Questions and Answers on Cancer

Cervical Carcinoma In Situ

Carcinoma in situ was diagnosed in a 46-year-old female by dilation and curettage and cold cone biopsy of the cervix. An abdominal panhysterectomy-salpingo-oophorectomy, bilateral with 2 cm. of vaginal cuff, was performed. The pathologist now reports that the hysterectomy specimen shows one area of very early invasion in the cervix. Both pathology reports were verified by competent pathologists. What is the further management of this patient?

M.D., Reading, Pennsylvania

A pathology report of "one area of very early invasion" does not give us quite enough information to make a specific recommendation in this case. The International Classification of cervical carcinoma now subdivides Stage I as follows:

Stage I
Carcinoma strictly confined to the cervix (extension to the corpus should be disregarded).
Stage Ia
Cases of early stromal invasion (preclinical carcinoma)
(1) Early stromal invasion
(2) Occult cancer
Stage Ib
All other cases of Stage I.
Stage Ia (1) refers to the very earliest phase of microinvasion where there is minimal breakthrough of the basement membrane. If this is the microscopic finding in the reported case, then I would consider the treatment complete and would recommend that nothing further be done except for vaginal smears at three-month intervals.

Stage Ia (2) on the other hand includes so-called occult carcinoma which refers to a more advanced form of microinvasive carcinoma. If this is the microscopic picture seen in the above patient, then I would be more concerned and would consider adding either radiotherapy or a pelvic node dissection and resection of the lateral ligaments and additional vaginal mucosa.

At the present time there is a grey zone between Stage Ia (1) and Ia (2) cancers which is more controversial. It includes minimal stromal invasion but with tumor emboli present in small vessels. Such a picture carries with it a poorer prognosis than the extent of the disease would lead one to believe. It also includes more extensive involvement of the stroma but in the immediate vicinity of the basement membrane. Where a tumor emboli in small vessels can be seen, most would agree that more radical treatment should be used. If this finding is present in this case, I would favor the treatment outlined for Stage Ia (2).

As this answer indicates, never has the clinician had to work more closely with the pathologist than at the present.

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Chemotherapy For Seminoma

In 1970, a man of advanced age was operated on for hydrocele, and a seminoma was discovered. An orchiectomy, but not a radical lymph node dissection, was performed. The lymph nodes of the groin and periaortic area were irradiated.

The patient felt well until recently. A tumor of the left suprACLavicular fossa has been biopsied, and the pathologic report is metastatic seminoma. Is there a good chemotherapy course for this patient?

M.D., Oak Hill, Ohio

First, carefully study the biopsy specimen to rule out elements which might indicate radioresistance. If the tumor is a pure seminoma, perform a lymphangiogram to make sure that all possible nodes within the abdominal cavity are detected. If no nodes are found, radiate the abdominal cavity, including the mediastinum and the left suprACLavicular mass with about 3500-3600 rads of megavoltage radiation in four weeks.

If, on the other hand, the biopsy indicates that the tumor is not a pure seminoma, give 30-40 mgs./kilo of Cytoxan every three weeks for two to three months. This regimen is best carried out in a specialized treatment center.

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Squamous Cell Carcinoma

A 65-year-old white male with hyperglycemia controlled by diet alone, an untreated (4 years) stasis ulcer encircling the middle third of the leg (dimensions: 10 cm. wide) and varicose veins, developed in the last four months a fungating (3.5 cm. diameter) area, diagnosed as squamous cell carcinoma with involvement of the underlying tibia.

Inguinal node biopsy was negative (two nodes; one deep, one superficial). Venography revealed incompetent saphenous system but no evidence of malignant involvement. Liver scan and liver function tests were normal. There was no evidence of metastases either clinically or chemically.

The ulcer bed and bone were resected and grafted successfully; amputation and complete groin dissection were deferred. After wound healing, the patient will receive methotrexate. Is this course reasonable and correct?

M.D., Philadelphia, Pennsylvania

This 65-year-old male with hyperglycemia controlled by diet alone with an untreated stasis ulcer and carcinoma invading the underlying tibia has been treated adequately provided that a wide enough excision of the underlying bone was carried out. It is quite reasonable to have deferred the amputation which should be an A.K. amputation if there is a recurrence. A more radical approach would involve a prophylactic groin dissection combined with an A.K. amputation. The difficulty in eradicating squamous cancer growing in bone is well known and resection of the underlying bone should be rather radical.

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Erythroleukemia

What is the treatment and life expectancy of the patient with erythroleukemia (Di Guglielmo's syndrome)?

M.D., Danbury, Connecticut

It is difficult to enunciate an accurate prognosis and a standard treatment for patients with erythroleukemia. First and foremost, precise criteria for the diagnosis of this disease have never been agreed on, and as a consequence, most studies of leukemia survival and treatment include such patients under the broad heading of acute myelocyte (or nonlymphocytic) leukemia. Second, the clinical course of this rare form of leukemia frequently includes a phase of refractory anemia which in some cases has lasted over a decade before a clearly malignant phase is apparent. On the other hand, other patients with similar (and perhaps identical) refractory anemias never develop leukemia. How and when, therefore, does the physician define the onset of erythroleukemia? At the first sign of any hematological abnormality? When megaloblastosis is first observed? When symptoms commence? Or when the course of the disease becomes rapidly progressive?

Despite these difficulties, a few small series and reviews present statistics on response and survival from the diagnosis of erythroleukemia to death. Most of these statistics are based on cases treated between 1956 and 1965, during which time 6-mercaptopurine with or without adrenocorticosteroids was the standard form of treatment for acute leukemia. Since 1965 there have been anecdotal reprints that cytosine arabinoside alone and in combination with other agents may be highly effective for erythroleukemia. These reported prognoses may be too conservative.

Reported survivals (diagnosis to death) range from two to 21 months with average (median) survivals of 3.5 to 7.0 months. In one study (Roath, Quarterly Journal of Medicine 33: 257, 1964), 73 percent of 18 patients survived six months or more, twice that of other categories of nonlymphocytic acute leukemia.

Erythroleukemia is generally considered to be relatively refractory to drug treatment, and remission induction rates in most reports are quite low. Again, this may reflect the uncertainty of the therapist as to when to initiate treatment in a slowly evolving malignancy (too early and too late, both being hazardous), but probably also reflects a more extensive marrow involvement and diminution of the ability of normal cells to regenerate from drug-induced injury analogous to the situation in the acute leukemic phases of chronic myelocytic leukemia or polycythema rubra vera. Accordingly, reported remission rates vary from inferior (one response in 18 patients) to perhaps identical (two of four) to results of treatment of acute myelocytic leukemia in its usual form.

Most authors agree that one should not use cytostatic drugs in patients whose only disease manifestation is disordered erythropoiesis. Such patients should receive transfusion support as needed together with careful monitoring of changes in clinical and bone marrow status. Progressive infiltration of the bone marrow with myeloblasts and promyelocytes or the development of life-endangering granulocytopenia should signal the need for antileukemic therapy. At that juncture, those agents and combinations of agents most effective in acute myelocytic leukemia should be administered, preferably in an institution and by personnel most knowledgeable in the treatment of leukemia.
and its complications. This will ensure the best possible care for the individual, and the most likelihood that more accurate and more current data on the response rate and prognosis of this category of leukemia will be accumulated.

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Metastatic Burkitt's Lymphoma

What is the management of a 9-year-old girl with Burkitt's lymphoma arising in the tonsils with spread to the stomach? What is the prognosis?

M. D., Danbury, Connecticut

While radiotherapy (in super-fractionated doses) is effective therapy for localized tumor deposits, the multicentric nature of Burkitt's lymphoma requires systemic chemotherapy. Cyclophosphamide, 40 mg./kg. I.V. in a single dose is the most effective therapy, and should be repeated every two weeks (upon recovery of the WBC) for a total of three to six courses. Methotrexate (15 mg./m.² p.o. daily for four days) with vincristine (1.4 mg./m.² I.V. on day one) is also effective in patients who become resistant to cyclophosphamide.

Frequent examination of cerebrospinal fluid to identify and treat meningeal involvement is important in initial evaluation and follow-up. Methotrexate 15 mg./m.² daily for four days administered intrathecally is effective. Thus far attempts at prophylaxis of central nervous system involvement have not been successful.

Future therapeutic trends to improve the outlook for patients with Burkitt's lymphoma include: (1) preventing meningeal involvement; (2) intensification of remission-induction chemotherapy; and (3) maintenance immunotherapy. These studies are currently in clinical trials, but it is too early to indicate whether the standard therapy recommended above should be altered.

Prognosis is obviously related to clinical stage on admission, although other variables such as EB virus titers to early antigen, immunological status, surgical reduction of tumor bulk and careful patient follow-up are all important prognostic determinants.

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Subcutaneous Bilateral Mastectomy

A woman with a past history of chronic cystic mastitis confirmed by biopsy had three negative mammograms which showed some deficit breast tissue from the previous surgical intervention. The patient has a marked breast phobia—her mother also had cystic mastitis and is now dying of breast cancer. Her present physician proposed that she have a subtotal bilateral mastectomy with follow-up silicone implants to reduce the risk of breast cancer from seven to eight percent to approximately one to two percent. Do you feel the proposed procedure is indicated?

M. D. Cranston, Rhode Island

The crux of the question is that the patient has a marked breast phobia. The recurrence of masses which are either watched or biopsied usually puts this type of patient into a severe depression. I would suggest a subcutaneous mastectomy, in this case, which allows for the removal of most of the breast tissue. All agree that 100 percent of the breast tissue cannot be removed, but with a care-
ful dissection it is possible to remove almost all of it.

When a careful dissection is carried out, skin flaps which are left behind, especially in the areas of the nipple and any previous excision sites, are extremely thin. I therefore prefer to wait until the flaps soften in about six months before insertion of the prosthesis. If one leaves the flap thick enough to allow for immediate insertion of the prosthesis, then all of the breast tissue has not been removed.

Even when a woman does not have a marked cancer phobia and has undergone three or more biopsies, it might be well to consider the possibility of doing a subcutaneous mastectomy with a later insertion of a prosthesis.

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Metastatic Liver Lesion

A 45-year-old menstruating female recently underwent a left mastectomy for advanced cancer of the breast. At the time of oophorectomy, a metastatic lesion of the liver was found. Please advise on therapy.

M.D. Springfield, Massachusetts

Oophorectomy remains the most effective means of systemic palliation for menstruating women with disseminated cancer of the breast; at least one-third obtain objective benefit for a minimum of six months. The chance of benefit increases progressively as the patient approaches menopause and decreases abruptly thereafter. Visceral metastases respond less frequently than do those in the bone or soft tissues. Nevertheless, secondary metastases in the liver regress in approximately 15 percent of patients, and the four to six weeks required to assess the response to oophorectomy by means of hepatic scans and serial liver function tests are well invested before proceeding to further therapy.

A favorable response to oophorectomy would influence the future choice between hypophysectomy or adrenalectomy when relapse occurs. Recent evidence also indicates that the presence of estrogen receptors in tumor tissue greatly favors a response to adrenalectomy. If involvement of the liver is limited, secondary endocrine ablations are often effective. Fluorouracil used concomitantly with adrenalectomy can improve the chance of remission, an important consideration if the disease is rapidly progressive. Androgens are rarely of value if castration fails, and estrogens are not indicated in premenopausal women. In the absence of hormonal responsiveness, non-hormonal chemotherapy, particularly with fluorouracil, to which hepatic metastases respond in about 40 percent of cases, or with a recognized program of combination chemotherapy, would be appropriate.

Hepatic metastases are an ominous development in this disease; 90 percent of such patients fail to survive more than 12 months after their recognition. For this reason, effective management is more urgent than usual. However, practical guidelines for a program of palliation include: (1) Have histologic proof of metastases whenever possible; (2) Employ the most effective methods of therapy early; (3) Have objective means for assessing tumor responses; (4) Continue with one method of treatment as long as it is successful; and (5) Have evidence of disease progression before going to another method.

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