Langerhans Cell Histiocytosis of the Head and Neck: Experience at a Rural Tertiary Referral Center

Tyler Schwartz, MD[1]; Leighton Elliott, MD[2]; Heather Fenley, MD[1]; Jagadeesh Ramdas, MD[3]; J. Scott Greene, MD[1]

[1] Department of Otolaryngology - Head and Neck Surgery, Geisinger Medical Center
[2] Medicine Institute, Geisinger Medical Center
[3] Pediatric Hematology and Oncology, Geisinger Medical Center

INTRODUCTION

Langerhans cell histiocytosis (LCH) is a disease characterized by proliferations of myeloid progenitor cells with a resemblance to Langerhans cells. These lesions are found predominantly within bone, however almost all organ systems can be involved. There is much debate in the literature regarding the classification of this process as an immunodysregulatory disorder or a true neoplastic disease.[2] Diagnosis is made by biopsy with characteristic cell types and confirmatory staining revealing S100 cytoplasmic protein and CD1a or CD207 glycoproteins. Treatment options are varied and include chemotherapy with systemic steroids, radiation therapy, and surgical resection. There is limited information in the literature regarding primary head and neck LCH.

METHODS

A retrospective chart review was performed of the electronic medical record utilizing ICD-9 and 10 codes between 2003 and 2019. Only charts with documented visits to dentistry, oral and maxillofacial surgery, otolaryngology, or neurosurgery were included in order to identify patients with head and neck involvement. 38 patients were identified. Inclusion criteria limited cases to those with biopsy proven disease and the accepted histopathologic markers. Upon manual review, 24 patients met criteria for primary head or neck LCH. Data collection included demographics, clinical presentation, primary physical exam findings, histopathology, imaging, treatment regimen, and recurrence. Length of follow-up was calculated from date of completion of treatment to the last documented hematology / oncology appointment. Additional data of interest included time from first documented symptom to biopsy, diagnosis, treatment, and overall survival.

RESULTS

Twenty-four patients with histopathologically confirmed LCH were included in the study (19 males, 5 females). Average age at diagnosis was 106 months (8.8yrs) and average length of follow-up information available was 68mos (5.7yrs). The presenting symptoms were otorrhea (n=6), scalp pain or mass (n=6), headaches (n=5), oral cavity lesions (n=4), frontal or facial pain (n=4), and orbital proptosis (n=1). Seven presented with primary temporal bone lesions, 13 with other facial or skull lesions, 3 with oral cavity involvement, and 1 with a cervical neck node. Ten of the 20 skull lesions demonstrated CNS risk lesions given lesion proximity to the dura. The subsites involved were the squamous and mastoid (n = 4 each), followed by EAC and middle ear (n = 2 each), with petrous portion in one patient.

Six patients were treated with primary surgical resection, 15 with primary chemotherapy (vinblastine with prednisone), and 3 with surgical resection and adjuvant chemotherapy. Nine patients had relapse of disease with average time to documented relapse being 11.4mo. All relapses were treated with salvage chemotherapy (cladribine, clofarabine, or cytarabine). All patients, except one who transferred care during salvage therapy, were disease-free at last documented follow-up. Relapse details are outlined in Table 1. Average time from initial reported symptoms to diagnosis was 190 days for non-temporal bone lesions and 300 days for primary temporal bone lesions.

Table 1: Clinical Features

Primary Symptom, n = 24	No. (%)
Otorrhea	6 (25%)
Scalp/skull lesion	6 (25%)
Headaches	5 (20.8%)
Oral cavity lesions	4 (16.7%)
Frontal/facial pain or mass	4 (16.7%)
Orbital proptosis	1 (4.2%)
Exam Findings, n = 24	**No. (%)**
Otitis media or externa	6 (25%)
EAC granulation tissue	4 (16.7%)
Gingival mass/dental abnormalities	5 (20.8%)
Skull mass	10 (41.7%)
Mastoid fluctuance	2 (8.3%)
Exophthalmos	1 (4.2%)
Scalp lesion	3 (12.5%)
Cervical lymphadenopathy	1 (4.2%)

Table 2: Recorded Time from Initial Symptom to Treatment in Days

	Time from Initial Symptom to Biopsy	Time from Biopsy to Diagnosis	Total Time from Initial Symptom to Diagnosis	Time from Diagnosis to Start of Chemotherapy (n = 16)	Total Time from Initial Symptom to Chemotherapy Start (n = 16)
Median	50.5	3.0	57.5	13.5	71.0
Average	185.1	5.2	190.3	22.3	219.6
Maximum	966	49	972	144	780
Minimum	11	0	14	0	20

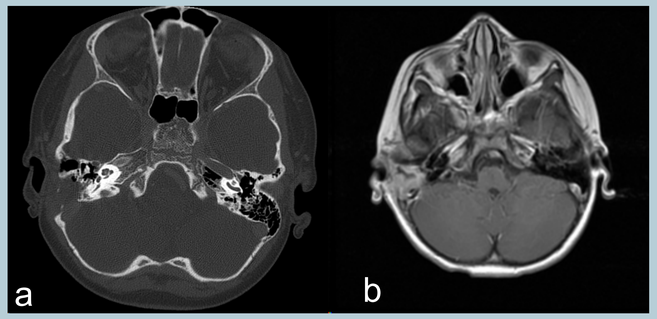

Figure 2: Unifocal LCH of the Right Temporal Bone. a) axial CT w/o contrast, osteolytic lesion of the right mastoid with erosion into the posterior fossa, b) axial MRI T1 with contrast, soft tissue lesion of right mastoid and intracranial extension into posterior fossa

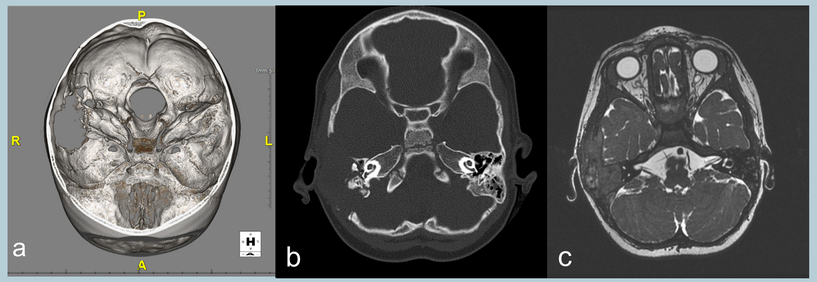

Figure 1: Aggressive right temporal bone lesion a) 3D reconstruction b) axial CT highlighting intracranial extension and zygomatic arch erosion c) MRI brain FIESTA image with demarcation between temporal lobe and mass elucidating intracranial, extracranial extension

Table 3: Recurrence Rates by Category

Treatment Modality	No. (% of Total)	No. Recurred (% of Category)
Primary Surgery	7 (29.2%)	2 (28.6%)
Primary Chemotherapy	14 (58.3%)	6 (42.9%)
Surgery with Adjuvant Chemotherapy	3 (12.5%)	1 (33.3%)
Salvage Chemotherapy for Recurrence	9 (37.5%)	2 (22.2%)
Site Location		
Temporal Bone	7 (29.2%)	4 (57.1%)
Other Skull/Facial	13 (54.2%)	4 (30.8%)
Oral Cavity	3 (12.5%)	0 (0%)
CNS Risk Lesions	10 (41.7%)	4 (40%)
Disease Extent		
Single System, Unifocal	14 (58.3%)	3 (21.4%)
Single System, Multifocal	3 (12.5%)	1 (33.3%)
Multisystem	7 (29.2%)	5 (71.4%)

DISCUSSION

LCH is a complex disease process in which diagnosis can be easily delayed since the most common presenting symptoms (otorrhea and headache) mimic more common diagnoses. Within the head and neck, the skull, including isolated temporal bone lesions, is the most common site of involvement. Treatment modality does not appear to have an influence on recurrence rates. Site of lesion was a factor in recurrence, with temporal bone lesions (4/7, 57%) and multisystem involvement (5/7, 71%) demonstrating higher rates of recurrence. All patients with recurrent disease were successfully treated with salvage chemotherapy. Diagnosis and treatment involve a multidisciplinary approach with long term follow-up. While the average time to recurrence was 11.4months in our study, one patient demonstrated recurrence 36 months post-diagnosis.

Time to diagnosis varied greatly between lesion sites: temporal bone lesions averaged 300 days, whereas other lesions averaged 190 days. Non-temporal bone lesions usually presented with a visible or palpable mass whereas temporal bones lesions presented with otorrhea mimicking common conditions (otitis media or otitis externa). Healthcare disparities for patients living in rural areas (limited access to transportation, social services, and low socioeconomic status) also contribute to delayed diagnosis.

This is the first study to report outcomes and presentation characteristics of LCH in a rural healthcare setting. This contribution to the body of knowledge of LCH will hopefully increase overall awareness of the disease, enable earlier diagnosis, and increase successful treatment.

CONTACT: Tyler Schwartz, MD; Phone: (219)718-1921; Email: trschwartz@gmail.com