Increased Cyclosporine Concentrations in the Absence of Cyclosporine Administration

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CASE

A 9-year-old girl was admitted to our hospital with juvenile metachromatic leukodystrophy (arylsulfatase A deficiency). Symptoms of this lysosomal storage disease, such as decreased school performance and compromised motor skills, had started 1 year earlier. She underwent bone marrow transplantation from a matched unrelated donor after receiving conditioning with fludarabine, treosulfan, and thiotepa, together with thymoglobulin, a rabbit antithymocyte globulin. Conditioning was well tolerated, and the posttransplantation period was uneventful except for 1 febrile episode. Graft-vs-host disease (GvHD) prophylaxis consisted of 3 methotrexate doses in combination with a starting daily cyclosporin A (CsA) dosage of 3 mg · kg $^{-1}$ · day $^{-1}$. Trough CsA concentrations were monitored with the antibody-conjugated magnetic immunoassay (ACMIA) for CsA (RxL Dimension; Siemens). CsA concentrations entered the therapeutic interval after 3 days, and the dosage was adjusted to achieve trough concentrations of 120–150 μg/L (Fig. 1). The patient received CsA for 16 weeks. During this period, the CsA concentration was measured 31 times, with results from 98 μg/L to 219 μg/L (mean, 156 μg/L). Four weeks after transplantation, the patient developed a mild GvHD of the skin, which disappeared immediately after commencement of prednisolone treatment. Because B lymphocytes were absent or low early after transplantation, the patient received immunoglobulins for 5 months (Fig. 1). Endogenous immunoglobulin production started only in the later phase of immune reconstitution. Six weeks after discontinuation of CsA therapy, a concentration of 147 μg/L was still detected in whole blood. Although the patient was not supposed to have received CsA and the parents had denied the administration of CsA or drugs other than those prescribed, CsA concentrations between 116 μg/L and 174 μg/L were obtained over the next 4 months.

Questions to Consider
• Has the CsA therapy really been discontinued?
• Can delayed drug elimination explain the continued increased CsA concentrations?
• What tests could be done to identify any potential analytical interference?

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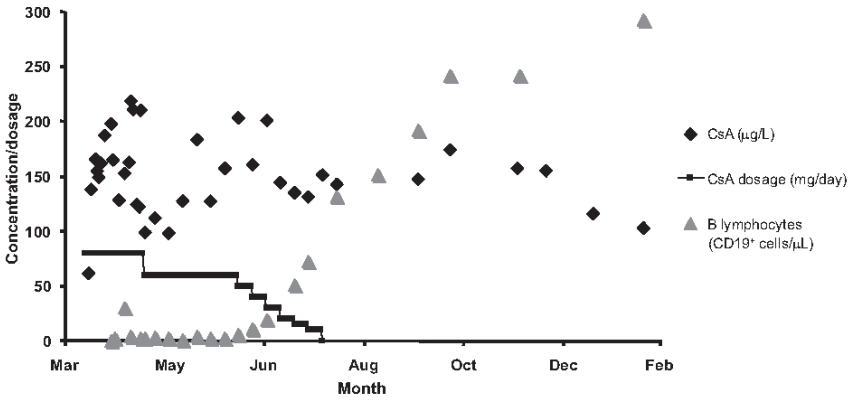

Fig. 1. Time courses of the whole-blood CsA concentration measured with the ACMIA CsA assay, the administered daily CsA dose, and the B-lymphocyte count.

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the May 2011 issue of *Clinical Chemistry*. To view the case and comments online, go to http://www.clinchem.org/content/vol57/issue5 and follow the link to the Clinical Case Study and Commentaries.

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