

Abnormal Growth Patterns and Adult Short Stature in 115 Long-Term Survivors of Childhood Leukemia

Schriock et al evaluated final height in 115 long-term survivors of acute lymphoblastic leukemia (ALL) treated at St. Jude's Children's Research Hospital during the years from 1967 to 1975. Subjects with trisomy 21, central nervous system (CNS) leukemia at diagnosis, or those older than 12 years of age at diagnosis were excluded from the analysis as were children who had not completed growth. None of the 115 patients had been treated with growth hormone (GH) and all experienced spontaneous puberty. A variety of chemotherapeutic protocols were utilized, although all patients received induction chemotherapy with prednisolone, vincristine, daunorubicin, and/or asparaginase. CNS prophylaxis consisted of 2,400 cGy cranial irradiation plus 5 concomitant doses of intrathecal methotrexate or 2,400 cGy craniospinal irradiation alone. Patients' heights were measured at diagnosis and at least annually utilizing a stadiometer. Heights were expressed as standard deviation scores (SDS). The final cohort consisted of 39 males and 76 females who had been followed for a mean of 13.8 ± 2.1 years since diagnosis.

Significant retardation was observed in height SDS from diagnosis to the completion of chemotherapy ($P < .0001$) and from the end of therapy to the last evaluation ($P < .0001$). Heights at diagnosis were >1 SD below population norms for 19% and >2 SD for 2%. At final evaluation, 74% of these patients had SDS ≤ 1 SD, and 37% had SDS ≥ 2

SD. Chemotherapeutic regimens did not appear to have differential effects on the findings; however, height SDSs were significantly different for those receiving cranial versus craniospinal irradiation. Six patients in the craniospinal group did not receive prophylactic irradiation until chemotherapy had been completed. Despite their growth decrement during chemotherapy ($P < 0.03$), they had no significant overall change in final height SDS. Height SDS had decreased at the end of chemotherapy in 90% of children treated with cranial irradiation, and 30% had final height scores of ≥ 2 SD below population means. Changes in height SDS were correlated with age at diagnosis for the patients who received cranial irradiation. Growth retardation was most prominent in those with early onset disease. In addition, girls whose disease was diagnosed before age 8 had significantly greater decreases in height SDS after chemotherapy than those who were older at diagnosis.

The authors state that the median change in height SDS from diagnosis to the last evaluation was -1.5 , corresponding to a mean height decrement of 9.1 cm. Their data contrast with that of other studies, which predict minimal effects on adult height in survivors of childhood leukemia. The authors state that this may be due to the failure of other investigators to follow patients until growth was complete. They further note that there have been changes in CNS prophylaxis over the last few years,

including a reduction in total cranial irradiation and the elimination of spinal irradiation.

Schriock E, et al. *Clin Oncol* 1991; 9: 400-405.

Editor's comments: *This well-conducted study demonstrates separate effects of chemotherapy and irradiation on final height in long-term survivors of childhood ALL. It is particularly interesting because only children who were younger than 12 years of age at diagnosis were studied, thus eliminating potentially minimal changes in height decrements that might be observed in pubertal children. GH evaluations were not reported for any of the subjects; thus, it is not known whether any had permanent loss of GH secretion. It is noteworthy, however, that all patients entered spontaneous puberty. It is hoped that future prospective studies will include the determination of GH secretion as well as insulin-like growth factor 1 levels, so that these findings might be more fully explained. In addition, it will be interesting to evaluate the effect of omitting spinal irradiation and lowering cranial irradiation doses on final height in survivors of childhood ALL. Dr. Stephen Shalet will cover the entire topic of growth and treatment of cancer, particularly leukemia, in GGH Volume 8, Number 3.*

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