



DISORDINI EMORRAGICI CONGENITI: ASPETTI
DIAGNOSTICI E CLINICI

PREVALENCE OF GASTROINTESTINAL BLEEDING IN GLANZMANN THROMBASTHENIA PATIENTS: RESULTS OF A WORLDWIDE SURVEY

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Background and Aims. Bleeding manifestations in Glanzmann Thrombasthenia (GT) are typically moderate-to-severe mucocutaneous hemorrhages, post-partum and post-surgical bleeding. Although gastrointestinal bleeding (GIB) is part of mucocutaneous hemorrhages, its prevalence and severity have not been systematically investigated in GT. GIB represents a clinically relevant complication due to the frequent delayed diagnosis, leading to significant blood loss, therapeutic challenges, and the need for repeated hospitalizations and transfusions. A potential underlying cause of occult GIB is gastrointestinal angiodysplasia (GIA), a vascular malformation associated with abnormal neoangiogenesis. GIA-related bleeding is frequent in von Willebrand disease, but it has not been explored in GT, in which it could reflect an impairment of integrin-B3 role in endothelial physiology. We aimed to assess the prevalence, severity, and current management of GIB, as well as its association with GIA, in a large international cohort of GT patients through a retrospective, international, multicenter survey.

Methods. A survey, supported by EHA and ISTH, was conducted across specialized centers managing patients with GT. All adult and pediatric patients with a confirmed diagnosis of GT or ITGA2B/ITGB3-related thrombocytopenia were included. GT diagnosis had to be based on genetic analysis and/or typical laboratory findings. A standardized, anonymized case report form (CRF) had to be completed for each GT patient followed at the participating centers, regardless of the presence or not of GIB. The CRF captured demographic and clinical data, detailed characteristics of the GIB episodes and treatment approaches.

Results. We enrolled 479 patients: 232 with ITGA2B variants, 125 with ITGB3 variants, and 122 with variant unknown. 252 were type I GT, 60 type II, 36 type III, 73 had ITGA2B/ITGB3-RT and 44 were not classified. 194 GIB episodes in 166 GT patients were reported. 34.1% of GT patients had at least one GIB (0.1%/year in the general population). Of the 166 patients with GIB, 68.7% were type I GT, 9.7% type II, 6% type III, 3.6% ITGA2B/ITGB3-RT, 12% not classified. The ISTH-BAT bleeding score (BS) was higher in patients with GIB than in those without (17.98±8 vs 12.8±10.1; p<0.0001). Among the overall GT population 6% had GIA (0.8% in the general population). The percentage of patients with GIB was similar in ITGA2B-mutated and ITGB3-mutated patients, while GIA was more frequent among ITGB3-mutated patients, although not significantly. GIB was more severe in ITGB3-mutated patients, in fact they experienced more bleeding episodes (3-10 in their life) and with a higher frequency (3-4 times/month). Red blood cell transfusions were the most frequently used treatment (58.7%), followed by platelet transfusions and antifibrinolytic agents; 34.6% of patients received combined treatments. DDAVP had the highest success rate, followed by combined treatments and argon plasma coagulation.

Conclusions. GIB is a frequent and clinically relevant complication in GT, often severe and associated with a high incidence of GIA. GT patients carrying ITGB3 variants seem to suffer more frequent and severe GIB. GIB carries a serious and often recurrent bleeding burden to GT patients. These findings support the need of systematic screening of GIB in GT patients and urge studies on the targeted prevention and management of this bleeding complication.