CASE REPORT

Long Term Survival in Aggressive NK-cell Leukemia

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Aggressive natural killer cell leukemia (ANKL) is a rare type of leukemia. It is rapidly progressing and the outcome is poor, with short survival. There is paucity of reports of ANKL in the Indian pediatric literature. We report a pediatric ANKL case that is in complete continuous remission after four years.

Key words: *Antineoplastic combined chemotherapy protocols, Leukemia, Outcome.*

Leukemia of natural killer (NK) cells was first described in 1986(1,2). The neoplasm of NK cells are classified into aggressive NK cell leukemia (ANKL), extranodal NK cell lymphoma, nasal type (ENKL), $CD4^+$/ $CD56^+$ hematodermic neoplasm, myeloid/NK cell precursor acute leukemia and chronic NK-cell lymphocytosis(3-5). Aggressive NK cell leukemia is common in young Asian and Latin Americans (median age of 40 years). The patients of ANKL present with fever, anemia, thrombocyto-penia and hepatosplenomegaly. The blasts are CD2, CD16, CD56, cCD3, HLA-DR positive; and express multidrug-resistant P-glycoprotein and Epstein–Barr virus (EBV)(6).

CASE REPORT

A 13 year-old male (weight 37 kg, height 160 cm, BSA 1.28 m^2) presented with fatigue, pallor, joint pains, sternal tenderness, palpable spleen and upper respiratory tract infection. His hemoglobin was 9.5 g/dL; platelet count was 80000/cmm and total count was 1100/cmm with 94% large granular mononuclear cells. These cells were positive for cyCD3 and CD56, while negative for CD3, CD5, CD10, CD 19, CD14, CD16, cyCD22, CD33, CD34, CD71, CD117, HLA-DR, IgG1, IgG2, and CD4. Cytogenetic analysis from bone marrow was normal. There was no evidence of extra-medullary involvement in imaging studies. Tumor cells could not be assessed for EBV and T-cell receptor status. He was put on AIEOP-95 high risk acute lymphoblastic leukemia regime. His bone marrow achieved complete remission after block 3 chemotherapy. He is in remission at the time of reporting (overall survival: 1721 days; days in CR: 1447).

DISCUSSION

Aggressive NK cell leukemia was diagnosed in our case, based on large granular lymphocytes, positive CD 56, cyCD3, and negative B, T and myeloid markers. T-cell antigens (CD2, CD7, and CD8), CD 16(NK cell antigen) and HLA DR were absent in our case but they can be present also(5). A nasal mass and negative CD16 favors diagnosis of ENKL. Germ line configuration of T cell receptors and demonstration of Epstein Barr virus differentiates ANKL+ENKL from other NK cell malignancies. The treatment of ANKL is not very effective and most patients die within two years(5). Due to its

rarity, large trials are few and there is no consensus about the treatment. Song, *et al.*(6) reported young age and anthracycline as good prognostic factors in a study of 13 cases. Progression free survival of 34% (28 patients) has been reported in an analysis of allogeneic hematopoietic transplantation (allogeneic BMT)(7). An analysis of L-asparaginase based chemotherapy reported 86.7% response rate and 53.8% complete remissions(8). SMILE protocol (dexamethasone, methotrexate, ifosfamide, L-asparaginase, etoposide) achieved 67% response and 50% complete response(9). Our patient was young and the chemotherapy given to him included anthracycline, L-asparaginase and etoposide, which are reported to be effective in ANKL(10). AIEOP therapy also has been reported to be useful in $CD4^+$/ $CD56^+$ hematodermic neoplasm(11). Our patient is in complete continuous remission for four years. Allogeneic BMT is an effective therapy but it was not considered in our case due to economical constraints(7).

In conclusion, ANKL is a rare type of leukemia and may achieve long term remission with aggressive multi-agent chemotherapy.

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