To the Editor:

Chronic immune thrombocytopenic purpura (ITP) is an autoimmune disorder in which autoantibodies, most commonly against either the platelet glycoprotein (GP) IIb/IIIa and/or GP Ib/IX complex, result in severe thrombocytopenia. Lasting complete and partial remissions are obtained in about 75% of patients with corticosteroids or splenectomy; refractory patients are usually treated with a variety of agents, including gammaglobulin, vinca alkaloids, danazol, colchicine, cyclophosphamide, azathioprine, or staphylococcal immunoadsorption columns. In many patients, these measures are unsuccessful and these patients suffer the consequences of severe thrombocytopenia and chronic immunosuppressive therapy.

The nucleoside, 2-chlorodeoxyadenosine (2-CdA), is activated by deoxycytidine kinase. Once incorporated into the nuclear DNA, it is capable of inducing single- and double-stranded breaks in dividing and nondividing cells. Cells rich in deoxycytidine kinase, such as lymphocytes, are the most sensitive to this agent. Because 2-CdA is active against lymphoid cells and has been used successfully in the treatment of a variety of low-grade lymphoid malignancies, it was thought that it might affect the antiplatelet antibody-producing plasma cell population in patients with chronic refractory ITP. We report our results on the treatment of seven such patients.

The patients are summarized in Table 1. Seven female patients with a disease duration ranging from 36 to 276 months were treated with one to three cycles of 2-CdA. All patients had failed to respond to high-dose corticosteroids, splenectomy, vincristine, danazol, cyclophosphamide, and intravenous gammaglobulin (IVIgG) therapy. Five patients had also failed other forms of treatment: patient no. 1, azathioprine, vinblastine, and anti-D; patient no. 2, vinblastine and a-interferon; patient no. 4, azathioprine, a-interferon, methotrexate, and plasmapheresis; patient no. 5, colchicine; patient no. 7, a-interferon, plasmapheresis, and staph A immunoadsorption.

Each cycle of 2-CdA was administered by continuous infusion at a dose of 0.1 mg/kg/d for 7 days, except for patient no. 2, whose first cycle dose was 0.05 mg/kg/d. Baseline studies consisted of a complete blood count, bone marrow aspirate, and immunoglobulin levels. All patients had a response to treatment, with a median response time of 4 weeks. The patients were then followed up for a median of 12 months, and all patients remained in remission.

Table 1. Patient Summaries

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (y)</th>
<th>Sex</th>
<th>Duration (mo)</th>
<th>Prior Therapies</th>
<th>Cycles of 2-CdA</th>
<th>2-CdA Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITP-1</td>
<td>43/F</td>
<td>204</td>
<td>P, Sp, V, D, Cy, IgG, A, Vb, Anti-D</td>
<td>2</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>ITP-2</td>
<td>21/F</td>
<td>36</td>
<td>P, Sp, V, D, Cy, IgG</td>
<td>2</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>ITP-3</td>
<td>35/F</td>
<td>132</td>
<td>P, Sp, V, D, Cy, IgG</td>
<td>1</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>ITP-4</td>
<td>42/F</td>
<td>60</td>
<td>P, Sp, V, D, Cy, IgG, A, Int, MTX, PP</td>
<td>3</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>ITP-5</td>
<td>46/F</td>
<td>144</td>
<td>P, Sp, V, D, Cy, IgG, Co</td>
<td>2</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>ITP-6</td>
<td>39/F</td>
<td>276</td>
<td>P, Sp, V, D, Cy, IgG</td>
<td>2</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>ITP-7</td>
<td>49/F</td>
<td>244</td>
<td>P, Sp, V, D, Cy, IgG, Int, PP, Staph</td>
<td>2</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: P, prednisone; Sp, splenectomy; V, vincristine; D, danazol; Cy, cyclophosphamide; IgG, gammaglobulin; A, azathioprine; Vb, vinblastine; Int, a-interferon; MTX, methotrexate; PP, plasmapheresis; Co, colchicine; Staph, Staphylococcal immunoadsorption.
plete blood cell count, chemistry panel, antinuclear antibody, chest x-ray, and EKG. Serial blood counts and chemistry panels were obtained during and after therapy. All patients received two cycles of 2-CdA except patient no. 4, who received three cycles, and patient no. 3, who, after receiving one cycle, withdrew from therapy for insurance purposes. Because of the severity of thrombocytopenia, all patients were hospitalized for each 7-day infusion. During and between each cycle of therapy, patients were supported when necessary with high-dose corticosteroids, gamma globulin, or platelet transfusions.

Response criteria were: complete (platelet count >180,000/µL), partial (platelet count >50,000/µL), or no response (platelet count <50,000/µL).

No patient responded to 2-CdA. The average platelet count after therapy did not differ significantly from the baseline counts before therapy. The only patient showing any improvement over the long term was patient no. 4, who noted a prolongation of her response to IVIgG from 1 to 2 weeks to 2 to 3 months. Whether this was due to 2-CdA or to the use of chronic IVIgG is unknown.

About 75% of patients with chronic ITP respond to corticosteroids or splenectomy. Refractory patients may respond to second-line therapies but lasting remissions are seldom achieved. We have treated seven patients with chronic refractory ITP with 2-CdA. No patient responded to treatment, although one patient (patient no. 4) appeared to become more responsive to IVIgG. These negative results in chronic ITP are probably due to the resistance of mature plasma cells to 2-CdA and are compatible with the lack of response to 2-CdA in patients with multiple myeloma. We conclude that this agent is ineffective in the treatment of chronic refractory ITP.

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REFERENCES

2-Chlorodeoxyadenosine in the treatment of chronic refractory immune thrombocytopenic purpura [letter]

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