To the Editor:

Kojima et al recently reported 20 patients with Down's syndrome and acute leukemia.1 Of these 20 patients, 14 who were 3 years old and less were diagnosed as having acute megakaryoblastic leukemia (AMKL). They were characterized by the presence of bone marrow fibrosis, a history of myelodysplastic syndrome (MDS), and a poor response to chemotherapy. Ten of the 14 patients were male, and platelet count ranged from 0.2 to 108 \( \times 10^9 \text{L} \) (median 25.0 \( \times 10^9 \text{L} \)). The median observation time between initial diagnosis and moment of overt leukemia for the seven patients with MDS was 6 months with a range of 3 to 9 months. All but one MDS-AMKL patients achieved a complete remission with anthracycline and cytosine arabinoside, but the duration of complete remission was short.

We recently observed a phenotypically normal 10-month-old boy with a white blood cell (WBC) count of 70 \( \times 10^9 \text{L} \), hemoglobin 7.4 g/dL, and platelet count 107 \( \times 10^9 \text{L} \), whose bone marrow showed ANAE, and PAS staining and reacted with anti CD33, CD42, and CD45 monoclonal antibodies. Following unsuccessful treatment with anthracycline and cytosine arabinoside, he received mitoxantrone and etoposide and achieved complete remission of short duration. Repeated follow-up chromosome studies during remission persistently showed normal karyotype on cells from both the peripheral blood and the bone marrow until relapse. In the infants with phenotypically evident Down's syndrome the likely outcome of an illness resembling congenital leukemia is spontaneous recovery. Transient leukemoid reaction and trisomy 21 mosaicism had been reported in a phenotypically normal newborn.2 Transient myeloproliferative disorder of the Down type was observed recently in two infants showing trisomy 21 apparently restricted to the leukemic clone, never detected in either PHA-stimulated peripheral blood cells or bone marrow, or in myeloid progenitor cells after resolution of the transient myeloproliferative disorder.3

According to the present knowledge, occurrence of any type of myeloproliferative disorders, both the transient leukemoid reaction or the AMKL, is not confined to infants with partial or complete systemic trisomy 21, but can occur in genetically normal newborns or infants whose leukemic cells contain a third chromosome 21.

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REFERENCES


RESPONSE

We are grateful to Dr Arico for pointing out an important aspect of our recent study of Down's syndrome and acute leukemia in children. We would like to complement the discussion with the following observation.

Recently, we observed transient myeloproliferative disorder of the Down type in two phenotypically normal infants showing trisomy 21 restricted to the proliferative blasts cells, which were shown to be of megakaryoblastic origin by use of ultrastructural and immunophenotyping studies. Trisomy 21 was not detected in either PHA-stimulated peripheral blood cells, bone marrow cells, or in skin fibroblasts after resolution of the transient myeloproliferative disorder, as was reported by Ridgeway et al. Brodeur et al have found a trisomy 21 clone in only 4 of 100 cultured skin fibroblasts from a phenotypically normal infant with similar transient myeloproliferative disorder of the Down type. The three infants described by Drs Arico and Ridgeway and our two infants may be genetically normal in view of usual cytogenetic analysis. However, we are not sure whether these infants have a small portion of trisomy 21 clone of normal tissue or not. More precise and extensive analyses, including molecular technique, are needed to elucidate this issue.

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REFERENCES


Acute megakaryoblastic leukemia and clonal trisomy 21 in a phenotypically normal infant [letter; comment]

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