Cytotoxic Chemotherapy for Cancer in Felty’s Syndrome: Role of Lithium Carbonate

By Richard Pazdur and Arthur H. Rossof

A 61-yr-old white man with Felty’s syndrome, who had previously undergone splenectomy, was referred to Rush-Presbyterian-St. Luke’s Medical Center for administration of this study because of the high-risk gastric cancer patients and was referred to Rush-Presbyterian-St. Luke’s Medical Center for administration of this treatment. Several granulocyte counts were then found to be approximately 0.7 x 10^9/liter.

Because of the patient’s persistent desire to proceed with therapy, a trial of lithium carbonate was instituted in March 1979, with an increase of the neutrophil count to 2.5 x 10^9/liter over the subsequent 2 wk. Chemotherapy was then administered according to the schedule and dosages depicted in Fig. 1. The patient tolerated the chemotherapy well with dose modifications (treatments B-D, see Fig. 1) subsequent to the neutropenia observed after treatment A. Because of a rising carcinoembryonic antigen (CEA) titer, an exploratory laparotomy was performed on day 238, which failed to demonstrate recurrent or persistent disease. Lithium carbonate was discontinued 2 days prior to the surgery. A culture-negative postoperative febrile illness resulted in an increased granulocyte count. After the febrile episode (and the discontinuation of lithium), the patient returned to his persistent neutropenic state (see Fig. 1).

DISCUSSION

Felty’s syndrome is characterized by splenomegaly, neutropenia, and rheumatoid arthritis. 14 The clinical course is frequently marked by repeated infections, often life-threatening. 14,15 A definite correlation between the severity of neutropenia and frequency of infection, as observed in leukemia, has not been delineated in Felty’s syndrome. 14,15 Nevertheless, the major clinical application of lithium carbonate in Felty’s syndrome has been aimed at increasing the granulocyte count to avert infections. 8,11,12 This report indicates an additional role of the drug in these patients. Lithium carbonate may increase the total neutrophil count to allow the initiation of cytotoxic chemotherapy.

In the present case, an absolute neutrophil count of 0.7 x 10^9/liter at the start of chemotherapy would have precluded the use of cytotoxic regimens effective in gastric carcinoma. However, with lithium carbonate, an increase of the neutrophil count to 2.5 x 10^9/liter allowed effective delivery of drugs without serious or unusual myelosuppression. Serum lithium levels were monitored weekly and were maintained in the therapeutic range for psychiatric patients. 17-19
Fig. 1. A graph illustrating the course of the patient described in this article. Each arrow indicates the day on which the particular chemotherapy course was initiated.
During therapy with lithium, the patient experienced a tolerable fine tremor that abated despite continuation of therapy. Interestingly, after discontinuation of lithium carbonate, a febrile episode was observed. The cyclic nature of the granulocyte count observed in this case is similar to that noted in hematologically normal individuals receiving the same chemotherapeutic regimen. The nadir of the granulocyte count after 5-fluorouracil occurs approximately 10 days after administration, whereas methyl-CCNU causes a delayed and prolonged nadir occurring approximately 28 days after receiving the drug. Myelosuppression on days 21–35, as experienced by our patient, has also been noted in some of our hematologically normal patients receiving the same drugs. In addition, after this period of myelosuppression, our patient’s neutrophil count rose abruptly to his new baseline level achieved after initiating lithium.

Splenectomy in Felty’s syndrome may initially give beneficial results. Although granulocyte counts in the normal range may be achieved initially, they may not be sustained. The lack of uniform response to splenectomy suggests that hypersplenism alone is not the cause of the neutropenia. Of the 18 reported patients given treatment with lithium carbonate for Felty’s syndrome, none has been reported to have undergone previous splenectomy. Our patient has had a prior splenectomy that failed to alter his granulocyte count permanently.

Decreased urinary and serum granulocyte colony-stimulating activity (CSA) has been documented in splenectomy suggests that hypersplenism alone is not the cause of the neutropenia. Of the 18 reported patients given treatment with lithium carbonate for Felty’s syndrome, none has been reported to have undergone previous splenectomy.

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R Pazdur and AH Rossof