to the hemostatic efficacy of DDAVP in such patients. but significant increase in FXI activity linked to the marked increase in FVIII:C, the slight though the observed APTT normalization is probably to predict hemorrhagic complications after surgery in patients with mild disease.

DDAVP therapy was well tolerated and no hemorrhagic complications occurred during or after surgery.

FXI deficiency is a rare inherited coagulation disorder characterized by rarity of spontaneous bleeding but the risk of severe hemorrhagic complications after trauma or surgery. There is often little direct correlation between the tendency to bleed and the severity of the disease itself, so it is extremely difficult to predict hemorrhagic complications after surgery in patients with mild disease.

Currently available therapeutic products for the treatment of bleeding in FXI deficient patients include fresh frozen plasma and virus-inactivated FXI concentrates: the former may carry blood-borne viruses, the latter, although the first choice treatment in patients with severe FXI deficiency, should be used cautiously because of its thrombotic risk.

Recent reports indicate that DDAVP has been used successfully to prevent surgical bleeding in FXI defective patients. Our case reports confirm these findings: we first tested and then utilized subcutaneous desmopressin in symptomatic heterozygous FXI deficient patients undergoing surgery. No hemorrhagic complications occurred peri-operatively.

It remains to be clarified how DDAVP acts in such patients: the administration of DDAVP causes a slight increase in FXI activity and a marked increase in FXI:C are rather unlikely as Castaman et al. have previously demonstrated parallel degrees of increase in both FXI:C and FXI:Ag after administration of DDAVP.

However, although the mechanism by which DDAVP increases FXI levels is still not clear, our data suggest that this drug is effective in preventing surgical bleeding in patients with mild factor XI deficiency.

References


Comparison between radial immunodiffusion and flow cytometry techniques for detecting antplatelet antibodies

The aim of our work was to compare radial immunodiffusion (RI) (in use for years) versus flow cytometry (FC) (a new technique). The discrepancies of the results in our patient population indicate that both techniques are valuable tools to understand the pathogenesis of thrombocytopenia.

Sir,

To evaluate the clinical use of RI and FC for detecting antplatelet antibodies, we analyzed platelet samples from 39 patients. The samples were grouped according to the etiology of the thrombocytopenia into: group A (n=12): immune thrombocytopenic purpura (ITP) (Table 1), group B (n=19): conditions associated to bone marrow failure or malignancy (Table 2) and group C (n=8): unexplained mild thrombocytopenia.

Surface platelet associated IgG (PAIgG) was assayed by FC using the procedure described by Lin et al. and total (PAIgG) by RI using the procedure described by M orse et al. We observed significant positive correlations between both methods when all 39 cases were examined (r=0.44, p=0.006). The main contribution to this significant positive correlation was given by group A results (r=0.8, p=0.0018).
Table 1. Results of platelet antibody tests in group A.

<table>
<thead>
<tr>
<th>PT</th>
<th>RI</th>
<th>FC</th>
<th>Clinical diagnoses (comments)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>44</td>
<td>ITP (C-I remission, normal platelet count)</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>18</td>
<td>ITP (C-I remission, normal platelet count)</td>
</tr>
<tr>
<td>3</td>
<td>2.5</td>
<td>19</td>
<td>ITP (C-I remission, normal platelet count)</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>34</td>
<td>ITP (past history of ITP) pregnancy</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>24</td>
<td>ITP (past history of ITP)</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>26</td>
<td>ITP (past history of ITP) pregnancy</td>
</tr>
<tr>
<td>7</td>
<td>9</td>
<td>47</td>
<td>ITP (taking corticosteroids, low platelet count)</td>
</tr>
<tr>
<td>8</td>
<td>9</td>
<td>67</td>
<td>ITP (taking corticosteroids, low platelet count)</td>
</tr>
<tr>
<td>9</td>
<td>15</td>
<td>32</td>
<td>ITP (taking corticosteroids, low platelet count)</td>
</tr>
<tr>
<td>10</td>
<td>9</td>
<td>49</td>
<td>ITP (antiphospholipid syndrome, low platelet count)</td>
</tr>
<tr>
<td>11</td>
<td>8</td>
<td>50</td>
<td>ITP (taking corticosteroids, low platelet count)</td>
</tr>
<tr>
<td>12</td>
<td>38</td>
<td>96</td>
<td>ITP (taking corticosteroids, low platelet count, autoimmune thyroiditis)</td>
</tr>
</tbody>
</table>

RI is expressed as median of arbitrary fluorescent intensity units (FIU). C-I: corticosteroid-induced.
FC is measured as median of arbitrary fluorescent intensity units (FIU). The normal surface PAIgG level was 33 ± 22 FIU. The normal total IgG value was below 7 fg/plt using RI (n=20).

FC is measured as median of arbitrary fluorescent intensity units (FIU). The normal surface PAIgG level was 33 ± 22 FIU. The normal total IgG value was below 7 fg/plt using RI (n=20).

In group A, although no patient had a recent diagnosis of ITP, the low platelet counts suggested an active disease. RI gave more abnormal results (6 of 12 patients) than FC (2 of 12 patients); the discrepancy between the methods is attributed to a high platelet turnover, yielding younger platelets with more IgG due to higher content of α-granules. Among these six patients we also found two patients with abnormal FC. This indicates the specificity of the FC method. Corticosteroid-induced remission or past history of ITP explains the normal results obtained by both methods in this group.

Three patients in group B gave abnormal results by both RI and FC. One patient had chronic lymphoid leukemia and a clinical picture of ITP. Another had paroxysmal nocturnal hemoglobinuria with severe thrombocytopenia; platelet kinetic studies showed decreased platelet production and, in spite of the normal platelet survival during treatment with corticosteroids and cyclosporin, we cannot exclude ITP. The patient probably had a combined mechanism explaining her thrombocytopenia. The third patient suffered from hepatitis of unknown serology.

The abnormal RI results with normal FC found in group B could be explained by an increased plasma IgG concentration causing elevated platelet α-granule IgG in liver disease. The clinical and laboratory findings of our HIV patients were not consistent with ITP implying that RI abnormalities are unspecific findings. The FC method proved specific for detecting platelet immune destruction.

All group C patients gave normal results using both methods (data not shown).

RI proved to be as good a marker for the intensity of thrombopoiesis as the reticulated platelet count. This last method also detects the dense granular pool of nucleotides, which appeared to cause a substantial proportion of non-specific labeling. Noris et al. concluded that there was no direct relation between platelet age and thioflavin orange fluorescence (TO) of platelets and, that the greater TO is largely dependent on the increased platelet volume. RI is also useful as a marker for thrombopoiesis, and not only for immune platelet destruction as is the case with FC. Moreover, RI can discriminate between the active and remission phases of ITP.

Cristina E. Farías,* Ana C. Kempfer,* Analia Sánchez Luceros,* Marila R. Silaf,º Gonzalo A. Carballo,º María A. Lazariº

*National Research Council (CONICET); ºDepartment of Hemostasis and Thrombosis, Hematologic Research Institute of the National Academy of Medicine, Buenos Aires, Argentina

Key words
Radial immunodiffusion, flow cytometry, PAIgG.

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Correspondence
Cristina E. Farías, M.Sc., Departamento de Hemostasia y Trombosis, Instituto de Investigaciones Hematológicas, Academia Nacional de Medicina, Pacheco de Melo 3081, 1425 Buenos Aires, Argentina. Phone: international +54-11-4805 5759 – Fax: international +54-11-4805 0712 – E-mail: farias@conmed.com.ar

References


G20210A homozygosity in antiphospholipid syndrome secondary to systemic lupus erythematosus

We report the first case of systemic lupus erythematosus (SLE)-associated antiphospholipid syndrome in a young female homozygous for the G20210A allele in the prothrombin gene who developed an extensive venous thrombosis while taking oral contraceptives.

Sir,

The risk of deep venous thrombosis (DVT) is increased by conditions that cause hypercoagulability or venous stasis.1 A variant of prothrombin (G20210A) represents the second most common genetic risk factor in Caucasians, after factor V Leiden.2,3 The mechanism of thrombosis is probably related to the high amounts of thrombin generated.2

We report a case of a 28-year-old woman who developed an extensive DVT after having taken oral contraceptives for one year. Venous ultrasonography demonstrated a femoral-iliac thrombosis with proximal extension to the common iliac vein. Past history was positive for oral ulcers and Raynaud’s phenomenon, since she was a teenager. She reported photosensitivity lasting years, with an important episode on the scalp some months earlier: scarring lesions with atrophy and alopecia were still evident. Platelet count, erythrocyte sedimentation rate and immunoglobulin levels were moderately increased and white cell count and fibrinogen were normal. The partial thromboplastin and prothrombin time, antithrombin III and fibrinogen were normal. The patient was treated with continuous intravenous non-fractionated heparin infusions followed by oral warfarin for 7 months (INR = 3.0). During the follow-up, antithrombin III digestion. The patient was a G20210A homozygote. Family members were asymptomatic and none of them had any events, despite I-2 having had 5 pregnancies, a condition known to favor thrombosis. Neither has II-2, a G20210A homozygote, had any events, but this situation has never been exposed to risk situations.

In conclusion, our study suggests that the thrombotic risk in G20210A variant is mild and requires additional factors to become manifest.

Piera Sivera,° Sandra Bosio, Maria Tiziana Bertero,* Monica Demoaestri,* Umberto Mazza, Clara Camassella

Dipartimento di Scienze Cliniche e Biologiche, Azienda Ospedaliera San Luigi; *Cattedra di Immunologia Clinica, Ospedale Mauriziano, Università di Torino, Italy

°Present address: Ospedale Mauriziano, Turin, Italy

Key words
Thrombophilia, prothrombin variant, antiphospholipid syndrome, SLE

Figure 1. Pedigree of the family studied. The age of each subject is shown in brackets. The results of the mutations studied and their inheritance are indicated.

with a 2.8 fold independent risk.2 Homozygotes are rare; although they present the highest prothrombin activity values2 data on their risk of thrombosis are controversial. This is not unexpected considering that a thrombotic event is the manifestation of a multifactorial disease.1 The patient described here had two acquired factors associated with a genotype at risk: APS and oral contraceptives. The relative risk in women with factor V Leiden using contraceptives is 34.7, that of carriers of prothrombin variant is unknown.1

APS is characterized by venous and arterial thrombosis and often by recurrent fetal loss in the presence of lupus anticoagulant, antiphospholipid antibodies or both. It has been proposed that anti-β2GPI, the presence of which correlates strongly with thrombosis, should be included in the APS biological score.9 In APS associated with SLE the risk of DVT is enhanced by the possible vasculitis process inherent to disease activity. The frequency of factor II mutation is not expected to be increased in patients with APS but, in analogy to that which occurs for factor V Leiden,10 when present may represent an independent risk factor for thrombosis.

The other members of the family had no history of DVT. The G20210A heterozygous parents are free of events, despite I-2 having had 5 pregnancies, a condition known to favor thrombosis. Neither has II-2, a G20210A homozygote, had any events, but this subject has never been exposed to risk situations.

In conclusion, our study suggests that the thrombotic risk in G20210A variant is mild and requires additional factors to become manifest.