The third patient had highly malignant T cell lymphoma. Owing to poor clinical response, after 7 days, intravenous TMP-SMZ therapy was switched to intravenous pentamidine therapy. *P. jiroveci* PCR results became negative for the first mtLSU nPCR step at day 9, but the results remained positive for the second step until day 17, when the patient died.

Other point mutations of the DHPS gene were not detected in this study. Because the 74 subjects had never received TMP-SMZ prophylaxis before presentation, this might explain the lack of mutations at codons 55 and 57 in our study.

The mutation at DHPS codon 171 has been only reported once (in 1999), and because eradication was achieved in 2 patients with TMP-SMZ, this mutation seems to be a spontaneous mutation and may not confer TMP-SMZ resistance. However, studies involving larger numbers of patients would be necessary to prove the suggested lack of clinical relevance.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

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Clinical Significance of Occult Hepatitis B Virus Infection Cannot Be Overlooked

Sir—In their recent article, Kempinska et al. [1] reported a case of reactivation of hepatitis B virus (HBV) infection following an allogeneic bone marrow transplant in a hepatitis B–immune patient. They pointed out that, although this event is rare, it is important to understand the clinical features associated with the development of HBV reactivation, as well as to avoid the development of such a potentially fatal complication [1]. We agree that reactivation of HBV infection is a serious event in this special clinical instance, and that it deserves much attention. Nevertheless, several critical points should be further addressed.

First, reactivation of HBV infection is not rare in areas where hepatitis B is endemic, such as the Asia-Pacific region [2, 3]. For example, a previous study in Taiwan revealed that among 388 bone marrow transplant recipients, nearly 100 had preexisting hepatitis B surface antigen carriage [2]. After transplantation, abnormal liver function was the most common complication, and 2 patients died of HBV-associated hepatic failure [2]. Consistent findings were reported by Lau et al. [3] from Hong Kong.

Second, in addition to overt HBV infection, occult HBV infection (defined as the presence of HBV DNA in blood or liver tissues in patients who are negative for hepatitis B surface antigen with or without any HBV antibodies [4]) was also not rare in areas where hepatitis B is endemic. It has been reported that the prevalence of occult HBV infection was quite high in these areas (~4–25% in the hepatitis B surface antigen–negative and hepatitis B core antibody–positive population) [5, 6].

Furthermore, as reviewed by Kempinska et al. [1], reactivation of HBV infection after transplantation can be potentially fatal. Unfortunately, this issue is often neglected clinically. Therefore, it is important for practicing physicians to identify recipients with pretransplantation occult HBV infection, which can be done with the use of sensitive assays to detect HBV DNA in serum or in liver tissue. A recent review shows that, in patients with occult HBV infection, serum HBV DNA levels range from 400 to 4 × 10^6 copies/mL in patients positive for isolated hepatitis B core antibody and from 10 to 10^6 copies/mL in patients positive for both hepatitis B surface antibody and hepatitis B core antibody [5]. Therefore, instead of insensitive hybridization-based assays, more-sensitive PCR-based or transcription-mediated amplification–based methods should be used [7]. Finally, the prior studies by us and our colleagues have suggested that hepatitis B core antibody is not a good marker of occult HBV infection and that the diagnosis of occult HBV infection could be missed if only hepatitis B core antibody is used as the diagnostic marker [8].
titis activity in patients with chronic hepatitis is always preceded by an increase in the serum HBV load [8, 9]. Taken together, the findings from the studies mentioned above show that, if we are to identify cases of HBV reactivation sooner after transplantation, it is paramount to monitor the dynamics of the serum HBV DNA level.

In summary, the significance of detecting occult HBV infection cannot be overlooked in bone marrow transplant recipients. Occult HBV infection can be manifested in different serological profiles. In the future, further studies should focus both on the serological profile associated with the risk of HBV reactivation and on the best time to initiate antiviral therapy to avoid such a catastrophic event.

Acknowledgments

Financial support. The study was supported by grants from the National Taiwan University Hospital; the National Science Council, Department of Health, Executive Yuan, Taiwan; and the National Health Research Institutes, Taiwan.

Potential conflicts of interest. All authors: no conflicts.

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Noninvasive Diagnosis of Mitochondrial Dysfunction in HAART-Related Hyperlactataemia

Sir—It has been suggested that hyperlactataemia that develops in patients who are receiving HAART is caused by mitochondrial dysfunction [1–6]. This hypothesis is based on the occurrence of mtDNA depletion and/or mitochondrial respiratory chain dysfunction in liver [1, 2], skeletal muscle [3, 4], and/or PBMCs [5, 6]. However, these techniques are laborious and time consuming, and some require invasive biopsies.

Noninvasive methods have been developed for the screening of mitochondrial function in subjects with primary myopathies [7–9], but these methods have not been applied to the study of HAART-mediated mitochondrial damage. We tested the utility of the forearm aerobic exercise test (FAET) [8] in 2 HIV-infected patients during an episode of HAART-related hyperlactataemia and after resolution of the episode. To determine mitochondrial function, we simultaneously measured mtDNA content by quantitative real-time PCR, and we determined complex IV mitochondrial respiratory chain enzymatic activity by spectrophotometry; homogeneously skeletal deltoid muscle biopsy specimens and PBMCs were used, as previously described [10, 11]. Results for HIV-infected subjects were compared with those for 10 healthy HIV-uninfected control subjects.

The FAET measures venous oxygen saturation in forearm blood before aerobic exercise (time 0), during aerobic exercise (minutes 1, 2, and 3), and after 1 min of resting (minute 4), to monitor oxygen saturation and to detect cellular oxygen uptake. The aerobic exercise consists of an intermittent static handgrip exercise at 33% of the intended maximum voluntary contraction force determined for each subject. In primary mitochondrial disorders, there is less oxygen desaturation in venous blood during aerobic exercise, indicating oxidative phosphorylation impairment [8].

Both HIV-infected patients, who had been infected before 1997, were receiving treatment with didanosine and stavudine (patient A was also receiving tenofovir, and patient B was also receiving efavirenz). The patients had been admitted to the hospital because of fatigue, as well as anorexia and weight loss for patient A. The serum lactate levels were 3.26 and 2.69 mmol/L (normal range, 0.4–2.0 mmol/L), the CD4 cell counts were 624 and 439 cells/mm³, and the HIV-1 RNA levels were 198 copies/mL and undetectable for patients A and B, respectively. The patients were both asymptomatic after experiencing either a 6-week interruption of HAART (patient A) or a 10-week treatment switch to lamivudine, tenofovir, and efavirenz (patient B).

The mitochondrial analysis performed on PBMCs and muscle homogenate specimens during the hyperlactatemic phase confirmed the occurrence of mitochondrial dysfunction, with a 20%–80% reduction in complex IV activity and a 65%–80% depletion of mitochondrial DNA, depending on tissue specimens. These deficiencies returned to normal levels after clinical resolution of hyperlactataemia (figure 1). At the same time, both patients...