Leukemia Following Cisplatin Therapy

Reed and Evans (1) reported a patient with myeloid leukemia that developed after treatment with several antitumor agents, including cisplatin. They discussed our previous brief report (2) of a patient who developed acute myelogenous leukemia after receiving cisplatin-only therapy of unusually long duration. Although the information provided in our report may have been unclear, the patient developed the leukemia soon (within the month) after receiving his 29th monthly dose of cisplatin. He probably would have been given a 30th cisplatin dose if the leukemia had not supervened.

It is of interest that Kempf and Ivanovics (3) demonstrated that cisplatin alone induced myeloid leukemia in six of 41 rats surviving more than 100 days after treatment. The clinical reports (1,2) and such animal studies (3) provide evidence for cisplatin leukemogenicity. Other such cases will probably be observed among patients who are long survivors after cisplatin therapy, with or without other antitumor treatment.

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References

Response

The occurrence of secondary leukemia after a period of meaningful response of the disease to chemotherapy is an unfortunate consequence of a desirable outcome. This should be kept in mind during discussions of secondary malignancies after treatment of Hodgkin’s disease, non-Hodgkin’s lymphoma, testicular tumor, and ovarian cancer. The fact that many good anticancer agents are also teratogens and carcinogens is only one of many unfortunate paradoxes in medicine.

The additional information given by Weiss (1) regarding a patient who was previously reported (2) is interesting in two respects: a) The cisplatin treatment regimen very closely parallels an experimental regimen that enhances malignant conversion of skin papillomas in mice (3), and b) the treatment regimen is consistent with the accepted notion that most cases of secondary leukemia in ovarian cancer are associated with chronic, low-dose therapy from DNA-damaging agents (4).

This poses an intellectual and medical challenge that has three primary facets. The first is to determine the circumstances that place a patient at risk for this undesirable outcome, and this has been the focus of most clinical reports to date. The second is to determine if there is a molecular basis for the occurrence of secondary malignancies in selected individuals, and if so, how the molecular parameter(s) of susceptibility can be favorably modulated; this is one of the goals of studies done to date on DNA adduct formation in human cancer patients and animal models (5). Third, if there is an identifiable molecular basis for the occurrence of secondary malignancies, can we separate that from the molecular basis of disease response to allow the two to be separately modulated?

To address the last two matters, more data are needed regarding the first. This is why it is so important to learn if the occurrence of secondary malignancy after curative therapy is simply a rare intellectual curiosity, or if it represents the opportunity to learn basic information about human biology that may have very practical and helpful applications.

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References

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1 Reed E, Listerl ER, Pointer MC: Cisplatin-DNA adduct persistence in renal and gonadal tissues of male and female rats. Manuscript submitted for publication.