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Letter to the editors

Acute myeloblastic leukemia following treatment with mitomycin C: a case report

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Sirs,

Mitomycin C is an alkylating agent that has been used in the treatment of various solid tumors [1]. Secondary acute nonlymphocytic leukemia induced by chemotherapy, particularly alkylating agents alone or with irradiation, is a well-recognized entity [3] but, to the best of our knowledge, has not yet been documented after mitomycin C. In this short report, a case of acute myeloblastic leukemia (AML) following treatment with mitomycin C is described.

Case report

A 74-year-old woman was hospitalized in January 1988 because of anemia and thrombocytopenia associated with vaginal bleeding. Her past history revealed the following: (1) Breast carcinoma, stage I, was diagnosed in January 1983 and treated by lumpectomy and axillary lymph node dissection, loco-regional irradiation, and tamoxifen. (2) Dukes' B_2 colon carcinoma was diagnosed in September 1983 and treated by a left hemicolectomy. Due to suspected abdominal relapse, between November 1983 and March 1984 she received 5-fluorouracil and leucovorin, followed by mitomycin C (20 mg/m^2 every 5 weeks, for a total dose of 120 mg), given between April and September 1984. (3) Villous adenomata with foci of carcinoma was diagnosed in March 1986 and treated by subtotal colectomy. (4) Renal-pelvic carcinoma was diagnosed in January 1984 and treated by nephrectomy. In February 1986, 22 months after mitomycin C, she first developed mild thrombocytopenia (80,000/mm^3), and in December 1986 macrocytic anemia developed, with 9 gm% hemoglobin (Hb).

On admission, the patient complained of fatigue, sore throat, dyspnea, and vaginal bleeding. A physical examination was unremarkable, and there was no lymphadenopathy, hepatosplenomegaly, or systemic bleeding diathesis. Laboratory tests showed: Hb, 6.0 gm%; mean corpuscular volume (MCV), 106 pm; platelets, 23,000/mm^3; and WBC, 7,200, with myeloblasts on the peripheral blood smear. Bone marrow aspiration and biopsy showed myeloblastic leukemia cells (M2, according to the FAB classification) and Auer rods were readily seen on the smears. Cytogenic analysis of the bone marrow was attempted but was technically unsuitable. Blood biochemistry showed mild renal dysfunction, a chest X-ray revealed a small right pleural effusion, and abdominal ultrasonography demonstrated mild hepatomegaly without metastatic disease. In view of her age, medical history, and expected prognosis, the patient was discharged without any specific treatment.

Discussion

Mitomycin C has been shown to be both carcinogenic and teratogenic in experimental animals and to produce chromosomal abnormalities in human lymphocytes [1]. Until now it has not been reported to be carcinogenic in humans, possibly because of the short survival of the patients treated with the drug. Our patient had four different solid malignancies, and the possibility that AML developed because of intrinsic host factors unrelated to mitomycin C cannot be excluded with certainty. Nevertheless, the time interval (22 months) between the administration of mitomycin C and the appearance of leukemia supports the possibility of a drug-induced leukemia and is consistent with that described in other reports [2]. 5-Fluorouracil and leucovorin are not considered leukemogenic, and the possibility that the local irradiation given for her breast carcinoma might have induced leukemia is unlikely.

In conclusion, although one cannot exclude the possibility that the radiotherapy given and a genetic constitution were additional predisposing factors in this particular case, this report suggests that mitomycin C might rarely be leukemogenic. This risk should be taken into account when the drug is used in an adjuvant setting or in patients expected to achieve long survival.

References

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