103e Principles of Cancer Treatment

Edward A. Sausville, Dan L. Longo

CANCER PRESENTATION

Cancer in a localized or systemic state is a frequent item in the differential diagnosis of a variety of common complaints. Although not all forms of cancer are curable at diagnosis, affording patients the greatest opportunity for cure or meaningful prolongation of life is greatly aided by diagnosing cancer at the earliest point possible in its natural history and defining treatments that prevent or retard its systemic spread. Indeed, certain forms of cancer, notably breast, colon, and possibly lung cancers in certain patients, can be prevented by screening appropriately selected asymptomatic patients; screening is arguably the earliest point in the spectrum of possible cancer-related interventions where cure is possible (Table 103e-1).

DETECTION OF A CANCER

The term *cancer*, as used here, is synonymous with the term *tumor*, whose original derivation from Latin simply meant "swelling," not otherwise specified. We now understand that the swelling that is a common physical manifestation of a tumor derives from increased interstitial fluid pressure and increased cellular and stromal mass per volume, compared to normal tissue. Tumors historically were referred to as *carcinomas*, or "crab-like" infiltrating tumors, or *sarcomas*, or "fleshy tumors," derived from the Greek terms for "crab" and "flesh," respectively. Leukemias are a special case of a cancer of the blood-forming tissues presenting in a disseminated form frequently without definable tumor masses. In addition to localized swelling, tumors present by altered function of the organ they afflict, such as dyspnea on exertion from the anemia caused by leukemia replacing normal hematopoietic cells, cough from lung cancers, jaundice from tumors disrupting the hepatobiliary tree, or seizures and neurologic signs from brain tumors. Hemorrhage is also a frequent presenting sign of tumors involving hollow viscera, as are decreases in the number of platelets and inappropriate inhibition of blood coagulation. Thus, although statistically the fraction of patients with cancer underlying a particular presenting sign or symptom may be low, the implications for a patient with cancer of missing an early-stage tumor call for vigilance; therefore, persistent signs or symptoms should be evaluated as possibly coming from an early-stage tumor.

Evidence of a tumor's existence can objectively be established by careful physical examination, such as enlarged lymph nodes in lymphomas or a palpable mass in a breast or soft tissue site. A mass may also be detected or confirmed by an imaging modality, such as plain x-ray, computed tomography (CT) scan, ultrasound, positron emission tomography (PET) imaging, or nuclear magnetic resonance approaches. Sensitivity of these technologies varies considerably, and the index of suspicion for a tumor should match the technology chosen. For example, low-dose helical CT scans are superior to plain chest radiographs in detecting lung cancers. Another way of initially establishing the existence of a possible tumor is through direct visualization of an afflicted organ by endoscopy.

TABLE 103e-1 SPECTRUM OF CANCER-RELATED INTERVENTIONS

Screening for cancer in an asymptomatic patient
Consideration of cancer in a differential diagnosis
Physical examination, imaging, or endoscopy to define a possible tumor
Diagnosis of cancer by biopsy or removal:
Routine histology
Specialized histology: immunohistochemistry
Molecular studies
Cytogenetic studies
Staging the cancer: Where has it spread?
Treatment
Localized
Systemic
Supportive care
During treatment: related to tumor effects on patient
During treatment to counteract side effects of treatment
Palliative and end of life
When useful treatments are not feasible or desired

ESTABLISHING A CANCER DIAGNOSIS

Once the existence of a likely tumor is defined, unequivocally establishing the diagnosis is the next step in the spectrum of correctly addressing a patient's needs. This is usually accomplished by a biopsy procedure and the emergence after pathologic examination of an unequivocal statement that cancer is present. The underlying principle in cancer diagnosis is to obtain as much tissue as safely as possible. Due to tumor heterogeneity, pathologists are better able to make the diagnosis when they have more tissue to examine. In addition to light microscopic inspection of a tumor for pattern of growth, degree of cellular atypia, invasiveness, and morphologic features that aid in the differential diagnosis, sufficient tissue is of value in searching for genetic abnormalities and protein expression patterns, such as hormone receptor expression in breast cancers, that may aid in the differential diagnosis or provide information about prognosis or likely response to treatment. Efforts to define "personalized" information from the biology of each patient's tumor and pertinent to each patient's treatment plan are becoming increasingly important in selecting treatment options. The general internist should make sure that a patient's cancer biopsy is appropriately referred from the surgical suite for important molecular studies that can advise the best treatment (Table 103e-2).

Similar-appearing tumors by microscopic morphology may have very different gene expression patterns when assessed by such techniques as microarray analysis for gene expression patterns using gene

TABLE 103e-2 DIAGNOSTIC BIOPSY: STANDARD OF CARE MOLECULAR AND SPECIAL STUDIES

Breast cancer: primary and suspected metastatic
Hormone receptors: estrogen, progesterone
HER2/neu oncoprotein
Lung cancer: primary and suspected metastatic
If nonsquamous non-small cell: epidermal growth factor receptor mutation; alk oncoprotein gene fusion
Colon cancer: suspected metastatic
Ki-ras mutation
Gastrointestinal stromal tumor
c-kit oncoprotein mutation
Melanoma
B-raf oncoprotein mutation
c-kit expression and mutation
Leukemia (peripheral blood mononuclear cells and/or bone marrow)
Cytogenetics
Flow cytometry
Treatment-defining chromosomal translocations
Bcr-Abl fusion protein
t(15,17)
inversion 16
t(8,21)
Lymphoma
Immunohistochemistry for CD20, CD30, T cell markers
Treatment defining chromosomal translocations:
t(14,18)
t(8,14)