Case Report

55 M with altered mental status, lower back pain, and weight loss
Case History

- Altered mental status, weakness, fatigue
- Lumbar back pain x4 days
- 15 lb weight loss in past 6 months
- Immigrated from Belize in 2002
- Physical Exam: inguinal lymphadenopathy
Calcium 18.2 (nl 9 - 10.5 mg/dL)
Ionized Calcium 9.27 (nl 4.5 - 5.5 g/dL)
BUN 60 (nl 8 - 20 mg/dL)
Creatinine 4.5 (nl 0.4 - 1.2 mg/dL)
Alkaline Phosphatase 309 (nl 38 – 126 U/L)
Initial Diagnosis/Plan

• Acute renal failure
• Altered mental status

Hypercalcemia

• Rx Calcitonin, Pamidronate, dialysis
• Radiology
• Workup of hypercalcemia, malignancy
• Hypercalcemia workup
  Serum PTH 9 (nl 10-65 pg/mL)
  Vitamin D25 27 (nl 14-42 ng/mL)

• Myeloma workup
  IgG level 759 (nl 694-1618 mg/dL)
  SPEP protein 5.4 albumin 2.8 γglobulin 0.76
  (nl 6.2-8.3 g/dL) (nl 3.0-5.0 g/dL) (nl 0.44-1.52 g/dL)

• Additional workup
  PSA 0.5 (nl 0.0-4.0 mg/dL)
Peripheral Smear
Bone Marrow
Bone Marrow
Flow Cytometry
Bronchoscopy
What is the diagnosis?
Additional Workup

- Bronchoscopy
  - Strongyloides
- Stool ova & parasites
  - Strongyloides
- HTLV I
  - positive ELISA
Nine weeks prior …

- CC: bilateral leg swelling for 1-2 weeks; chronic diarrhea with foul-smelling stools, weight loss, abdominal pain x6 months
- Abdominal CT: edematous changes of the small bowel with focal dilations
- Albumin: 1.6 g/dL (3.5-5.5 g/dL)
- SPEP: hypoproteinemia, hypoalbuminemia
HTLV-I infection causes inhibited Th2 response

Adult T-cell Leukemia/Lymphoma

1. Hypercalcemia, ↑ PTHrP
2. Multiple lytic lesions on radiology
3. Flower cells on peripheral blood smear
4. Bone marrow
   - Osteoclasts along trabeculae
   - Positive CD2, CD3, CD4, CD5, CD25
   - Negative CD7, CD8, B-cell markers
5. Strongyloides stercoralis
6. HTLV-I
White Blood Cell Count

WBC (K/cumm)
Regions of endemic HTLV infection

HTLV-I Transmission

Requires live, infected cells, not virions

– Breastfeeding
– Transplacental
– Sexual intercourse
– Sharing of contaminated needles
– Blood transfusions
HTLV-I in USA

Risks for infection

• being from the Caribbean or Japan
• having had sexual contact with persons from the Caribbean or Japan

Seropositivity in donated blood

• American Red Cross: 0.014%
• Council of Cmty Blood Centers: 0.021%

• Lifetime risk of Adult T-cell Leukemia/Lymphoma (ATLL) is about 5% in people infected before the age of 20 years

• Occurs mostly in adults, at least 20-30 years after HTLV-I infection.

• Men > women (1.5 : 1)
ATLL Epidemiology

- Localized to the Caribbean, southeastern US, and most notably southern Japan.
  
  In southern Japan, ATLL is the most common form of non-Hodgkin’s lymphoma.

- Mean age at diagnosis
  
  Japan: 60y
  
  Caribbean & South America: 40-50y

<table>
<thead>
<tr>
<th>Proportion of cases</th>
<th>Box 1 Clinical forms of adult T-cell leukaemia/lymphoma (ATLL)</th>
<th>Medial survival time</th>
</tr>
</thead>
<tbody>
<tr>
<td>55%</td>
<td>Acute&lt;/ul&gt; Leukaemic picture, organomegaly, high lactate dehydrogenase (LDH) and often hypercalcaemia</td>
<td>6 m</td>
</tr>
</tbody>
</table>
| 20%                 | Chronic<ul> Lymphocytosis &gt;4x10<sup>9</sup>/l with ATLL cells, skin, lung, liver or node involvement</li>  
|                     | Calcium levels normal, LDH normal or less that twice the upper normal limit | 24 m |
| 5%                  | Smouldering<ul> Skin and/or lung infiltrates</li>  
|                     | No other organ involvement</li>  
|                     | Normal lymphocyte count (1–5% ATLL cells), normal calcium and LDH | .. |
| 20%                 | Lymphoma<ul> Organomegaly</li>  
|                     | Less than 1% circulating leukaemic cells</li>  
|                     | High LDH and possible hypercalcaemia | 10 m |

Key Features of ATLL

**Lab**
- \( \uparrow \text{Ca}, \uparrow \text{PTHrP} \)
- hypoproteinemia
- (+) HTLV

**Peripheral Blood**
- transformed T cell nucleus has multiple lobules

**Physical Exam**
- lymphadenopathy
- hepatomegaly
- ± splenomegaly
- cutaneous lesions

**Immunophenotyping**
- (+) CD2, CD3, CD4, CD5, CD25
- (-) CD7, CD8

**Opportunitic Infections**
- Strongyloides
Differential Diagnosis

- Mycosis fungoides and Sézary Syndrome
- Cerebriform variant of T-prolymphocytic leukemia
- Other peripheral T-cell lymphomas, not specified
- Rarely Hodgkin disease
- Rarely angioimmunoblastic T-cell lymphoma
Sézary cells

- Medium to large lymphocytes with ceribriform nuclei
- Nucleus has been said to resemble a monocyte nucleus
## Differential Diagnosis

<table>
<thead>
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<th>ATLL</th>
<th>Sézary Syndrome</th>
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<tr>
<td>CD2 +</td>
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<tr>
<td>CD3 +</td>
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</tr>
<tr>
<td>CD5 +</td>
<td>CD5 +</td>
</tr>
<tr>
<td>CD7 –</td>
<td>CD7 + (30%)</td>
</tr>
<tr>
<td>CD4 + &gt;&gt; CD8 +</td>
<td>CD4 + / CD8 –</td>
</tr>
<tr>
<td>CD25 +</td>
<td>CD25 –</td>
</tr>
<tr>
<td>Integrated HTLV</td>
<td>No integrated HTLV</td>
</tr>
</tbody>
</table>
ATLL Treatment

• Multiple therapies have been studied:
  Conventional lymphoma chemotherapy (CHOP)
  Nucleoside analogues
  Topoisomerase inhibitors
  Interferon-α
  Zidovudine
  Monoclonal antibodies (anti-CD25, anti-CD52)

• Median survival is less than 1 year and has not significantly improved significantly in the past two decades.

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