AN UNUSUAL CASE OF MILIARY MOTTLING – LCH WITH PULMONARY INVOLVEMENT

D. BALAKUMARAN
RN, a 5 year old boy
Was referred here for further evaluation and treatment of a recurrent scalp swelling.
TREATMENT OBTAINED ELSEWHERE

- Child had a history of scalp swelling one year before.
- H/O recurrent ear infection
- He was seen elsewhere only by neurosurgeon and was not evaluated by any investigations
- Excision of the swelling in a private pediatric hospital by neurosurgeon and biopsy (done in Dec 2009) proved LANGERHANS CELL HISTIOCYTOSIS to be the diagnosis
Biopsy report
CONSISTENT with LCH CD1a positivity
After few months developed a scalp swelling in another site
The rpt CT scan head done on 1.2.2011 showed a recurrent lesion in the same site and another soft tissue swelling in the left posterior aspect of the parietal bone
He was referred to us.
History

- Except for scalp swelling
- No h/o any polyuria, fever, skin rash and any other swelling.
- h/o ear infections reported by physicians but no h/o ear discharge
Scalp showed a left parietal swelling 3 X 2 cms
PR:90/minute
RR:24/minute
BP:80/60mmHg
Height:108 cms
Weight: 16.9kgs
Systems were normal
INVESTIGATIONS :
<table>
<thead>
<tr>
<th>Date</th>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>08.03.2011</td>
<td>Hemoglobin</td>
<td>11.5 (11–14)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>Total counts</td>
<td>10910 (4000–11000)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>P 65.7 l 26.2 e 1.9 m 3 and baso 0.2</td>
<td></td>
</tr>
<tr>
<td>08.03.2011</td>
<td>RBC count</td>
<td>4.72 (4.5–5.5)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>Platelets</td>
<td>2.68</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>PCV</td>
<td>34.9 (41–59)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>MCV</td>
<td>73.9 (76–96)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>MCH</td>
<td>24.4 (27–32)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>MCHC</td>
<td>33.0</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>ESR</td>
<td>13 (5–15)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>MP</td>
<td>negative</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>Peripheral smear</td>
<td>Microcytic hypochromic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal in number size</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Platelets adequate</td>
</tr>
<tr>
<td>Date</td>
<td>Test</td>
<td>Result</td>
</tr>
<tr>
<td>------------</td>
<td>------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>Blood osmolarity</td>
<td>283.58(275–295)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>Urine osmolarity</td>
<td>828(50–1200)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>LDH</td>
<td>187(100–190)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>Uric acid</td>
<td>3.4(2.6–7.2)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>BUN</td>
<td>14(7–18)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>Creatinine</td>
<td>0.3(0.6–1.3)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>Bicarbonate</td>
<td>23(21–28)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>SGOT</td>
<td>21(15–37)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>SGPT</td>
<td>27(30–65)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>Alkaline phosphate</td>
<td>215(54–369)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>Total protein</td>
<td>6.9(6.4–8.2)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>Albumin</td>
<td>4.3(3–4.5)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>Globulin</td>
<td>2.6(2–3.5)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>Total bilirubin</td>
<td>0.40(0.1–1)</td>
</tr>
<tr>
<td>08.03.2011</td>
<td>Direct bilirubin</td>
<td>0.05(0–0.3)</td>
</tr>
</tbody>
</table>
An array of radiological investigations were ordered LCH staging:
- X ray of the skull
- X ray of the chest AP
- X ray pelvis and
- X ray spine
Skull xray
Chest xray
X ray lumbosacral spine AP and Lateral views
No lytic or sclerotic lesion seen
IMP: normal study
X ray pelvis was also normal
CT chest
In view of chest xray finding evaluation done to rule out TB
- Mantoux done was negative.
- No contact history
- GJ aspirate for AFB negative
- TB Quantiferon test negative
Final diagnosis

- LCH with pulmonary involvement
- Group III multi organ involvement with risk organ involvement
MANAGEMENT:
# Histiocyte Society

**Langerhans Cell Histiocytosis Protocol LCH III**

## ‘Risk’ Induction Arm A

<table>
<thead>
<tr>
<th>Course</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Week</strong></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Date</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Vinblastine</strong> 6mg/m² IV bolus Day 1 of each week</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td><strong>Prednisolone</strong> 40mg/m²/day in 3 divided doses, weeks 1 to 4, tapering dose to zero during weeks 5 and 6</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Prednisolone</strong> 40mg/m²/day in 3 divided doses Day 1-3 every week for 6 weeks commencing week 7*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Infants with body weight under 10kg:*
- <6mths 50% of dose calculated from BSA
- >6mths <12mths 75% of dose calculated from BSA
- >12mths 100% of dose calculated from BSA

**Baseline Evaluations:**
- FBC, EUC, ESR, LFTs, coagulation studies, iron studies, urine osmolality
- Chest and Skeletal x-ray
- BMA and trephine
- HLA-typing
- See protocol Section 4.3 for evaluations for specific indications

**Laboratory Guidelines:**
- Low blood counts may reflect disease activity rather than toxicity
- Essential to discuss with primary physician before giving any dose if platelets <100x10⁹/L or ANC <1.0x10⁹/L

---

*If no active disease after week 6, go directly to continuation therapy and omit course 2*

**Supportive Care:**
- Omeprazole/Ranitidine whilst on Prednisolone
- Co-Trimoxazole 5mg/kg/day (Trimethoprim content) in two divided doses M/W/F
- Laxative use with Vinblastine
- Consider G-CSF if prolonged neutropenia

**Modifications for toxicity:** See protocol section 9.6

**Response evaluation:** See protocol section 10.3.1

---

LCH-III: Protocol date 11/09/2003  WCH flow sheet date 19/9/05

CPC review 29/9/05  Do not use after September 08
HISTIOCYTE SOCIETY
LANGERHANS CELL HISTIOCYTOSIS PROTOCOL LCH III

Continuation therapy – Arm A, Group 3 (multifocal bone disease and special sites)

<table>
<thead>
<tr>
<th>Week</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycle 1</td>
<td>SA:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cycle 2</td>
<td>SA:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cycle 3</td>
<td>SA:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vinblastine 6mg/m²/day IV bolus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisolone 40mg/m²/day in 3 divided doses on Day 1 to 5 every 3 weeks commencing at week 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FBE + LFTs + U+E + creatinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

THERAPY CONTINUES UNTIL 6 MONTHS FROM START OF TREATMENT

Infants with body weight under 10kg:
- <6mths: 50% of dose calculated from BSA
- >6mths <12mths: 75% of dose calculated from BSA
- >12mths: 100% of dose calculated from BSA

Laboratory Guidelines:
- Commence each 3 week course when ANC > 1.0 x 10⁹/L and platelets > 100 x 10⁹/L

Modifications for toxicity: See protocol section 9.6

Supportive Care:
- Co-Triamoxazole 5mg/kg/day (Trimethoprim contents) in two divided doses M/W/F. Continue until 3 months after completion of treatment.
- Consider laxative use with Vinblastine.
- Consider G-CSF if prolonged neutropenia

Post treatment pictures
DISCUSSION:

• Rare disorder in which lesions contain cells with features similar to the Langerhans cell of the epidermis
Clinical Presentations

- Skin disease
- Bone/Dental disease
- Liver/Spleen involvement
- Lymph node involvement
- Lung disease
- Bone marrow involvement
- CNS disease
  - Endocrine
  - Thymic disease
LITERATURE REVIEW OF UNUSUAL PULMONARY PRESENTATIONS:
Pulmonary LCH occurs both as an isolated finding, or more frequently, as part of multi-system involvement.


Ha et al., found lung involvement in 42% of 61 children with LCH, but none of them had isolated pulmonary involvement.

In another review 12 cases were reported, but only 2 were found with isolated pulmonary involvement.


Isolated pulmonary LCH, although rare, is seen more frequently in adults and very rarely in children and there is a strong association with cigarette smoking which is reported in over 90% of the patients. 

Bela Nagy et al studied the association of maternal smoking and isolated pulmonary LCH in a toddler*.


Lung involvement in LCH is usually parenchymal except the one reported by Farhan et al., who described a left intraluminal lesion in left main bronchus in a 2 year old girl.

5 case reports described the association of pneumothorax with pulmonary LCH*


Adults with pulmonary Langerhans’-cell histiocytosis may be at increased risk for malignant neoplasms. The association between pediatric pulmonary Langerhans’-cell histiocytosis and the occurrence of malignant neoplasms is rarely reported*.


Neumann MP, Frizzera G. The coexistence of Langerhans’ cell granulomatosis and malignant lymphoma may take different forms: report of seven cases with a review of the literature. *Hum Pathol* 1986;17:1060-5

Early responders to treatment have a high likelihood of becoming free of disease. However, pulmonary fibrosis is an important mechanism of lung remodelling in pulmonary Langerhans cell histiocytosis and the long-term prognosis is unclear.


Burns BF, Colby TV, Dorfman RF. Langerhans’ cell granulomatosis (histiocytosis X) associated
TAKE HOME MESSAGES:

LCH with isolated pulmonary involvement can be a close differential diagnosis for miliary tuberculosis.
THANK YOU