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Treatment of Childhood Leukaemia in Singapore

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INTRODUCTION

Acute leukaemia is the commonest childhood malignancy. In Singapore, acute lymphoblastic leukaemia accounts for about 24% of cancers reported in the age group 0 to 14 years.¹⁾ The incidence is comparable to those of other countries.²⁾⁻⁴⁾

All the patients with leukaemia died prior to 1973 in Singapore. The treatment then was poor and without central nervous system prophylaxis. Median survival time after diagnosis was three months. By 1973, there were reports of relative success in prolonging survival times that cure seemed possible in some patients.⁵⁾ Since then, we have started treatment of childhood leukaemia and the results were encouraging.

ROUTINE INVESTIGATIONS

Besides the usual clinical and laboratory investigations, the following were carried out for every patient with leukaemia :

- 1) Full blood count, including haemoglobin levels, total white cell counts, differential counts, platelet counts, reticulocytes
- 2) Peripheral blood film and buffy coat preparation
- 3) Blood grouping : -ABO and Rh
- 4) Bone marrow or trephine biopsy for Romanowsky, PAS, Peroxidase, other histochemical stains, immunological markers and chromosome culture
- 5) Haemoglobin electrophoresis for foetal haemoglobin and haemoglobin A₂

- 6) Lumbar puncture and the spinal fluid examined for leukaemic cells
- 7) Blood urea, creatinine and serum electrolyte levels
- 8) Blood uric acid level
- 9) Liver function tests
- 10) Chest X-rays
- 11) Other investigations as indicated, e.g. X-rays of bones, blood cultures and cell markers

SELECTION OF PATIENTS

The regime differs for good and bad risk patients based on the clinical and laboratory parameters. Poor risk parameters are :

- 1) High total white cell counts
- 2) Age 3 years or 7 years
- 3) Male sex
- 4) Large liver and spleen
- 5) T-cell and null-cell leukaemia

TREATMENT REGIME

Our treatment regime consist of induction with intravenous Vincristine (1.5mg/m²) weekly and daily oral prednisolone (40mg/m²). A third medicine will be added for the poor prognostic patient, i.e. intravenous asparaginase 10,000 IU/m² for 6 doses.

Central nervous system (CNS) prophylaxis comprises intrathecal injection of methotrexate (the dose varying with age, from 6-12mg) and cranial irradiation of 2400, (recently reduced to 1800) rads. Maintenance therapy is carried out for about 3 years. The detailed treatment regime has been published earlier.⁶⁾

More recently, bone marrow transplantation

is preferred for treatment of AML in first remission and ALL in second or subsequent remission.⁷⁾

TREATMENT OF CNS LEUKAEMIA

If the initial cerebrospinal fluid shows evidence of CNS leukaemia, the patient is treated with weekly intrathecal methotrexate (10mg/m², maximum 12mg) until the CSF is normal. When haematological remission is established with induction therapy, the patient will receive cranial irradiation and then put on CNS pulsing with alternate intrathecal methotrexate or intrathecal cytosine arabinoside.

RESULTS OF TREATMENT

From 1973 to 1981, there were 49 patients with acute lymphoblastic leukaemia (ALL) referred for treatment. 6 were lost to follow-up leaving 43 patients for analysis. Of all the ALL patients, there were 30 males and 19 females with the usual male predominance. There were no particular racial bias, there being 33 Chinese, 9 Malays, 5 Indians and 2 other racial groups.

The survival rates were calculated on the life table. The 5 year survival rate was 59%.⁶⁾ This is not equivalent to cure. For those patients who had been followed up long enough, the 5 year continuous remission rate is 38.1%.

There were 22 cases of acute non-lymphoblastic leukaemia, and the 5 year survival rate was only 18.6%.

Because of the poor result, bone marrow transplantation was preferred for non-lymphoblastic leukaemia in first remission or ALL in second remission. So far, 4 cases (5 transplants) had been done and one had graft-versus-host disease and died of interstitial pneumonitis on day 94 post-transplant. The other one died after a second relapse.

DISCUSSION

The results of our treatment is encouraging. When comparing the survival rate of ALL treatment at various centres, many factors have to be taken into consideration, eg. patient

selection, availability of medical staff and facilities, different treatment schedules, drug availability and dosages, length of follow-up, life-table analysis or actual length of follow-up, number of cases and so on.

Excellent survival rates were reported in the United States. 53.9% 5 years survival was reported for St Jude's Hospital.⁸⁾ Another follow-up of 70 cases of childhood ALL revealed a 5-year survival rate of 57.1% by life table analysis.⁹⁾ In the U.K., 2 cohorts were followed up.¹⁰⁾¹¹⁾ The first cohort comprised 72 patients from 1972-1973 and the 5 years survival rate was 38.8% while the 1974-1975 cohort of 78 patients had a 5 year survival rate of 50%. The better survival of the later cohort was presumably due to better treatment regimes of therapy. Our figure of 59% 5 year survival, also obtained by life table analysis, compares favourably with those figures from U.K. and U.S.A.

However, other reports of acute cohort follow-up studies are not as promising as the above figures. A report from Italy of 727 cases of ALL collected from 8 countries, the actual 5 year survival rate was only 27.5%.¹²⁾ In the U.S.A., another report of 341 ALL from 1970-1973, the actual 5 year survival rate was 34%.¹³⁾ These workers noted the disparate 5 year survival rates between various centres in the same country and commented that selection of cases, different therapeutic regimes, modes of survival assessment of life table analysis or actual cohort long-term follow-up may account to some extent for the difference in survival figures. It is pertinent to recall that our actual cohort survival was 38% which is much lower than the overall 5 years survival of 59%.

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