

Piastrinopenie immuni

DOWNREGULATION OF MARKERS OF PLATELET ACTIVATION, PLATELET TURNOVER AND PLATELET DESIALYLATION IN GOOD RESPONDERS TO FIRST-LINE TREATMENT(S) FOR IMMUNE THROMBOCYTOPENIA

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Background and Aims. In immune thrombocytopenia (ITP), thrombocytopenia is the result of immune-mediated accelerated platelet clearance and impaired megakaryopoiesis. Evidence suggests that the pathogenic mechanisms of ITP may be heterogeneous across patients and modulated by treatment. Flow cytometry (FC) platelet profiling may help identify residual pathogenic pathways and support mechanism-based treatment tailoring. With this study, we aimed to investigate FC platelet markers in recipients of first-line ITP treatment(s).

Methods. We included adult ITP patients followed up at the Haematology outpatient clinic of hospital San Paolo, Milan, sampled before and after ITP-specific first-line treatment (high-dose corticosteroids and/or intravenous immunoglobulin, IVIG), administered as per current clinical guidelines. Post-treatment samples were obtained at least 14 days after the start of corticosteroids and 3 days after the start of IVIG. For this analysis, patients were classified as good responders, responders and poor responders based on their post-treatment platelet counts (≥100x10^9/L, 50-99x10^9/L and ≤49x10^{9}L, respectively). We evaluated markers of circulating activated platelets [surface p-selectin expression, platelet-monocyte and platelet-granulocyte aggregates (PMAs, PGAs)], platelet turnover (reticulated platelets) and platelet desialylation (platelet β-galactose exposure) through FC. The cut-off was the 95th centile of 20 healthy subjects. This project was funded by the Italian Ministry of Health (SG-2021-12375578).

Results. Thirty-two patients were enrolled in this study (20 females). All patients had been treated with ITP-directed first-line treatment(s). Based on their post-treatment platelet counts, 14 patients were classified as good responders, 8 as responders, and 10 as poor responders. With regards to markers of circulating activated platelets, the highest proportion of patients with p-selectin positive platelets was found in the poor response group (5/10, 50%) compared to the response (2/8, 25%) and good response (0/13, 0%) groups (poor responders vs good responders, p=0.01). Similar trends were observed for PMAs [6/10 (60%), 3/8 (38%) and 3/13 (23%)], PGAs [7/10 (70%), 3/8 (38%) and 5/13 (38%)], increased reticulated platelets [3/10 (30%), 2/8 (25%) and 0/13 (0%)] and platelet desialylation [2/7 (29%), 1/6 (17%) and 1/11 (9%)] in poor responders, responders and good responders, respectively. Ten patients had samples drawn before and after treatment, all with post-treatment platelet counts ≥50x10^9/L. The proportions of patients with increased reticulated platelets [pre- vs post-treatment: 4/9 (44%) vs 0/10 (0%), p=0.03], p-selectin positive platelets [3/7 (43%) vs 0/9 (0%), p=0.06], PGAs [8/10 (80%) vs 4/9 (44%), p=0.17], PMAs [9/10 (90%) vs 2/9 (22%), p=0.01] and platelet desialylation [5/8 (63%) vs 1/9 (11%), p=0.05] declined post-treatment.

Conclusions. In the examined cohort, there was an overall trend towards the improvement of FC markers of platelet turnover, activation and desialylation in good responders to ITP-directed first-line treatment, suggesting that the successful downregulation of ITP pathogenic mechanisms may be measurable. Persistent abnormalities in these markers may help identify residual mechanisms of thrombocytopenia and guide personalized treatment escalation in ITP.