Neuroblastoma and Treatment-Related Myelodysplasia/Leukemia: The Memorial Sloan-Kettering Experience and a Literature Review

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Background

Neuroblastoma is the most common solid childhood tumor occurring outside the brain. The majority of patients with neuroblastoma present with metastatic disease and require intensive therapy if hope for a cure is to be entertained. Over the last several decades therapy for metastatic (or high risk) neuroblastoma patients has evolved to include higher doses of chemotherapy.

As physicians increase chemotherapy dose in the hope of increasing survival, a concomitant increase in side effects is unfortunately expected. One known side effect of chemotherapy is the development of leukemia. In fact, it is now well established that certain chemotherapy drugs give rise to specific types of leukemia. For example, alkylating chemotherapy medications such as cyclophosphamide are associated with acute myeloid leukemia that commonly occur four to seven years after treatment and have abnormalities of chromosomes 5 and/or 7. In contrast, the topoisomerase class of chemotherapy drugs that include adriamycin and etoposide cause acute myeloid leukemia quicker and with different genetic alterations.

Large studies in patients receiving high doses of etoposide for lymphoid cancers have reported the incidence of acute myeloid leukemia to range from 6% to 18%. The incidence of acute myeloid leukemia following treatment of neuroblastoma is rare, however, only recently have patients with neuroblastoma received high doses of leukomogenic agents like etoposide and cyclophosphamide. To assess the risk of developing acute myeloid leukemia after treatment of neuroblastoma with high dose chemotherapy, researchers at Memorial Sloan-Kettering Cancer Institute reviewed their experience and reported the results in the December issue of the Journal of Clinical Oncology.

Materials and Methods

A total of 380 patients received high dose chemotherapy for high-risk neuroblastoma. This group of patients was compared to 50 low-risk neuroblastoma patients who did not receive any chemotherapy. In total six cases of acute myeloid leukemia occurred in the group receiving high dose chemotherapy and none in the group not receiving chemotherapy. In the cohort of patients who received the most intense chemotherapy regimen, the 36-month incidence of developing acute myeloid leukemia was 7%. The clinical and genetic findings of the acute myeloid leukemia cases were consistent with what is described in the literature for treatment related acute myeloid leukemia.

Results
Identifying which chemotherapy agent is most responsible for causing acute myeloid leukemia is very difficult, and it may well be a combination of the agents used that has led to the high rate of acute myeloid leukemia. Also possible is that children with neuroblastoma are at increased risk for developing acute myeloid leukemia regardless of the therapy received. However, the association between leukemia and increasing dosage of chemotherapy and the fact that no cases of acute myeloid leukemia occurred in the group of children not receiving chemotherapy argues against this point.

Conclusions

The authors conclude that efforts must be made to devise treatment strategies that decrease the risk of leukemia but maintain the current standard rate of cure.