CORRESPONDENCE

An Ethical Approach to Chemotherapy in Private Practice

Over the past several decades, several key principles have evolved in medical oncology which limit the dose range and length of chemotherapy courses. The first principle states that, when a tumor is shown to progress during a course of chemotherapy, continued treatment with that same chemotherapy protocol no longer benefits the patient. A corollary to this contends that, when cancer is seen to relapse while a patient is on adjuvant chemotherapy, further treatment with the same regimen does not benefit the patient. These precepts are based on the idea that a particular drug therapy has no anticancer effect when the bulk of tumor cells is resistant to those drugs. Patients continuing to receive the same drugs still suffer adverse side effects but no longer achieve palliation or remission from their malignancy. Rational alternatives include second-line regimens of merit, palliative radiation, supportive care, or participation in a clinical trial of a new drug.

Another principle argues that optimal adjuvant chemotherapy is limited to a rather brief course, somewhere between 4 and 12 months. Patients are unlikely to gain from continuing adjuvant chemotherapy for durations in excess of 1 year. For example, a 6-month regimen appears to be all that is necessary for successful adjuvant chemotherapy with cyclophosphamide, methotrexate, and fluorouracil in breast cancer. A final principle, once debated, is that for the majority of malignancies, full-dose intensity must be sought after to achieve a meaningful anticancer effect. This last concept has been borne out in many retrospective analyses and is now uniformly accepted.

There are physicians who disregard these principles in order to maintain a very lucrative chemotherapy practice. Patients are routinely continued on ineffective chemotherapy despite obvious progression of disease. Others are given adjuvant chemotherapy for long periods, even extending to 5 years for high-risk resected tumors, despite a lack of supportive studies. Patients are sometimes treated with doses as little as one fourth of those in recommended regimens in order to facilitate sustained compliance. Furthermore, patients are compelled to undergo weekly complete blood cell counts despite little or no myelosuppression. This kind of unscrupulous routine is self-serving, costly, and detrimental to the patient. It is unsettling that this practice can continue unchecked in the face of efforts at cost containment. Physicians who knowingly prescribe ineffective chemotherapy to patients with refractory cancers are unlikely to be challenged, given that community non-oncologists and insurance representatives have no mechanism to identify ineffective treatment.

I am surprised that the issue of ethical treatment in cancer patients has not been addressed in our standard oncology textbooks or has not been brought up by the American Society of Clinical Oncology. I believe that the time has come to publish a code of ethical standards for oncologists regarding the proper use of chemotherapy, particularly regarding the duration of treatment and treatment in the setting of tumor resistance. I have brought this concern to the attention of several members of the American Society of Clinical Oncology and hope that work will be done to achieve this goal.

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Interleukin-2 and Splenic Enlargement

Recombinant interleukin-2 (rIL-2) has been used with some success in the treatment of human and murine malignancies, but it has many well-documented side effects (*1*). Splenomegaly during rIL-2 therapy has been noted in mice but, to date, has not been reported in humans.

A retrospective study was carried out using the hematologic and radiologic results obtained from 16 patients who had had metastatic colorectal or renal tumors (Table 1) and had been in the Eurocetus rIL-2 trials between 1988 and 1991 (*2*,*3*). The treatment schedules involved intravenous rIL-2 given at a standard dose of 3×10^6 Cetus units/m^2 per day for a continuous period of 120 hours; this treatment was given once a month for those with colorectal cancer and twice a month for those with renal cancer. Two to 3 weeks after completion of each month's treatment, patients had their disease status assessed with computed tomography and/or ultrasound scans unless there was obvious disease progression. Those patients whose disease remained static or who experienced tumor shrinkage were given four cycles with two additional treatments of rIL-2 if a partial or complete remission had been obtained.

Only seven of the 16 patients completed four or more courses of rIL-2; the remaining nine patients were withdrawn from the trial as a result of progressive disease. Hematologic and radiologic findings are as tabulated in Table 1. Eosinophilia was noted in 15 of the 16 patients during treatment, and a significant rebound lymphocytosis was achieved by 11. Of the 16 patients, only nine had scans that, on each review, included the spleen. Of these, five were found to have an increase in their splenic size, ranging from 24% to 65% of the initial length, and none had evidence of metastatic disease. Four of the five had completed five or more courses of rIL-2. Patient 6 had only 2.5 pulses but had increasing hepatomegaly, as did patient 12, and raised portal venous pressure may have contributed to the splenic enlargement. No other assessable patients had evidence of metastatic liver disease. Apart from patient 6, no patient who had four or fewer pulses of rIL-2 had significant splenic enlargement.

Rebound lymphocytosis has been found to be associated with better response to rIL-2 (*4*), but we were unable to demonstrate this association and rebound lymphocytosis was not significantly associated with increasing splenic size. Splenomegaly has been noted in transgenic mice expressing the IL-5 gene (*5*), which is associated with