cancer Sci*. 2018;109(12):3707–3713. doi:10.1111/cas.13817
38. Chen J, Zhao A-L, Duan M-H, et al. Diverse kinase alterations and myeloid-associated mutations in adult histiocytosis. *Leukemia*. 2022;36(2):573–576. doi:10.1038/s41375-021-01439-3
39. Champaneri H, Banerjee AD. Pediatric Langerhans Cell Histiocytosis with BRAF mutation affecting sacral vertebra: a case report and disease review. *Pediatr Neurosurg*. 2020;55(3):169–174. doi:10.1159/000508940
40. Bielamowicz K, Dimitrion P, Abila O, et al. Langerhans cell histiocytosis: NACHO update on progress, chaos, and opportunity on the path to rational cures. *Cancer*. 2024;130(14):2416–2439. doi:10.1002/cncr.35301

41. Cournoyer E, Ferrell J, Sharp S, et al. Dabrafenib and trametinib in Langerhans cell histiocytosis and other histiocytic disorders. *Haematologica*. 2024;109(4):1137–1148. doi:10.3324/haematol.2023.283295
42. Veys PA, Nanduri V, Baker KS, et al. Haematopoietic stem cell transplantation for refractory Langerhans cell histiocytosis: outcome by intensity of conditioning. *Br J Haematol*. 2015;169(5):711–718. doi:10.1111/bjh.13347

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