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Acute Leukemia Following Therapy for Teratoma

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Abstract—*Three cases of acute leukemia are reported following aggressive therapy for inoperable germ cell tumors. Two patients were treated by radiation plus cytotoxic chemotherapy and the third received only drugs. The time between onset of these therapies to death from leukemia was* 4, 17 *and* 61 months.

INTRODUCTION

THE SUCCESS of chemotherapy in the treatment of childhood leukemia and Hodgkin's disease has been clouded by the late occurrence of second malignancies [1–5]. Chemoresistant leukemia has been the predominant form of late cancer, and has been clearly related to the type of drug, the dose, duration of exposure and combination with radiotherapy [6, 7]. Germ cell tumors have lately been added to the small list of cancers cured by chemotherapy [8], and it was expected that sooner or later a price would be paid in the form of late complications. Two isolated case reports, one of acute leukemia [9] and one of cancer of the bladder [10], have appeared in the last three years, and we now add three patients with teratomatous tumors, all of whom developed acute non-lymphocytic leukemia.

Patient A, a 36-yr-old white male, was treated in 1977 with radiotherapy to the abdomen (37 Gy), mediastinum (12 Gy), supraclavicular areas (30 Gy), lungs (12 Gy) and left femur (30 Gy) for a testicular teratoma (malignant undifferentiated form). In 1979 he underwent chemotherapy amounting to a total dose of cisplatin of 450 mg, vinblastine 40 mg and bleomycin 180 mg. In 1983 he developed pancytopenia and a myelodysplastic syndrome, characterised by ring sideroblasts in the bone marrow and abnormal chromosomes. He developed blasts and transformed into leukemia several months later, and died.

Patient B was a 23-yr-old white male who underwent chemotherapy for a mediastinal malignant teratoma intermediate form. The total dose of cisplatin was 805 mg, vinblastine 72 mg, bleomycin 300 mg, etoposide 750 mg and methotrexate 500 mg. This was followed by 45 Gy radiotherapy with a linear accelerator to the lung and mediastinum. Nine months later he developed a normocytic anemia with 29% myelomonocytic blasts in the peripheral blood. The patient refused bone marrow analysis and he died shortly thereafter.

Patient C was a 25-yr-old white male who also had a malignant teratoma intermediate presenting in the mediastinum. Over 6 months he was treated with a total dose of cyclophosphamide of 1000 mg, chlorambucil 56 mg, actinomycin-D 2.8 mg, doxorubicin 60 mg, etoposide 600 mg, cisplatin 600 mg, vinblastine 24 mg and bleomycin 300 mg. While still receiving chemotherapy, he developed normoblasts in the peripheral blood smear, and a bone marrow puncture confirmed a myelodysplastic syndrome. An autopsy several weeks later confirmed the diagnosis of acute myelomonocytic leukemia.

DISCUSSION

A retrospective study published in abstract form revealed that 52 of 1150 patients treated with germ cell tumors of the testis between 1945 and 1977 in one institute went on to suffer a second tumor (20 contralateral testis tumors, 5 leukemias and 27 solid tumors) [11]. As the majority of these patients were stage 1 or 2, the principal therapy was radiation. Two of the patients described in our report received radiation, which must be taken into account as an etiological factor. All three, however, received combination chemotherapy, including the three constituents of the successful Einhorn regime [8]. None of these drugs has yet been proven to be carcinogenic in man [12–14], so this report of three new leukemia

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patients will hopefully alert clinicians to the possibility. In the five years since 1978, a total of 99 patients have been treated in our institute for teratoma, and these three patients represent the only deaths due to late complication or second malignancy. Patients A, B and C died 61, 17 and 4 months respectively from the start of chemotherapy. We conclude that patients with a germ cell tumor must not be denied an effective chemotherapeutic regime, but that long-term follow-up is mandatory to further evaluate the possible carcinogenic effect of these relatively new treatments. Further, we would suggest that there is now a case against overtreatment in the form of maintenance therapy or adjuvant therapy within or outside of a clinical trial.

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