Clinical Correlates in Patients with Elevated Platelet-Associated Immunoglobulins*†

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ABSTRACT

Studies are reported pertaining to platelet-associated IgG (PAIgG) and IgM (PAIgM) in patients with thrombocytopenias considered possibly immune-mediated on clinical grounds. Approximately 14 percent of all patients with these disorders had elevated PAIgM but normal levels of PAIgG. Of patients with classic autoimmune thrombocytopenia (ITP), there was a trend toward more frequently normal levels of PAIgG in chronic ITP compared with patients with acute ITP, but this was not statistically significant. Patients with acute ITP had higher levels of PAIgG and PAIgM in general than those with chronic ITP. Patterns of PAIgG and/or PAIgM elevation were not significantly different when chronic and acute ITP were compared, nor when childhood ITP was compared with adult ITP. Patients with immune thrombocytopenias owing to malignant disorders were likely to have lower levels of PAIgG compared with those with classic ITP. Treated patients with immune thrombocytopenias showed a trend toward earlier response to therapy if they had only elevated PAIgG as opposed to elevated PAIgM alone or elevated PAIgM and PAIgG (p = 0.17). There appear to be great overlaps in the patterns and quantities of PAIgG and PAIgM in patients with immune-mediated thrombocytopenias in widely varied clinical settings. This suggests some underlying common pathophysiologic mechanisms for thrombocytopenia in these clinically diverse disorders. It is believed that the data are most consistent with the hypothesis that thrombocytopenia in patients with elevated PAIgG and/or PAIgM is most probably of immune origin even in such diverse disorders as systemic lupus erythematosus, cirrhosis of the liver, lymphoma, leukemia, cancer, or septic conditions, as well as in ITP.

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Introduction

Over the past decade, sensitive and relatively simple laboratory tests have been developed for measuring platelet-associated immunoglobulins and com-
plement components that mediate immune destruction of these cells.\textsuperscript{6,9} Many questions remain concerning the interpretation of these tests and their role in explaining the pathophysiology of thrombocytopenia in a wide variety of clinical circumstances.\textsuperscript{10} However, there is little doubt that in most patients with idiopathic thrombocytopenic purpura (ITP) the mechanism of platelet destruction is largely immune, and that in 80 to 90 percent of these patients elevations of cell surface IgG can be demonstrated.\textsuperscript{6,9} Nonetheless, autoimmune thrombocytopenia has remained a clinically based diagnosis in which the role of platelet antibody tests is controversial. It is believed that the presence of increased amounts of platelet-surface immunoglobulins and/or complement can be of potential clinical significance regardless of the pathophysiologic mechanisms involved. However, the amount of platelet-associated immune components is only one of several factors which determine the fate of these peripheral blood cells in immune-mediated disease. One critical factor is the avidity with which the monocyte-macrophage network (reticuloendothelial system) recognizes and destroys cells with increased amounts of surface immunoglobulins.\textsuperscript{8} Because it is not certain whether the finding of elevated platelet-associated immunoglobulins in thrombocytopenic patients is a specific marker for immune destruction or can be non-specific, it would be of interest to compare the levels and patterns of surface IgG and IgM in patients with diverse disorders complicated by thrombocytopenia.

To assist in the evaluation of thrombocytopenic patients, our laboratory performs assays of platelet surface IgG (PAIgG) and IgM (PAIgM). A retrospective clinical review of patients is reported and is intended to address a number of questions. It would be of interest to know whether differences in the pattern of PAIgG and PAIgM correlated with response to treatment in patients with immune thrombocytopenia. Since many patients with thrombocytopenias of questionable immune origin also have increased PAIgG and PAIgM, patients with "classical ITP" were evaluated to see whether they differed from other thrombocytopenic patients in the quantitative or qualitative pattern of IgG and IgM on their platelets. Because adult and childhood ITP differ significantly in their clinical course, with children having a lower incidence of chronic ITP, the pattern of elevated PAIgG and PAIgM in these two groups was examined. It is hoped these data might shed light on possible differences in pathophysiology, and also provide information of potential prognostic utility, as has been the case in the area of red cell immunology.

**Methods of Analysis**

**Patients**

This study was a retrospective medical record review of patients who had samples evaluated for PAIgG and PAIgM during the two year period 1984 to 1985. Patient samples were referred from approximately 10 different hematologists practicing at five different hospitals in our area. Obviously, this population of patients is highly biased towards patients in which the practitioner felt there was a high \textit{a priori} likelihood of an immune mechanism. Information about patient age, sex, clinical diagnosis, date of diagnosis, duration of illness (days to platelet counts greater than 50,000 and 100,000), bone marrow exam, complete blood counts, tests for red cell or other autoimmunity or immunological parameters, treatment employed, duration of treatment, and serial platelet counts after diagnosis were collected. Many patients had incomplete information or followup.
Any history of malignancy, autoimmune disease, coagulopathy, recent viral illness, blood product transfusion, and recent drug use were also noted. Many patients, especially children, received no specific therapy for their thrombocytopenia. Tests for circulating immune complexes were only rarely performed; PAIgG and PAIgM as determined by our laboratory were recorded. Unless otherwise noted, all patients had platelet counts <150,000 per μl at the time of testing, although several were rapidly recovering and had normal counts within a few days after sampling.

Patients were classified in the “classic ITP” group if they had an initial platelet count of <100,000 per μl, normal physical examination except for signs related to thrombocytopenia, normal laboratory findings, and the clinical picture was not complicated by recent drug use, autoimmune disease, concurrent malignancy, sepsis, pregnancy or trauma. All patients in the “classic ITP” group met the criteria proposed by Kelton for “probable ITP,” with the vast majority having bone marrow examinations. Most of these patients also met the criteria for “definite ITP” once the results of therapy or clinical course were evaluated. Only eight of 110 patients, all with severe hemorrhage, received platelet transfusions. None of the patients classified as having classic ITP were transfused.

Other patients with elevated PAIgG and/or PAIgM were classified according to their primary diagnosis, such as autoimmune disease, malignancy, infection, etc. These groups and those with classic ITP were compared by their pattern of test results in each of four categories: (1) Elevated PAIgG and normal PAIgM; (2) Normal PAIgG and elevated PAIgM; (3) Both elevated; and (4) Both normal.

Patients in each of these categories were then subdivided into adults versus children (12 years old or less at date of diagnosis), acute versus chronic (>six month duration of platelet count <100.00 per μl) “classic ITP” versus other diagnoses (sepsis, malignancy, pregnancy, other autoimmune, drug-related, or trauma), and time from diagnosis to remission (defined as platelet count >100,000 per μl), and finally treatment versus no treatment.

In order to see if the level of elevated PAIgG was of prognostic significance or differed in the various groups, patients with elevated PAIgG were further placed in one of four categories, (10.1 to 20.0; 20.1 to 50.0; 50.1 to 100.0, or 100.1+) dependent on level of PAIgG (normal is <10 fg per platelet in soluble IgG equivalents). A similar analysis was performed for PAIgM levels.

**Statistical Analysis**

All analyses were carried out using a microcomputer* and software.† Comparison of frequencies of events was performed using Chi-square contingency tables, with individual frequencies being further compared to each other employing Fisher’s exact test. It was recognized that the performance of these multiple comparisons could lead to statistically significant findings merely on a probabilistic basis (i.e., one in 20 comparisons). Thus, results of statistical significance derived from multiple 2 by 2 contingency tables and Fisher’s exact test should be viewed with caution. An exploratory study such as this requires something of a “fishing expedition” statistically and is intended to point toward further useful comparisons in larger and better controlled studies.

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Laboratory Techniques

INTRODUCTION AND PRINCIPLES

The assay for PAIgG has been previously described.1 Soluble IgG standards or PAIgG compete with solid-phase IgG for binding to an alkaline phosphatase-linked anti-IgG antoglobulin reagent. The principle of the assay is that increased concentrations of soluble IgG or PAIgG will compete for anti-IgG and reduce anti-IgG binding to the solid-phase IgG. This assay can reproducibly detect changes of about 50 molecules per platelet of IgG. Results are reported in "fg per platelet in soluble IgG equivalents" (normal = 0 to 10). Whole platelets are employed so that measurements reflect only surface PAIgG and PAIgM. The assay for PAIgM is essentially similar except that the assay does not use soluble IgM as a standard curve.

PROCEDURE FOR PAIgM ASSAY, INCLUDING REAGENTS, SOLUTIONS AND APPARATUS

Immulon II microtiter plates‡ were washed three times using distilled water. A murine monoclonal antibody that reacts with an undefined antigen present on all human platelets (UR 1-6.6 produced by the Laboratory Medicine Division Hybridoma Facility) was added to each well in the amount of 100 μl at a concentration of approximately 10 μg per ml in coating buffer (1.59 g per L Na₂CO₃, 2.93 g per L NaHCO₃, pH 9.6). The plate was then incubated for two hours at 37°C, then overnight at 4°C. The antibody was used as crude mouse ascitic fluid. Platelets were first sedimented and resuspended in PBS-EDTA (0.01 M Na₂HPO₄/NaH₂PO₄, 0.15 NaCl, 3 g per L Na₂EDTA, pH 7.0) prior to adhering to the plate. After resuspension in PBS-EDTA at a count of 370,000 per μl, a 100 μL aliquot of platelets was added to each of two wells for each sample to be tested. After platelets have been added, the microtiter plate was centrifuged at 1800 RPM in a GLC-4 centrifuge for 10 minutes to sediment the platelets onto the monoclonal antibody coated surface. The plate was then incubated at room temperature for 50 minutes. It was then washed semi-automatically, without need for centrifugation, three times utilizing PBS (pH 7.2) and a Mini-Wash.‡ One hundred μl of PBS-1 percent bovine serum albumin§ were added to each well to reduce non-specific adsorption of enzyme-antiglobulin conjugate during a subsequent step. This required a 30 minute room temperature incubation, and was followed by two further washes with PBS-1 percent BSA.

One hundred μl of alkaline phosphatase linked to affinity-purified antihuman IgM (Sigma) were added at a dilution previously optimized to the lot in question. The conjugates were usually employed at 1:800 or 1:1000 dilutions. Two wells received no conjugate to serve as negative controls for non-specific binding by the anti-IgG-enzyme conjugate. A further incubation at room temperature for 60 minutes was performed, followed by three PBS-1 percent BSA washes. Substrate, one mg per ml paranitrophenyl phosphate∥ in 0.05 M Na₂CO₃, 0.001 M MgCl₂, pH 9.8 was added at 100 μl per well. Color development was measured spectrophotometrically with a MR600 microtiter plate reader∥ coupled to an Apple IIe microcomputer for which kinetic-ELISA programs have been written.¶ At this stage,

‡ Dynatech, Chantilly, VA.
§ BSA, BCA, West Chester, PA.
∥ Sigma.
¶ Dr. Jonathan Cowles, Pittsford, NY 14534.
ΔA405nm per minute × 1000 was computed by least squares linear regression of absorbance readings taken at 20, 25, 30, and 35 minutes after substrate addition. The correlation coefficient for the linearity of the ΔA405nm versus time was usually 0.99, thus confirming the measurement of first-order enzyme kinetics, which has been shown previously to correlate linearly with the amount of immunoglobulin and anti-immunoglobulin bound. The assay was linear throughout the range used. The amount of IgM bound to the solid-phase platelet layer was reported as the mean of the duplicate determinations of ΔA405nm per minute × 1000. The duplicates were usually within 10 to 20 percent. Because the kinetic measurement of enzyme activity is made at ambient temperature, controls were run to normalize the results from day to day.

**Normal Range**

The IgM bound to platelets of non-thrombocytopenic hospitalized patients yielded a normal range of 0–1.36 for ΔA405nM per minute × 1000 (mean ± 2 S.D., n = 268).

**Discussion, Sources of Error and Interpretation**

As in previous reports, clinical review suggested that 80 to 90 percent of patients with classic ITP have elevated levels of PAIgG in our assay. Likewise, normal levels of PAIgG in our experience with over 200 patients usually suggested a non-immune etiology for the thrombocytopenia. Artifactual causes of falsely normal PAIgG in thrombocytopenic patients known to have ITP include the early beneficial effects of therapy, the onset of clinical remission, and recent platelet transfusions. In our experience, falsely elevated levels in thrombocytopenia were restricted to conditions of rapid platelet destruction and the elevations were modest (e.g., 10 to 20 fg per platelet of IgG). About five to 10 percent of non-thrombocytopenic hospitalized patients also had elevated levels, the vast majority in the lower end of this range. This latter finding was partially due to intentional definition of the normal range as excluding the upper 2.5 percent of normals in the Gaussian distribution, and partially due to the slightly skewed distribution of PAIgG and PAIgM that was typical of most biological measurements.

**Results**

Over the last two years 176 samples from patients with thrombocytopenia or a history of a thrombocytopenic illness were tested by the present authors. Most of these patients were suspected of having ITP or immune thrombocytopenia owing to their underlying primary disease, such as lupus or lymphoma. Some of these patients were known to be in remission from ITP, and some were known to have non-immune thrombocytopenia. Of these tests, 49 of 176 showed normal levels of both PAIgG and PAIgM. Of those with elevated platelet surface immunoglobulins, 18 of 127 (14 percent) had elevated PAIgM only, 44 of 127 (35 percent) had elevated PAIgG only, and 65 of 127 (51 percent) had elevated levels of both immunoglobulins. Based upon availability of medical records and likelihood of adequate time for followup, patients were chosen for investigation whose samples were received prior to mid-1986 and who had been seen in our local area. A total of 110 patients were investigated; of these, 15 were excluded from the analysis because the initial platelet counts were found to be spurious or because the thrombocytopenia was mild and platelet counts did not drop below 100,000.

Of the 95 patients remaining, 48 had probable "classic ITP." Of the 47 thrombocytopenic patients without classic ITP
CLINICAL ASPECTS OF ELEVATED PAIgG/IgM

whose platelets were tested for PAIgG and PAIgM, eight had a solid tumor, six were pregnant but not thought to have classic ITP, six had systemic lupus erythematosus, six were septic, six had leukemia, five had lymphoma, three had possible drug induced thrombocytopenia, three had myelodysplastic syndromes, and one each had aplastic anemia, sickle cell crisis, cirrhosis of the liver, or post-surgical thrombocytopenia.

Of the 48 patients with classic ITP, eight had insufficient follow up (< 6 months) to classify as acute or chronic, and two others were not tested for levels of PAIgM owing to insufficient blood sample. Of the 10 patients who had elevated values for neither PAIgG or PAIgM, seven were entering remission at the time the test was run, and three were chronic ITP patients who continued to have a low platelet count. The 31 patients with active disease could be grouped as shown in table I. None of the 14 acute ITP patients had both PAIgG and PAIgM's that were normal, as compared with three of 17 of those who had chronic ITP (p = 0.15). There were no differences in pattern of elevated PAIgG and/or PAIgM between those with acute or chronic ITP.

Because of the finding of normal values of PAIgM and PAIgG in a few patients with chronic ITP, the amount of PAIgG was examined in the 42 patients from both the “classic ITP” and “other” groups who had elevated levels of this immunoglobulin. These data are shown in table II. There was a significant trend toward higher levels of PAIgG in patients with acute immune thrombocytopenia as compared to chronic immune thrombocytopenia. Of 24 patients with elevated PAIgM whose thrombocytopenias could clearly be classified as acute or chronic, there was a significant trend toward higher levels of PAIgM in the chronic thrombocytopenias, although the numbers of patients is quite small. Of the nine patients with chronic immune thrombocytopenia, only two (22 percent) had modest elevations of PAIgM in the range of 1.37-2.00 (normal is ≤ 1.36), whereas seven (78 percent) had levels > 2.00 (p = 0.03). In contrast, amongst 15 patients with acute immune thrombocytopenia, six had modest elevations of PAIgM versus nine with levels >2.00 (p = 0.23).

The patterns of PAIgG and PAIgM are shown in the 36 patients with clinically active “classic ITP” according to age in table III. Not included in the table are an additional five patients who had no PAIgM measurements and an additional seven patients who were adults in recovery phase of acute ITP with normal PAIgG and PAIgM. None of the differences shown are statistically significant, perhaps owing to inadequate sample size. Two children were the only classic ITP patients with isolated elevations of IgM (two of 13) versus none of 23 adults with classic ITP with this pattern (p = 0.09).

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**Table I**

| Patterns of Platelet-Associated IgG and Platelet-Associated IgM in Acute or Chronic Classic Autoimmune Thrombocytopenia |
|---|---|---|
| Group | Acute | Chronic |
| Elevated PAIgG only | 7 (50%) | 6 (29%) |
| Elevated PAIgM only | 0 (0%) | 1 (5%) |
| Both elevated | 7 (50%) | 7 (33%) |
| Neither elevated* | 0 (0%) | 3 (33%) |
| Total | 14 (100%) | 17 (100%) |

*Seven patients, four with chronic autoimmune thrombocytopenia and three with acute autoimmune thrombocytopenia were in recovery phase and had normal PAIgG and PAIgM at the time of testing and are not included in the table.

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**Table II**

| Levels of Platelet-Associated IgG in Patients with Chronic or Acute Autoimmune Thrombocytopenia |
|---|---|---|---|
| Group | 10.1 - 20 fg | 20.1 - 100 fg | p |
| Chronic | 9 of 19 (47%) | 10 of 19 (53%) | 0.5 |
| Acute | 8 of 23 (35%) | 15 of 23 (65%) | 0.04 |
| p | 0.30 | 0.30 | |

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Of the 95 patients with classic ITP or other types of thrombocytopenia, 88 had levels of both PAIgG and PAIgM measured. To determine if the patterns of PAIgG and PAIgM elevations varied between those with "classic ITP" as opposed to other potentially immune-mediated thrombocytopenias (malignancy, other autoimmune disease, pregnancy, sepsis, drugs, etc.), the patients were grouped as shown in table IV. No significant difference is seen between these two groups in PAIgG/PAIgM patterns. Amongst patients with elevation of PAIgG and/or PAIgM there was a trend toward more patients with increased PAIgM in patients in the “other” group (24 of 34, 71 percent) as compared with those with classic ITP (18 of 33, 55 percent) (p = 0.13).

To assess whether or not the quantity of PAIgG correlated with diagnosis amongst those with elevated PAIgG, those with classic ITP and those with other diagnoses were divided into groups of PAIgG = 10 to 20 and PAIgG = >20. "Other" patients with autoimmune disease, sepsis, drugs, etc. as the probable cause of their autoimmune thrombocytopenia had a similar distribution to patients with classic ITP. However, patients with malignancies (solid tumors, lymphoma, leukemia) tended to have lower levels of PAIgG compared with patients with classic ITP (table V). Of classic ITP patients with elevated PAIgG, 26 of 36 (72 percent) had elevations greater than twice the upper limit of normal, compared with five of 14 patients (36 percent) with malignancies (p = 0.02). Similarly, classic ITP patients with elevated PAIgM were somewhat more likely (70 percent) to have higher levels of PAIgM (>2.00) than patients with malignancy (50 percent) although this difference was not statistically significant (p = 0.28).

To examine whether or not patterns of PAIgG and PAIgM correlated with response to treatment, patients were divided into treated and untreated groups and the number of patients noted whose platelet count had risen to >100,000 per μl within 21 days of treatment initiation, or within this time after initial diagnosis if no treatment was given. Results employing a platelet count of ≥50,000 per μl as the measure of response gave similar results. Most patients were treated with corticosteroids, but some received in addition, or alternatively, splenectomy, high dose intravenous IgG, or cytotoxic chemotherapy for their underlying disease. The results of this division of the data are shown in table VI. No statistically significant differences were found. The treated patients were no more likely to have platelet counts >100,000 per μl within three weeks (21 of 44, 48 percent) as compared with untreated patients (10 of 24, 42 percent). However, there is a trend for the patients with only

### Table III

Patterns of Platelet-Associated IgG and Platelet-Associated IgM by Patient Age in Classic Autoimmune Thrombocytopenia

<table>
<thead>
<tr>
<th>Group</th>
<th>Adults</th>
<th>Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated PAIgG only</td>
<td>9 (39%)</td>
<td>6 (46%)</td>
</tr>
<tr>
<td>Elevated PAIgM only</td>
<td>0 (0%)</td>
<td>2 (15%)</td>
</tr>
<tr>
<td>Both elevated</td>
<td>13 (57%)</td>
<td>3 (23%)</td>
</tr>
<tr>
<td>Neither elevated</td>
<td>1 (4%)</td>
<td>2 (15%)</td>
</tr>
<tr>
<td>Total</td>
<td>23 (100%)</td>
<td>13 (100%)</td>
</tr>
</tbody>
</table>

### Table IV

Patterns of Platelet-Associated IgG and Platelet Associated IgM According to Primary Diagnosis

<table>
<thead>
<tr>
<th>Group</th>
<th>Classic ITP</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated PAIgG only</td>
<td>15 (35%)</td>
<td>10 (22%)</td>
</tr>
<tr>
<td>Elevated PAIgM only</td>
<td>2 (5%)</td>
<td>5 (11%)</td>
</tr>
<tr>
<td>Both elevated</td>
<td>16 (37%)</td>
<td>19 (42%)</td>
</tr>
<tr>
<td>Neither elevated</td>
<td>10 (23%)</td>
<td>11 (24%)</td>
</tr>
<tr>
<td>Total</td>
<td>43 (100%)</td>
<td>45 (100%)</td>
</tr>
</tbody>
</table>

ITP = autoimmune thrombocytopenia
increased IgG on their platelets to respond to therapy (eight of 13, 62 percent) better than those with IgM, or IgM and IgG on their platelets (nine of 23, 39 percent) (p = 0.17).

**Discussion**

Our findings, limited by the retrospective method which was employed, revealed few statistically significant differences in patterns or quantitation of PAIgG and PAIgM in patients with widely differing clinical settings. This confirms the results in a much larger study by Helmerhorst and colleagues in which patients with primary immune thrombocytopenia ("classic ITP") differed little from those with secondary immune thrombocytopenias (e.g., cancer, lupus, etc.). Recently, Panzer and colleagues from Vienna reported virtually identical results—patients with ITP differ very little, if at all, from thrombocytopenic patients with malignancy, aplasia, infection, etc. in terms of the level or patterns of platelet-associated immunoproteins. McFarland and her colleagues have reported essentially similar findings. As reported by others, failing to test for PAIgM and/or platelet associated complement components will miss perhaps as many as 15 percent of patients with probable autoimmune phenomena involving platelets.

Some of these patients with elevations only of PAIgM undoubtedly have “classic ITP”. It is suggested that combined tests of PAIgG and PAIgM will yield evidence for increased immunoglobulins in perhaps 95 percent of patients with active ITP. The rest presumably represent instances of IgA sensitization only, or immune thrombocytopenia on the basis of increased removal of normal platelets by abnormal monocytic, lymphoid, or phagocytic effector cells.

No clearcut prognostic utility for these tests has emerged from our data or those of others. Some modest heterogeneity in the clinical course of patients with immune thrombocytopenias is suggested by the results of others and those herein reported. As noted by Helmerhorst and associates, there is a trend toward normal levels of PAIgG and PAIgM in those with chronic ITP (table I). Patients with acute ITP are significantly more likely to have higher levels of PAIgG and PAIgM in those with chronic ITP (table I). Patients with chronic ITP were significantly more likely to have higher levels of PAIgM, but the numbers of patients studied in this regard were small. There remained approximately five percent of our patients with probable immune thrombocytopenia whose PAIgG and PAIgM were normal.

Despite the well known clinical distinctions between ITP of childhood and adulthood, the patterns of PAIgG and PAIgM in these two groups were similar.
Likewise, patients with probable autoimmune thrombocytopenia owing to drugs, sepsis, malignancy, etc., did not differ in their pattern of PAIgG and IgM from those with classic ITP (table IV). Patients with malignancy as their underlying cause of autoimmune thrombocytopenia were slightly, but significantly more likely to have normal or lower levels of PAIgG and PAIgM than those with classic ITP, who tend to have greater amounts of immunoglobulin on their platelets (table V). However, there is a great overlap in these two groups of patients.

There was a trend toward more rapid response to treatment in patients with elevated PAIgG as their only abnormality (table VI). McFarland and associates reported that those patients with higher PAIgG levels were significantly more likely to achieve a corticosteroid-induced complete remission than those with lower levels. Court and colleagues recently reported that patients with treatment resistant immune thrombocytopenia were more likely to have normal or lower levels of PAIgG than those who responded to therapy.

Some have interpreted the observed elevations of PAIgG and PAIgM in thrombocytopenic patients with sepsis, malignancy, etc. as being non-specific as markers of immune destruction. It is our belief the opposite is possible. Many patients with thrombocytopenia and non-immune primary disorders such as infection, splenomegaly, cirrhosis, cancer, etc. may nonetheless have an immune etiology for their low platelet counts. The marked similarities between the clinically diverse groups reported in this communication could indicate that many thrombocytopenias, whether acute or chronic, adult or pediatric, classic ITP or associated with other clinical conditions, share an underlying pathophysiology.

Acknowledgments

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