CORRESPONDENCE

TREATMENT OF DIC ASSOCIATED WITH APL

To the Editor:

The recent report by Rodeghiero[1] suggests that uncertainty still exists on how to prevent intracerebral hemorrhage in patients with acute promyelocytic leukemia undergoing induction therapy. Patients treated with either heparin, antifibrinolytics, and supportive care alone all experienced a comparable incidence of early hemorrhagic death (approximately 9%).

While controversy may still persist in relation to optimal therapy, it should be clearly understood that virtual elimination of intracerebral hemorrhage occurs with the application of intravenous heparin, 7.5 to 12.5 U/kg/h accompanied by infusions of fresh frozen plasma with 6 U of platelets every 12 hours.

This method has now been applied to induction therapy in 61 consecutive patients, with only one instance of intracerebral hemorrhage in a patient who failed to receive the platelet transfusion at 12 hours.[2] Further refinements may ultimately reduce the theoretical risk of allosensitization because of multiple transfusions, but intracerebral hemorrhage rates of 10%[1] or 15%[3] still represent an unacceptably high risk in patients with disseminated intravascular coagulopathy and acute leukemia.

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RESPONSE

Every hematologist would easily agree with the statement of Drs Arlin and Feldman that a rate of 10% or 15% of fatal cerebral hemorrhage is still unacceptable in patients with DIC and acute leukemia, but we do not understand how Drs Arlin and Feldman can state that virtual elimination of intracerebral hemorrhage can be obtained with the administration of intravenous heparin at low dosage plus fresh frozen plasma and platelet transfusion every 12 hours. If the data on which the investigators base their statement are those reported in 1989,[1] several comments seem appropriate.

(1) This paper reports data on 32 patients to whom a total of 46 separate induction courses were administered. Of them, only 12 were treated at diagnosis whereas the majority were treated at relapse. As a consequence, the overall incidence of DIC was very low (37%) in comparison with that commonly observed in this subtype of acute leukemia.[2] In fact, the burden of leukemic cells may be smaller than in patients treated at diagnosis. Our patients were all treated at diagnosis and about 65% had DIC.[3] The difference between the two patient populations is further demonstrated by the different platelet count at admission (32% of cases $<50{,}000/\mu L$ *v* 60% $<30{,}000/\mu L$; median $78{,}000/\mu L$ *v* $25{,}000/\mu L$, respectively, in Dr Arlin's and our study).

(2) In their article the investigators report one case of fatal cerebral hemorrhage out of 46 induction courses. It is not specified if this patient was treated at diagnosis or at relapse. If the patient was treated at diagnosis, the incidence of fatal hemorrhage ($^1/_{12}$ or 8.3%) would be very similar to that observed in our study, whatever the significance of an estimation based on such a small number of cases.

While waiting for a full report of the data mentioned by Drs Arlin and Feldman in their letter, we would like to re-emphasize that only prospective randomized trials, rather than anecdotal reports, can definitely clarify the effectiveness of any antihemorrhagic treatment for acute promyelocytic leukemia. Such a prospective study has been recently proposed to all Italian centers treating leukemic patients and it is in its preliminary phase.

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