Reply

Sir—We appreciate Dr. Jenny-Avital’s thoughtful comments on and shared experience with the use of rifabutin (RBT) in HIV-infected patients with tuberculosis (TB) receiving highly active antiretroviral therapy (HAART) including protease inhibitors (PIs) [1], and we also appreciate Dr. Slain’s interest in and comments on [2] our article [3].

As Dr. Jenny-Avital points out, one of the reasons for virologic failure associated with the use of PIs is that PI trough levels fall short of the inhibitory concentration. Although it has now become our practice to measure peak and trough levels of PIs, at the time our study was designed, it was decided to measure the drug levels of PIs at the time of “standard” monitoring of TB drug levels (i.e., at 2 and 6 h after dosing). Nonetheless, 20 (80%) of 25 patients achieved a virus load of <500 copies/mL prior to discharge, which was comparable to the results of previous studies, in which 45%–85% of zidovudine-experienced subjects attained virus loads of <500 copies/mL at 24 weeks [4, 5]. Once again, 500 copies/mL was used as the lower limit of detection because of the sensitivity of the tests available at the time.

We share Dr. Jenny-Avital’s concerns regarding why, in subanalysis, only 4 of 8 antiretroviral therapy (ART)—naive patients achieved a virus load of <500 copies/mL while receiving a PI and rifabutin, and why the patients who were not ART-naive fared better (7 of 9 achieved a virus load of <500 copies/mL). However, this may be due to the small number of patients in subanalysis. Findings of a comparison of 3 groups (ART-naive patients, nuclease reverse transcriptase–experienced patients, and PI-experienced patients) were not statistically significant (P > .3).

We reiterate that the purpose of our original study was to evaluate the utilization of PIs and rifabutin, with regard to a patient’s clinical response, drug side effects, and pharmacokinetics. Although deferring HAART may be a consideration, there has been no study to compare aggressive HAART with deferred HAART with regard to the clinical outcome of patients dually infected with HIV and TB. Because TB may accelerate the natural progression of HIV disease, further studies are necessary to delineate the best approach for treatment of individuals with this increasingly more prevalent combination of deadly diseases.

With regard to Dr. Slain’s comment, we received the same questions by e-mail soon after the electronic publication of our article. We asked Clinical Infectious Diseases to print an erratum, which appeared on page 992 of the June 2000 issue (volume 30, number 6).

Masahiro Narita,1,2,3 Jerry J. Stambaugh,1 Elena S Hollender,1 Arthur E. Pitchenik1,4 David Ashkin1,2,4
1A.G. Holley State Tuberculosis Hospital, Lantana; 2Florida Department of Health, Bureau of Tuberculosis Control and Prevention, Tallahassee, Florida; 3Division of Pulmonary and Critical Care, Department of Medicine, University of Miami School of Medicine, and 4VA Medical Center, Miami

References


Clinical Infectious Diseases 2001;32:323–329
© 2001 by the Infectious Diseases Society of America. All rights reserved. 1058-4838/2001/3202-0030$03.00

Good’s Syndrome: The Association of Thymoma and Hypogammaglobulinemia

Sir—Among the many causes of recurrent airway infections is the rare Good’s syndrome, a classic example of which is reported in the following patient. In 1992, a 59-year-old woman presented with a 6-month history of productive cough. She had never smoked and mentioned having a “spot” on a chest radiograph that was obtained in 1943, for which she had to take bed rest for several months, at the time her mother had tuberculosis diagnosed. A chest radiograph obtained in 1992 revealed a homogenous oval consolidation in the region of the left upper lobe; comparison of this radiograph with earlier routine preoperative radiographs indicated that the consolidation had not changed. Cultures of sputum samples yielded Haemophilus species. Results of a cytological examination of the mass were inconclusive and the mass was presumed to have resulted from an old case of tuberculosis with residual atelectasis. Antibiotic treatment resulted in gradual resolution of her symptoms. However, from 1992 through 1997, she required antibiotic treatment of bronchitis at least 3 times per year. In 1998, she was admitted to the hospital with increased dyspnea and cough which produced green sputum. She complained of fatigue, had a temperature up to 39°C, and had experienced night sweats during the past months; she also had gradually lost 12 kg of weight since 1992. On physical examination, she appeared ill and bi-
lateral basal inspiratory crackles were heard. Her \( \text{Pao}_2 \) was 6.9 kPa with 88% oxygen saturation while breathing room air. Laboratory studies disclosed the following findings: erythrocyte sedimentation rate, 24 mm/h; C reactive protein level, 152 mg/L (normal, <10 mg/L); WBC count, \( 2.04 \times 10^9 \) cells/mm\(^3\) with 80% polymorphonuclear leukocytes, including 10% band forms; total serum protein level, 68 g/L with 6% gamma-globulin; IgG level, 2.9 g/L (normal, 7–16 g/L); IgM level, <0.2 g/L (normal, 0.4–2.3 g/L); and IgA level, 0.2 g/L (normal, 0.7–4 g/L). The results of the tuberculin skin test were negative.

Cultures of sputum samples yielded \textit{Haemophilus} species; no other pathogens were detected. Staining for acid-fast bacilli yielded negative results. A radiography indicated that the intrathoracic mass had increased in size. A CT scan showed the mass in the anterior mediastinum and bronchiectasies with peribronchial inflammation (figure 1). A CT-guided biopsy specimen of the mass showed mesenchymal cells without signs of malignancy.

In November 1998, an encapsulated multinodular solid tumor of 11 cm \( \times \) 9 cm \( \times \) 6 cm was resected uneventfully; its histology was compatible with that of a benign thymoma. Postoperatively, the patient frequently had airway infections. Treatment with iv gammaglobulin substitutions (monthly dose, 18 g) and antibiotics resulted in a considerable reduction in the frequency of infections.

Good’s syndrome, which involves the combination of thymoma and hypogammaglobulinemia, was first described in 1954 [1]; single case reports followed [2–5]. An estimated 10% of the patients with adult-onset hypogammaglobulinemia have a thymoma, and among patients with a thymoma, 5% will have hypogammaglobulinemia [6].

Radiologic findings for the thymoma-hypogammaglobulinemia syndrome vary from a mediastinal mass in an asymptomatic patient to acute and chronic pulmonary infiltrates secondary to infection [7]. High-resolution CT was found to be more sensitive than chest radiography for the detection of pulmonary abnormalities; it could show progression of bronchiectasies despite adequate immunoglobulin substitution [8]. Like that described in literature on the subject [6], the hypogammaglobulinemia in our patient did not improve after thymectomy and the patient required Ig substitution. Mortality is considerably higher in patients with thymoma-associated hypogammaglobulinemia than in patients with X-linked agammaglobulinemia or common-variable immunodeficiency [9], a finding that underscores the importance of timely substitution therapy to prevent irreversible lung damage.

Diagnosis of Good’s syndrome should

---

**Figure 1.** Top, CT scan (without contrast enhancement) showing a homogenous mass without invasion of contiguous structures that is located in the anterior mediastinum and that extends into the left pectoral lung segment. Histology of the resected mass showed benign thymoma. Bottom, CT scan with contrast enhancement. At the level of the lower lung fields, the thymoma is not visible, but dilated airways and peribronchial infiltration diagnostic of bronchiectasies are seen predominantly in the left lower lung field.
be considered in patients presenting with recurrent airway infections and an anterior mediastinal mass and/or any of the paraneoplastic syndromes associated with thymoma, such as myasthenia gravis.

Sandra M. Arend,1 Hans Dik,2 and Jaap T. van Dissel1
1 Department of Infectious Diseases, Leiden University Medical Center, Leiden; and 2 Department of Pulmonology, Rijnland Hospital, Leiderdorp, The Netherlands

References

Reprints or correspondence: Dr. Sandra M. Arend, Dept. of Infectious Diseases, C5F, Leiden University Medical Center, PO Box 9600, 2300 RC Leiden, The Netherlands (s.marend @lumc.nl).

Clinical Infectious Diseases 2001;32:323–5 © 2001 by the Infectious Diseases Society of America. All rights reserved. 1058-4838/2001/3202-0031$03.00

Influence of the Normal Menstrual Cycle on Vaginal Microflora

SIR—We read with interest the article by Eschenbach et al. [1] in Clinical Infectious Diseases. The authors presented a detailed description of the vaginal microflora at 3 points during the menstrual cycle, as detected by means of culture methodology. Women both with and without bacterial vaginosis (BV) were studied. Among the women without BV, it was noted that there was a significant increase in the recovery rate of high concentrations of Lactobacilli species over the course of the menstrual cycle, with only 70% of subjects having high levels during menses. They also noted a significant shift from high to low levels of non-Lactobacillus flora from the time of menses to the later parts of the cycle.

We have also been interested in changes in the vaginal microflora, and we have described daily changes in the flora during the course of the menstrual cycle among 51 women who had no evidence of BV or other lower genital tract infections [2]. Using the vaginal Gram stain method described by Nugent et al [3], we have described daily changes in the vaginal microflora, and we have described daily changes in the flora during the course of the menstrual cycle among 51 women who had no evidence of BV or other lower genital tract infections [2]. Using the vaginal Gram stain method described by Nugent et al [3], we examined vaginal smears that were self-obtained from these women daily, and we found significant, transient changes in the vaginal flora. The most significant point of change was during the time of menses. Only 11 (22%) of the 51 women maintained a lactobacillus-predominant flora throughout the menstrual cycle. Other factors that were associated with shifts in the flora included a greater number of sexual partners and more frequent unprotected vaginal intercourse.

Therefore, our data concur with those of Eschenbach et al. regarding the instability of vaginal flora at the time of menses in the majority of women. Behaviors associated with instability in our study suggest that sexual activity may also be associated with this pattern.

Jane R. Schwebke1 and Heidi Weiss2
1Department of Medicine and 2Biostatistics Unit, Comprehensive Cancer Center, University of Alabama at Birmingham

Correspondence

Immune Restoration Disease in HIV-Infected Patients after Antiretroviral Therapy

SIR—We were interested to read the paper on “immunorestitution disease” by Cheng et al. [1], since we, too, have argued for several years that infectious and/or inflammatory disease in HIV-infected patients who are responding to antiretroviral therapy (ART) is a manifestation of immune restoration. When zidovudine monotherapy was introduced into clinical practice, our group observed that Mycobacterium avium complex (MAC) disease developed in a small proportion of patients during the first few weeks of therapy and that this development was associated with the restoration of a delayed-type hypersensitivity (DTH) response to mycobacterial antigens [2]. We argued that this reflected restoration of an immune response against subclinical MAC infection [3]. Disease presentation was atypical; in particular, the infection was usually localized to tissues rather