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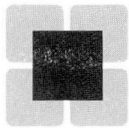

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What does tumor shrinkage mean to the patient receiving chemotherapy?

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ONCOLOGISTS generally consider a therapy effective if it causes the tumor to diminish in size. However, what does tumor shrinkage really mean to the patient and his or her quality of life? Does the therapy alleviate the patient's symptoms? Does it prolong the patient's life?

Because the drugs used to cure or palliate advanced cancers cause serious side effects (eg, emesis, fatigue, renal dysfunction, bone marrow suppression), it is important to evaluate their effectiveness in these ways after they are started to determine whether to continue them.

DOES TUMOR SHRINKAGE REDUCE SYMPTOMS?

Tumor-related symptoms, if any are present, may abate as the tumor shrinks. In situations in which it is difficult to document tumor shrinkage objectively (eg, diffuse abdominal carcinomatosis, lymphangitic spread of tumor to the lung), relief of symptoms (eg, less dyspnea or pain, better appetite, weight gain) is often a reasonable surrogate for response of the cancer to the treatment.

It is important to document if chemotherapy does make the patient feel better, because a major aim of antineoplastic treatment is to maximize the patient's quality of life. In addition, even if side effects occur, continuing the chemotherapy can often be justified if it causes less discomfort than the cancer symptoms it has relieved. For example, a woman with advanced ovarian cancer may accept moderately severe emesis due to cisplatin treatment if the treatment produces a major reduction in malignant ascites, a reduction in abdominal pain, and a significant increase in appetite. This type of symptomatic benefit is generally fairly simple to determine.

DOES TUMOR SHRINKAGE PROLONG SURVIVAL?

A more difficult question is whether tumor shrinkage leads to prolonged survival.

Partial response

Oncologists define a response to treatment as a decrease in tumor mass of at least 50%.[1] Will a patient who demonstrates such a "partial response" survive longer than a patient whose cancer responds less, or not at all?

Unfortunately, available evidence provides little support for this assumption. In fact, numerous randomized trials of chemotherapy in many tumor types have failed to prove that patients survive longer with regimens that produce statistically higher partial response rates than with regimens that produce lower response rates.[2,3] Why should this be?

Although a 50% reduction in the size of a cancerous mass may reduce symptoms strikingly and produce impressive changes on physical or radiographic examination, it generally represents a relatively small reduction in the body's tumor burden, ie, the total number of cancer cells present in the body. If the cancer begins to grow only slightly faster or if a

larger fraction of malignant cells begins to divide, any benefit gained from reducing the tumor mass is relatively quickly overcome, and the treatment will have little or no impact on survival. Partial tumor responses have led to only modest increases in survival in non-small cell lung cancer and metastatic cancers of the colon and prostate.

Complete remission

In contrast, in a complete remission the tumor shrinks so much that at the end of treatment there is no longer any clinical evidence of disease by physical examination, by biochemical and radiographic evaluation, or by the patient's symptoms. To achieve complete remission, the number of tumor cells killed is likely several orders of magnitude greater than in a partial response. Patients achieving a complete remission generally survive much longer than those whose tumors fail to respond to treatment or who have only a partial response. Complete remissions are possible in lymphomas, leukemias, germ cell tumors, and cancers of the breast and ovary.

EXCEPTIONS AND COMPLEXITIES

There are exceptions to these generalizations. Some patients with tumors that are usually resistant to chemotherapy can have major responses to treatment; conversely, some patients with tumors that are usually very sensitive to chemotherapy do not have any response to therapy.

Slow- vs fast-growing tumors

In addition, a major factor influencing the survival of any cancer patient is the inherent growth rate and metastatic potential of the tumor, sometimes referred to as the "natural history" of the disease. A patient may survive a long time with a relatively slow-growing tumor, whether or not it responds to treatment. Conversely, a rapidly growing tumor may kill quickly, even if the patient experiences a major, but transient, response to treatment.

Stable tumors

Adding to this complexity is a category of response called "stable disease," in which a cancerous mass neither grows nor shrinks. Is stable disease the result of antineoplastic drugs killing enough cancer cells to balance the continued growth of a chemotherapy-resistant tumor cell population? Or is it another manifestation of the natural history of disease in certain persons, in which chemotherapy does not really help at all?

This is an important issue. Many studies have demonstrated that cancer patients with stable disease can enjoy an excellent quality of life for an extended time. If anticancer drugs cause this prolonged survival, their cost and potential toxicity is justified. However, if patients would survive just as long without the cytotoxic drugs (and their side effects, inconvenience, and expense), it is appropriate to question the use of such treatment.

A PERSPECTIVE ON TREATMENT

A major reduction in tumor size may prolong a patient's life, but in general only if the patient has a complete or near-complete response to treatment. Less-impressive reductions in tumor bulk, including stable disease, may also extend survival, but in general only modestly. Therefore, to the patient, the major benefit of tumor shrinkage is a lessening or prevention of cancer symptoms. This point bears keeping in mind when attempting to balance the toxicity and cost of treatment with the potential benefit to the individual patient.

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