Langerhans cell histiocytosis (LCH) is a rare entity of unknown origin, currently considered as an orphan disease. Here we report five adult cases diagnosed and treated between 1997 and 2017 at the National Institute of Cancerology in Colombia. Three patients developed a metachronous cancer. First-line treatments were based on etoposide (ETO), vinblastine (VB), and prednisone (PDN); response was good. Cladribine (2-CdA) was used as a rescue therapy.

**Background**

LCH may cause single-system or multisystem involvement, with bone and lung as the most commonly affected organs. Multisystem involvement is frequent. The disease is commonly associated with central diabetes insipidus and other endocrinopathies.

Few cases have been reported in children and the incidence rate in adults is estimated at one case per million. The BRAF V600E mutation is present in at least 50% of the cases. Currently, there are no definite treatment guidelines for adults. LCH shows a good response to regimens based on VB and PDN.

**Objective**

The purpose of this paper is to present a case series of five patients diagnosed with LCH and treated in a leading cancer treatment center in Colombia.

**Langerhans Cell Histiocytosis in Adults: Report of Five Cases**

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**Abstract**

Langerhans cell histiocytosis (LCH) is a rare entity of unknown origin, currently considered as an orphan disease. Here we report five adult cases diagnosed and treated between 1997 and 2017 at the National Institute of Cancerology in Colombia. Three patients developed a metachronous cancer. First-line treatments were based on etoposide (ETO), vinblastine (VB), and prednisone (PDN); response was good. Cladribine (2-CdA) was used as a rescue therapy.

**Cases Description**

**Table 1. Data of the patients included in the series**

<table>
<thead>
<tr>
<th>Case</th>
<th>Gender</th>
<th>Age</th>
<th>Date of diagnosis</th>
<th>Sex</th>
<th>Date of last follow-up</th>
<th>Immunophenotype</th>
<th>Involvement</th>
<th>Treatment description</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>60</td>
<td>2001</td>
<td>M</td>
<td>2016</td>
<td>S100+, CD1a+, KIT 70%</td>
<td>Single-system disease</td>
<td>CP + PDN: CR. Relapsed two years later (2003). ETO + VB were given as rescue regimen. Following second relapse, 2-CdA (five cycles) was given through August 2015.</td>
<td>CR confirmed by PET/CT</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>60</td>
<td>2001</td>
<td>M</td>
<td>2016</td>
<td>CD10, CD1a, CD3, CD56, KIT 70%</td>
<td>Multisystem disease</td>
<td>ETO + PDN, VB followed as maintenance therapy every three weeks: PR. Progression was reported afterwards. 2-CdA (five cycles) was prescribed: PR</td>
<td>CR confirmed by PET/CT</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>60</td>
<td>2011</td>
<td>M</td>
<td>2016</td>
<td>S100+, CD1a+, p53, CD56, AE1, AE3, CD20, CD1a, CD56, KIT 70%</td>
<td>Multisystem disease</td>
<td>VB + PDN (six cycles) with no response. Persistent bone involvement (facial and long bones) in addition to anorectal zone involvement. 2-CdA was given as rescue therapy from July to November 2013. RT consolidation (IMRT) to maxillary sinuses, orbital region. Therapy ended in May 2014.</td>
<td>CR confirmed by PET/CT</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>54</td>
<td>2017</td>
<td>F</td>
<td>2017</td>
<td>S100+, CD1a+, S100+, CD20, keratin, EMA, chromogranin, and antinucleosome factor were all negative</td>
<td>Multisystem disease</td>
<td>VB + PDN (six cycles) with no response. Persistent bone involvement (facial and long bones) in addition to anorectal zone involvement. 2-CdA was given as rescue therapy from July to November 2013. RT consolidation (IMRT) to maxillary sinuses, orbital region. Therapy ended in May 2014.</td>
<td>CR confirmed by PET/CT</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>55</td>
<td>2017</td>
<td>F</td>
<td>2017</td>
<td>CD1a+, S100+, CD68+, vimentin+, HLA-DR+, CD34, CD117, MPO, CD3, and ACL were all negative</td>
<td>Multisystem disease</td>
<td>CD1a, S100, CD68, HLA-DR, CD34, CD117, MPO, CD3, and ACL were all negative</td>
<td>CR confirmed by PET/CT</td>
</tr>
</tbody>
</table>

**Case 1: Cladribine Therapy**

- **Five cycles through August 2015:**
  - **CR confirmed by PET/CT:**
  - **CR confirmed by PET/CT:**

**Outcome**

- **CR confirmed by PET/CT:**
- **CR confirmed by PET/CT:**
- **CR confirmed by PET/CT:**

**Secondary malignancies**

- **Low-risk basal cell carcinoma (2011):**
- **Papillary thyroid carcinoma metastasized to the lung:**
- **Gastric adenocarcinoma (2017):**

**Other diseases**

- **Hypothyroidism, Hypopituitarism:**
- **Hypothyroidism:**
- **Insulin-requiring type 2 DM:**
- **Hypothyroidism:**

**Patient status**

- **Alive without relapse:**
- **Dead:**
- **No relapse at the time of last follow-up (2016):**

**Summary**

LCH is an extremely rare disease of clonal origin and an indolent course mainly involving the skeletal system. Presence of the BRAF V600E mutation at least in 50% of the patients would be the reason for resistance to VB regimens. Pulmonary disease is associated with smoking and shows a good response to cigarette cessation.

Therapy is poorly defined and is based on VB, ETO, and steroid combinations. Given the promising disease control results, 2-CdA regimens seem to be among the best treatment options.

**Discussion**

To the best of our knowledge, this is one of the largest series reported in Latin America. We highlight the fact that two female patients had genital involvement. The association of LCH with second malignancies was another interesting finding.

The most frequent regimens used as front-line therapies were based on steroids plus VB, ETO, and radiation therapy. Cladribine is an excellent option for front-line treatment.

**References**