Increased glyocalicin index and normal thrombopoietin levels in patients with idiopathic thrombocytopenic purpura with a decreased rate of platelet production

Platelet kinetic studies in idiopathic thrombocytopenic purpura (ITP) have shown that in a subgroup of patients a shortened mean platelet life (MPL) is associated with a decreased platelet production rate (PPR). Other methods of studying certain aspects of thrombopoiesis are the plasma concentrations of thrombopoietin and glyocalicin.

Clinical studies have shown elevated plasma levels of thrombopoietin in conditions with diminished megakaryocyte production. Glyocalicin is the soluble, external part of membrane glycoprotein Ibα (GPIbα). The glyocalicin-index, normalized for individual platelet count, has been introduced as a parameter of platelet turnover. We investigated thrombopoietin and glyocalicin levels in ITP patients and correlated them to the platelet kinetic parameters MPL and PPR. Platelet kinetic studies. In order to study platelet kinetics, autologous platelets were labeled with Indium-111 tropolonate according to the recommendations of the International Committee for Standardization in Hematology. The platelet production rate (PPR) is defined as the number of platelets entering the circulation to maintain the platelet count. The normal values of PPR is 223×10³/day (158–268) and the normal mean platelet life (MPL) is 9.2±1.4 days (8.9–9.4).

Plasma thrombopoietin concentrations were determined with an enzyme-linked immunosorbent assay (Quantikine, R&D systems, Minneapolis, USA). The normal value in this assay is 114 pg/mL (93-146). Plasma glyocalicin concentrations were measured by enzymatic immunoassay (Takara Shuzo Co, Ltd). The glyocalicin index is derived from the glyocalicin value (mg/mL)×250×10³/L divided by the individual platelet count. The normal value is 0.7 (0.6-0.9).

Table 1. Characteristics of patients.

<table>
<thead>
<tr>
<th></th>
<th>Production decreased</th>
<th>Production normal or increased</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n</td>
<td>9</td>
<td>26</td>
<td>0.9</td>
</tr>
<tr>
<td>Female</td>
<td>4</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>62 (30-68)</td>
<td>44 (32-67)</td>
<td>0.9</td>
</tr>
<tr>
<td>Platelet count at diagnosis,×10⁹/L</td>
<td>22 (13-46)</td>
<td>63 (43-89)</td>
<td>0.02</td>
</tr>
<tr>
<td>Mean platelet life, days</td>
<td>2.6 (1.4-3.7)</td>
<td>1.9 (1.1-3)</td>
<td>0.5</td>
</tr>
<tr>
<td>Platelet production rate, 10⁹/d</td>
<td>100 (88-145)</td>
<td>255 (188-325)</td>
<td>0.004</td>
</tr>
<tr>
<td>Thrombopoietin, pg/mL</td>
<td>109 (71-172)</td>
<td>111 (64-171)</td>
<td>0.8</td>
</tr>
<tr>
<td>Glyocalicin-index</td>
<td>12 (7-25)</td>
<td>5 (3-10)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Results are expressed as median (25%;75% percentile).

Figure 1. Correlation of glyocalicin index with platelet production rates.
10) among patients with a MPL >2 days (p<0.3). Most studies point to elevated thrombopoietin levels and low levels of glycocalcin in the case of a hypomegakaryocytic thrombocytopenia. However, in our study a reduced PPR was not associated with elevated thrombopoietin levels, but rather with a high glycocalcin-index. Comparable results were recently obtained in myelodysplastic patients. These data suggest that the reduced PPR is not due to a decline in the mass of Mpl-bearing cells in the bone marrow, but indicate an increased release of GP-Ibα complex in the circulation. This might be a consequence of shedding of the receptor complex from destroyed megakaryocytes and/or platelets in the bone marrow. This is also in concordance with the lack of significant correlation observed between the glycocalcin index and MPL, suggesting that the platelet antibody not only affects platelets but also megakaryocytes.

The finding of a lower PPR in patients with more pronounced thrombocytopenia suggests more prominent intramedullary destruction in more severe ITP. In conclusion, the present study indicates that (i) that thrombopoietin levels and the glycocalcin index are related to the dynamics of megakaryocyte and platelet kinetics in bone marrow and peripheral blood; (ii) in ITP patients with a decreased PPR, increased platelet and/or megakaryocyte destruction might occur in the bone marrow, as recently demonstrated by ultrastructural studies. Further research is needed to evaluate the usefulness of determining the glycocalcin index in ITP in clinical practice.

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Key words: glycocalcin, ITP, platelet production.

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References


Thrombosis

Risk of thromboembolism in patients with idiopathic autoimmune hemolytic disease and antiphospholipid antibodies: results from a prospective, case-control study

During a period of 4 years, 21 consecutive patients with newly diagnosed idiopathic autoimmune hemolytic disease (IAHD) and 42 healthy, sex- and age-matched subjects, were tested for the presence of antiphospholipid antibodies (APA). At diagnosis, APA were detected in 10/21 (47.6%) patients and in 2/42 (4.76%) controls (p<0.01). No thromboembolic events were registered during the follow-up period.


From January 1996 to January 2000, 47 patients aged > 20 years were diagnosed with autoimmune hemolytic disease (AHD) at the Hematology Department of the University “La Sapienza” of Rome. Of these 47 consecutive patients, 26 had secondary AHD (SAHD) and 21 had idiopathic AHD (IAHD). The main characteristics of the IAHD patients at diagnosis are reported in Table 1. All these patients were tested for antiphospholipid antibodies (LP anticoagulant, anticardiolipin and anti–b2-glycoprotein I antibodies) at diagnosis, after 8 to 10 weeks and then every six months or when clinically required. We did not test the anti-phospho-ethanolamine antibodies usually associated with IAHD. The results were then compared to those obtained in 42 healthy, sex- and age-matched subjects who tested negative to a panel of several auto-antibodies. Controls were tested at the entry into the study and when APA-positive, after 8-10 weeks for confirmation. LP anticoagulant (LAC) was detected according to the criteria indicated by the ISHT, utilizing two procedures: the kaolin clotting time (KCT) and the diluted Russel’s viper venom time (DRVVT). Tested plasmas were considered LAC positive only if at least one of the two procedures was diagnostic for LAC. Anticardiolipin antibodies (ACA) of Ig-G type (ACA-IgG) and anti-b2-glycoprotein I (anti-b2 GPL) antibodies were measured with standardized ELISA assays. The differences between the variables, were calculated by the chi² test, using a 2×2 table. Differences were considered statistically significant when p<0.05 (two tailed).

Overall, at diagnosis, 10/21 (47.6%) IAHD patients and