

Disordini emorragici acquisiti: aspetti diagnostici e clinici

UPDATING MANAGEMENT OF ACQUIRED HEMOPHILIA A USING EMICIZUMAB: REAL-WORLD OUTCOMES BY A COLLABORATIVE NETWORK OF 3 ITALIAN CENTERS

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Background. Acquired Hemophilia A (AHA) is a rare, life-threatening autoimmune bleeding disorder caused by autoantibodies (inhibitors) against coagulation factor VIII (FVIII). Traditional management focuses on immediate hemostatic treatment for acute bleeding and the eradication of autoantibodies via immunosuppressive therapy (IST). However, patients remain at high risk of severe hemorrhage until complete remission is achieved, and prolonged IST is associated with significant morbidity. Recently, emicizumab—a bispecific monoclonal antibody that mimics FVIII activity by bridging activated factor IX and factor X—has emerged as an innovative approach for AHA. Originally authorized for bleeding prophylaxis in congenital hemophilia (with or without inhibitors), emicizumab may reduce the bleeding burden even in AHA and allow for more flexible IST regimens. In Italy, the drug is currently accessible for this indication under the provisions of Law 648/1996.

Methods. We reviewed a cohort of AHA patients who received emicizumab at the Hemophilia Center of Parma or through consultations at the Centers in Piacenza and Reggio Emilia. Due to the requirement for chromogenic assays with bovine reagents, monitoring of FVIII and inhibitor levels was centralized at the Parma laboratory. Results are reported as means ± 1 standard deviation.

Results. Five patients (3 men, 2 women) were diagnosed with AHA (idiopathic in 3 cases) at mean age of 81±6 years. All but one patient presented with poor prognostic factors, including FVIII:C <1% and/or high inhibitor titers (mean: 47±31 BU/mL). All patients exhibited severe muscle and subcutaneous hematomas and anemia (Hb <7 g/dL in 3 cases); elbow joint bleeding and gastrointestinal hemorrhage were also observed in one patient each. Initial hemostatic treatment with recombinant activated FVIII (rFVIIa) and red blood cell (RBC) transfusions was administered to all patients as needed. Emicizumab was introduced following the loading schedule in this setting (6 mg/kg on day 1, 3 mg/kg on day 2, and 1.5 mg/kg on day 8) after a mean of 17 days of hospitalization. Maintenance doses were administered weekly for 3 weeks in four patients, while one patient was treated for 4 weeks. Compared to the pre-emicizumab phase, the mean RBC transfusion requirement decreased from 7.2±4.9 to 1±0, and mean rFVIIa consumption fell from 124±72 mg to 71±23 mg (with three patients requiring no further administration). Three patients were discharged 7–9 days after initiating emicizumab, continuing with outpatient monitoring. In two cases, emicizumab helped avoid the intensification of IST and inhibitor eradication was achieved after 42–98 days (FVIII >20% reached within 17–45 days). Despite the reduction in bleeding, two patients died due to complications of the underlying condition (acute leukemia) and sepsis, respectively. No adverse events related to emicizumab were observed, including thrombotic or cardiovascular complications.

Conclusions. A collaborative network of centers providing specialized laboratory and clinical expertise facilitated the integration of emicizumab into the management of these poor-prognosis AHA patients. Emicizumab prophylaxis effectively reduced both the clinical bleeding burden and the treatment requirements, enabling earlier discharge and outpatient follow-up in patients without severe IST-related complications or comorbidities.

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