Oral Presentation

Priscila Medeiros
Pediatric Rheumatology Fellow
Ribeirão Preto Medical School- University of São Paulo
**Identification**

3 year-old, mullato, Brazilian boy

**First appointment:**
May/06/2010

**Main complaints:**
Fever, pallor and skin lesions since 3 months of age

**History:**
Persistent daily fever (39°C) since 3 months of age, associated with pallor, apathy, irritability and failure to thrive. In addition, he presented erythematous cutaneous lesions initially over the face, progressing to trunk, abdomen, arms and legs.

**Family history:**
Parents were first-degree cousins
Single child
No similar cases in the family
Physical examination

Positive findings:

• Dysmorphic face (saddle nose, thicker lips, undefined filter, lipodistrophy)
• Multiple indurated erythematous violaceous skin lesions
• Periorbital and limb swelling
• Subcutaneous nodules
• Lymphadenopathy
• Hepatosplenomegaly
• Bony overgrowth of PIP joints and knees
• Limping gait
# Laboratory findings

<table>
<thead>
<tr>
<th></th>
<th>May 10</th>
<th>Nov 10</th>
<th>Fev 11</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hb / Ht</strong></td>
<td>7 g/dl/ 23%</td>
<td>9 g/dl/ 29%</td>
<td>8,3 g/dl/ 27%</td>
</tr>
<tr>
<td><strong>WBC</strong></td>
<td>6 400/µL</td>
<td>3 000/µL</td>
<td>3 300/µL</td>
</tr>
<tr>
<td><strong>Lym</strong></td>
<td>1 472/µL</td>
<td>1 080/µL</td>
<td>1 452/µL</td>
</tr>
<tr>
<td><strong>Plat</strong></td>
<td>216 000/µL</td>
<td>206 000/µL</td>
<td>302 000/µL</td>
</tr>
<tr>
<td><strong>CRP</strong></td>
<td>16,9 mg/dl</td>
<td>6,48 mg/dl</td>
<td>--</td>
</tr>
<tr>
<td><strong>ESR</strong></td>
<td>62 mm</td>
<td>40 mm</td>
<td>58 mm</td>
</tr>
<tr>
<td><strong>LDH</strong></td>
<td>1045 U/L</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td><strong>Ferritin</strong></td>
<td>899 ng/ml</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td><strong>IgG</strong></td>
<td>2 250 mg/dl (&gt;p97)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td><strong>IgA</strong></td>
<td>297 mg/dl (&gt;p97)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td><strong>IgM</strong></td>
<td>149 mg/dl (&gt;p97)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td><strong>AST/ALT</strong></td>
<td>25/06</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td><strong>FA/GGT</strong></td>
<td>574/93</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>
Laboratory and biopsy findings

- Negative autoantibodies
- Investigation for virus (CMV, EBV, HERPES, PARVOVIRUS), bacteria (blood, urine and liquor culture) and fungus infection was negative
- Inborn errors of metabolism were discarded

Skin biopsy:
Dermal histiocytic infiltration associated with some mononuclear cells. Immunofluorescence CD 68+

Liver biopsy:
Mild fibrosis peri central vein and microgoticular steatosis
Previous diagnosis

• Jul 2008
  First diagnosed as Sweet’s syndrome in another centre, received corticosteroid and dapsone for 16 months, with no improvement

• Nov 2009
  The diagnosis was revised, and NOMID (Neonatal Onset Multisystem Inflammatory Disease) hypothesis was made. Methotrexate was associated to the treatment for 6 months, without any improvement.
Follow up

• May 2010- First appointment at our service.

• Aug 2010- After thalidomide was introduced, fever and edema improved; no new cutaneous lesions appeared.

• Feb 2011- Due to drowsiness and appearance of new lesions, thalidomide was changed for colchicine

• Mar 2011- patient did not return to our centre

• June 2012- we received the information that this boy had died at 4 years old in March 11, after a sudden episode of vomiting and seizures.
Genetic analysis

- **Jan 2011:**
  CIAS1 gene: no mutations on exons 1 to 9
  “Hereditary autoinflammatory syndromes: a Brazilian multicentre study” - Jesus AA

- **March 2012:**
  PSMB8 gene: homozygous T75M mutation performed at NIH Lab for Adriana de Jesus, MD

- **Final diagnosis:**
  CANDLE syndrome (Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated Temperature).
Questions to the audience

How can we treat a patient with undefined autoinflammatory syndrome without genetic study?

What else could be used to treat this patient?
Thank you