T8. **THE ROLE OF ANTITHROMBIN-III THERAPY IN REDUCTION OF HEMATOPOIETIC STEM CELL TRANSPLANTATION RELATED TOXICITY.**

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Introduction: Antithrombin III (ATIII) is a potent inhibitor of the coagulation cascade. It is a nonvitamin K-dependent protease that inhibits coagulation by lysing thrombin and factor Xa. Antithrombin III's activity is markedly potentiated by heparin; potentiation of its activity is the main mechanism by which both heparin and low molecular weight heparin result in anticoagulation.

Acquired antithrombin III deficiency is a deficiency of antithrombin primarily due to consumption. It is observed in situations in which activation of the coagulation system is inappropriate. Common conditions that result in acquired antithrombin III deficiency include disseminated intravascular coagulation (DIC) , microangiopathic hemolytic anemias due to endothelial damage and veno-occlusive disease in patients undergoing allogeneic bone marrow transplantation.

A hypercoagulable state has been shown to follow high-dose chemotherapy for bone marrow transplantation (BMT). Deficiency of the natural anticoagulants, antithrombin III (ATIII), protein C and protein S correlates with organ dysfunction following bone marrow transplantation (BMT).

Material and methods: We treated 8 patients pre-emptive or with severe post-BMT organ dysfunction with ATIII concentrate (Baxter AT III). Indications for treatment included ATIII anticoagulant level less than 80% and life-threatening single or multiorgan dysfunction. All patients were loaded with 50 units/kg ATIII/ day for 3-5 days. Clinical improvement was seen within 1-7 days of start of therapy in all patients.The study group was composed of 4 childrens (age range 3 years 7 months-16 years) and 4 adults (age 35-56) who underwent allogeneic peripheral stem cell transplantation from February 2012 to March 2013: 6 patients from related matched donors and 2 from unrelated matched donors.The underlying disease was: myelo-monocytic AML 2 cases, B-ALL 3 cases, aplastic anemia 1 case, JMML 1 case, beta thalasemia major 1 case. Total and conjugated bilirubin, aspartame, alanine and γ-glutamyl transferase, prothrombin time, activated partial thromboplastin, protein C and S and fibrinogen were determined at baseline and three times per week thereafter until at least day +30 after HSCT. ATIII activity (normal range 70-120%) was measured at least three times per week beginning prior to conditioning (baseline) and ending at day +40.

Results: From the study group 6 patients received pre-emptive replacement with ATIII, 1 patient in condition of multiorgan failure and 1 in confirmed VOD.Four from the pre-emptive group are in remission after day+100, one relapsed and died from progressive AML at 6 months after BMT, one died at day +45 by hemofagocytic syndrome.In cases of graft failure and multiorgan dysfunction and VOD death occured at day +64 respectively +38.

Patients receiving pre-emptive or therapeutic AT-III replacement therapy had no detectable toxicity or adverse effects.

Conclusions: Significant improvements in organ dysfunction following ATIII treatment in this small study supports a causal relationship between ATIII deficiency and post-BMT chemotherapy-induced organ dysfunction. In conclusion, the encouraging results of this study suggest that this antithrombin III treatment should be further considered in patients with allogeneic bone marrow transplantation with or without defibrotide.