ELSEVIER

Blood 142 (2023) 3962–3964

The 65th ASH Annual Meeting Abstracts

# POSTER ABSTRACTS

## 311.DISORDERS OF PLATELET NUMBER OR FUNCTION: CLINICAL AND EPIDEMIOLOGICAL

### Coagulation in Patients with Immune Thrombocytopenia and Other Associated Autoimmune Disorders

*Nora Butta, PhD*[1,2], *Elena Monzón Manzano, PhD*[3,2], *Paula Acuña*[3,2], *Elena G Arias-Salgado, PhD*[2,3], *Maria Isabel Rivas Pollmar, PhD MD*[3,2], *Monica Martin Salces, PhD MD*[3,2], *Ana Mendoza-Martínez*[3], *Víctor Jiménez-Yuste, MD PhD*[3,4,2], *Waleed Ghanima, MDPhD*[5,6,7], *Maria Teresa Álvarez-Roman*[2,4,3]

[1] Hospital Universitario La Paz, Madrid, Spain
[2] IdiPAZ, Madrid, Spain
[3] Department of Haematology, Hospital Universitario La Paz, Madrid, Spain
[4] Faculty of Medicine, Universidad Autonoma de Madrid, Madrid, Spain
[5] Østfold Hospital, Gralum, Norway
[6] Østfold Hospital and Institute of Clinical Medicine, University of Oslo, Oslo, Norway
[7] Østfold Hospital, Gralum, NOR

**Introduction**

Chronic immune thrombocytopenia (ITP) is characterized by perturbations of immune homeostasis with hyperactivated effector cells as well as defective regulation of the adaptive immune system. It has been reported that, with varying frequency, patients with ITP may also have associated other autoimmune disorders, with circulating autoantibodies such as lupus anticoagulant antibodies (LACs), anti-nuclear antibodies (ANA), anticardiolipin (aCL), anti-beta2-glycoprotein I (anti-beta2GPI), anti-thyroid peroxidase (ATPA), and rheumatoid factor (RF).

**Objectives**

To evaluate coagulation in patients with ITP with autoantibodies associated to other autoimmune diseases.

**Methods**

This is a prospective study that was approved by the Ethics Committee from Hospital Universitario La Paz. Informed consent was signed before sampling. Adult ITP patients (n=182) without and with associated autoantibodies such as LACs, ANA, aCL, anti-beta2GPI, ATPA, and RF and healthy controls (n=180) were recruited.

To evaluate the kinetics of clot formation and fibrinolysis, ROTEM® was performed on fresh platelet rich plasma adjusted to 25x10$^9$ platelets/L with the subjects own platelet poor plasma (PPP). Recalcification (NATEM) was used to induce coagulation. Clotting time (CT = time from start of measurement until initiation of clotting, in seconds); alpha angle (tangent to the curve at 2 mm amplitude, in degrees, which reflects the rate of fibrin polymerization); maximum clot firmness (MCF = maximum clot firmness, in mm, which reflects the maximum tensile strength of the thrombus); and lysis at 60 min (LI60) were recorded.

Thrombin generation was measured in citrated PPP by calibrated automated thrombogram (CAT). To evaluate procoagulant capacity of plasma, coagulation was triggered by proper recalcification and the addition (final concentrations) of 1 pmol/L of recombinant human tissue factor (TF) and 4 μmol/L of phospholipid mixture (PPP-Reagent LOW, Thrombinoscope BV, Maastricht, The Netherlands). Procoagulant activity of microparticles (MPs) associated with their content of either TF or phosphatidylserine (PS) was determined, respectively, with MP reagent (4 μM phospholipids) or PRP reagent (1 pM of recombinant human TF) by CAT. The following parameters were determined: Lag time (LT), or time from the start of the assay until 10 nM thrombin is formed, in min; time-to-peak (ttPeak), or time required to reach the maximum thrombin concentration, in min; peak height (Peak), or maximum thrombin concentration reached, in nM; and endogenous thrombin potential (ETP), or total amount of thrombin generated over time, in nMxmin.

**Results**

Fifty of the 182 patients with ITP (27.5%) were positive for autoantibodies associated with other autoimmune diseases, distributed as shown in Table 1. ANA were the most frequent antibodies present in these patients, and 22% had more than one kind of associated antibodies.

Patients with ITP without antibodies had a shorter clot formation time (CT) than healthy controls. Presence of associated autoimmune diseases prolongs CT and resulting in values similar to controls. Both groups of patients with ITP had a diminished fibrinolysis (Table 2).

Thrombin generation triggered by TF plus phospholipids as well as that dependent on TF content of microparticles (MP-reagent) was impaired in patients with other associated autoimmune disorders as shown by the prolonged LT and the diminution in either ETP or peak of generated thrombin (Table 2).
When thrombin generation relayed on phospholipids of MPs, all patients with ITP generated less thrombin.

**Conclusion**

Association of other autoimmune diseases with ITP seemed to produce a delay in clot formation and in thrombin generation whereas did not affect the diminished fibrinolysis observed in ITP patients.

*Work supported by Instituto de Salud Carlos III (ISCIII) (PI19/00772, PI22/01489), co-funded by the European Union.*

**Disclosures Butta:** *Novo Nordisck, Novartis:* Speakers Bureau; *Takeda, Novo Nordisck:* Research Funding. **G Arias-Salgado:** *Novo Nordisck, Novartis:* Speakers Bureau; *Grifols:* Research Funding. **Rivas Pollmar:** *Novo Nordisck, Novartis:* Speakers Bureau. **Martin Salces:** *Novo Nordisck, Novartis:* Speakers Bureau. **Jiménez-Yuste:** *Grifols:* Consultancy, Honoraria, Research Funding; *Novo Nordisk:* Consultancy, Honoraria, Research Funding; *F. Hoffmann-La Roche Ltd:* Consultancy, Honoraria, Research Funding; *Takeda:* Consultancy, Honoraria, Research Funding; *Bayer:* Consultancy, Honoraria, Research Funding; *CSL Behring:* Consultancy, Honoraria, Research Funding; *Pfizer:* Consultancy, Honoraria, Research Funding; *BioMarin:* Consultancy; *Sanofi:* Consultancy, Honoraria, Research Funding; *Sobi:* Consultancy, Honoraria, Research Funding. **Ghanima:** *BMS:* Honoraria, Research Funding; *UCB:* Consultancy, Honoraria; *Grifols:* Consultancy, Honoraria; *Bayer:* Consultancy, Honoraria, Research Funding; *Argenx:* Consultancy, Honoraria; *Sobi, Pfizer:* Consultancy, Honoraria, Research Funding; *hibio:* Consultancy, Honoraria; *Sanofi:* Consultancy, Honoraria; *cellphire:* Consultancy, Honoraria; *Kedrion:* Consultancy; *alpine:* Consultancy, Honoraria; *Amgen:* Consultancy, Honoraria; *Novartis:* Consultancy, Honoraria. **Álvarez-Roman:** *Roche:* Honoraria, Speakers Bureau; *Grifols:* Honoraria, Speakers Bureau; *Amgen:* Honoraria, Speakers Bureau; *LFB:* Honoraria, Speakers Bureau; *Novartis:* Honoraria, Speakers Bureau; *Novo Nordisk:* Honoraria, Speakers Bureau.

| | N (%) |
|---|---|
| Anti-Nuclear Antibodies (ANA) | 25 (50) |
| Anti-Thyroid Peroxidase Antibodies (ATPA) | 9 (18) |
| Lupus Anticoagulant Antibodies ((LACs) | 1 (2) |
| Rheumatoid Factor (RF) | 4 (8) |
| RF+ATPA | 1 (2) |
| ANA+ATPA | 3 (6) |
| Anti-beta2-glycoprotein I (Anti-beta2GPI, IgG)+ Anticardiolipin (Acl, IgM) | 2 (4) |
| Anti-beta2GPI (IgM)+ATPA | 1 (2) |
| Anti-beta2GPI (IgM)+ Acl (IgM+IgG)+LACs | 3 (6) |
| Anti-beta2GPI (IgM)+ Acl (IgM+IgG)+LACs+ANA | 1 (2) |

TABLE 1-Distribution of circulating factors associated to other autoimmune diseases in patients with ITP.

| | ITP w/o associated autoI disorders | ITP with associated autoI disorders | CONTROLS |
|---|---|---|---|
| PLATELET COUNT ($X10^9$/L) | 133±114~ | 157±129~ | 252±76 |
| CT (s) | 782.8±159.9~ | 949.6±197.3# | 901.7±195 |
| MCF (mm) | 43.64±8.45 | 42±8.95 | 42.3±7.14 |
| ALPHA (°) | 44.68±10.4 | 40.64±12.44 | 40.96±8.24 |
| Ly60 (%) | 97.14±3.23~ | 96.89±2.42~ | 93.67±2.94 |
| LT-PPP LOW (min) | 4.98±1.27 | 7.24±5.1~# | 4.94±1.51 |
| ETP-PPP LOW (nMxmin) | 1462±315.7 | 1198±579.4~# | 1484±574.7 |
| PEAK-PPP LOW (nM) | 257.4±88.2 | 239.5±113.5 | 243±79.4 |
| LT-MP (min) | 12.33±3.88 | 17.65±9.62~# | 13.63±5.20 |
| ETP-MP (nMxmin) | 1352±342.8 | 1209±508.6 | 1360±364.3 |
| PEAK-MP (nM) | 312.3±92.6 | 245.9±111.8~# | 291.3±83.2 |
| LT-PRP (min) | 6.49±2.29~ | 6.71±2.9~ | 5.17±1.46 |
| ETP-PRP (nMxmin) | 1155±404.7~ | 1033±443.0~ | 1359±419.0 |
| PEAK-PRP (nM) | 96.9±56.1~ | 96.6±66.7~ | 149.2±66.1 |

TABLE 2- Coagulation in patients with ITP. ROTEM parameters (CT, MCF, ALPHA and Ly60) and thrombin generation test (CAT) parameters (LT, ETP and peak) are shown in patients with ITP without and with associated autoimmune disorders (autoI) and in healthy controls. CAT was triggered with different reagents as mentioned in text. One-way ANOVA and Dunn's multiple comparison test were performed and $P < 0.05$ was considered significant.~ denotes significant differences with control group, and # between patients with ITP without and with other associated autoimmune diseases.

**Figure 1**

https://doi.org/10.1182/blood-2023-188452