prolongation [2]. In conclusion, Ebola virus–infected patients with Plasmodium spp. parasitemia should receive optimal antimalaria treatment. However, whether such treatment, in particular AL, should be given to all Ebola virus–infected, patients regardless of a malaria test result, needs to be investigated.

Note

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References


Reply to Colebunders

To the Editor—We read with interest the letter by Colebunders [1] regarding our recently published article in Clinical Infectious Diseases [2]. In our study, we found an association between Plasmodium parasitemia and survival of Ebola virus–infected individuals. Patients coinfected with Plasmodium parasites were 20% more likely to survive the Ebola virus infection. This effect was dose dependent as survival in the group with the highest level of parasitemia was 83% compared to 46% in patients infected with Ebola virus alone. All patients in our cohort received antimalarial artemether–lumefantrine (AL) treatment, independent of the outcome of the malaria diagnostic test. In his letter, Colebunders questions whether there really is an association between Plasmodium parasitemia and survival or whether this effect is somehow explained by the AL treatment. He states that Ebola virus–infected patients with an untreated Plasmodium coinfection may have an increased mortality risk compared with patients infected with Ebola virus alone and that antimalarial treatment would thus benefit coinfected patients. Although this is an interesting hypothesis, our cohort only consisted of AL-treated patients either infected with Ebola virus alone or patients coinfected with Ebola virus and Plasmodium parasites. The increased survival in the coinfected patients thus cannot be due to the resolution of the Plasmodium coinfection by the antimalarial treatment, as the other group was not infected with Plasmodium to begin with.

Colebunders further argues that AL treatment itself may be detrimental to Ebola virus–infected patients by prolonging the QT interval. Although AL treatment can indeed result in QT interval prolongation, it is not clear how this could have a selective effect only in patients infected with Ebola virus alone. The study by Gignoux et al from Foya, Liberia [3], and referenced by Colebunders, included a group of patients infected with Ebola virus alone who were not treated with antimalarial drugs. When survival in this group was compared to that of patients infected with Ebola virus alone who did receive AL treatment, there was no statistically significant difference in survival, suggesting that AL treatment did not have a negative effect on patient outcome [3].

If there is an indication that AL treatment can have a negative effect on patient outcome in Ebola virus–infected patients, we should consider replacing this treatment scheme with a more appropriate choice of antimalarial drugs, as suggested by Gignoux et al [3] and by Colebunders [1]. However, this does not change our observation of increased survival in patients coinfected with Plasmodium parasites in the patient cohort from Monrovia, Liberia.

What to Do for the Asymptomatic Pulmonary Coccidioidal Nodule or Cavity in Immunosuppressed Patients? A Focus in the Recent Coccidioidomycosis Guidelines

To the Editor—Asymptomatic pulmonary Coccidioidal nodules can be seen in immunocompromised patients such as those with cancer, transplant, or other chronic immunosuppressing conditions [1,2]. Not uncommonly, the significance of this finding is unclear as the condition simulates nodular cancer lung metastasis [1,2].
Also, frequently no information beyond histopathology is available because no cultures from the biopsy material were sent due to low suspicion of an infection. The recently released, comprehensive Coccidioidomycosis guidelines [3] do not directly address what strategy or strategies are to be considered in this situation. Realizing the available quality of evidence is very low, I suggest that these asymptomatic patients be treated with an oral azole-based regimen for at least 3 months followed by close monitoring. For patients with high risk for an opportunistic mold infection, such as hematologic malignancy or allogeneic transplant, perhaps a mold-active azole is preferable to fluconazole, especially in the setting of a cavitating Coccidioidal nodule, where secondary colonization by another mold (eg, Aspergillus) could occur. I offer the following rationale for supporting a trial of “preemptive” azole treatment. First, there is, although unmeasured, risk for progression or dissemination of this occult lung infection in the setting of subsequent immune impairment [2,4], and there are no clinical or immunogenetic predictors to prognosticate this event. Second, the possibility of extrapulmonary Coccidioidal lesions beyond the dominant Coccidioidal nodule exists; therefore, the burden of fungal disease might be underestimated by conventional computerized tomography of the lung. As Coccidioidal lesions are 18F-Fluorodeoxyglucose-avid [5] and in view of the well-known poor sensitivity of Coccidioides serology in immunosuppressed patients [2], positron emission tomography/computed tomography as a baseline to look for the extent of lung involvement and to evaluate for cryptococgenic disseminated diseases [6] could be informative in selected cases. Third, as pulmonary Coccidioidal lung nodules simulate cancer [1,2], it would be important in a patient with underlying cancer and an asymptomatic pulmonary Coccidioidal nodule to eradicate these nodules with antifungals. This can facilitate the downstream differential diagnosis in case the patient subsequently develops new pulmonary lesions.

In view of the availability of oral azoles that have excellent efficacy and long-term safety, the benefit of treating preemptively far outweighs the risk. Finally, surgical resection can be an alternative modality in selected patients with solitary culture-proven Coccidioidal cavitating lung nodule, if no further chemotherapy is planned and azole treatment is not feasible or is undesirable. Again, more studies are needed in order to validate this proposed strategy. I thank Galgiani et al for their significant contribution with their guidelines to the clinical management of a complex disease.

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References


Overcoming Outpatient Loss to Follow-up as a Barrier to Efficiently Instituting Hepatitis B Liver-related Care

To the Editor—Following the recent publication by Spradling et al [1], we want to bring to attention that loss to follow-up of hepatitis B virus (HBV)–infected outpatients is a barrier to efficiently instituting liver-related specialty care.

An estimated 72% of HBV patients in countries of low endemicity are untreated [2], which can be attributed to disease factors, physician factors, and patient factors, such as ignorance regarding seriousness of the disease with subsequent loss to follow-up [3,4]. Outpatient loss to follow-up does not necessarily indicate failure on behalf of the patient, but instead may indicate flaws in the outpatient-care system [5]. By identifying those at risk, optimal liver-related care can be given with subsequent deceleration of disease progression. We aimed to identify factors associated with outpatient loss to follow-up in a case-control study.

Data from all HBV-infected patients in a Dutch center were collected from electronic health records. Brief Illness Perception (IPQ-K) and Social Support List 12 (SSL-12) questionnaires were additionally sent to these patients. Loss to follow-up was defined as no outpatient visit for at least 18 months between the first outpatient appointment and 1 April 2016. Deceased patients or those with hepatitis B surface antigen clearance were not considered lost to follow-up.

Three hundred forty-three consecutive HBV patients were followed for a median of 3.9 (interquartile range [IQR], 1.4–8.0) years by an infectious disease specialist or gastroenterologist; 17% of patients were innate Dutch, 17% European immigrants, 59% non-European immigrants, and 7% refugees. At baseline, median age, alanine aminotransferase, bilirubin, and HBV DNA were 35 (27–49) years, 34 (22–64) U/L, 9 (6–15) μmol/L, and 3.1 (2.3–4.9) log10 IU/mL, respectively. Seven percent had fibrosis of Metavir stage F3 or higher.

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