Langerhans Cell Histiocytosis of the Orbit: Spectrum of Clinical and Imaging Findings

Karoly Lakatos, MD[1,*], Katharina Sterlich, MD[2,*], Ulrike Pötschger, MSc[3], Elfriede Thiem, MSc[3], Caroline Hutter, MD[3,4], Helmut Prosch, MD[5], and Milen Minkov, MD, PhD[2,3,6]

Objective To evaluate the clinical and imaging characteristics of orbital lesions of pediatric Langerhans cell histiocytosis (LCH).

Study design A retrospective analysis of clinical data and central review of magnetic resonance imaging scans in patients with LCH, enrolled into one of the consecutive international trials LCH I-III, or submitted for a second opinion between 1994 and 2015.

Results Data from 31 children (34 involved orbits) were analyzed. Orbital LCH was the only disease manifestation in 15, part of a multifocal skeletal in 5, or a multisystem LCH in 11 patients. Orbital LCH was part of the initial disease presentation in 23 or developed at relapse in 8 cases. Orbital involvement was unilateral in 28 and bilateral in 3 patients (34 affected orbits). Proptosis was present in 9 patients. Frontal and zygomatic bone were most commonly affected. All orbital lesions were extraconal. Associated extraorbital imaging findings were dural tail sign in 19, neurodegeneration in 8, and hypothalamic-pituitary mass in 3 patients. Sixteen patients (52%) had at least 1 documented disease relapse. Permanent consequences were prominent proptosis in 1, diabetes insipidus in 8, growth hormone deficiency in 2, radiologic neurodegeneration in 8, and clinical neurodegeneration in 3 patients.

Conclusions Predominantly unilateral orbital LCH can be the only disease manifestation or part of a disseminated disease. Orbital lesions in LCH are exclusively extraconal, typically located at the roof and the lateral wall of the orbit. The optimal treatment approach of unifocal LCH of the orbit remains controversial and warrants a prospective evaluation. *(J Pediatr 2021;230:174-81)*.

Langerhans cell histiocytosis (LCH) is an inflammatory myeloid neoplasia characterized by the accumulation of clonal histiocytes and granuloma formation in affected tissue.[1] It is a rare disorder with a yearly incidence of 4-9 cases per million children younger than 15 years of age.[2-5] The definitive diagnosis of LCH is based on characteristic morphology and positive immunochemical staining for CD1a and CD207 (Langerin).[6]

The clinical spectrum of LCH ranges from a single system to a multisystem (MS-LCH) disease.[7] Orbital lesions can be the only disease location or a manifestation of a multifocal single system LCH of bone (MFB) or an MS-LCH. Proptosis is a characteristic, though a rare sign of LCH.[8,9] There is no uniformly accepted definition of orbital LCH. The term is used interchangeably in the literature with the terms proptosis, exophthalmos, and eye involvement. In fact, the orbital lesions can be variable, ranging from a circumscribed osteolysis to large mass lesions with extension into the adjacent structures (forehead, temporal fossa, or anterior cranial fossa). Erythema, upper eyelid edema, periorbital swelling, tenderness, pain, and proptosis are possible manifestations of orbital lesions. Orbital lesions are associated with increased risk for diabetes insipidus and central nervous system (CNS)-LCH of nongranulomatous type (neurodegeneration).[10]

We present a detailed characterization of the orbital lesions in patients with pediatric-onset LCH based on a retrospective analysis of clinical data and central review of magnetic resonance imaging (MRI) scans, and discuss the controversies related to their management.

Methods

The database of the International LCH Clinical Trials of the Histiocyte Society was retrospectively searched for patients with orbital involvement enrolled by the countries of the Gesellschaft für Pädiatrische Onkologie und Hämatologie (German Society for Pediatric Oncology and Hematology) Sub-Center (Austria,

CNS	Central nervous system
LCH	Langerhans cell histiocytosis
MFB-LCH	Multifocal single system Langerhans cell histiocytosis of bone
MS-LCH	Multisystem Langerhans cell histiocytosis

From the [1]Medical University of Vienna, St. Anna Children's Hospital, Department of Pediatric Radiology; [2]Vienna Nord Hospital, Department of Pediatrics, Neonatology and Adolescent Medicine; [3]CCRI, St. Anna Kinderkrebsforschung; [4]Medical University of Vienna, St. Anna Children's Hospital, Department of Pediatric Hematology/Oncology; [5]Medical University of Vienna, Department of Radiology; and [6]Sigmund Freud Private University, Vienna, Austria

*Contributed equally.

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Germany, and Switzerland). The patients were either enrolled in one of the consecutive clinical trials LCH I-III, or were submitted for a second opinion between 1994 and 2015. The database screening for "eye involvement," "exophthalmos/proptosis," or involvement of bones anatomically constituting the orbit, revealed 517 patients with potential orbital involvement. A closer review of the lesion locations revealed involvement of orbital structures in 41 cases, whereas 476 had skull bone lesions not affecting the orbit (eg, affection of the mastoid of the temporal bone or part of the frontal bone not touching the orbit). The latter were excluded from further analysis. At least 1 MRI scan of sufficient quality was available for detailed radiologic review in 31 patients. Serial (on average, 3) MRI scans were available in 26 patients.

Two radiologists independently reviewed the MRI scans and documented their findings on a spreadsheet designed for a structured image assessment. Items evaluated included: laterality (one-sided vs bilateral), number of lesions (single vs multiple), involved part of the orbit (lateral, medial, roof, and base), location (intraconal vs extraconal), affected bone (maxilla, frontal bone, ethmoid bone, lacrimal bone, sphenoid bone, zygomatic bone, and temporal bone), involvement of the eye globe; compression of the optic nerve; exophthalmos; intracranial tumor extension and dural affection; margins of the lesion (distinct vs nondistinct), presence of CNS-LCH or involvement of the hypothalamus-pituitary region and involvement of the sella turcica. We assessed the characteristics of the mass lesions on T1- and T2-weighted images (hyperintense, isointense, or hypointense). In patients with available serial MRI scans, the dynamics of the orbital findings over time were analyzed in addition. Disease extent categories were: single-system, single site LCH (unifocal orbital LCH), single system, multifocal bone LCH, and MS-LCH. Statistical analysis were performed using methods and definitions (ie, median and range) of descriptive statistics.

Results

We evaluated 73 MRI scans in 31 patients with LCH with orbital involvement. The demographic characteristics of the patients are summarized in **Table I**.

Disease Extent at Orbital Involvement

An orbital lesion was the only disease site in 15 patients (unifocal orbital LCH), whereas it was a manifestation of a MFB-LCH or MS-LCH in another 5 and 11 patients, respectively.

Timing of the Orbital Lesions

The involvement of the orbit was part of the initial presentation of LCH in 23 cases or developed later (in the setting of a progression or relapse) in 8 cases. In those 8 cases, the median time from LCH diagnosis to orbit involvement was 16 months (range, 3-62 months).

Clinical Manifestations of Orbital Lesions

Orbital lesions manifested in 26 patients with one or more of the following: eyelid swelling or palpable mass (n = 15), temporal swelling (n = 10), proptosis (n = 9), eyelid redness (n = 5), pain (n = 1), and strabismus convergens (n = 1). In 5 patients the lesions were not clinically manifest and were detected on imaging performed for evaluation of disease extent.

Detailed Characterization of Orbital Lesions at First MRI

The left orbit was affected in 15 patients, the right orbit in 13 patients, and 3 patients had a bilateral orbit involvement (**Table II**; available at www.jpeds.com). The lesions margins were distinct in 14 and blurred in 17 patients. The frequency of affection of the individual orbit-forming bones is depicted in **Figure 1**. Respectively, the lateral orbital wall was affected in 25 patients, the medial wall in 2 patients, and 1 patient had extensive lesions involving both the lateral and medial orbital walls, and 3 patients had lesions confined to the roof only. Orbital roof was affected by extension from the lateral (n = 20) or medial (n = 3) wall in another 23 patients. Orbital base was affected by extension of lateral lesions in 3 patients only. In 16 patients bone destruction was associated with an extensive soft tissue mass. Intracranial extension of the lesion was documented in 4 patients.

Interestingly, all lesions were extraconal (**Figure 2** and **Figure 3**), and none of the patients had involvement of the eye globe or compression of the optic nerve. On T1W images, the lesions were hyperintense in 3 patients and isointense to hypointense in 28 patients. On T2W images, the lesions appeared hyperintense in 21 patients and isointense to hypointense in 7 patients (T2W images were not available in 3 patients). Contrast enhancement was rated as strong in 26 (87%) and weak in 3 of 29 (13%) evaluable MRI scans. In 22 MRI scans, the bone marrow enhancement was judged as homogeneous and in nine as inhomogeneous.

Extraorbital Imaging Findings

A dural tail sign was found in 19 patients, nongranulomatous (neurodegenerative) CNS lesions in 8 patients, and hypothalamus-pituitary mass in 3 patients.

Course of the Orbital Lesions

Serial scans were available in 26 patients (median, 3 patients; range, 2-6 patients). MRI scans performed at 1 and 2 years after manifestation of orbital LCH, documented resolution of the orbital lesions in 39% and 50% of the cases, respectively.

Clinical Course and Permanent Consequences

Sixteen patients (52%) had at least 1 documented disease relapse. Relapse in a previously involved orbit was observed in 1 patient only. The following permanent consequences were reported: permanent prominent proptosis in 1 (3%), diabetes insipidus in 8 (26%), growth hormone deficiency

Table I. Population characteristics of the study cohort

LCH extents at orbital involvement	SS-SS orbital LCH	SS-MFB LCH	MS-LCH	Total
No. of patients	15	5	11	31
Sex (m:f)	8:7	4:1	6:5	18:13
Age at LCH diagnosis (years)	median 5.0 (range, 0.3-14.8)	median 2.6 (range, 0.4-11.2)	median 1.4 (range, 0.1-13.2)	median 2.6 (range, 0.1-14.8)
Age at orbital involvement	median 5.2 (range, 2.2 -14.8)	median 2.6 (range, 0.4-11.2)	median 1.9 (range, 1.0-13.2)	median 3.5 (range, 0.4-16.8)
Timing of orbital involvement				
At LCH diagnosis (n)	12	3	8	23
Developed later (n)	3	2	3	8
LCH diagnosis to orbit involvement (months)	7, 35, 45	3, 10	16, 16, 62	median 16 (range 3-62)
Laterality of orbit involvement:				
Right orbit	5	2	6	13
Left orbit	10	2	3	15
Bilateral	-	1	2	3
Observation time (years)	median 3.3 (9.9-10.8)	median 7.0 (range, 4.3-13.8)	median 6.3 (0.9-21.8)	median 5 (range, 0.9-21.8)
Relapse of LCH (no. of patients)	6 (40%)	2 (40%)	8 (73%)	16 (52%)
Permanent consequences				
Number of patients	4*	1	5	0
Spectrum†				
Permanent proptosis	1	-	-	1
Diabetes insipidus	3	1	4	8
Growth hormone deficiency	-	-	2	2
Radiologic neurodegeneration	2 (1)‡	1 (0)‡	5 (2)‡	8 (3)‡

SS-MFB single-system, multifocal bone; *SS-MFB LCH*, single system, multifocal bone LCH; *SS-SS,* single-system, single site (orbit).
*All patients with progression or relapse.
†Some patients had more than 1 permanent consequences.
‡Brackets indicate patients with clinical neurodegeneration.

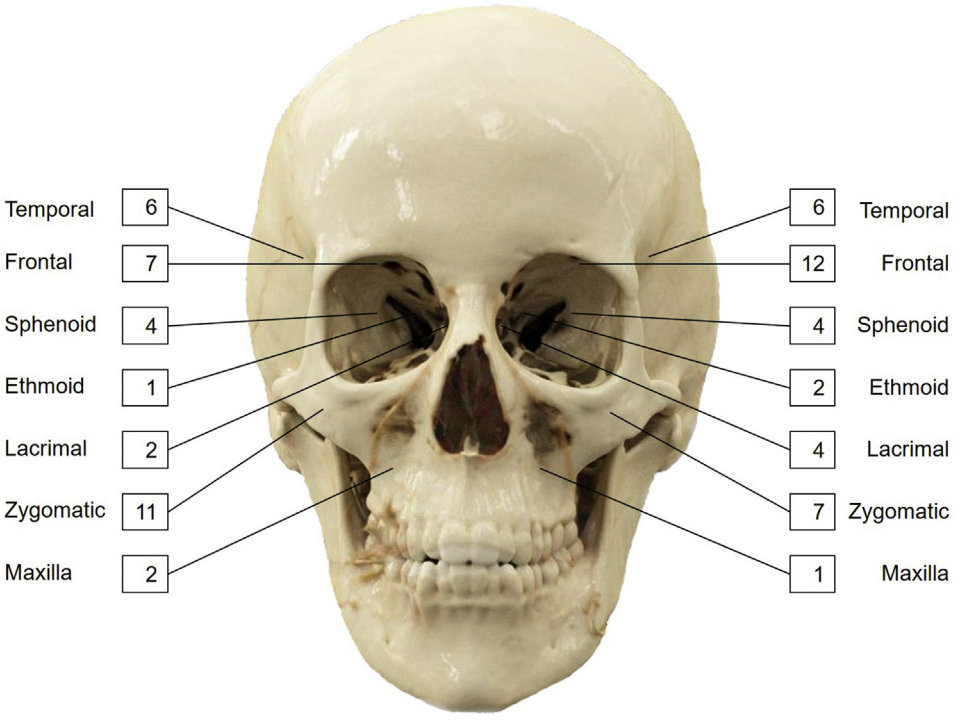

Figure 1. Frequency of involvement of the individual orbit-forming bones.

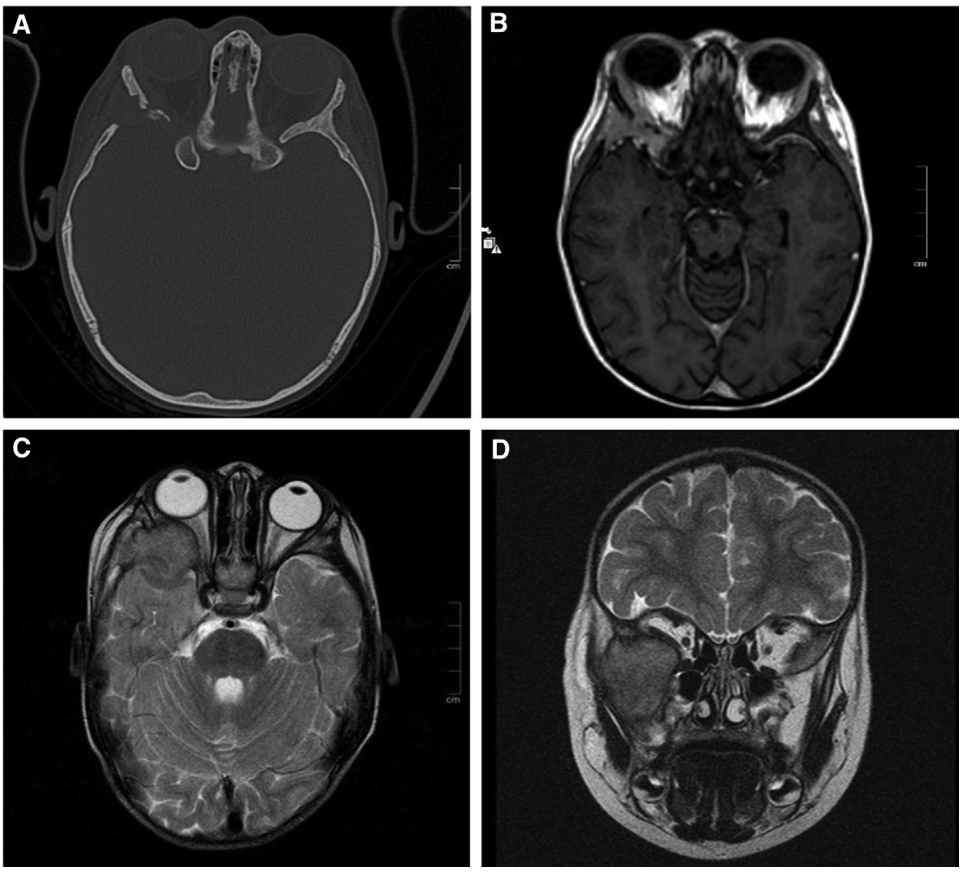

Figure 2. **A,** Axial computed tomography scan and **B,** T1-weighted MR images of an extraconal destructive lesion of the right lateral orbit. **C,** Axial and **D,** coronal T2-weighted images of a solid extraconal mass of the right orbit revealing displacement of the lateral rectus muscle with infiltration of the greater sphenoidal wing and the temporal muscle, clinically presenting with a proptosis.

in 2 (6%), radiologic neurodegeneration in 8 (26%), and clinically manifest neurodegeneration in 3 (10%) patients. Diabetes insipidus was present at LCH diagnosis in 2 patients and developed later in another 6 patients (median time after diagnosis, 2.5 years). Neither radiologic nor clinical neurodegeneration were documented at initial diagnosis of LCH, and they developed in 7 patients during disease course at median of 4.9 years (range, 2.7-8.7) after a diagnosis of LCH.

Discussion

Orbital lesions and associated symptoms (eg, proptosis) are a well-recognized presentation of LCH.[8,9,11,12] The frequency of orbital LCH depends on the denominator used for its calculation. Among orbital tumors and tumor-like lesions of any age, orbital LCH accounts for 1% or less of the cases; however, it makes 7% of the pediatric orbital tumors causing proptosis.[13-17] In published LCH series, involvement of the orbit was reported in 12.0%-37.5% of the cases.[13,18,19] Our database search identified orbital involvement in 41 of 517 patients (8%). In the case series published by ophthalmologists and oculoplastic surgeons, unifocal orbital LCH was the dominating form; however, it can be a manifestation of a MFB-LCH or a MS-LCH.[13,19-22] In our study, 52% of the patients with LCH with orbital involvement had a disseminated LCH. In agreement with other authors, orbital involvement in our cohort affected predominantly young children with male predominance.

Orbital LCH manifests with a range of complaints, signs, and symptoms. Those most consistently described in the literature are proptosis, diffuse periorbital swelling with or without redness, discrete swelling of the upper and occasionally the lower eyelid, palpable soft tissue mass, and ptosis.[13,22-25] Respectively, the clinical differential diagnosis of orbital LCH in children encompasses inflammatory processes (eg, preseptal cellulitis, orbital phlegmone, dacryoadenitis, and inflammatory pseudotumor), dermoid cysts, fibromatosis, fibrous dysplasia, vasculogenic masses, rhabdomyosarcoma, lymphoma, leukemia (chloroma), Ewing tumor, and neuroblastoma metastases. Finally, other histiocytic disorders (Rosai-Dorfman disease, Erdheim-Chester disease, and juvenile xanthogranuloma) can manifest in similar way and require consideration. Interestingly, proptosis, which is a very well recognized sign of LCH develops in less than 50% of patients with orbital involvement.[26] Proptosis was a presenting symptom of orbital LCH in 9 of our patients (29%).

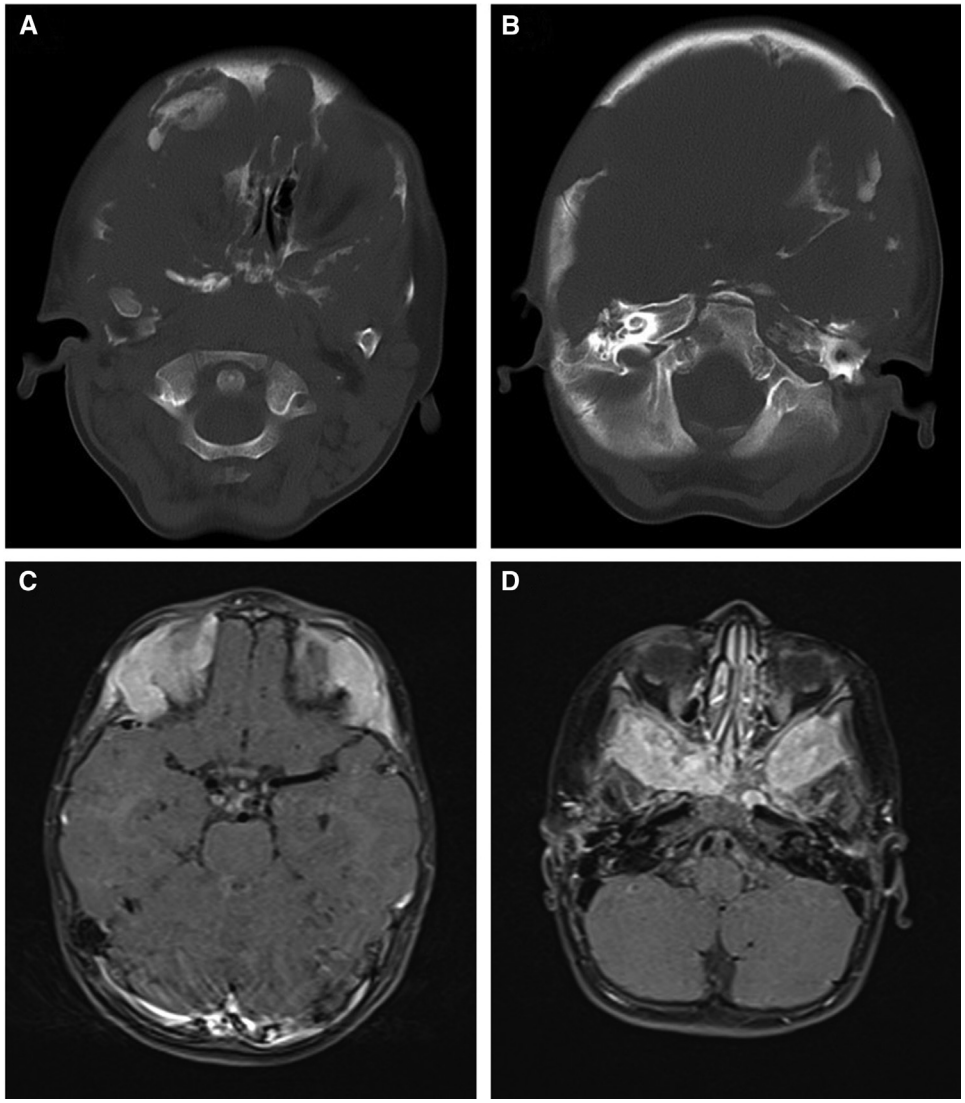

Figure 3. Extensive destruction of the skull base and both orbits causing bilateral proptosis in a 3-year-old girl. **A, B**, Axial computed tomography images illustrating extensive destruction of the skull base with involvement of both orbits. **C, D,** Axial contrast enhanced T1-weighted MR images depicting the soft tissue masses adjacent to the bone lesions.

In our experience and according to previous publications, proptosis is invariably associated with a lytic lesion of the orbital wall.[13,26,27] Our observation confirms previous report, that orbital lesions can be clinically silent and incidentally detected at imaging performed for initial systemic assessment.[13,26]

Orbital LCH is mostly unilateral and rarely bilateral.[13,18,20-22,25] It presents as bone destruction associated with a soft tissue mass of varying size and extent. Displacement of adjacent structures, particularly the eye globe, may cause proptosis, palpable mass, or tissue swelling. The lesions are typically extraconal and are most commonly located at the superolateral part of the orbit (affecting the lateral wall and the roof), and much less frequently at the orbital floor, medial wall, or apex.[13,18,19,22,28,29] Respectively, the frontal, zygomatic, and sphenoid bones are the most commonly affected orbit-forming bones in all published series and case reports. The eye globe and the intraocular structures seem to be rarely affected by LCH.[28] Neuro-ophthalmic complications, such as papilledema, optic atrophy, secondary glaucoma, or cavernous sinus syndrome, have been reported in anecdotal cases only.[13,30-34] This observation is not surprising, considering the typically extraconal location of the orbital lesions in patients with LCH. Likewise, none of our patients had an intraocular LCH. Depending on size and location, the orbital lesion can extend into adjacent extraorbital structures, such as the anterior cranial fossa, infratemporal fossa, and the paranasal sinuses.[18,21,22,25,35] There are rare reports of extension of orbital LCH into the middle cranial fossa.[36,37]

On plain radiography, LCH appears as osteolytic lesions with beveled or irregular margins, with or without sclerosis.[38]

The radiologic appearance of orbital LCH can vary depending on the developmental stage of the lesion. At early stage, it is an aggressive-looking osteolytic lesion, with a large transition zone and a discontinuous periosteal reaction.[39] At later stages, these lesions regain a benign appearance with well-limited peripheral osteosclerosis and a small transition zone. On computed tomography scan, LCH appears as soft tissue masses that replace and destroy the osseous structures.[38] Compared with plain radiography, a computed tomography scan is more sensitive for determining cortical disruption and assessing bone destruction and soft tissue masses, but it is associated with radiation burden. MRI offers a high-resolution visualization of the normal structures of the orbit and captures well soft tissue masses, bone destruction, dural affection, and lesions of the hypothalamic-pituitary region and the brain structures. Therefore, MRI is particularly suited for the evaluation of the intracranial extension of LCH. Combined with the advantage of being free of radiation, it is a preferred method for imaging orbital lesions in children.[34,37] A LCH lesion is seen as a mass of heterogeneous signal intensity that replaces the bone.[38] Orbital lesions of LCH are isointense to iso-hypointense on T1W and reveal a mixed (hyperintense to hypointense) pattern on T2W images.[20,25,34,38,39] They usually show moderate to marked enhancement after contrast application.

Orbital LCH is mostly part of the disease presentation, but as evidenced by our experience and that of other authors it may develop later in the setting of disease progression or relapse.[13,19,37,40,41] Furthermore, there are reports documenting that orbital lesions can recur after treatment.[13,42]

The management of orbital LCH is a matter of ongoing debate: there are 2 opposite attitudes.[10,19,28,43-47] Although ophthalmologists and orbital surgeons advocate a "more conservative" approach including subtotal curettage with intralesional steroids, pediatric oncologists recommend systemic therapy, driven by concerns for associated debilitating permanent consequences and the belief in the preventive role of systemic treatment.[10,19,22,44-46,48,49] Case reports and case series published by ophthalmologists and orbital surgeons are obviously skewed toward LCH confined to orbit ("unifocal orbital LCH" or "eosinophilic granuloma of the orbit").[20-22,28,34,35,37,40,47-51] Subtotal curettage and intralesional steroids are able to cure the majority of those cases, as evidenced by the low recurrence rates and the lack of CNS-related permanent consequences. However, our experience (4 of 15 patients) and other larger series, show that patients presenting with unifocal orbital LCH can progress to more disseminated disease and end up with permanent consequences.[19,22,37] Patients with incomplete response, progression or relapse, could be cured by subsequent systemic therapy.[22,37,52] An analysis of the pertinent literature does not provide convincing evidence for unifocal orbital LCH being a risk factor for CNS-related permanent consequences.[10,43-46,48,53] Nevertheless, systemic therapy may be the less risky option in patients with extensive lesions or large retrobulbar mass.[54]

Regarding orbital involvement in the setting of MFB-LCH or MS-LCH, there is an agreement for a multidisciplinary management and systemic treatment.[10,19,22,44,45] This agreement is based on the increased risk for diabetes insipidus and neurodegeneration in patients with disseminated LCH and orbital involvement, which has been substantiated by several studies.[10,43,55] A prospective validation of the concept of "CNS-risk lesions" introduced by Grois et al, is expected from a respective stratum from the ongoing LCH-IV clinical study of the Histiocyte Society.[10] Central diabetes insipidus is due to a permanent loss of antidiuretic hormone, which can be managed by replacement therapy with desmopressin. However, patient with diabetes insipidus have an increased risk to develop neurodegeneration. Neurodegeneration, or CNS-LCH of nongranulomatous type is the most devastating complication of LCH, owing to inflammation and neuronal loss.[56-58] It usually develops insidiously and can manifest many years after LCH diagnosis even in the absence of active extracranial disease. Importantly, not all patients with characteristic MRI findings will develop overt clinical manifestations.[59,60] The speculation about the preventive role of timely initiated systemic therapy stems from a comparison of published cohorts with unknown reporting or selection bias.[43] The fact that in that study, 10% of the patients with disseminated LCH developed diabetes insipidus despite 12 months of combination chemotherapy, questions the preventive role of systemic therapy per se, limiting the speculation to possible risk minimizing.[43] Subsequent analysis of a larger dataset failed to demonstrate difference among regimens of different treatment intensity and duration.[10] The preventive role of systemic therapy on endocrine or CNS-related permanent consequences has been questioned by other authors, as well.[53,61] The common weakness of these cited studies is that they all have been done in retrospect. Randomized prolongation of treatment duration from 6 to 12 months in the low-risk group of the LCH-III study, failed reducing the rate of central diabetes insipidus in MS-LCH.[62] The currently ongoing LCH-IV study of the Histiocyte Society strives for further improvement of outcomes in MS-LCH in a 2×2 factorial design trial (randomizing for treatment duration of 12 vs 24 months, as well as for addition of mercaptopurine to the standard combination of steroids and vinblastine). The data are expected to definitively prove or rebut the preventive role of the standard first-line treatment regimen on neuroendocrine permanent consequences of LCH.

Although the dispute about the optimal treatment of orbital LCH cannot be solved without robust prospective data, it is obvious that the optimal approach in an individual case requires multidisciplinary cooperation and a weighted use of local and systemic treatment modalities. Orbital involvement in pediatric LCH is predominantly unilateral and can be the only disease manifestation or part of a more disseminated disease. Orbital lesions in LCH are exclusively extraconal, typically located at the roof and the lateral wall of the orbit. Hence, the zygomatic and frontal bones are most commonly affected. The optimal treatment approach

of unifocal LCH of the orbit remains controversial. Prospective data from the ongoing LCH-IV clinical study (https://clinicaltrials.gov/ct2/show/NCT02205762) are expected to provide evidence needed for informed clinical decisions. ■

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Reprint requests: Milen Minkov, MD, PhD, Professor of Pediatrics, International LCH Study Reference Center, CCRI, St. Anna Kinderkrebsforschung, Zimmermannplatz 10, A-1090 Vienna, Austria. E-mail: milen.minkov@stanna.at

Data Statement

Data sharing statement available at www.jpeds.com.

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Table II. MRI findings

			TW-characteristics and contrast enhancement										Lesion location						Affected bones								Eye	Nerves	Margins		Mass	Extention	Extracran. findings		
Patient Number	LCH extent	Laterality of orbit involvement	T1hyper	T1hypo	T1iso	T2hyper	T2hypo	T2iso	Contrast enhancement strong	Contrast enhancement weak	Signal homogenous	KM inhomogenous	extraconal	intraconal	lateral	medial	roof	b ase	Os frontale	Maxilla	Os ethmoidale	Os palatinum	Os lacrimale	Os spheniodale	Os zygomaticum	Os temporale	Eye buld affection	Optic nerve affection	Distinct margin	Blurred margin	Soft tissue mass	Intracranial extention	Radiol neurodegeneration	Sellar mass	dural tail sign
1	MFB	left	no	no	yes	yes	no	no	yes		no	yes	yes	no	yes	no	yes	no	no	no	no	no	no	L	no	no	no	no	no	yes	yes	no	no	no	yes
2	SS-LCH	left	no	no	no	yes	no	no	yes		yes	no	yes	no	yes	no	yes	no	no	no	no	no	L	no	no	no	no	no	no	yes	yes	no	no	no	yes
3	SS-LCH	left	no	no	yes	yes	no	no	yes		yes	no	yes	no	yes	no	yes	no	no	no	no	no	no	no	L	no	no	no	no	yes	yes	no	no	no	yes
4	SS-LCH	right	no	no	yes	no	yes	no	yes		yes	no	yes	no	yes	no	yes	no	no	no	no	no	no	no	R	no	no	no	no	yes	no	no	no	no	no
5	SS-LCH	left	no	yes	no	yes	no	no	yes		yes	no	yes	no	yes	no	yes	no	no	no	no	no	L	no	no	no	no	no	no	yes	no	no	no	no	yes
6	MS-LCH	right	no	yes	no	yes	no	no	yes		yes	no	yes	no	yes	no	yes	no	R	no	no	no	no	no	R	no	no	no	no	yes	yes	no	yes	no	yes
7	SS-LCH	right	yes	yes	no	yes	no	no	yes		no	yes	yes	no	yes	no	no	no		no	no	no	no	no	R	R	no	no	no	yes	yes	no	no	no	yes
8	SS-LCH	left	no	no	yes	no	no	yes	no	yes	yes	no	yes	no	yes	no	yes	no	L	no	no	no	no	no	no	no	no	no	yes	no	yes	no	no	no	yes
9	SS-LCH	left	no	no	yes	yes	no	no	yes		no	yes	yes	no	no	yes	yes	no	L	no	L	no	no	no	no	no	no	no	no	yes	yes	no	no	no	yes
10	MS-LCH	left	no	no	yes	yes	no	no	yes		yes	no	yes	no	no	no	yes	no	L	no	no	no	L	no	no	no	no	no	yes	no	no	no	yes	no	yes
11	MS-LCH	right	no	no	yes	yes	no	no	na	na	yes	no	yes	no	yes	no	yes	no		no	no	no	no	R	no	no	no	no	no	yes	no	no	no	no	no
12	MS-LCH	left	no	no	yes	no	no	yes	yes		yes	no	yes	no	yes	no	yes	no	L	no	no	no	no	no	no	L	no	no	yes	no	no	yes	no	no	yes
13	SS-LCH	right	no	no	yes	yes	no	no	yes		yes	no	yes	no	yes	no	yes	no		no	no	no	R	no	no	no	no	no	yes	no	yes	no	no	no	yes
14	MFB	left	no	yes	no	no	yes	no	no	yes	yes	no	yes	no	yes	no	yes	no	L	no	no	no	no	no	no	no	no	no	yes	no	yes	no	no	no	no
15	MFB	right	no	no	yes	yes	no	no	yes		yes	no	yes	no	yes	no	yes	no	R	no	no	no	no	no	R	no	no	no	yes	no	no	no	no	no	yes
16	MFB	Bilat	yes	no	no	no	no	yes	yes		yes	no	yes	no	yes	no	yes	no	RL	RL	no	no	RL	RL	RL	RL	no	no	no	yes	yes	no	no	no	yes
17	SS-LCH	left	no	yes	no	no	yes	yes	no	yes	yes	no	yes	no	yes	no	no	yes		no	no	no	no	L	no	no	no	no	yes	no	no	no	no	no	no
18	SS-LCH	right	no	yes	no	yes	no	no	yes		no	yes	yes	no	yes	no	no	no		no	no	no	no	no	R	no	no	no	yes	no	yes	yes	no	no	yes
19	MS-LCH	right	no	yes	no	yes	no	no	yes		yes	no	yes	no	no	no	yes	no		no	no	no	no	no	R	no	no	no	yes	no	no	no	no	no	no
20	MFB	right	no	no	yes	yes	no	no	yes		yes	no	yes	no	no	yes	yes	no	R	no	no	no	no	no	no	no	no	no	no	yes	no	no	yes	yes	no
21	MS-LCH	right	no	yes	no	yes	no	no	yes		yes	no	yes	no	yes	no	yes	no		no	no	no	no	no	no	R	no	no	yes	no	no	no	no	no	no
22	SS-LCH	right	no	yes	no	yes	no	no	yes		no	yes	yes	no	no	no	yes	no		no	no	no	no	no	R	R	no	no	yes	no	no	yes	no	yes	yes
23	MS-LCH	right	no	yes	no	no	no	yes	yes		yes	no	yes	no	yes	no	yes	no		no	no	no	no	no	R	no	no	no	yes	no	no	no	yes	no	yes
24	MS-LCH	Bilat	no	yes	no	yes	no	no	yes		yes	no	yes	no	yes	no	no	yes	RL	R	no	no	no	no	L	RL	no	no	yes	no	no	no	no	no	no
25	SS-LCH	left	no	no	yes	na	na	na	na	na	yes	no	yes	no	yes	no	no	no		no	no	no	no	no	L	L	no	no	no	yes	yes	no	no	no	no
26	MS-LCH	left	no	yes	yes	na	na	na	yes		yes	no	yes	no	yes	no	yes	no	L	no	no	no	no	no	no	no	no	no	no	yes	no	no	yes	no	no
27	MS-LCH	right	no	yes	no	yes	no	no	yes		no	yes	yes	no	yes	no	yes	no	R	no	no	no	no	R	R	no	no	no	no	yes	yes	no	yes	no	yes
28	MS-LCH	Bilat	no	yes	no	yes	no	no	yes		no	yes	yes	no			yes	yes	RL	no	RL	no	no	RL	RL	RL	no	no	no	yes	yes	no	no	no	yes
29	SS-LCH	left	no	yes	no	na	na	na	yes		no	yes	yes	no	yes	no	yes	no	L	no	no	no	no	no	L	no	no	no	no	yes	yes	yes	yes	yes	yes
30	SS-LCH	left	yes	no	no	yes	no	no	yes		no	yes	yes	no	yes	no	yes	no	L	no	no	no	no	no	no	no	no	0	yes	no	no	no	yes	no	no
31	SS-LCH	left	no	yes	no	yes	no	no	yes		yes	no	yes	no	yes	no	yes	no	L	no	no	no	no	no	L	L	no	0	no	yes	yes	no	no	no	no

Bilat, bilateral; *KM*, contrast enhancement; *L*, left; *na*, not available; *R*, right; *RL*, right and left; *SS-LCH*, single-system, single site (orbit).