Sudden Decompensation in a Heart Transplant Patient

Brit Shackley, M.D.
University of Los Angeles, California
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Clinical History

• 64 year old male presents with:
  – History of heart transplantation for dilated cardiomyopathy 2 weeks prior to presentation
  – Acute onset of diarrhea
  – Intermittent fevers
  – Echocardiogram shows decrease in ejection fraction to 35% from 45% the previous week
Clinical Differential Diagnosis

• The sudden decrease in ejection fraction is suspicious for acute cellular rejection, and the patient’s immunosuppressive regimen is decreased.

• Infectious etiologies were also considered to explain the patient’s gastrointestinal symptoms.

• Despite these measures, the patient continues to deteriorate and eventually goes into cardiac failure.
Clinical Findings

- Stool cultures, ova and parasite microscopy, and CMV DNA quantification are negative.
- An endomyocardial biopsy was performed which showed no evidence of acute cellular rejection, but was suspicious for humoral rejection.
- A routine CBC and peripheral smear was performed with abnormal results, prompting a second review of the cardiac biopsy.
### Laboratory Findings

<table>
<thead>
<tr>
<th>TEST</th>
<th>RESULT</th>
<th>REFERENCE RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC count, ×103/μL</td>
<td>4.22</td>
<td>3.28-9.29</td>
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<tr>
<td>Hemoglobin, g/dL</td>
<td>10.1</td>
<td>12.3 – 16.3</td>
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<tr>
<td>Hematocrit, %</td>
<td>30.9</td>
<td>37.4 – 47.0</td>
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<tr>
<td>Platelet count, ×103/μL</td>
<td>108</td>
<td>143 – 398</td>
</tr>
<tr>
<td>Prothrombin time, s</td>
<td>28.4</td>
<td>23.7 – 30.8</td>
</tr>
<tr>
<td>International normalized ratio</td>
<td>6.5</td>
<td>2 – 3</td>
</tr>
</tbody>
</table>
Peripheral Blood Smear

Wright-Giemsa stain, 40x
Peripheral Blood Smear

Wright-Giemsa stain, 100x
Cardiac Biospsy

Hematoxylin and eosin stain, 40x
• *Trypanosoma cruzi*
  – Intracellular amastigotes seen on endomyocardial biopsy
  – Flagellated trypomastigotes seen on peripheral blood smear
• The organ donor was a 23 year old Hispanic male and was found to have traveled to Guadalajara for 1 month in 2003. His blood sample tested positive for *T. cruzi* antibodies by radioimmunoprecipitation assay (RIPA) and borderline-positive by immunofluorescent antibody testing (IFA).

• The organ recipient had never lived in or traveled to an endemic area and had no other risk factors for Chagas disease prior to transplant.
The etiologic agent of Chagas disease is the protozoal parasite *Trypanosoma cruzi* which is transmitted by bloodsucking insects of the Triatominae subfamily, also known as Reduviid bugs.

It is estimated that 8-11 million people in Mexico, Central America, and South America have Chagas disease and it causes 45,000-70,000 deaths annually in those regions.
Life Cycle

Trypanosomiasis, American (Chagas disease)
(Trypanosoma cruzi)

1. Trypanosome bug stage: Trigemal trypanosome takes a blood meal (pores metacyclic trypanosomes in feces. trypanosomes enter bite wound or mucosal membranes, such as the conjunctiva)

2. Metacyclic trypanosome stage: Penetrate various cells at bite wound site. Inside cells they transform into amastigotes.

3. Amastigotes stage: Multiply by binary fission in cells of infected tissues.

4. Intracellular amastigotes stage: Transform into trypomastigotes, then burst out of the cell and enter the bloodstream.

5. Trypanosome stage: Trigemal trypanosome stage. Takes a blood meal (trypanosomes ingested).

6. Epimastigote stage: Multiples in midgut.

7. Multiples in midgut.

1 = Infective Stage
2 = Diagnostic Stage

<www.lib.uiowa.edu/.../cdc/PHIL_3384_lores.jpg>
• The acute phase of *T. cruzi* infection may be asymptomatic or may manifest as mild non-specific symptoms approximately one week after acquiring the parasites and include:
  – fever, skin rash, generalized lymphadenopathy, and hepatosplenomegaly
• The acute phase generally resolves in 4 to 8 weeks, but is fatal in up to 10% of infected children.
• In immunosuppressed patients, the acute phase is often fatal if not diagnosed.
Clinical Presentation

• Following a latent phase of years to decades, approximately 30-40% of infected individuals develop symptoms associated with the chronic phase of Chagas disease. Manifestations include:
  – cardiomyopathy, megacolon, and achalasia

• It is believed that low levels of parasites in the affected tissue provoke a chronic inflammatory response, which leads to denervation and eventual dysfunction.
The diagnosis of acute Chagas disease relies on examination of peripheral blood preparations, PCR, IgM antibodies detection, and occasionally blood culture.

On Giemsa stain, *T. cruzi* can be visualized as a C or S-shaped parasite with an undulating membrane and a large circular mass of DNA known as the kinetoplast.

Chronic Chagas disease is usually diagnosed by detecting IgG antibodies against *T. Cruzi* using enzyme linked immunosorbent assay (ELISA), indirect hemagglutination, and indirect immunofluorescence.

In immunosuppressed patients, antibody testing may be negative. PCR testing for *T. Cruzi* should be done in these patients.
• Direct autochthonous infection in the U.S. is rare and secondary routes of transmission are the most important sources of infection.
  – This includes blood transfusions, organ transplantation, transplacental transmission, and consumption of food contaminated by triatomine feces or from infected animals.
  – *T. cruzi* infection by these routes is of particular concern in areas such as southern California, Texas, and Florida with large immigrant populations from endemic areas.

• In the US, there have been three cases of infected organ donors transmitting *T. cruzi* to a total of five organ recipients, and many more transfusion associated cases.
Currently, approximately 65% of the US blood supply is routinely screened for antibodies to *T. cruzi* via ELISA testing for *T. cruzi* antibodies.

There is still no routine testing for *T. cruzi* infection in the area of solid organ transplantation.

However, cases such as this indicate that screening both blood and organ donors with risk factors for *T. cruzi* infection may be beneficial in areas with high rates of emigration from Latin America.
References