Acta Haemat 1989;81:58-59

Antifibrinolytic Therapy in Acute Promyelocytic Leukemia

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Fig. 1, 2. Clinical courses of 2 patients. 1 L.A., a 46-year-old man; M3. 2 P.B., a 14-year-old girl; M3. a Days on which daunorubicin(DNR), tranexamic acid (TA) and heparin (Hep.) were given, b Percentage of peripheral blast cells (PB) and marrow blasts, c Plasma concentration of fibrinogen (FG;) and fibrinogen degradation products (FDP;). d Plasma concentration of antithrombin (AT II; O), plasminogen (PG; •) and α 2-AP (Δ).
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The treatment of acute promyelocytic leukemia (APL) presents special problems because of the coagulopathy that often accompanies the disease [1]. Intravenous heparin has been attempted to control intra-vascular coagulation in APL patients with minor bleeding complications [2]. However, some authors report that fibrinolysis persists in patients with APL and DIC, in spite of heparin [3] and many patients develop major bleeding problems.

Results of several studies (4), in agreement with ours [5], have shown low levels of α_2 -antiplasmin (α_2 -AP) inhibitor in patients with APL.

Recently, Schwartz et al. [6] suggested that epsilon-aminocaproic acid could be an effective therapy for patients affected by APL who developed a coagulopathy associated with α_2 -AP inhibitor depletion.

On the basis of our previous data [5], we administered tranexamic acid instead of α -aminocaproic acid to 2 APL patients (a 46-year-old man and a 14-year-old child) who presented coagulopathy during heparinic treatment (10 IU/kg/h i.v.); tranexamic acid was started after the fall of α_2 -AP below 50% and plasminogen below 60% (assayed with S-2251 chromogenic substrates), a finding which coincided in both cases with daunorubicin (80 mg/M²) for 4 and 6 days respectively.

In contrast with the observation of Schwartz et al. [6] and Imaoka et al. [3], no sign of hemorrhagic diathesis was observed in our patients during induction therapy or in aplastic phases, although α_2 -AP levels were maintained below the normal range (fig. 1, 2); α_2 -AP and plasminogen raised to normal values together with progressive bone marrow clearing from leukemic cells, even before fibrinogen normalization, and both patients achieved hematological remission.

These data underline the possible efficacy of antifibrinolytic agents in the prevention of hemorrhagic events in APL patients in addition to heparinic treatment and suggest a potential role of α_2 -AP as a marker of hematological remission in acute leukemia.

References

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