All patients received the first plasma exchange employing fresh frozen plasma, and CPP was used in the following procedures. PE was performed daily until normalization of the platelet count and serum LDH level.

Two patients (B.S. and P.M.L.) died 8 and 5 days, respectively, after beginning plasma exchange, and the addition of high-dose iv immunoglobulins in one case did not produce any effect. Clinical remission was reached in four patients. In one case, neurological disorders at onset such as amnesia and paresis improved after three PE procedures.

Normalization of platelet count was obtained after 7, 11, 13 and 17 plasma exchange procedures, respectively. Our experience confirms the data reported by Perotti et al. regarding hematological recovery, while the neurological disorders that appeared during the treatment in two patients did not seem to be influenced by the addition of CPP.

These observations seem to limit the efficacy of CPP as compared to fresh frozen plasma in the treatment of TTP.

Riccardo Centurioni
Cristina Rebi
Alessandro Cecchelli
Istituto di Clinica Medica Generale, Ematologia ed Immunologia Clinica, Università di Ancona and *Servizio di Immunoematologia e Trasfusione, Ancona, Italy.

References

Correspondence: Riccardo Centurioni, MD, Istituto di Clinica Medica, Ospedale di Torrette, 60020 Ancona, Italy.

Lymph node myeloid metaplasia associated with chronic neutrophilic leukemia

Sir,
chronic neutrophilic leukemia (CNL) is a rare disorder characterized by neutrophilia due to mature elements and organ infiltration, including both hepatosplenomegaly and lymph node infiltration. Around 78 cases have been reported up to now and no one else has described the presence of myeloid metaplasia in lymph nodes as we have in this study.

A 68-year-old man presented weight loss, enlarged lymph nodes, hepatosplenomegaly and ascites. WBC count was 156 × 10^9/L (84% neutrophils, 1% monocytes, 2% basophils, 3% bands, 2% atypical lymphocytes, 5% metamyelocytes, 5% myelocytes). Hemoglobin was 8.7 g/dL, platelets 68 × 10^9/L, uric acid was 15.8 mg/dL, alkaline phosphatase 2457 U/L, LDH 915 U/L, granulocytic alkaline phosphatase 300 U. Renal and liver function was normal. Paracentesis revealed ascitic liquid with 3.6 × 10^9/L cells (85% mature neutrophils). Bone marrow biopsy displayed increased cellularity and granulocytic hyperplasia compatible with CNL. Cytogenetic study was normal (46,XY). Molecular biology did not demonstrate a bcr-abl translocation. A lymph node biopsy showed massive substitution of the normal lymph node architecture by hematopoietic cells, including elements of all three series; within the granulocytic line numerous polymuclear cells were conspicuously intercalated among immature cells. Megakaryocytes were also frequent, and some of them presented phagocytic phenomena.

The patient was treated with hydroxyurea, which provided good WBC count control; however, two months later he developed hepatorenal failure and died on day +71 after diagnosis.

Myeloid metaplasia has not been previously described in CNL. Chronic neutrophilic leukemia was recently characterized as a distinct myeloproliferative disease with a specific molecular marker (bcr/abl with C3/A2 junction). Our finding of myeloid metaplasia is consistent with the myeloproliferative nature of CNL.

José A. Pérez-Simón
José M. Hernández-Rivas
Teresa Flores
Servicio de Hematología, Hospital Universitario de Salamanca, Paseo de San Vicente 58-182, Salamanca, Spain.

Correspondence: José A. Pérez-Simón, MD, Servicio de Hematología, Hospital Universitario de Salamanca, Paseo de San Vicente 58-182, 37007 Salamanca, Spain. Tel. international +33 23 291100-291200. Fax. international +33 23 291131.

Prolonged low doses of oral etoposide may be effective in individual patients with advanced lymphoproliferative disorders refractory to aggressive chemotherapy

Sir,
etoposide, a semisynthetic podophyllin derivate, is currently employed in the treatment of several malignancies. The antitumor efficacy of etoposide is highly schedule dependent and it has been demonstrated that five-day administration is superior to single day administration. Oral etoposide has greatly facilitated the use of multiple-day schedules and the drug displays good activity in many extrahematological malignancies as well as in lymphoma. From December ’93 to May ’94, we treated with prolonged low doses of oral etoposide 24 patients with advanced hematological malignancies not eligible for further intensive approaches due to age >60 years and/or severe previous or infective complications. Of these, ten patients had ALL, 8 AML, 4 NHL and 2 had CML.

Etoposide (50 mg/m^2 per day) was administrated orally for 21 consecutive days; patients who showed a response or stable disease on day 28 received a second and a third cycle of the same treatment. Responder patients received maintenance etoposide at the same dosage 10 days/month until relapse. Three patients (12.5%) died during the first cycle of intracerebral hemorrhage (1 patient) or infective complications (2 patients); no other toxic deaths were observed. All other patients received at least 2 cycles. Two ALL and 1 NHL patient (12.5%) obtained a complete remission of short duration (2, 3, 7 months); 1 ALL and 2 NHL patients (12.5%) achieved a partial response. No patient with myeloproliferative disease attained a response. Data from responder patients are shown in Table 1.

As for toxicity, 15/24 patients (62.5%) suffered febrile episodes during treatment (4 sepsis, 6 bronchopneumonia, 1 fungal sinusitis and 4 fever of unknown origin). One patient developed an intracerebral hemorrhage, while 8/24 patients (33.3%) displayed cutaneous hemorrhagic manifestations. Ten patients (41.6%) had mild nausea (WHO < 2) and vomiting, and 6/24 (25%) mucosis (WHO 2).

Table 1. Laboratory parameters and clinical manifestations at onset in six patients with TTP.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (g/dL)</td>
<td>6.5</td>
<td>no</td>
</tr>
<tr>
<td>PB × 10^9/L</td>
<td>9.0</td>
<td>no</td>
</tr>
<tr>
<td>LDH (U/L)</td>
<td>2750</td>
<td>no</td>
</tr>
<tr>
<td>Neurological findings</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Kidney findings</td>
<td>yes</td>
<td>no</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Finding</th>
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</thead>
<tbody>
<tr>
<td>RR</td>
<td>6.8</td>
<td>1498</td>
</tr>
<tr>
<td>MD</td>
<td>11.0</td>
<td>5786</td>
</tr>
<tr>
<td>CM</td>
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</tr>
<tr>
<td>PLM</td>
<td>6.7</td>
<td>1474</td>
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<tr>
<td>BS</td>
<td>7.2</td>
<td>1570</td>
</tr>
</tbody>
</table>

References
Despite the heterogeneity and low number of patients treated, some preliminary observations can be made. The 25% overall response rate achieved is encouraging and compares favorably with other single-agent approaches, as well as with intravenous etoposide.

Previous studies have also reported encouraging results using oral etoposide in untreated elderly AML patients. By contrast, the results reported in all patients are disappointing. No AML patient in our study responded. However, all patients showed a 30% response rate (2/10 CR and 1/10 PR). Overall, oral etoposide achieved better results in advanced lymphoproliferative disease (6/14 responder patients) than in advanced myeloproliferative disease (0/10 responder patients). The reason for this behavior is unclear.

The toxicity of the schedule was acceptable and no patient discontinued the treatment because of nausea. As expected from the advanced disease status and heavy pretreatment of these patients, median response and survival duration were short. The use of oral etoposide in less advanced disease and/or its association with other drugs are possible ways of improving these results.

Circulating antiplatelet antibody specificity in children with immune thrombocytopenic purpura at onset

Sir, immune thrombocytopenic purpura (ITP) is caused by the interaction of platelet reactive antibodies with platelet surface antigens, which determines accelerated platelet destruction of antibody-coated platelets. Two forms of childhood ITP may occur: a syndrome similar to adult chronic ITP, and an acute self-limiting form of the disease. Only few reports have been published about antiplatelet antibody specificity in paediatric ITP; some of them studied the specificity of circulating antiplatelet antibodies by testing patient sera by immunoblotting. However, certain conformational antigens on platelet membrane are destroyed by this technique. Moreover, these reports concerned small pediatric ITP populations. It was suggested that the presence of circulating anti-GPllb/llla antibodies may be useful in differentiating acute from chronic ITP in children; however, in a recent pediatric survey no difference between the two ITP forms was found. We investigated the specificity of circulating antiplatelet antibodies of ITP children at onset, in order to assess whether it may represent a marker of evolution of the disease. Sera were collected from 74 ITP children (4 months to 13 years, mean age of 5.5 years) at onset before beginning therapy. Forty-nine patients recovered within 6 months from the initial diagnosis (acute ITP), whereas 25 patients developed chronic disease (mean duration 2.2 years, range 1 to 5 years). Antibody specificity was assessed by indirect MAIPA assay refined according to Kiefel et al., we looked for anti-GPllb/llla and anti-GPllb/llla IgG antibodies.

Anti-GPllb/llla antibodies were found in 19/49 (38.8%) and in 8/25 (32.0%) acute and chronic ITP, respectively. Antibodies to GPllb/llla were detected in 15/49 (30.6%) acute ITP and in 7/25 (28.0%) chronic ITP. Thus, in our experience we did not find any significant difference between acute and chronic ITP, evaluating both anti-GPllb/llla and anti-GPllb/llla/IXA antibodies. This study reports on the investigation of circulating antiplatelet antibodies specificity in the largest sample of acute and chronic ITP children at onset ever analyzed at our knowledge. We conclude that circulating antiplatelet IgG specificity in childhood ITP at onset does not represent a marker to the early recognition of those patients devoted to chronicize. We cannot rule out that autoantibodies against platelet antigens other than GPllb/llla and GPllb/llla/IXA were responsible for thrombocytopenia in some of our patients; moreover, antiplatelet IgM should be investigated especially in acute ITP patients. Finally, more useful information could be obtained performing directly MAIPA on patient’s platelets.

References


Correspondence: Roberto Latagliata, MD, Ematologia, Divisione Medica, Ospedale di S. Severino Marche (MC); Italy. Fax. international +39.644241984.