

Special issues in Opportunistic Infections



Case presentation

- 7 year old female presents for follow-up visit one month after starting d4T, 3TC and NVP.
- The day she started on ARV therapy, she was also treated for oral candidiasis.
- When she came back for her one month visit, she still had thrush.
- What may be the reason(s) for this?



Case presentation 1

- Three potential reasons:
 - Did not take the antifungal
 - Drug-resistant candida
 - Inadequate dose of antifungal
 - Wrong prescribed dose
 - Drug interaction that reduced levels of antifungal
 - Which antifungal is contraindicated with NVP?



Case presentation 1

- Nevirapine is an inducer of P450 system
 - Therefore, has many drug interactions, often to reduce levels of other drugs metabolized by P450.
 - Contraindicated with ketoconazole
 - Ketoconazole levels are decreased by nevirapine
 - Use fluconazole instead



Case presentation 2

- A married couple presents for initiation of ART. The wife was diagnosed simultaneously with pulmonary TB and HIV. Because the wife's CD4 counts were so low (<50), the clinician decided to treat her TB and give ARVs simultaneously.
- The wife was pregnant and in the first trimester of pregnancy. The clinician gave her d4T, 3TC and NVP to avoid first trimester effects of EFV, with plans to change to EFV later in the pregnancy
- The husband was given d4T, 3TC and EFV.



Case 2, cont'd

- The wife initially did well clinically and immunologically with a rise of her CD4 count to 120 by the time she delivered. However, her CD4 stopped rising and actually dropped to 100.
 - What may have been the reason(s)?
 - What are the consequences of this?
 - What could have been done to avoid this?



Case 2, cont'd

- Immunologic failure

- May come from not taking the ARVs
- May come from taking inadequate doses of ARVs
- May come from drug interactions that reduce the dose of ARVs
 - In her case, the rifampicin may have reduced the levels of NVP, and then she may have gotten resistance
 - This may have led to her own drug resistance and drug resistance in the baby!
 - Could have been avoided by giving only TB meds and co-trimoxazole until she was far enough in the pregnancy to give EFV



Case 2, cont'd

- The husband did not do well initially. He has fever and it appears that he is having respiratory difficulty. He states that he takes his ARVs every day as prescribed.
- What may have been the cause of this?
- What should be done for the patient?



Case 2, cont'd

- He likely has immune reconstitution syndrome
 - TB symptoms were masked in him because he could not mount a sufficient immune response previously
- He should continue ARVs and give steroids. May want to consider give anti-TB meds as well.



HIV and TB: Treatment Implications

- Drug – drug interactions common
 - Can affect the levels of either anti-TB meds or antiretrovirals
 - Can lead to resistance or increased toxicity
 - CRITICAL to look up interactions of meds and adjust doses where necessary
- Sometimes cause similar side-effects
 - Difficult to determine which med caused the side effect
 - Example: Isoniazid can also cause peripheral neuropathy
- Adherence problem: pill burden
 - Taking 3-4 drugs for TB plus 3 antiretrovirals plus taking any recommended prophylactic medication

Other OIs

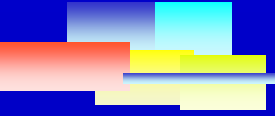
- Patients who develop other OIs should be treated with ARVs unless there are major interactions
- In contrast to the situation with TB, drug interactions with standard ARV regimens do not pose a significant problem
 - Ketoconazole may boost PI levels
 - Co-trimoxazole may exacerbate anemia from AZT
- Prompt initiation of ART should be considered when OIs occur for which treatment is not available or for which it is suboptimal
 - Improvement of the immune system may enhance recovery
 - Ex: chronic diarrhea with cryptosporidium



Hepatitis

- Patients coinfectd with hepatitis B or C can safely be treated with several ARV regimens
- Avoid regimens which have ARVs that can cause additive hepatotoxicity
- 3TC and TDF are both active against hepatitis B and may even have a protective effect against new infections.
 - Patients receiving 3TC or TDF who are known to have hepatitis B and experience ARV regimen failure may wish to continue these medications when the ARV regimen is switched.

Immune Reconstitution Syndrome

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- For many OIs, including TB, there can be a transient worsening of infection 2-3 weeks after initiation of ART.
 - This is called immune reconstitution syndrome. Initiation of ART can unmask previously undiagnosed infections by augmenting the inflammatory response
 - Cause is thought to be improving the inflammatory response due to the repairing of the immune system
 - Risk is higher in those with advanced HIV
 - Patients may discourage others from taking ARVs!



Immune reconstitution syndrome, continued

- Clinical presentation:
 - fevers
 - lymphadenopathy
 - worsening pulmonary lesions
 - expanding lesions of the central nervous system

- Management:
 - Reactions are self-limiting although they may require a brief course of corticosteroids to reduce inflammation of CNS or severe respiratory symptoms

 - ART should not be interrupted if immune reconstitution syndrome occurs