Minimally invasive diagnosis of Langerhans cell histiocytosis: a retrospective review of the use of fine needle aspiration.

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Introduction
Paul Langerhans, the namesake of Langerhans cell histiocytosis, initially described the "Langerhans cell" as belonging to the nervous system. Despite the many advances in diagnosis and treatment seen in the decades since the Langerhans cell was first described in 1868, the cause of Langerhans cell histiocytosis (LCH) remains elusive. LCH is a disease characterized by the clonal proliferation of Langerhans cells, an antigen-presenting cell. It is purported to have both reactive and neoplastic qualities, and is not classified as a solely inflammatory or a solely malignant disease. LCH, previously known by the terms Histiocytosis X, eosinophilic granuloma, Hand-Schüller-Christian disease, and Letterer-Siwe disease, is now known as a Class I childhood histiocytosis by the International Histiocyte Society.¹

Langerhans cell histiocytosis is a rare disease. There are estimates to be 2.6-8.9 cases per million children (less than 15 years old) per year.² Despite the rarity of LCH, a significant percentage of cases of LCH involve the head and neck. Several retrospective studies spanning decades have found 67-82% of cases of LCH involve the head and neck.³,⁴ Bony involvement occurs in 75% of cases.²

In general, the prognosis of single system LCH is excellent. Even more striking is the potential, and sometimes proclivity, of LCH to spontaneously resolve in children. Although treatment strategies vary from institution to institution and are dependent on the extent of disease, such findings have led many authors to advocate the role of surgical intervention be limited to that of diagnosis.³,⁴,⁵

Biopsy is required for the diagnosis of LCH. The diagnosis of LCH requires finding the representative Langerhans cell, as well as the finding that that representative Langerhans cells stain positively for CD1a and/or CD207 (Langerin).⁶ Although such diagnostic findings can be achieved by means of surgical curettage and surgical excision, it is essential to note that such findings can also be achieved by means of a minimally invasive approach: fine needle aspiration.

Objective and Study Design
OBJECTIVE: To assess the usefulness and accuracy of fine needle aspiration as a diagnostic tool for Langerhans cell histiocytosis in the patient population at large, as well as the subset of patients affected by Langerhans cell histiocytosis of the head and neck.

STUDY DESIGN: A retrospective study of patients who were diagnosed with Langerhans cell histiocytosis (LCH) between December 1986 and February 2014 at Lurie Children’s Hospital (formerly Children’s Memorial Hospital) in Chicago, Illinois.

Results
Ninety-nine patients were diagnosed with LCH at our institution during this time period. Fourteen of the 99 total patients were evaluated by means of fine needle aspiration (FNA). Eleven of the 14 patients (79%) were diagnosed on the first attempt at FNA. Twelve of the 14 (86%) were diagnosed by the second attempt at FNA.

Of the 99 total patients diagnosed with LCH between 1986 and 2014, 78 (79%) were diagnosed with lesions of the head and neck. Eight of the 78 patients with disease diagnosed in the head and neck had FNAs performed as part of the diagnostic evaluation. Of the patients diagnosed with LCH of the head and neck who also had FNAs performed, 6 out of 8 (75%) were diagnosed with LCH on the first attempt at FNA. Seven out of 8 (88%) were diagnosed by the second attempt at FNA.

Discussion
Langerhans cell histiocytosis is a rare cause of lytic bony lesions in pediatric patients. A majority of pediatric LCH lesions occur in the head or neck. Fine needle aspiration is a minimally invasive technique that can successfully diagnose LCH. FNA as the first, and often only, step in diagnosis is useful because it is safe, simple and efficacious. FNA can avoid the higher morbidity associated with surgical curettage or surgical excision. If diagnosed by FNA, management of LCH lesions of the head or neck may not require further surgical intervention as many lesions resolve spontaneously or are treated with medical therapy alone. In cases where an FNA is non-diagnostic or further surgical intervention is required, surgical curettage and surgical excision remain as more invasive options to obtain tissue for diagnosis or for further surgical management of LCH lesions.

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Table 1. Results of retrospective review.

<table>
<thead>
<tr>
<th>Diagnosis of LCH</th>
<th>LCH (all sites)</th>
<th>LCH (head &amp; neck)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FNA, on 1st attempt</td>
<td>11 (79%)</td>
<td>6 (75%)</td>
</tr>
<tr>
<td>FNA, by 2nd attempt</td>
<td>12 (86%)</td>
<td>7 (88%)</td>
</tr>
<tr>
<td>FNA, nondiagnostic</td>
<td>2 (14%)</td>
<td>1 (13%)</td>
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<tr>
<td>Total FNA biopsies</td>
<td>14</td>
<td>8</td>
</tr>
<tr>
<td>Total patients</td>
<td>99</td>
<td>78</td>
</tr>
</tbody>
</table>

References
2. Defina Oncology of Infancy and Childhood, 1st ed. Chapter 24: Histiocytosis. Langerhans Cell Histiocytosis