HIV-1 containing the 150V mutation to amprolovir. Thus, if N88S can be maintained, future treatment options for this patient, who harbors 150V-containing virus, may include amprolovir, perhaps in combination with ritonavir. Although the change was less dramatic, N88S also lowered the level of resistance to lopinavir imparted by 150V. The congruence of directionality in the effect of N88S on amprolovir and lopinavir is consistent with observations we have published elsewhere with regard to cross-resistance between these 2 PIs [6]. Although N88S is a relatively rare mutation in clade B viruses from PI-experienced patients, recent reports indicate that it may be more common in other subtypes [7–9]. Thus, the importance of the findings described here may increase as PIs begin to be used in areas where non-clade B HIV-1 is predominant, as well as after the introduction of new PIs, such as atazanavir [4].

References


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Linezolid and Serotonin Toxicity

Sir—The possibility, suggested by the report by Bernard et al. [1], that linezolid may cause serotonin syndrome (serotonin toxicity) via action as an monoamine oxidase inhibitor (MAOI) is of great importance. The spectrum of the iatrogenic, drug-induced reaction of toxicity ranges from side effects to toxicity (thus, thinking of it as a syndrome is less helpful) [2, 3]. General physicians need to know that severe serotonin toxicity—that is, toxicity of a possibly life-threatening/fatal degree—may be expected to result from combinations of MAOIs with serotonin reuptake inhibitors [3].

If linezolid produces significant monoamine oxidase inhibition, then there will be a risk of severe toxicity if it is coadministered with any serotonin reuptake inhibitor; serotonin reuptake inhibitors include some narcotic analgesics (e.g., tramadol and pethidine), all selective serotonin reuptake inhibitors, and “dual action” antidepressants (i.e., serotonin and noradrenaline reuptake inhibitors), such as duloxetine and venlafaxine (and similar drugs, such as sibutramine).

I have presented the evidence for the accuracy of the spectrum model of serotonin toxicity in 2 major review articles [3, 4]. The spectrum model aids persons in understanding that the degree of elevation of serotonin levels dictates the severity of the toxicity, and that severe, life-threatening toxicity only results from large elevations in the serotonin level caused by combinations of MAOIs and serotonin reuptake inhibitors.

The features that distinguish serotonin toxicity from other toxic syndromes are hyperreflexia, hypertension, myoclonus, fever, agitation, and late-stage/severe pyramidal rigidity [2]. Serotonin toxicity typically presents as neuromuscular hyperactivity (tremor, clonus, myoclonus, and hyperreflexia), altered mental status (excitement, agitation, and late-stage/severe confusion), and autonomic hyperactivity (diaphoresis, fever, mydriasis, tachycardia, and tachypnea).

Clinically, the onset of serotonin toxicity is often rapid; at first, the patient is quick to detect the symptoms, with tremor and hyperreflexia. Clonus and myoclonus starts in the lower limbs and may become generalized. Autonomic features (tachycardia, tachycardia, and hypertension) fluctuate and are not usually difficult to manage. Other symptoms may include shaking, shivering, chattering of the teeth, and trismus. Pyramidal rigidity is a late development and may impair respiration if it affects truncal muscles. Rigidity and fever (temperature, >39.5°C) indicate serious toxicity.

The case reported by Bernard et al. [1] illustrates the importance of knowing the aforementioned information and what to look for and report to establish the presence and severity of toxicity. The spectrum concept predicts the high-risk cases that may sometimes require aggressive treatment intervention with cyproheptadine; endotracheal intubation, neuromuscular paralysis, and cooling; or chlorpromazine. I maintain a summary (based on peer-reviewed publications) of all aspects of serotonin toxicity and the implicated drugs on my Web site (http://www.psyhotropical.com/SerotoninToxicity.doc).
Isolated Antibody to Hepatitis B Core Antigen in Individuals Infected with HIV-1

Sir—We read with interest the article by Gandhi et al. [1] concerning the factors associated with the presence of isolated antibody to hepatitis B core antigen (anti-HBc) in patients with human immuno-deficiency virus type 1 (HIV-1) infection. Patients in this study who were seronegative for hepatitis B surface antigen (HBsAg) and for antibody to HBsAg (anti-HBs) had a relatively higher CD4+ cell count (median, ~350 cells/mm³) and lower plasma virus load (median, ≤3.75 log₁₀ copies/mL) than patients who were not; 42% of these 142 patients had a history of percutaneous exposure to blood. In order to determine whether the prevalence of isolated anti-HBc might be different among patients who had acquired HIV infection mainly through sexual transmission and who were at a late stage of HIV infection, we analyzed the data in a prospective observational study of 716 nonhemophiliac patients infected with HIV-1, aged ≥15 years, in an area where hepatitis B (HBV) infection is hyperendemic [2, 3]. All statistical analyses were performed using SAS statistical software (Version 8.02, SAS Institute). Categorical variables were compared using χ² or Fisher’s exact test, whereas noncategorical variables were compared using Wilcoxon’s rank-sum test. The Spearman correlation coefficient was used to compute the relationship between ordinal and continuous variables.

Of the 716 patients enrolled in our study between June 1994 and June 2002, 416 (58.1%) had a complete diagnostic study of hepatitis B status (i.e., the presence of HBsAg, anti-HBs, and anti-HBc) performed at enrollment. Their clinical characteristics are shown in table 1 (overleaf). Most of them were at the late stage of HIV infection, with a depleted CD4 cell count and a high plasma virus load (PVL), and had acquired HIV infection through sexual transmission; only 2.4% of the patients had a history of exposure to blood. Approximately 10% of our patients had chronic hepatitis C virus (HCV) infection. Of the 416 patients who had a complete study diagnostic study of hepatitis B status performed, 140 (33.7%) were negative for HBsAg and anti-HBs; isolated anti-HBc was detected in 113 patients (80.7%). The prevalence of isolated anti-HBc appeared to increase with the severity of immunosuppression (Spearman correlation coefficient, −0.84; P = .07) (table 1). In a multivariate analysis, we did not find that either chronic HCV infection or a history of exposure to blood was associated with prevalence of isolated anti-HBc (data not shown), which finding may be related to the small number of patients with chronic HCV infection in our study. In addition, isolated anti-HBc was not associated with an increased risk for mortality or with progression of HIV infection either before or after the introduction of HAART.

Our findings suggest that the prevalence of isolated anti-HBc will vary with the epidemiologic characteristics of the patients enrolled in the study and the background seroprevalence of HBV infection. In an area of hyperendemicity of HBV infection and low endemicity of HCV infection, the prevalence of isolated anti-HBc will be high among patients at a late stage of HIV infection.

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