Aclarubicin in the treatment of elderly patients with acute nonlymphocytic leukemia.

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Aclarubicin in the treatment of elderly patients with acute nonlymphocytic leukemia.*

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Abstract

Thirteen previously untreated patients aged 70 and above with acute nonlymphocytic leukemia were treated with aclarubicin (ACR) alone. Among 10 cases (3, acute myelocytic leukemia; 4, acute myelomonocytic leukemia; 2, acute monocytic leukemia; and one, acute erythroleukemia) in which an evaluation was possible, 5 cases (3, acute myelomonocytic leukemia; and 2, acute monocytic leukemia) obtained complete remission (CR). The CR rate was 83% in 6 patients with acute myelomonocytic leukemia or acute monocytic leukemia. The median CR duration and survival was 7.5 and 10 + months, respectively. Although side effects of the drug on digestive system such as nausea, vomiting and anorexia were observed in all patients, they were controllable by conventional treatments. The results suggest that ACR is effective for the clinical management of elderly patients with acute nonlymphocytic leukemia, especially those with acute myelomonocytic leukemia or acute monocytic leukemia.

KEYWORDS: acute leukemia in elderly patients, chemotherapy of acute leukemia, aclarubicin

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Thirteen previously untreated patients aged 70 and above with acute nonlymphocytic leukemia were treated with aclarubicin (ACR) alone. Among 10 cases (3, acute myelocytic leukemia; 4, acute myelomonocytic leukemia; 2, acute monocytic leukemia; and one, acute erythroleukemia) in which an evaluation was possible, 5 cases (3, acute myelomonocytic leukemia; and 2, acute monocytic leukemia) obtained complete remission (CR). The CR rate was 83% in 6 patients with acute myelomonocytic leukemia or acute monocytic leukemia. The median CR duration and survival was 7.5 and 10+ months, respectively. Although side effects of the drug on digestive system such as nausea, vomiting and anorexia were observed in all patients, they were controllable by conventional treatments. The results suggest that ACR is effective for the clinical management of elderly patients with acute nonlymphocytic leukemia, especially those with acute myelomonocytic leukemia or acute monocytic leukemia.

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The recent increase in acute nonlymphocytic leukemia (ANLL) among the aged has received much attention. Progress in intensive induction chemotherapy has given excellent results for patients with ANLL, but chemotherapeutic trials for elderly patients are not always successful. Recently, low doses of cytosine arabinoside (LD ara-C) have been used for the treatment of elderly patients with ANLL and myelodysplastic syndromes (1-3). Aclarubicin (ACR), an anthracycline antibiotic with antileukemic activity, has been found to be less cardiotoxic than doxorubicin (4). ACR also has been found to induce in vitro differentiation of human acute promyelocytic leukemia cell line HL-60 (5). The present paper describes a trial of ACR in ANLL patients aged 70 and above.

Thirteen patients with ANLL (4, acute myelocytic leukemia; 5, acute myelomonocytic leukemia; 2, acute monocytic leukemia; and 2, acute erythroleukemia) were treated with ACR alone. All patients were previously untreated. The ratio of male to female was 11:2, and the ages of the patients ranged from 71 to 86 years (median: 76). ACR was diluted in 200 ml of dextrose-
electrolyte solution and administrated by intravenous drip infusion at a dose of 14 mg/m²/day for 7 to 10 days, and repeated after the recovery from myelosuppression. Complete remission (CR) was defined by less than 5% of blasts in bone marrow and by the normalization of peripheral blood. Consolidation and intensification therapies were done by infusing the same dose of ACR as that used in the induction therapy for 4 or 5 days. Antimicrobial chemotherapy and blood transfusion were done according to the conditions of patients.

Table 1 Type of acute leukemia and the response to aclacinomycin

| Type of leukemia          | Patients treated | Patients evaluated | Patients with CR a
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Acute myelocytic leukemia</td>
<td>4</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Acute myelomonocytic leukemia</td>
<td>5</td>
<td>4</td>
<td>3(75%) b</td>
</tr>
<tr>
<td>Acute monocytic leukemia</td>
<td>2</td>
<td>2</td>
<td>2(100%) b</td>
</tr>
<tr>
<td>Acute erythro-leukemia</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

a: CR, Complete remission
b: Percent of complete remission

The therapeutic results of ACR are outlined in Table 1. In 10 of the 13 patients treated, an evaluation of the response was possible. Two patients, one suffering from gastrointestinal bleeding and another from renal failure on admission, could not receive an adequate doses of ACR. One patient was discharged from the hospital at will before the evaluation of the response. Five of the 10 evaluated (50%) obtained CR, including 3 acute myelomonocytic leukemia and 2 acute monocytic leukemia patients. The days required for achieving CR ranged from 24 to 97 days (median: 28), and the total doses of ACR used ranged from 140 to 400 mg (median: 200). The CR duration, including that in 2 patients without intensification therapy, was from 1.3 to 11.3 months (median: 7.5). The survival time was from 6.6 to 15.6 months (median: 10+) in patients with CR. The nadir of the cell count and days to nadir were 1,000/cmm and 18 days for neutrophils, 15,000/cmm and 13 days for platelets, and 18,000/cmm and 24 days for nucleated bone-marrow cells, respectively. Although gastrointestinal toxicities such as nausea, vomiting and anorexia were observed in all patients, they were controllable by conventional treatments. No patients showed acute cardiotoxicity. Fever was observed in 5 of 10 patients: one patient with an episode of septicemia, 2 with pneumonia and one with fever of undetermined origin. The fever was controllable in all of the patients by antimicrobial chemotherapy.

The introduction of more active agents in therapeutic regimens and the progress in supportive therapy have improved the CR rate and survival in elderly patients with ANLL. However, for patients aged 70 and above, chemotherapeutic trials are not always satisfactory. Actually, most past trials achieved CR in less than 40% of the patients aged 70 and above, Keating et al. (6) obtained a 33% CR rate in 24 patients treated with a ROAP (rubidazone, vincristine, ara-C and prednisolone) regimen, and Kahn et al. (7) obtained a 28% CR rate in 40 patients treated with a combination of daunorubicin, ara-C and 6-thioguanine. In our previous trial, a 33% CR rate was achieved in 6 ANLL patients aged 70 and above treated with a NCMP (neocarzinostatin, ara-C, 6-mercaptopurine and prednisolone) regimen. Although the reasons for the lower CR rate in elderly patients have not been precisely defined, less tolerance to myelosuppression is considered to be one of the possible causes. Recent laboratory investigations have demonstrated that various agents, including ara-C and other cytotoxic agents, can induce in vitro differentiation.
of cultured myeloid leukemia cells (8). Based on these findings, LD ara-C has been used in a new therapeutic strategy for elderly patients with ANLL. Degos et al. (2) obtained a 50% CR rate in 48 patients aged 70 and above using a LD ara-C regimen. ACR seems to be favorable for the treatment of aged patients because of its lower cardiotoxicity. Furthermore, ACR has been found to induce in vitro differentiation of human acute leukemia cell line HL-60 (5). In the present study, ACR treatment resulted in a 50% CR rate in 10 patients with ANLL aged 70 and above. In patients with acute myelomonocytic leukemia and acute monocytic leukemia, the CR rate was 83%. All patients with CR experienced transient cytopenia. Therefore, the effect of CR is considered to be due to the cytopenic action of ACR rather than the induction of differentiation of leukemic cells.

In summary, the present results suggest the clinical usefulness of ACR in elderly patients with ANLL, especially those with acute myelomonocytic leukemia and those with acute monocytic leukemia. However, since the present trial was done with a small number of patients, the results need to be confirmed in a larger randomized study.

References


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