Update on Opportunistic Infections in the Era of Effective Antiretroviral Therapy

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KEYWORDS

• HIV • Opportunistic infections • Antiretroviral therapy • Diagnostics

KEY POINTS

- New diagnostic tests are improving the ability to detect tuberculosis (TB), cryptococcal meningitis (CM), and pneumocystis pneumonia (PCP) in human immunodeficiency virus (HIV)-infected patients.
- Randomized trials support early initiation of antiretroviral therapy (ART) in HIV-infected patients with TB; however, a slight delay in the initiation of ART in patients with CM may be warranted.
- Although new therapies have been tested in HIV-infected patients with progressive multifocal leukoencephalopathy (PML), ART is still the mainstay of therapy.
- Young HIV-infected males and females should receive the quadrivalent human papillomavirus (HPV) vaccine.
- Varicella vaccine is recommended for nonimmune HIV-infected individuals with CD4 cell count greater than 200/mm^3. Zoster vaccine seems to be safe and immunogenic in HIV-infected patients with high CD4 cell counts on ART.

INTRODUCTION

Despite efforts to diagnose and treat HIV infection before patients develop advanced disease, opportunistic infections (OIs) continue to occur in the era of effective ART, particularly in those who have not yet been diagnosed with HIV and in those who are not receiving therapy. In the United States, approximately one-third of patients have a CD4 cell count less than 200/mm^3 at the time of HIV diagnosis, placing them at risk for OIs.[1]

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Although most OIs occur in patients with CD4 cell counts less than 200/mm^3, a small residual risk remains even in those with higher counts. A recent analysis of patients with CD4 cell counts greater than 200/mm^3 found that esophageal candidiasis, Kaposi sarcoma, and pulmonary TB were the most common opportunistic conditions in this population.[2] Factors associated with increased risk of acquired immunodeficiency syndrome (AIDS)-defining illness (ADI) in patients with a CD4 cell count greater than 500/mm^3 included injection drug use, older age, and having more than 10,000 copies/mL of HIV RNA.[2] The incidence of OIs seems to level off at a CD4 cell count of 750/mm^3, suggesting that immune reconstitution is near complete at this level.[2]

This review focuses on TB and cryptococcal infections, the most common OIs in patients living with HIV around the world, as well as on new developments in progressive multifocal leukoencephalopathy and PCP. In the sections on these conditions, updates on diagnosis, treatment, and complications, as well as information on when to start ART is provided. The article concludes with a discussion of new data on 2 vaccine-preventable OIs, HPV and varicella-zoster virus (VZV) infections. For information on other OIs, the readers may consult the recently updated US Department of Health and Human Services (DHHS) Guidelines for the Prevention and Treatment of Opportunistic Infection in HIV-Infected Adults and Adolescents, which provides a comprehensive review.[3]

TB in HIV-Infected Patients

Epidemiology

Since the widespread use of ART and intensive TB control efforts in the 1990s, TB incidence among HIV-infected individuals in the United States has declined; in fact, the decrease outpaces those seen in HIV-uninfected individuals.[4,5] In 2012, there were 9945 cases of TB in the United States, of whom 625 (7%) were coinfected with HIV.[4,5]

Latent TB infection

Patients should be tested for latent TB infection (LTBI) at the time of HIV diagnosis; if the result is negative, the test should be repeated if the patient is exposed to TB.[3] LTBI in HIV-infected individuals is defined as a tuberculin skin test (TST) with more than 5 mm of induration without clinical or radiographic evidence of active disease. However, a positive TST result is not completely specific for TB: patients who are infected with some nontuberculous mycobacteria or who have recently received BCG vaccination may have a false-positive result. A false-negative TST result may occur in patients with severe immunodeficiency; therefore, if the test result is negative when the patient's CD4 cell count is less than 200/mm^3, the test should be repeated after the patient receives ART and achieves immune reconstitution. Finally, the TST has several logistic disadvantages, including the need for a return visit for the test to be read and variability in how it is placed and interpreted.

Interferon gamma release assay (IGRA), a blood test, requires only a single visit and has higher specificity than the TST for diagnosis of LTBI. In HIV-uninfected individuals, there is good concordance (89%) between the IGRA and TST.[6] However, in HIV-infected individuals in low-TB-prevalence areas, the concordance between TST and IGRA results is not as good.[7] In addition, those with a CD4 cell count less than 200/mm^3 are more likely to have indeterminate results.[7] Nevertheless, both the TST and IGRA are considered appropriate tests for diagnosis of LTBI in HIV-infected patients.[8] Of note, although a recent study found that an IGRA had good sensitivity for active TB in HIV-infected patients,[7,8] other studies have found that the result of TST

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