Programmatic Challenges in the care of HIV and TB co-infection

Maunank Shah M.D.
Johns Hopkins University
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Disclaimer

• This presentation will ask many questions for which I don’t have answers

• No financial disclosures

Goal

• To frame the programmatic challenges in the management of HIV/TB co-infection

• Encourage discussion from the group

• Solicit ideas/solutions

Overview

• Issues from a TB program perspective
  – HIV diagnosis and monitoring
  – HIV treatment and ART initiation
  – Management of IRIS

• Issues from an HIV program perspective
  – TB screening
  – TB diagnosis

• “Who’s in charge”
  – Adverse events
  – Program integration
Introduction

• Management of HIV/TB co-infection requires coordinated efforts between TB and HIV programs

• Currently HIV and TB programs operate separately

• HIV and TB programs have separate funding streams

• Better communication and integrated policies are necessary

Issues from a TB program perspective

• Identifying areas of success and challenges
  • Data from Baltimore City to illustrate

Estimated HIV Coinfection in Persons Reported with TB, United States, 1993–2008*

<table>
<thead>
<tr>
<th>Year</th>
<th>All Ages</th>
<th>Aged 25–44</th>
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</thead>
<tbody>
<tr>
<td>1993</td>
<td>0%</td>
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<tr>
<td>1996</td>
<td>~8%</td>
<td>~8%</td>
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<td>1999</td>
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<td>~10%</td>
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<tr>
<td>2002</td>
<td>~15%</td>
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<td>2005</td>
<td>~20%</td>
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<tr>
<td>2008</td>
<td>~25%</td>
<td>~25%</td>
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*Updated as of May 20, 2009.
Note: Minimum estimates based on reported HIV-positive status among all TB cases in the age group.

HIV diagnosis

• Things we likely do well:
  • All active TB patients are recommended to have HIV testing*:
    – Baltimore City: ~100%
    – 15% of all TB cases HIV-coinfected

*CDC guidelines: Treatment of TB. MMWR June 20,2003; Vol 52
HIV Diagnosis:
Contact Investigations

• Contact Investigations:
  – CDC recommends Voluntary Counseling and Testing for all contacts
  – Maryland TB guidelines also advocate VCT
• Challenges: Baltimore City 2008-2010
  – 358/392 contacts (91%) did not have HIV testing
  – Poll: What % of contacts are being tested in other jurisdictions?

HIV Diagnosis

• QUESTIONS:
  • Where should VCT take place? Privacy concerns
  • Staff training/Comfort: TB nurses not necessarily trained in HIV counseling
  • Availability of rapid HIV tests
  • How to test during large CI’s (i.e. schools)
  • Time/Resources for large CI’s lacking

HIV Diagnosis: LTBI

• Maryland TB guidelines: HIV testing should be considered for all individuals with LTBI
• Baltimore City 2009-2011
  – 1285 referrals for Latent TB evaluation
  – 974 patients seen for Latent TB evaluation
  – 32/974 (3%) were diagnosed with HIV infection
  – 268/974(26%) refused or HIV test result not available
• QUESTION: What is an appropriate target goal/program indicator?

HIV Monitoring

• 28 y/o male diagnosed with disseminated TB (lungs, blood, ascites)
• Diagnosed with HIV. CD4 15. Viral load >100K
• Did well on RHZ and Efavirenz/emtricitabine/tenofovir started
• 2 months CD4 75, viral load undetectable
• Adherence issues with DOT
• Communication with HIV provider reveals:
  – Given 1 year supply of Efavirenz/emtricitabine/tenofovir?
  – Didn’t go to any HIV visits once feeling better
  – 6 months: CD4 20, Viral load 55K, K103N, M184V
**HIV monitoring: Who’s in charge?**

- **Initial testing:**
  - CD4, viral load, genotype, CMV, Toxo serology, Viral hepatitis screening, STD screening

- **Ongoing monitoring:**
  - CD4, Viral load every 3 months*

- Is this the responsibility/role of the TB program?

*Primary Care Guidelines for the Management of Persons Infected with Human Immunodeficiency Virus: Update by HIVMA/IDSA. CID 2009;49: 651-81

**HIV Monitoring**

- **QUESTION/CHALLENGES:**
  - Can TB programs initiate workup or do lab testing (separate budgets)?
  - How to handle/communicate HIV results (CD4, VL)
  - What to do when HIV provider not monitoring appropriately?

**HIV treatment**

- **When to start ART?**
  - SAPIT trial: Sequential therapy worse outcomes
    - All HIV patients should be started on ART prior to completion of TB treatment
  - NEJM Oct 2011: 3 papers on this topic
    - Early initiation (2 weeks): mortality benefit in CD4<50
    - ‘Late’ initiation (8 weeks): may be considered in those with CD4 >50 (less IRIS, no difference in mortality)

**HIV treatment**

- If ART initiation is important...
- Questions/Challenges:
- How do we do it?
  - TB programs usually not funded to provide ARV drugs
  - HIV expertise among TB clinicians may be lacking
  - Social Work support may be lacking
    - Ryan White, ADAP
HIV treatment issues continued

- How do we streamline referrals to HIV providers? Delayed appointments.
  - Pre-established referral process
- Even if early HIV enrollment possible:
  - How can we initiate ART in 2 weeks if TB programs can’t send initial labs (i.e. genotypes)
- Counseling necessary prior to ART treatment initiation to maximize adherence
- Should TB programs provide ART DOT initially?

HIV treatment

- Drug interactions:
  - Should we be increasing EFV doses with rifamycins?
  - Is Rifabutin 150 QOD appropriate?
    - How do you handle ART non-adherence (i.e. suboptimal rifamycin dosing)
- Communication with HIV provider regarding ART changes

TB IRIS

- 30 yo with pulmonary TB, diagnosed with HIV
- Started on RHZE and Efavirenz/emtricitabine/tenofovir as an inpatient
- Resolution of infiltrates on CXR at 1 month
- 2.5 months into therapy, develops DOE and cough
- CXR shows recurrent pulmonary infiltrates
- Concern for relapse vs. IRIS
- Sputums sent—smear negative, MTD negative
- Diagnosed with TB IRIS

TB IRIS

- Programmatic challenges:
  - Prednisone prescribed for this patient by TB program
    - Not covered by MADAP or TB program in Maryland
    - No other insurance coverage
    - Creative solutions: Grocery store gift cards used to buy prednisone in this case
  - Who is in charge of monitoring/treatment?
    - Case: HIV provider stopped steroids at 2 weeks
      - TB IRIS flared
    - Role of rapid molecular testing to rule out relapsed TB/drug-resistance
Unmasked TB

- Unmasked TB/Subclinical TB: TB diagnosed shortly after ART initiation
- Data from endemic settings suggests highest TB incidence in first 6 months following ART initiation
- Active Case-Finding studies in some endemic areas suggest 5-20% of HIV+ patients have active TB at the time of enrollment
  - Usually asymptomatic and smear-negative

WHO Intensified Case Finding (3 I’s)

Key recommendations

1. Adults and adolescents living with HIV and screening with a clinical algorithm for TB, and who report any one of the symptoms of current illness (fever, weight loss, or night sweats) on at least two days in a month. Strong recommendation, moderate-quality evidence

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WHO guidelines for TB ICF and IPT in PLWH in resource-limited; 2011
TB ICF for individuals from endemic areas

• QUESTIONS:
  • Are individuals from endemic areas being appropriately screened for TB?
  • Should all HIV positive individuals from endemic areas receive sputum smear and culture during as part of initial screening?

WHO TB testing/IPT

3. Adults and adolescents living with HIV who have an unknown or positive TST status and are unlikely to have active TB should receive TB testing prior to starting IPT as part of a comprehensive package of HIV care and treatment.
   Strong recommendation, high quality of evidence

4. Adults and adolescents living with HIV who have an unknown or positive TST status and who are unlikely to have active TB should receive at least 36 months of IPT (79a) should be given to such individuals irrespective of the degree of immunosuppression, and also to those on ART, those who have previously been treated for TB and pregnant women.
   Conditional recommendation, moderate quality of evidence

5. TST is not a requirement for initiating IPT in people living with HIV.
   Strong recommendation, moderate quality of evidence

6. People living with HIV who have a positive TST should benefit more from IPT. TST can be used where feasible to identify such individuals.
   Strong recommendation, high quality of evidence

TB testing/IPT in US

• QUESTION:
  • In light of evidence from SA, Botswana, and WHO recommendations:
  • Should all HIV positive individuals from an endemic area be considered for INH preventative therapy?

CDC: TB Screening

• TB screening should be done upon enrollment in HIV care
• Repeat testing recommended for those with prior negative TST once CD4>200
• Close contacts of TB cases
• Annual testing should be considered for those with ongoing TB exposures

Primary Care Guidelines for the Management of Persons Infected with Human Immunodeficiency Virus: Update by HIVMA/IDSA. CID 2009;49: 651-81
Other issues: Who’s in charge?

- Adverse events:
  - Liver toxicity:
    • How do you sort out ART toxicity from TB drug toxicity?
    • What to do if HIV provider stops (or recommends stopping) TB therapy?
- Inappropriate ART therapy:
  - What to do when you recognize patient is on inappropriate regimen:
    • Case 1: Pt viremic and on CBV/Tenofovir DF/Maraviroc/DRV/r
    • Case 2: Pt viremic and on dual PI therapy

Who’s in charge

- Should HIV programs be allowed primary management of TB patients to avoid confusion?
- Should HIV programs transfer care of their patient to TB programs for the duration of TB therapy?—could allow integrated DOT
- HIV/TB liaisons

Conclusion

- Management of HIV/TB co-infection requires coordinated efforts between TB and HIV programs
- Better communication and integrated policies are necessary
- Discussion/Thoughts?