Juvenile Chronic Myelogenous Leukemia: Therapeutic Trial with Interferon Alpha 2B

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Juvenile chronic myelogenous leukemia (JCML) is a rare malignant hematopoietic disorder representing only 2% of all childhood leukemias. The disease has a rapid course and has a median survival of less than 10 months when untreated or undertreated(l,2). Patients are often difficult to diagnose because of their clinical heterogeneity. A remarkable feature is increased synthesis of HbF and excessive proliferation of exclusively monocyte-macrophage CFU-C colonies in the absence of added growth factors with an abnormally high plating efficiency(l,3,4). Considering the highly malignant nature of the disease the response to chemotherapy is poor and variable. Here we report a case of JCML with the results of our bone marrow *in vitro* CFU-C assay and attempts to treat the child with interferon alpha-2 (alpha-IFN).

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Case Report

A 4 month old male child presented with low grade fever, progressively increasing pallor and splenohepatomegaly of 3 months duration. Liver was 5 cm palpable and spleen was 10 cm palpable below the costal margin. There was no skin rash, icterus, generalized lymphadenopathy or any bleeding tendency. There was no family history of any hematblogical disorders. Laboratory parameters showed a Hb of 8.1 g/dl, total WBC count of 65,400/mm^3, platelet count of 20,000/mm^3. Peripheral smear revealed 11% monocytes, 10% immature granulocytes and 4% nucleated red cells *(Table I)*. Bone marrow aspirate showed a hypercellular marrow with increased granulopoie^sis, suppressed erythropoiesis and no megakaryocytes. Bone marrow was layered on Ficoll-Hypaque gradients and centrifuged to obtain the mononuclear cell (MNC) fraction. MNC were plated at 2.0 x 10^5 MNC/ml in 2.5% methylcellulose and incubated in 5% Co_2 at 37°C for 14 days with 10% HPCM (human placental conditioned medium) for CFU-GM assay. This yielded more numbers of pure monocyte colonies (n=68) than granulocyte monocyte colonies (n=13). The normal range of CFU-GM is 120-198 colonies in our experimental conditions. The HbF **was** 17.8% (normal 5-8%) and leucocyte alkaline phosphate score was 110 (n=50-150). Biochemistry was normal. With the above results, a diagnosis of JCML was confirmed and patient was started on 1.5 million units per day subcutaneously of Intron-A (alpha-interferon 2b). In addi-

TABLE I-*Partial Response to Therapy with Interferon-Alpha 2 in JCML*

Time period	Liver (cm)	Spleen (cm)	Hb (g/dl)	Total WBC Count (/mm^3)	Differential WBC Count			
					Mono-cytes (%)	Blast (%)	Immature granulo-eytes(%)	NR (%)
At diagnosis	6	10	8.1	65400	11	5	10	4
D20 after diagnosis (begin therapy with Intron-A)	6	10	9.0	140000	19	8	15	4
D7 after treatment	6	9	8.5	47000	11	1	14	1
D14 after treatment	6	9	6.7	32000	6	0	5	0
D21 after treatment	5.5	9.5	9.2	32000	6	0	2	0

tion he received 2 units of packed red cell transfusions. Liver and spleen remained the same. Daily counts were monitored. As shown in *Table I,* there was a partial hematological response. Subsequently after 3 weeks the child was reported to have died of gastroenteritis at home.

Discussion

JCML is a disease of childhood with most patients being less than 4 years of age. The median survival period is usually 10 months and patients succumb to the disease unless adequately treated. Clinical features usually consist of splenomegaly which in almost 40% of cases extends below the umbilicus, hepatomegaly, lymphadenopathy and pallor, as seen in our case. Eczematous skin rash which is commonly seen in JCML was, however, not present in our patient('i,2). Symptoms suggestive of pulmonary involvement were not observed in our patient.

Peripheral blood and bone marrow findings at diagnosis were similar to those published in other series(l). The patient had leucocytosis, monocytosis with immature granulocytes, blast forms and nucleated red cells. There was increased production of HbF. Attempts to culture mononuclear cells yielded more numbers of pure monocyte colonies as expected. However, autonomous growth of these cells could not be studied(3). Thus clinical course and laboratory findings were consistent with a diagnosis of JCML.

Our decision to treat the child with alpha IFN was based on the following aspects: *(a)* previous attempts to treat with chemotherapy protocols like for

ALL or adult CML failed to achieve remission or resulted in frequent relapses due to persistence of leukemic cells(l,2,5,8,9); (b) Allogeneic BMT in early remission is one of the possibilities for achieving cure(l,2). However, it was not possible in this case due to unavailability of a suitable donor and financial constraints; (c) Remission has been induced in various other malignancies including CML with use of alpha IFN(7); *(d)* Evidence of *in vitro* inhibition of growth of JCML cells by alpha IFN(IO). The patient was treated with alpha-IFN for 3 weeks. Liver and spleen did not show any progressive increase during this period. The total WBC counts reduced partially to 32,000/mm^3 though they did not reach the normal range. There was considerable reduction in the percentage of blasts, immature granulocytes, monocytes and nucleated red cells in the peripheral blood. A similar trial by Hazani *et al* with alpha-IFN did not show any clinical. response(2). In our case a partial hematologic response was seen. Hence, we suggest that alpha-IFN may be effective in treating infants with JCML. Further larger clinical trials over longer periods need to be carried out.

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