




Resolution and Re-ossification of Orbital-Wall Langerhans Cell Histiocytosis Following Stereotactic Needle Biopsy

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Abstract

Introduction Langerhans cell histiocytosis (LCH) is a rare disease that encompasses a spectrum of clinical syndromes. It is characterized by the proliferation and infiltration of white blood cells into organs or organ systems. Reports of management of these lesions have included biopsy, resection, curettage, radiation, and/or chemotherapy.

Case Presentation A 40-year-old man presented with a history of right proptosis and retro-orbital pain and was found to have a lytic mass involving the greater wing of the sphenoid extending into the right orbit. A stereotactic needle biopsy using neuro-navigation demonstrated this to be LCH. After no further treatment, the mass spontaneously resolved, with virtual normalization of the orbital magnetic resonance imaging at 10 months following the needle biopsy. The bony defect of the temporal bone caused by the mass also re-ossified following the needle biopsy.

Discussion This report highlights the potential for an isolated LCH lesion to regress after simple needle biopsy, an outcome only rarely reported previously. Thus, expectant management of such lesions following biopsy or initial debridement should be considered prior to proceeding with additional treatment.

Keywords

- ▶ Langerhans cell histiocytosis
- ▶ biopsy
- ▶ stereotactic
- ▶ resolution
- ▶ re-ossification

Introduction

Langerhans cell histiocytosis (LCH) was first described by Alfred Hand Jr. in 1893 in a pediatric patient.¹ In general, the disease is characterized by the accumulation and infiltration of white blood cells, specifically Langerhans cells, into organs or organ systems.² LCH can affect a single system (unifocal or multifocal) or have multisystem involvement. Single system, unifocal LCH has been termed eosinophilic granuloma (EG) and multifocal LCH has been termed Hand–Schuller–Chris-

tian disease. The acute multisystem form of LCH has been named Letterer–Siwe disease.³ Prognosis for patients with solitary lesions is generally good, while individuals with multiple lesions may have extensive disease-related morbidity.^{2,4}

LCH is exceedingly rare, with an incidence of approximately five to six per 1 million and is typically seen in the pediatric population.⁵ Histologic characteristics of LCH include positive staining for S-100 protein and CD1a antigen or electron microscopy revealing Birbeck's granules.⁶ Sites

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affected may include bone, skin, central nervous system, liver, spleen, hematopoietic system, lungs, and lymph nodes.² The disease course is known to be unpredictable—it can remain indolent or rapidly progress to cause severe multisystem injury and death, highlighting the complex nature of the disease.

The treatment of LCH is dependent on the site(s) affected and if the lesion is unifocal, multifocal, or multisystem. In the setting of a solitary lesion, such as with an EG of the orbit, a variety of treatments have been described. These include: incisional biopsy, excisional biopsy, curettage of the lesion, steroid injection of the lesion, postbiopsy radiation, and systemic chemotherapy.⁷ We present the case of a 40-year-old man who had spontaneous resolution with re-ossification of an orbital EG after stereotactic needle biopsy with no additional treatment. The aim of this report is to summarize the current literature on management of LCH in the orbit, and to highlight the fact that LCH with bony involvement can resolve and re-ossify following needle biopsy without additional treatment in adult patients.

Illustrative Case

History and Examination

A 40-year-old man presented with a 1-week history of right proptosis and retro-orbital pain. Laboratory tests performed at an ophthalmology clinic did not reveal any abnormalities. Computed tomography (CT) imaging revealed an osteolytic expansive lesion involving the lateral posterior wall of the orbit, at which point he was referred for neurosurgical evaluation (►Fig. 1B). At the time of initial presentation, the patient

had a normal neurologic exam without deficits. The patient had an unremarkable past medical history and his only complaint was headache since the onset of the right proptosis and retro-orbital pain. The only notable physical examination finding was right-sided proptosis. An magnetic resonance imaging (MRI) scan with and without contrast revealed a lesion involving the right greater wing of the sphenoid with contrast enhancement and irregular margins, measuring approximately 11 × 14 mm in size (►Fig. 1A). The lesion was noted to extend extracranially in the temporal fossa and into the lateral orbital apex. It was predicted that the lytic lesion was the cause of the proptosis and the next step was to obtain a tissue diagnosis to elucidate the nature of the lesion.

Operative Technique

Intraoperative navigation was used to accurately identify the entry point on the lateral portion of the right temporal region. A standard 3.5-inch, 18-gauge spinal needle was registered with the intraoperative navigation system and then advanced through the scalp and temporalis muscle to the lateral margin of the lesion to serve as a guide cannula. The stylet was then removed, and the lesion was biopsied through the 18-gauge spinal needle using a 5-inch, 20-gauge spinal needle and syringe. After several 20-gauge needle aspirates were obtained, additional biopsy material was obtained by advancing the 18-gauge needle fully into the lesion with aspiration.

Histopathological Findings

Aspirate smears and tissue cell blocks showed a cellular lesion composed of a mixed inflammatory infiltrate with

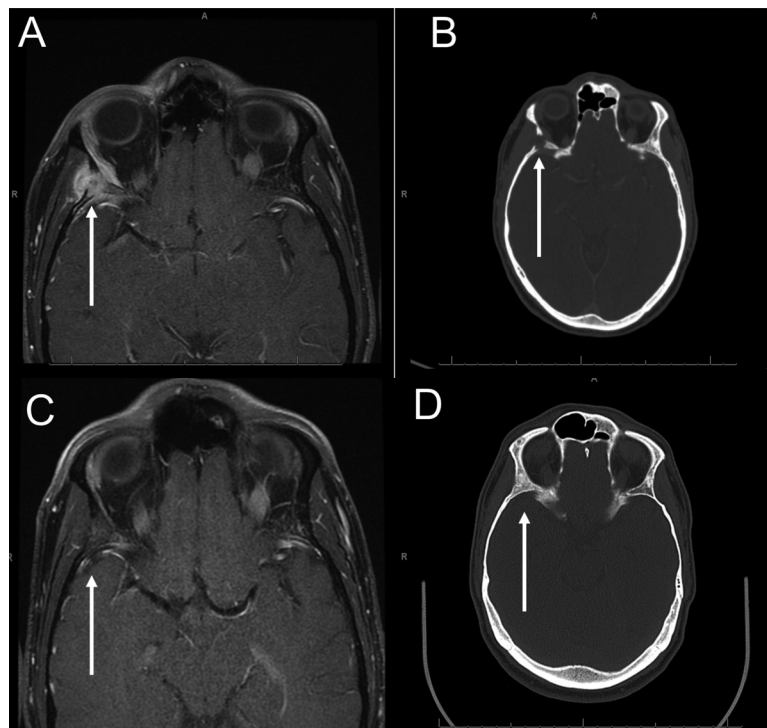


Fig. 1 Preoperative MR axial fat saturation T1-weighted postcontrast (A) and CT (B) images demonstrating the mass in the right greater wing of the sphenoid. Postoperative axial T1-weighted MR image 3 months after the initial biopsy (C), and CT scan 17 months after biopsy showing complete re-ossification of the bony architecture (D). CT, computed tomography; MR, magnetic resonance.

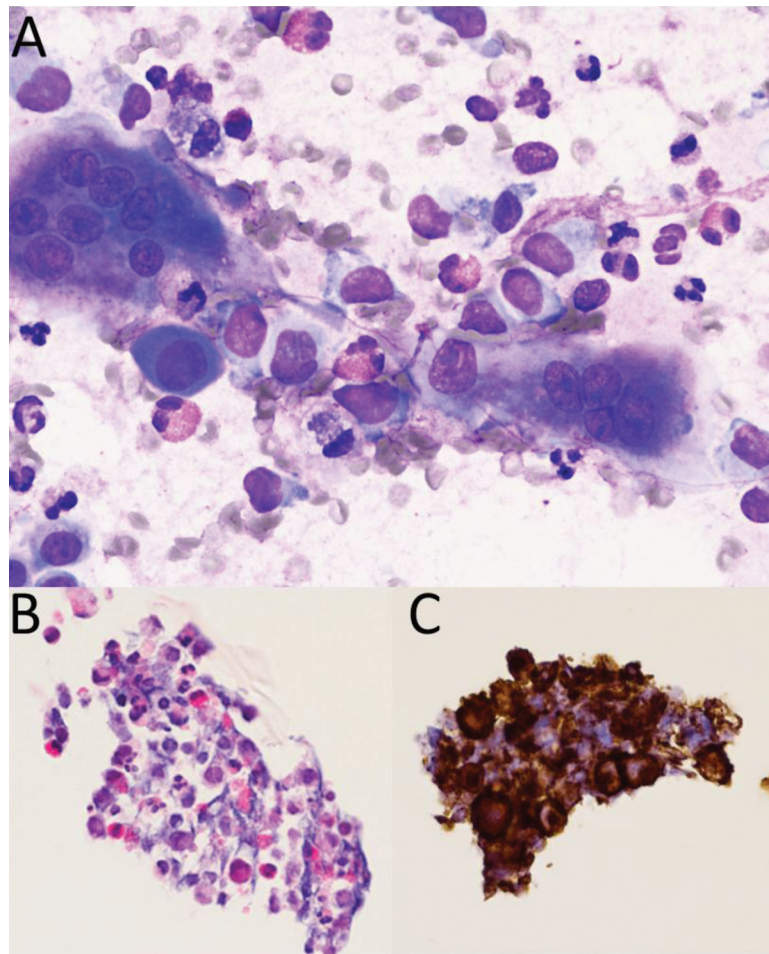


Fig. 2 (A) Diff-Quik stained aspirate smears at 60 \times magnification shows a cellular smear with a mixed inflammatory infiltrate, conspicuous eosinophils, occasional multinucleated giant cells, and abundant bland histiocytoid cells with moderate cytoplasm and oval to bean-shaped nuclei with nuclear grooving. (B) Similar features are seen on H&E-stained cell block (60 \times) and immunohistochemical stains performed on the cell block show positive staining of the histiocytoid cells with CD1a (C). H&E, hematoxylin and eosin.

conspicuous eosinophils and occasional multinucleated giant cells (**Fig. 2A, B**). Abundant bland histiocytoid cells with moderate cytoplasm and oval to bean-shaped nuclei with nuclear grooving were also present. Immunohistochemical staining with CD1a (**Fig. 2C**) and S100 showed positivity in the histiocytic cells noted on hematoxylin and eosin stained cell block sections confirming the diagnosis of LCH.

Postoperative Course

The patient did not experience any complications and was discharged the same day. Further workup included full-body positron emission tomography/CT with 18F-fluorodeoxyglucose, which demonstrated uptake in the orbital lesion, but no evidence for other lesions. Endocrine evaluation demonstrated no abnormalities. The patient was referred to hematology/oncology and, after discussion of options, the patient elected to pursue observation rather than any additional treatments. The proptosis and retro-orbital pain progressively resolved without additional treatment. Ten months after the biopsy, a follow-up MRI scan demonstrated complete resolution of the enhancing abnormality

(**Fig. 1C**). Seventeen months after the biopsy, a CT scan demonstrated re-ossification of the lesion with re-establishment of the bony architecture (**Fig. 1D**). An additional head MRI was obtained 4 years after the needle biopsy, which demonstrated normal orbital anatomy.

Discussion

LCH, including EG, is a well-known entity that is typically seen in the pediatric population. EG is typically seen in the skull, mandible, spine, ribs, and pelvis and usually presents between 5 and 15 years old.⁵ EG is a benign, unifocal lesion, typically managed with a conservative approach. Orbital LCH is extremely rare, comprising approximately 1% of all orbital tumors.⁸⁻¹⁰ Common clinical indications of orbital LCH include: swelling of the eyelid, proptosis, or global displacement.³ Due to the rarity of the disease, there is no “gold standard” treatment for orbital LCH. Reported treatment methods vary from biopsy to complete surgical excision with steroid administration.^{3,11}

Table 1 Summary of prior studies reporting spontaneous resolution of LCH

Authors and year	Patient gender	Patient age (y)	Treatment	Time to resolution or re-ossification following biopsy
Glover and Grove, ¹¹ 1987	Male	13	Incisional biopsy	14 mo
Smith et al, ¹⁴ 1999	Female	3	Fine needle aspiration biopsy	6 mo
Rajendram et al, ³ 2005	Male	17	Incisional biopsy	5 mo
Harzallah et al, ¹³ 2005	Male	5	Fine needle aspiration biopsy	N/A
El Ayadi et al, ¹² 2007	Female	3	Incisional biopsy	2 wk
Satoh et al, ¹⁵ 2012	Male	22	Endoscopic endonasal biopsy	7 mo

Abbreviation: LCH, Langerhans cell histiocytosis.

Six prior reports in the literature described the regression of LCH in the orbit; most of which were published in the ophthalmological literature (►Table 1).^{3,11–15} All the cases were single, unifocal lesions that were confirmed histologically to be LCH. A report by Glover and Grove was the first to describe the spontaneous resolution and re-ossification of LCH in a 13-year-old boy with a right orbital EG. The patient underwent surgery for an incisional biopsy. Resolution and re-ossification occurred 14 months after the initial surgery.¹¹ A report by Smith et al was the first to describe spontaneous resolution and re-ossification after a fine needle biopsy in a 3-year-old girl with a left orbital EG.¹⁴ Since their initial description, there have been four reports including ours that describe the spontaneous resolution of an EG in the orbit with re-ossification of anatomical bone defect caused by the mass after simple needle biopsy.

Rajendram et al described the first spontaneous regression of a LCH that was histologically confirmed in a 17-year-old patient. The patient initially had a needle biopsy of a left lacrimal mass, which was histologically confirmed as a LCH. Five months after the initial biopsy, the patient underwent a second surgery where curettage was performed and steroids were administered. Pathology from the second surgery did not show any evidence of LCH, histologically confirming resolution of the mass.³ Satoh et al presented a case as the first report of “truly spontaneous” regression of LCH in the orbit in a 22-year-old patient who had a left orbital mass. Imaging revealed that the mass was gradually regressing but due to irreversible damage to the left eye, indicated by optical coherence tomography, the patient had the mass biopsied via an endoscopic endonasal approach, which confirmed the diagnosis of LCH. The mass resolved 7 months after the biopsy.¹⁵ The present case is the first report of regression of LCH in the orbit after stereotactic needle biopsy in an older patient, and is the first report of this phenomenon in the neurosurgical literature.

In our report the patient presented at the age of 40 years, which is interesting, as these lesions usually present in the pediatric population and adults have been reported to have a higher rate of recurrence. After imaging revealed a lytic lesion as the cause of his proptosis, it was decided to biopsy the mass to obtain a tissue diagnosis. The Histiocyte Society

recommends systemic chemotherapy if the craniofacial bone lesions extend into the dura, as it is a risk factor for diabetes insipidus and neurodegeneration.¹⁶ Endocrine evaluation was normal, and after the tissue diagnosis confirmed LCH, a “wait and see” approach was performed due to the benign nature of the lesion, and according to the preferences of the patient.

An MRI 10 months after biopsy revealed that the enhancing mass in the right sphenoid wing had completely resolved. A CT scan 17 months after the initial biopsy demonstrated complete re-ossification of the bony defect with mild bony sclerosis in the re-ossified area. An additional follow-up MRI 4 years after the needle biopsy demonstrated normal orbital anatomy without evidence of recurrence. Careful monitoring is imperative as recurrence has been described up to 10 years out.¹⁷

Orbital LCH is extremely rare and there is a paucity in the literature discussing its clinical management. Prior cases have reported that a simple biopsy may induce regression of the mass and re-ossification of bone, and this case demonstrates this may happen in older adult patients, as well. A conservative mode of treatment can be employed initially to manage orbital LCH in pediatric or adult patients. If the entity continues to be aggressive, more invasive or systemic treatments may be sought including surgery, radiation, or chemotherapy.

This report demonstrates that simple needle biopsy can be adequate to promote complete resolution of LCH involving the bony anatomy of the skull, with ensuing reestablishment of normal bony anatomy. In light of reports of other similar cases, this case suggests that a conservative approach to managing patients with solitary LCH involving the skull may be appropriate in selected cases, including in adult patients.

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Conflict of Interest

None declared.

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References

- 1 Hand A. Polyuria and tuberculosis. *Arch Pediatr* 1893;10:673–675
- 2 Donadieu J, Chalard F, Jeziorski E. Medical management of langerhans cell histiocytosis from diagnosis to treatment. *Expert Opin Pharmacother* 2012;13(09):1309–1322
- 3 Rajendram R, Rose G, Luthert P, Plowman P, Pearson A. Biopsy-confirmed spontaneous resolution of orbital langerhans cell histiocytosis. *Orbit* 2005;24(01):39–41
- 4 Lee SK, Jung TY, Jung S, Han DK, Lee JK, Baek HJ. Solitary Langerhans cell histiocytosis of skull and spine in pediatric and adult patients. *Childs Nerv Syst* 2014;30(02):271–275
- 5 DiCaprio MR, Roberts TT. Diagnosis and management of langerhans cell histiocytosis. *J Am Acad Orthop Surg* 2014;22(10):643–652
- 6 Giovannetti F, Giona F, Ungari C, et al. Langerhans cell histiocytosis with orbital involvement: our experience. *J Oral Maxillofac Surg* 2009;67(01):212–216
- 7 Harris GJ, Woo KI. Eosinophilic granuloma of the orbit: a paradox of aggressive destruction responsive to minimal intervention. *Trans Am Ophthalmol Soc* 2003;101:93–103, discussion 103–105
- 8 Garrity JA, Henderson JW, Cameron JD. Henderson's Orbital Tumors. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:267
- 9 Kiratli H, Tarlan B, Söylemezoglu F. Langerhans cell histiocytosis of the orbit. *Eur J Ophthalmol* 2013;23(04):578–583
- 10 Shields JA, Shields CL, Scartozzi R. Survey of 1264 patients with orbital tumors and simulating lesions: The 2002 Montgomery Lecture, part 1. *Ophthalmology* 2004;111(05):997–1008
- 11 Glover AT, Grove AS Jr. Eosinophilic granuloma of the orbit with spontaneous healing. *Ophthalmology* 1987;94(08):1008–1012
- 12 El Ayadi C, Benharbit M, Lezrek M, Tachfouti S, Boutimzine N, Daoudi R. Solitary eosinophilic granuloma of the orbit: a case report [in French]. *Bull Soc Belge Ophtalmol* 2007;(305):33–36
- 13 Harzallah L, Braham N, Ben Chérifa L, et al. Solitary eosinophilic granuloma of the orbit: a case report [in French]. *J Fr Ophtalmol* 2005;28(09):983
- 14 Smith JH, Fulton L, O'Brien JM. Spontaneous regression of orbital Langerhans cell granulomatosis in a three-year-old girl. *Am J Ophthalmol* 1999;128(01):119–121
- 15 Satoh K, Tada M, Shimizu H, Yoneoka Y. Early adult-onset orbital apex Langerhans cell histiocytosis histologically confirmed during “truly spontaneous” regression. *Acta Neurochir (Wien)* 2012;154(02):301–302
- 16 Abla O, Egeler RM, Weitzman S. Langerhans cell histiocytosis: current concepts and treatments. *Cancer Treat Rev* 2010;36(04):354–359
- 17 Wladis EJ, Tomaszewski JE, Gausas RE. Langerhans cell histiocytosis of the orbit 10 years after involvement at other sites. *Ophthalm Plast Reconstr Surg* 2008;24(02):142–143