CUTANEOUS LEISHMANIASIS:
Standardization Of An Evolving Disease With Ancient Roots

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INTRODUCTION: AUBMC Archives
Delay in diagnosis?

- Lebanon is non-endemic for Cutaneous Leishmaniasis.
- Lack of exposure.
- Low index of suspicion.
- Broad clinical and microscopic spectrum.
- Known mimicker.
Delay in diagnosis?

☑️ Lebanon is non-endemic for Cutaneous Leishmaniasis.
☑️ Lack of exposure.
☑️ Low index of suspicion.
☑️ Broad clinical spectrum.
☑️ Known mimicker.
• **Protozoan** disease
  • Transmitted by the female sandfly, *phlebotomus* genus
  • **Promastigotes** (Blood) $\rightarrow$ **amastigotes** (Macrophages)

• Three forms of disease:
  1. **Cutaneous** Leishmaniasis (CL)
  2. **Mucocutaneous** Leishmaniasis
  3. **Visceral** Leishmaniasis
HISTORY AND EPIDEMIOLOGY

2,000 B.C.: Ancient Egyptian mummies.
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550-330 BC: Silk Persian carpets, Achaemenid dynasty

700 B.C.: Tablets from King Ashurbanipal.
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550-330 BC: Silk Persian carpets, Achaemenid dynasty

10th century: Avicenna describes the “Balkh sore”

1901: Leishman identifies organisms

1911: Incrimination of Phlebotomus as disease vector
Year-wise trend of CL cases
(from Salam et al. 2014)

Migration patterns of refugees with cutaneous leishmaniasis identified in Lebanon
(from Saroufim et al. 2012)
OBJECTIVES

1. Resurgence of Old World CL in endemic and nonendemic regions.
2. High index of suspicion.
3. Ability to produce extensive, mutilating chronic lesions.
4. To challenge traditional information.
5. Standardized and revisited understanding of the disease.
RESEARCH METHODS AND DESIGN

• N = 396.

• Data collection:
  ➢ Demographic information:
    • Age, gender, geographic origin.

  ➢ Clinical history:
    • Insect bite.
    • Duration, size, anatomic location and number of lesions.
# RESEARCH METHODS AND DESIGN

<table>
<thead>
<tr>
<th><strong>CLINICAL STAGE</strong></th>
<th>Inflammatory</th>
<th>Proliferative/reorganizing</th>
<th>Healed</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>LESION TYPE</strong></th>
<th>Papule</th>
<th>Plaque/nodule</th>
<th>Ulcer</th>
<th>Scar</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
<td><img src="image7.png" alt="Image" /></td>
<td><img src="image8.png" alt="Image" /></td>
<td><img src="image9.png" alt="Image" /></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>ERUPTION TYPE</strong></th>
<th>Wet</th>
<th>Dry</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image10.png" alt="Image" /></td>
<td><img src="image11.png" alt="Image" /></td>
<td><img src="image12.png" alt="Image" /></td>
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</tr>
</tbody>
</table>
EXTENSIVE DISEASE
EXTENSIVE DISEASE

• >3 cm in diameter
EXTENSIVE DISEASE

• >3 cm in diameter
• Facial disfigurement
• Threatening sensory organs
EXTENSIVE DISEASE

• >3 cm in diameter
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• Threatening sensory organs
• >5 lesions
EXTENSIVE DISEASE

- >3 cm in diameter
- Facial disfigurement
- Threatening sensory organs
- >5 lesions
- Sporotrichoid spread
EXTENSIVE DISEASE

• >3 cm in diameter
• Facial disfigurement
• Threatening sensory organs
• >5 lesions
• Sporotrichoid spread
• Persistence >12 months
ACKERMAN’S PATTERN

- Superficial
- Superficial and deep
- Diffuse
- Nodular
## RESEARCH METHODS AND DESIGN

### RIDLEY’S PATTERN

<table>
<thead>
<tr>
<th>Stage I</th>
<th>Stage II</th>
<th>Stage III</th>
<th>Stage IV</th>
<th>Stage V</th>
</tr>
</thead>
<tbody>
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<td><img src="image1.png" alt="Image" /></td>
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<td><img src="image4.png" alt="Image" /></td>
<td><img src="image5.png" alt="Image" /></td>
</tr>
</tbody>
</table>
## Identification of Organisms

<table>
<thead>
<tr>
<th>Amastigotes per standard section</th>
<th>PI</th>
<th>PI category</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 or more</td>
<td>1+</td>
<td>Low</td>
</tr>
<tr>
<td>10 or more</td>
<td>2+</td>
<td>Low</td>
</tr>
<tr>
<td>100 or more</td>
<td>3+</td>
<td>Intermediate</td>
</tr>
<tr>
<td>1000 or more</td>
<td>4+</td>
<td>Intermediate</td>
</tr>
<tr>
<td>10,000 or more</td>
<td>5+</td>
<td>High</td>
</tr>
<tr>
<td>100,000 or more</td>
<td>6+</td>
<td>High</td>
</tr>
</tbody>
</table>

### Research Methods and Design
# Research Methods and Design

## Epidermal Features
- Epidermal status
- Status of the stratum corneum
- Ulceration
- Serum crust
- Follicular plugging
- Spongiosis
- Basal cell hydropic degeneration
- Interface dermatitis.

## Host Inflammatory Response
- Neutrophils
- Lymphocytes
- Plasmocytes
- Eosinophils
- Histiocytes
- Granulomas
- Giant cells
- Panniculitis
- Perineural inflammation
- Necrosis
RESEARCH METHODS AND DESIGN

Confirmation by polymerase chain reaction analysis.

Speciation by restriction fragment length polymorphism analysis.
OUTLINE

• Introduction
• History and epidemiology
• Objectives
• Research methods and design
• Results
• Conclusion
RESULTS: Patient Demographics and Clinical History

• **Equal gender** based distribution.

• **Age range:** 1 to 92 years (mean 27.6).

• **Pediatric population:** 41.4%.

• **Head and neck:** 47.2%.

• **Insect bite** in 52.5%.
RESULTS: Clinical Presentation

<table>
<thead>
<tr>
<th>Duration of lesion (mean, SD)</th>
<th>7.3 months (±9.8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of lesions (mean, range)</td>
<td>2.3 (1-23)</td>
</tr>
<tr>
<td>Lesion size (mean, SD)</td>
<td>4.1 cm (±2.4)</td>
</tr>
</tbody>
</table>

**Clinical Stage**
- Inflammatory: 29.2%
- Proliferative/reorganizing: 55.8%
- Healed: 14.4%

**Lesion Type**
- Papule: 3.8%
- Plaque/nodule: 52%
- Ulcer: 42.7%
- Scar: 1.5%
RESULTS: Eruption type

- Eruption type:
  - 79.9% Dry
  - 12.5% Wet
  - 7.6% Mixed

- Leishmania Tropica:
  - Dry: 77.2%
  - Wet: 7.4%
  - Mixed: 15.4%

- Leishmania Major:
  - Dry
Disease was extensive in **71.8% of cases**
RESULTS: Microscopic Examination

Epidermal status

- Atrophy: 35.6%
- Normal: 25.1%
- Hyperplastic: 11%
- PEH: 28.3%

Stratum corneum status

- Unremarkable: 49.3%
- Hyperkeratosis: 41.8%
- Parakeratosis: 8.8%
Transepidermal elimination: 29.2%

- Perforating plug: 25.7%
- All layers: 25.7%
- Basal layer: 20.2%
Transepidermal elimination: 29.2%

- Perforating plug: 25.7%
- All layers: 25.7%
- Basal layer: 20.2%

CD1a
Basal cell hydropic changes | Spongiosis | Interface dermatitis | Follicular plugging | Ulceration | Serum crust
---|---|---|---|---|---
90.3% | 75.3% | 72.7% | 61.4% | 58.2% | 37.5%
INFLAMMATORY INFILTRATE

- Histiocytic
- Lymphocytic
- Plasmocytic
- Eosinophilic
- Neutrophilic

CUMULATIVE PRESENCE

- Histiocytic: 99.2
- Lymphocytic: 98.9
- Plasmocytic: 78
- Eosinophilic: 12.3
- Neutrophilic: 0.5
GRANULOMATOUS INFLAMMATION AND SUBTYPE

- **Absent**: 45%
- **Present**: 55%

**Subtypes**:
- Tuberculoid: 82.5%
- Caseating: 14.5%
- Suppurative: 1.5%
- Sarcoidal: 1.5%
PARASITIC INDEX VERSUS LESION AGE
PARASITIC INDEX VERSUS LESION AGE

RESULTS

All histological features were related to the PI. Since the general tendency is for the parasite load to decline progressively during the course of CL, the mean PI of a group of biopsies was indicative of the stage of evolution of the disease.
TRADITIONAL CLASSIFICATIONS VERSUS LESION AGE
TRADITIONAL CLASSIFICATIONS VERSUS PARASITIC INDEX
CONCLUSION

- Resurgence of Old World CL.
- High index of suspicion.
- Extensive, mutilating chronic lesions.
- Challenge traditional information.
- Revisit understanding.