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Antifibrinolytic Therapy in Acute Promyelocytic Leukemia

E.M. Pogliani, M. Salvatore, G. Masera, G. Corneo

Istituto Scienze Biomediche, Università di Milano, Ospedale S. Gerardo Monza, Milano, Italia

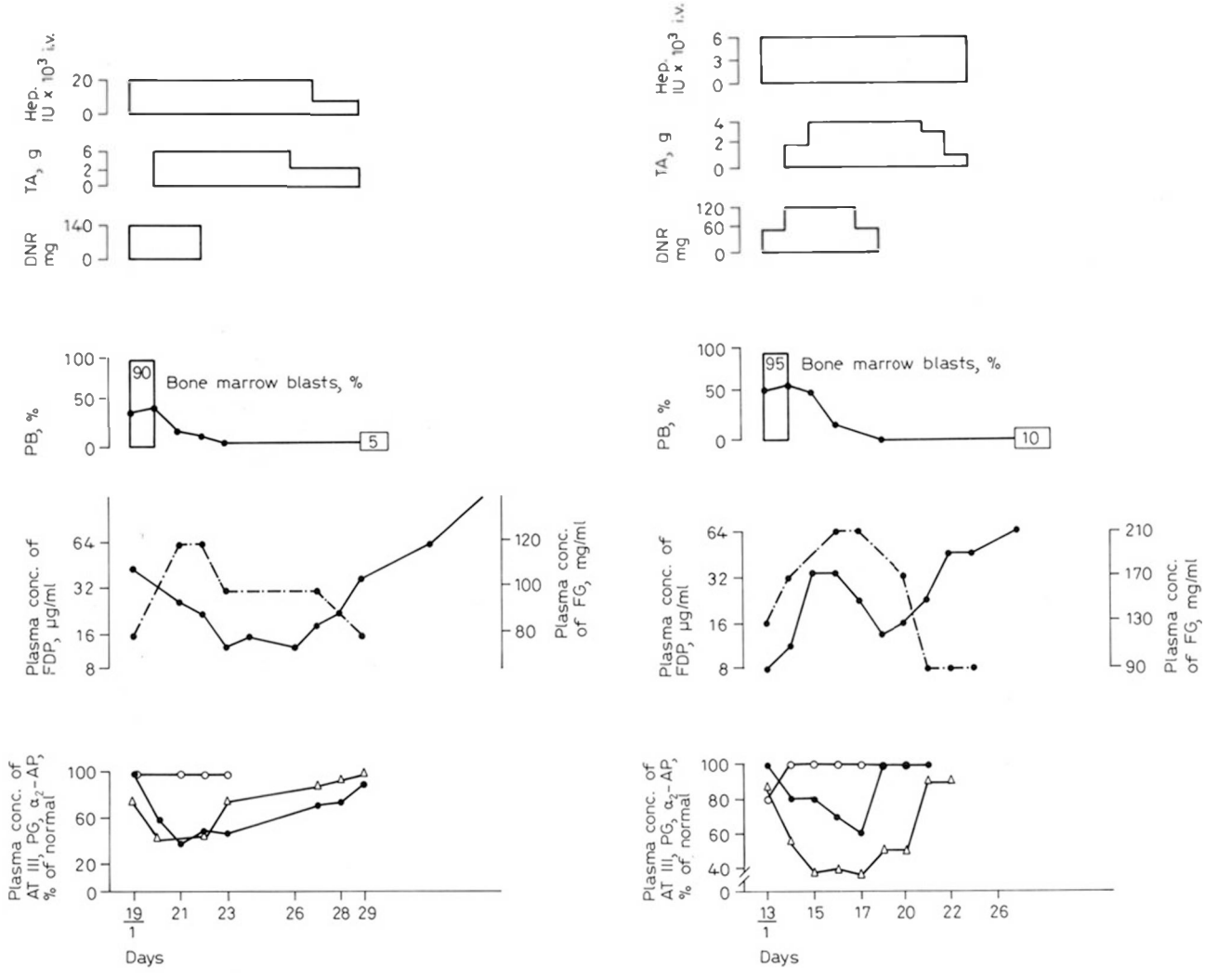

Fig. 1, 2. Clinical courses of 2 patients. **1** L.A., a 46-year-old man; M_3. **2** P.B., a 14-year-old girl; M_3. **a** Days on which daunorubicin (DNR), tranexamic acid (TA) and heparin (Hep.) were given. **b** Percentage of peripheral blast cells (PB) and marrow blasts. **c** Plasma concentration of fibrinogen (FG; ——) and fibrinogen degradation products (FDP; — · —). **d** Plasma concentration of antithrombin (AT II; ○), plasminogen (PG; ●) and α_2-AP (△).

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 intravascular 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/M_2) 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

1 Baker W, Bang NU, Nachman RL, et al: Hypofibrinogenemic hemorrhage in acute myelogenous leukemia treated with heparin. Ann Inter Med 1986;61:116–123.
2 Gralnick HR, Bagley J, Abbell E: Heparin treatment for the hemorrhagic diathesis of acute promyelocytic leukemia. Am J Med 1972;52:167–174.
3 Imaoka S, Ueda T, Shibata H, et al: Fibrinolysis in patients with acute promyelocytic leukemia and disseminated intravascular coagulation during heparin therapy. Cancer 1986;57:1736–1738.
4 Velasco F, Torres A, Andreis P, et al: Changes in plasma levels of protease and fibrinolytic inhibitors induced by treatment in acute myeloid leukemia. Thromb Haemost 1984;52:81–84.
5 Pogliani EM, Cofrancesco E, Boschetti C, et al: Treatment-induced changes in plasma levels of alpha-2-anti-plasmin in acute leukemia. Thromb Haemost 1985;54:202.
6 Schwartz BS, Williams EC, Conrad MG, et al: Epsilon-aminocaproic acid in the treatment of patients with acute promyelocytic leukemia and acquired alpha 2-plasmin inhibitor deficiency. Ann Intern med 1986;105:873–877.

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E.M. Pogliani
Istituto Scienze Biomediche
Università di Milano
Ospedale S. Gerardo Monza
Milano (Italy)