

MANAGEMENT OF L-ASPARAGINASE INDUCED PROTHROMBOTIC STATE IN ACUTE LYMPHOBLASTIC LEUKEMIA

Matteo Parma, Daniela Belotti, Enrico Maria Pogliani

Istituto di Scienze Biomediche, Università degli Studi di Milano, Div. di Ematologia, Ospedale S. Gerardo, Monza, Italy

Sir,

in their report *Inefficacy of fresh frozen plasma in the treatment of L-asparaginase induced coagulation factor deficiencies during ALL induction therapy*, Nowak-Göttl and coll.¹ reported that the prophylactic administration of fresh frozen plasma in acute lymphoblastic leukemia (ALL) patients treated with L-asparaginase (L-Ase) is of no use in correcting the hemostatic imbalance. In fact, they observed no increase in antithrombin III (ATIII) or plasminogen levels, and only a minimal increase in thrombin and α_2 -antiplasmin levels. It has been established that L-Ase used in ALL patients can induce thrombotic events by reducing coagulation inhibitors² (ATIII, protein C and protein S) and inducing endothelial damage.³ We wish to report our experience in the prevention of coagulation disorders induced by L-Ase therapy in adult ALL patients.⁴ As suggested by some authors,⁵ we administered ATIII concentrates during L-Ase therapy to restore hemostasis altered by chemotherapy. In these patients, and in a control group of non-supported patients, we studied two hypercoagulability markers: the thrombin-antithrombin complex (TAT) and D-dimer.

Our study confirms that L-Ase treatment can induce a hypercoagulability state which can be corrected by the administration of ATIII concentrates. In fact, in the ATIII supported group TAT and D-dimer levels returned to normal, while the same hypercoagulability markers

increased in the control group, who experienced some thrombotic events. The administration of ATIII concentrates alone cannot restore hemostasis, but may be important in regulating the prothrombotic state related to possible endothelial injury. Our study suggests that ATIII concentrates are more suitable than fresh frozen plasma infusion for normalizing the prothrombotic state. In our Department, prophylactic administration of ATIII concentrates is currently performed in all ALL patients treated with L-Ase. We have not observed thrombotic events in any of the thirty patients treated so far.

References

1. Nowak-Göttl U, Rath B, Binder M, et al. Inefficacy of fresh frozen plasma in the treatment of L-asparaginase induced coagulation factor deficiencies during ALL induction therapy. *Haematologica* 1995; 80:451-3.
2. Gugliotta L, Mazzucconi MG, Leone G, et al. Incidence of thrombotic complication in adult patients with acute lymphoblastic leukemia receiving L-asparaginase during induction therapy: a retrospective study. The GIMEMA group. *Eur J Haematol* 1992; 49:63-6.
3. Jane SM, Hau L, Salem HM. Extracts from malignant tissue reduce thrombomodulin expression on cultured human endothelial cells. *Haematol Rev* 1991; 5:85-95.
4. Pogliani EM, Parma M, Baragetti I, et al. L-Asparaginase in acute lymphoblastic leukemia treatment: the role of human antithrombin III concentrates in regulating the prothrombotic state induced by therapy. *Acta Haematol* 1995; 93:5-8.
5. Mattioli Belmonte M, Gugliotta L, Devols U, et al. A regimen for antithrombin III substitution in patients with acute lymphoblastic leukemia under treatment with L-asparaginase. *Haematologica* 1991; 76:209-14.