HIV Case Presentation

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General Background

*Human Immunodeficiency Virus* (HIV) is widely known as the pathogenic source of the AIDS pandemic.
YOU CAN GET HIV VIA...

- Sex without a condom
- Passed from mother to baby
- Sharing injecting equipment
- Contaminated blood transfusions & organ transplants

AVERT.org
YOU CAN’T GET HIV FROM...

- Kissing
- Hugging
- Sharing food
- Insect bites
- Toilet seats
- Bathing
- Sneezes and coughs
- Sweat
General Background

It infects specific cells of the immune system which express the binding protein CD4.
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- Dendritic cells
- Macrophages
- Monocyes
- Helper T-lymphocytes
General Background

Damage to the immune system via HIV infection allows opportunistic infections to flourish.

- TB (Tuberculosis)
- HIV
- Toxoplasmosis
- Karposi’s sarcoma

Images:
- Tuberculosis
- Toxoplasmosis
- Double Trouble (TB and HIV)
- Karposi’s sarcoma
HIV anatomy and physiology
HIV anatomy and physiology

Reverse Transcription

CD4 Cell

HIV RNA

Reverse Transcriptase

HIV DNA

CD4 Cell Nucleus

HIV-1 protease
Highly Active Antiretroviral Therapy (HAART/cART)

NNRTIs
- Nevirapine
- Delavirdine
- Efavirenz
- Etravirine
- Rilpivirine

NRTIs (also 3TC)
- AZT
- d4T
- FTC
- ddI
- Abacavir
- Tenofovir
- Amdoxovir
- Apricitabine
- Elvucitabine
- EFV
- EFVα
Highly Active Antiretroviral Therapy (HAART/cART)

Protease inhibitors (Ritonavir, Lopinavir, etc...)
HIV/AIDS in South Africa

South Africa currently has the largest population living with HIV of any country at over 7 million people \(^4\).

Efforts to fight the spread of HIV were hindered by “HIV denialists” in the government from the 1990s into the 2000s, with some claiming antiretroviral medications were poisonous \(^5\).
Case 18-2010

7-Year-Old Boy with Elevated HIV RNA Levels despite Antiretroviral Medications

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Case History

Antepartum:

- The patient’s mother received prenatal care but was not tested for HIV infection.

Age Three:

- Admitted to hospital due to pneumonia.
- Diagnosed with TB.
- Received a anti-tuberculosis medication regimen including rifampin, isoniazid, and pyrazinamide.
26 Months Prior to Evaluation:

- Patient presented an episode of suppurative otitis media.

18 Months Prior to Evaluation:

- Tests for HIV antibodies returned positive.
- HIV RNA (copies per mL): 2,239,206.
- CD4 T cells (per mm$^3$): 9.
- Ceftriaxone, clarithromycin, trimethoprim–sulfamethoxazole, albuterol, and hydrocortisone were administered.
- Rifampin, isoniazid, and pyrazinamide daily as well as ritonavir, lamivudine, and zidovudine (Table 1) were begun.
13-12 Months Prior to Evaluation:

- HIV RNA (copies per mL): 3,342.
- CD4 T cells (per mm$^3$): 236.
- A supraclavicular abscess developed which did not respond well to antibiotics. A biopsy test revealed numerous leukocytes but no microorganisms.
- A pathological examination revealed granuloma necrosis consistent with active TB.
8 Months Prior to Evaluation:

- Patient was referred to the McCord Hospital to renew his retroviral medication.
- Reportedly followed his antiretroviral regimen.

Evaluation:

- HIV RNA (copies per mL): 4,300.
- CD4 T cells (per mm$^3$): 146.
- Ritonavir alone was replaced with lopinavir–ritonavir combination therapy, doses of zidovudine and lamivudine were increased.
- Administration of multivitamins was begun and trimethoprim–sulfamethoxazole was continued.
Post-Evaluation:

- Test results determined normal white-blood cell and platelet counts.
- CD4 T cells (per mm$^3$): 471.
- HIV RNA (copies per mL): 22,000.

**Differential Diagnosis**

It was determined that an improper regimen as well as an ineffective combination of medication resulted in elevated HIV RNA levels and antiretroviral resistance.
Table 1. The Patient’s Weight, Height, Laboratory Data, and Medications for Each Clinical Visit.

<table>
<thead>
<tr>
<th>Variable</th>
<th>First Hospital, 18 Mo Earlier</th>
<th>Doctor’s Office, 12 Mo Earlier</th>
<th>Pediatric HIV Clinic, on Presentation</th>
<th>Pediatric HIV Clinic, 3.75 Mo Later</th>
<th>Pediatric HIV Clinic, 5.5 Mo Later</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>5 yr 10 mo</td>
<td>6 yr 4 mo</td>
<td>7 yr 4 mo</td>
<td>7 yr 7.75 mo</td>
<td>7 yr 9.5 mo</td>
</tr>
<tr>
<td>Months on antiretroviral medication</td>
<td>0</td>
<td>6</td>
<td>18</td>
<td>22</td>
<td>23.5</td>
</tr>
<tr>
<td>HIV RNA (copies per ml)</td>
<td>2,239,206</td>
<td>3342</td>
<td>4300</td>
<td>22,000</td>
<td></td>
</tr>
<tr>
<td>CD4 T cells (per mm³)</td>
<td>9</td>
<td>236</td>
<td>146</td>
<td>471</td>
<td></td>
</tr>
<tr>
<td>CD4 T cells (%)</td>
<td>1</td>
<td>6</td>
<td>6.1</td>
<td>17.9</td>
<td></td>
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<tr>
<td>Weight (kg)</td>
<td>14</td>
<td>15</td>
<td>17.8</td>
<td>19.4</td>
<td>19.4</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>100</td>
<td>100</td>
<td>107.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiretroviral medications (mg/day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zidovudine</td>
<td>200</td>
<td>200</td>
<td>400</td>
<td>400</td>
<td>400</td>
</tr>
<tr>
<td>Lamivudine*</td>
<td>120</td>
<td>120</td>
<td>140</td>
<td>180</td>
<td>180</td>
</tr>
<tr>
<td>Ritonavir†</td>
<td>480</td>
<td>480</td>
<td>100</td>
<td>120</td>
<td>120</td>
</tr>
<tr>
<td>Lopinavir‡</td>
<td>400</td>
<td>480</td>
<td></td>
<td>120</td>
<td>120</td>
</tr>
</tbody>
</table>

* Lamivudine solution is administered twice daily and contains 10 mg of lamivudine per milliliter.
† Ritonavir solution alone is administered twice daily and contains 80 mg of ritonavir per milliliter.
‡ Lopinavir–ritonavir oral solution is administered twice daily and contains 80 mg of lopinavir and 20 mg of ritonavir per milliliter, with 42.4% alcohol.
Problems with Diagnosis:

- despite receiving prenatal care, mother was never tested for HIV while pregnant despite living in a high risk area.
- Not officially diagnosed until he was 5 years of age, despite presenting symptoms consistent with tuberculosis at the age of 3, and suppurative otitis media several months later.
- International guidelines now suggest that all infants in high risk areas be treated with antiretroviral therapy, and HIV testing be done for infants possibly presenting with opportunistic infections.
Problems with Adherence:

- Mother initially received no training on how to administer antiretroviral therapy, or the importance of strict adherence to the treatment plan.
- The patient was never told about his diagnosis.
Regimen Problems:

- Normally a mix of two NRTIs and one NNRTI or protease inhibitor is prescribed to prevent drug resistant strains from being able to develop.
- Regimen initially consisted of two NRTIs (Zidovudine, and Lamivudine) and a protease inhibitor, Ritonavir.
- Ritonavir is normally paired with lopinavir.
- Alone, ritonavir can increase the risk of drug resistant mutations developing.
- Ritonavir is not recommended for use alongside the medications he was receiving to treat tuberculosis, nor is it recommended for his age group.
- Recommended third drug in this antiretroviral regimen is the NNRTI efavirenz.
- Antiretroviral regimen not changed to reflect his growth, or when unchanged viral RNA levels suggested drug resistance.
Solving the Regimen Problem:

- Patient’s infection developed several mutations that made it resistant to the drugs he was receiving.
- Regimen switched to the nonpeptide protease inhibitor darunavir and the NNRTI efavirenz.
- NRTIs were also changed, as his infection showed signs of resistance to them.
- New regimen was more effective at controlling viral levels, and viral suppression was eventually achieved.
Table 2: Results and Interpretation of HIV Resistance Genotype Mutations.

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Mutations Detected</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protease inhibitor</td>
<td>M46I, I54V, L76V, V82A, L90M (major resistance mutations); L10F/I, Q58E, A71V (minor resistance mutations)</td>
<td>High-level resistance to atazanavir, fosamprenavir, indinavir, lopinavir, nelfinavir, and saquinavir; intermediate resistance to darunavir and tipranavir</td>
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<tr>
<td>Reverse-transcriptase inhibitor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nucleoside reverse-transcriptase inhibitor</td>
<td>M41L, D67N, M184V, L210W, T215Y, G333E</td>
<td>High-level resistance to lamivudine, abacavir, zidovudine, stavudine, and emtricitabine; intermediate resistance to didanosine and tenofovir</td>
</tr>
<tr>
<td>Nonnucleoside reverse-transcriptase inhibitor</td>
<td>None</td>
<td>Susceptible to delavirdine, efavirenz, etravirine, and nevirapine</td>
</tr>
</tbody>
</table>
Solving the Adherence Problem:

- Patient must be informed of his diagnosis
- Patient should join a support group
- His mother also eventually enrolled in adherence training
Future Directions:

- Research is being done that suggests that AAV-delivered eCD4-IG (a fusion of CD4 immunoglobulin and a small CCR5-mimetic sulfopeptide) can function as a more effective HIV-1 vaccine.
- It acts by binding to the HIV-1 envelope glycoprotein and neutralizing the virus.
- Studies have shown that this may be a more effective potential means of HIV-1 vaccination than the use of broadly neutralizing antibodies (bNAbs) which are also under investigation as a potential vaccine.\(^2\)
THANK YOU
References


