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Accepted: August 19, 1987


Low-Dose Cytosine Arabinoside in the Treatment of Acute Nonlymphocytic Leukemia

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We have read with interest the article of Jensen and Stentoft [1] about the treatment of relapsed and refractory acute nonlymphocytic leukemia (ANLL) with low-dose cytosine arabinoside (ARA-C). We would like to report our clinical experience of the treatment with low-dose ARA-C in 11 patients with ANLL.

The patients were classified according to the FAB criteria [2]; 2 cases had M↑ type, 5 M2 type, 1 M3, 2 M4, and 1 patient had chronic granulocytic leukemia (CGL) in myeloblastic transformation (table I). Three patients developed ANLL after myelodysplastic syndromes (MDS); 4 other patients were refractory to standard chemotherapy for remission induction, which was one course with daunorubicin 50 mg/m2 day for 3 days, ARA-C 100 mg/m2/12 h and thioguanine 100 mg/m2/12 h on days 1–7, followed by one course with one day daunorubicin and 5 days ARA-C and thioguanine treatment. Also included were 3 elderly patients with de novo ANLL. The patient with CGL in the blast phase was unresponsive to the two courses of combination chemotherapy.

Treatment regimen. ARA-C was administered 10 mg/m2 s.c. every 12 h, usually for 21 days. To patients who had a response, ARA-C was given for 10 days every 4–6 weeks. Complete remission (CR) was defined as a reduction of bone marrow blasts to < 5% in the presence of peripheral granulocytes count > 2×109/1, a platelet count > 100×109/1 and a hemoglobin level > 12 g/dl; partial response (PR) was defined as > 50% reduction in bone marrow blasts, an increase of the hemoglobin values > 10 g/dl, with an increase of > 50×109/1 platelets and > 1.5×1011 granulocytes. Eight patients responded to therapy; there were 5 CR and 3 PR (table I).

<table>
<thead>
<tr>
<th>Patients No.</th>
<th>Clinical data and response to low-dose ARA-C of 11 patients with ANLL</th>
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<tbody>
<tr>
<td>1–3</td>
<td>had ANLL after MDS, No. 4–8 had refractory disease, and No. 9–11 de novo ANLL. NR = No response.</td>
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10 and 26 months, respectively. Among the 3 cases who showed PR, patient No. 5 previously refractory to conventional chemotherapy had improved bone marrow function, resumed his daily activities and was well for 18 months (table I). Patient No. 9 with de novo ANLL is still alive after 14 months from diagnosis. Patient No. 8 with CGL in blast crisis died 7 months after the start of low-dose ARA-C for infection and disease progression. The 3 patients who did not respond died within 3 months from diagnosis.

The therapy was well tolerated; none of the patients had gastrointestinal symptoms. The most severe toxic effect was myelosuppression: 4 patients showed serious trombocytopenia ( < 20×10^9/1) and 3 had granulocytopenia ( < 0.5×10^9/1). There were no deaths related to the treatment.

In conclusion, low-dose ARA-C induced responses in 8 of 11 patients with ANLL; it must be emphasized that 4 responses (2 CR and 2 PR) were obtained in 5 patients who were refractory to heavy combination chemotherapy and these data seem to confirm the results reported by Jensen and Stentoft [1].

References
