To the editor:

Central nervous system (CNS) disease in Abelson virus–induced leukemia

In the original description and isolation of the murine Abelson leukemia virus, we described a "massive degree of meningeal involvement" as a characteristic of the disease process.\(^1,2\) As in the Bcr/Abl murine bone marrow transplantation model, the latent period to tumor appearance was very short. We suggested that the meningeal disease could serve as a model for testing chemotherapy.

Herbert T. Abelson

To the editor:

ADAMTS13 and thrombotic thrombocytopenic purpura–hemolytic uremic syndrome

We read with interest the paper by Vesely et al concerning ADAMTS13 (a disintegrin-like and metalloprotease with thrombospondin type 1 repeats) activity in relation to presenting features and clinical outcomes of patients suffering from thrombotic thrombocytopenic purpura–hemolytic uremic syndrome (TTP-HUS).\(^3\) We would like to make a few comments.

First, in regards to the etiology, we are surprised that in a large prospective cohort of 142 patients, only 2 patients were HIV positive. In a recent retrospective review of 55 adults admitted to our renal intensive care unit (ICU) between 1990 and 1998, 18 suffered HIV infection.\(^5\) It was the main factor influencing the in-hospital mortality and the requirement for hemodialysis. HIV-1 infection has been reported to account for up to 30% of TTP-HUS.\(^3\) In a similar fashion, a 1.4% incidence of TTP-HUS was reported in patients with acquired immunodeficiency syndrome.\(^4\) It is known that this incidence of HIV-related TTP-HUS decreased until the introduction of highly active antiretroviral therapy (HAART).\(^4\) The registry enrolled all patients from January 1, 1989, to December 31, 2001, thus including a period before the HAART era. There is no explanation for this low number of HIV-positive patients.

Concerning the treatment, Vesely et al argue that the standard practice is to treat all adult patients with plasma exchange. This conviction is based mainly on the result of a large prospective study reporting therapeutic plasma exchange to be superior to plasma infusion.\(^3\) In this study, however, the volumes of plasma administered in the plasma infusion group were low compared with those of the therapeutic plasma exchange group. A previous report suggests that high-dose plasma infusion may be as effective, less cumbersome, and less invasive than therapeutic plasma exchange.\(^6\) The efficiency of high-dose plasma infusion (\(> 30 \text{ mL/kg per day}\)) has been confirmed in a larger and more recent study.\(^7\) We think that the use of therapeutic plasma exchange is of limited interest in the case of bone marrow transplantation–associated TTP-HUS. A recent review reports a low response rate (45%) and an overall low survival (18%) in this special form of TTP-HUS.\(^6\) After correcting high blood pressure and blocking the renin-angiotensin system, drugs such as tumor necrosis factor \(\alpha\) (TNF-\(\alpha\)) antagonist, defibrotide, or nitric oxide donors may be superior to plasma exchange.\(^8\)

We are surprised by the rate of death that, except for pregnancy/postpartum-related TTP-HUS, is between 40% (bloody diarrhea) and 100% (stem cell transplantation).\(^5\) In a recent study of 30 patients admitted to the ICU for management of TTP-HUS (mean simplified acute physiology score II [SAPS II] 37.3 \(\pm\) 18.7,\(^9\) 57% under mechanical ventilation), only 27% of patients died.\(^10\) Of most importance is that 9 of 30 patients were infected with HIV, one of the main factors influencing the prognosis in multivariate analysis in our report (odds ratio [OR], 20.3; range, 2.5-167.5; \(P = .0002\)).\(^2\) The death rate of TTP-HUS patients is especially high in patients with moderate deficiency or normal levels of ADAMTS13 activity (respectively, 61% and 35%). Is it possible to conclude that plasma exchange is of poor efficacy in the case of hemolytic and uremic syndrome, and of value in the case of thrombotic thrombocytopenic purpura detected by a severe deficiency (\(< 5\% \) activity)\(^10\) of ADAMTS13? This hypothesis was suggested in a recent review by Tsai.\(^12\) We believe that adjuvant treatments such as cortisosteroids and antihypertensive agents are of great importance in hemolytic uremic syndrome. Finally, we agree that ADAMTS13 deficiency will not detect all patients with TTP-HUS who may respond to treatment.

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References

Response:

Thrombotic thrombocytopenic purpura–hemolytic uraemic syndrome (TTP-HUS): treatment, mortality, and the frequency of HIV infection

Vincent et al raise 4 points about our recent publication that require a response and clarification. First, Vincent et al are surprised by the low frequency of HIV infection among our patients with TTP-HUS. We feel that the explanation for the widely different frequencies of HIV infection among different case series must be related to patient selection and to the location of the study; for example, some urban areas in some regions have a high rate of HIV infection while other regions have lower rates. In our publication, we reported that 2 (1.4%) of 142 patients were HIV positive. This is the same frequency as in our total 14.5-year experience of the Oklahoma TTP-HUS Registry: 4 (1.4%) of 295 patients were HIV positive. Because the Registry includes all patients with clinically diagnosed TTP-HUS in our region and because 295 of 301 patients in the Registry have been tested for HIV infection at presentation, these data accurately reflect the frequency of HIV infection in patients with clinically diagnosed TTP-HUS in our region.

Second, Vincent et al cite a previous study to support their practice that high-dose plasma infusion is as effective as plasma exchange for the treatment of TTP-HUS. However, in that retrospective, nonrandomized study, 8 of 19 patients initially treated with plasma infusion were switched to plasma exchange because of fluid overload or lack of response. Therefore, we believe that this study is not convincing for the use of plasma infusion instead of plasma exchange. However, it does suggest that plasma infusion is appropriate for urgent care until plasma exchange is available.

Third, we agree with Vincent et al that patients diagnosed with TTP-HUS following allogeneic hematopoietic stem cell transplantation rarely respond to plasma exchange. However, many, perhaps most, of these patients are unresponsive because they are subsequently diagnosed with systemic fungal and/or viral infections, therefore they would also be unresponsive to the other modalities mentioned by Vincent et al.

Fourth, Vincent et al note the poor response to plasma exchange and the high mortality among patients with moderate ADAMTS13 deficiency (a disintegrin-like and metalloprotease with thrombospondin type 1 repeats) deficiency (10%-25%) in our report, compared with patients with severe ADAMTS13 deficiency (<5%). They interpret these data to suggest that patients with moderate deficiency have HUS and patients with severe deficiency have TTP, and that plasma exchange treatment is less effective for HUS than it is for TTP. However, defining patients in different categories of ADAMTS13 deficiency as having distinct syndromes, HUS and TTP, is not possible. While patients with moderate ADAMTS13 deficiency did have a higher frequency of acute renal failure than patients with severe ADAMTS13 deficiency, they also had a higher frequency of severe neurologic abnormalities; the severity of thrombocytopenia and anemia was the same in both groups.

Our interpretation is that patients with moderate ADAMTS13 deficiency, as well as the patients with normal ADAMTS13 activity, often had additional disorders at presentation (eg, autoimmune disorders) or alternative disorders discovered after presentation (eg, disseminated malignancy and sepsis). Moderate ADAMTS13 deficiency has been previously reported in acutely ill patients with systemic disorders. We believe that these additional and alternative disorders were the reason for the poor response to plasma exchange and the high mortality in patients with moderate ADAMTS13 deficiency.

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References

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