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REPORT TO PHYSICIANS

OCTOBER 2009 VOL. 54, NO. 10

Oncology

Early Testicular Cancer

Strategies that mitigate the risk of recurrence have boosted the long-term success of treatment.

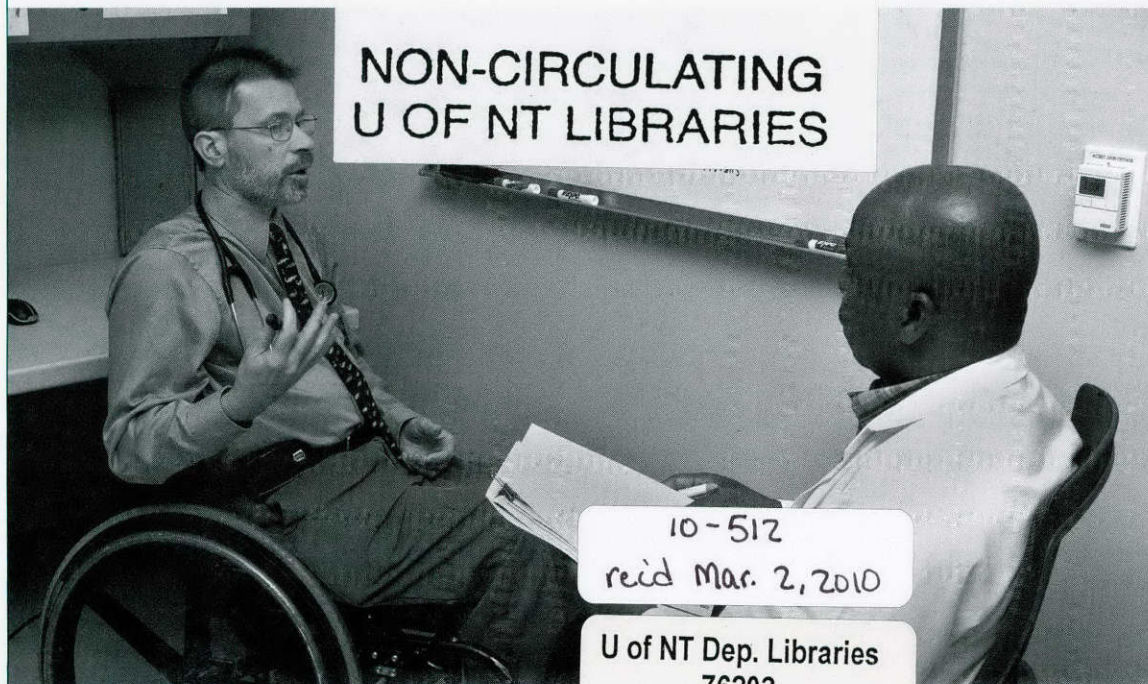
By John LeBas

When testicular cancer is found early—that is, when the tumor is confined to the testicle—the cancer is almost always curable.

In fact, patients treated at this disease stage can typically expect to lead full lives with few long-term effects from the cancer or its treatment on their fertility or health.

Much of this success in curing testicular cancer has resulted from treating potential metastasis of the primary tumor. Physicians at The University of Texas M. D. Anderson Cancer Center continue to refine treatment approaches for early-stage testicular cancer to achieve an optimal outcome for each patient.

“There have been significant advances in how chemotherapy, surgery, and radiation are integrated to produce an optimal outcome for patients with early testicular tumors,” said Lance C. Pagliaro, an associate professor in the Department of Genitourinary Medical Oncology at The University of Texas M. D. Anderson Cancer (Continued on page 2)



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Dr. Lance Pagliaro (left) and nurse practitioner William Osai discuss the treatment plan for a patient with testicular cancer. Treatment of the disease at its earliest stage can usually be done in a way that limits both recurrence risk and side effects, Dr. Pagliaro said.

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Early Testicular Cancer

(Continued from page 1)

Center. "This involves a balance between minimizing the long-term risk of recurrence and minimizing the long-term risks of treatment side effects."

Early-stage testicular cancer characteristics

In the United States, about 7,000 men each year are newly diagnosed with testicular cancer, most commonly of germ cell origin. About half of those germ cell tumors are seminomas; the rest are single- and mixed-histology non-seminomas. About 85% of patients are cured with surgery alone or surgery followed by chemotherapy or radiation therapy, and the chance of a cure is highest when the tumor is confined to the testis (clinical stage I).

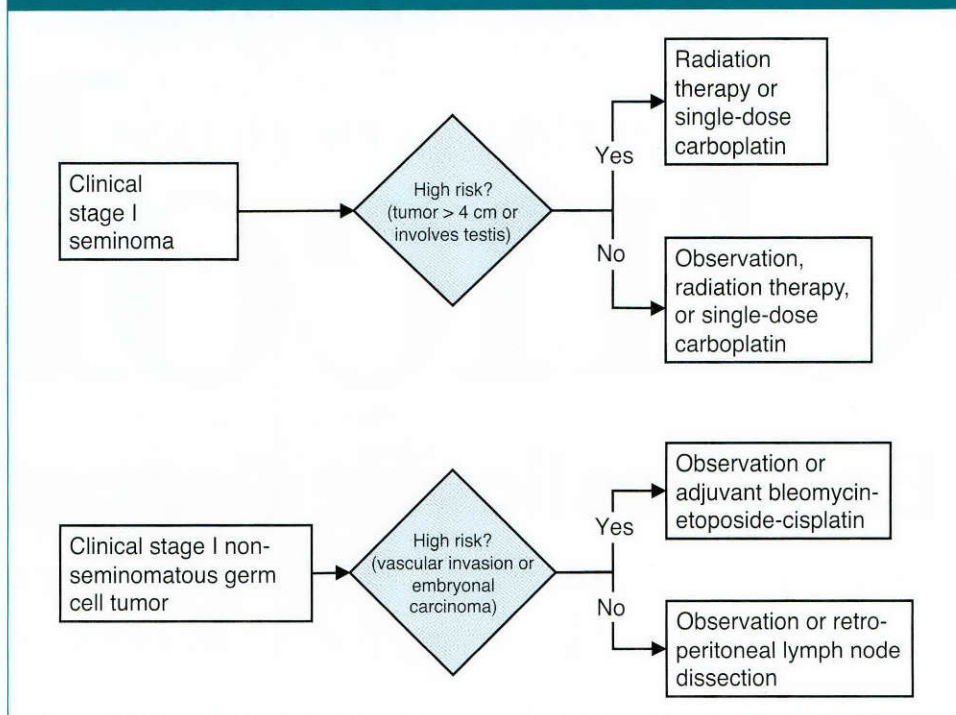
For confined tumors, only one testicle is usually removed (orchidectomy). After orchidectomy, a decision about whether to give further treatment is made based on the likelihood that an apparently confined tumor may have actually already metastasized.

Some patients are considered to have high-risk clinical stage I disease, in which histologic characteristics of the tumor indicate a higher chance of metastasis. For both seminoma and non-seminoma, evidence of lymphovascular invasion indicates that a tumor is at high risk of spread; in addition, the presence of embryonal carcinoma in non-seminomas increases the risk of spread. Patients with such tumor characteristics are candidates for immediate adjuvant (post-orchidectomy) treatment or careful observation, in which further treatment is delayed unless testing reveals evidence of metastasis.

The standard adjuvant treatment options depend on the disease type, which is determined by pathologic examination of the tumor after orchidectomy, and alternative treatment options for each type have emerged. The refinement of available treatments has not only decreased occurrence but also allowed fertility to be preserved in a majority of clinical stage I testicular cancer patients—important since the disease usually develops in late adolescence or early adulthood.

"However, we have not eliminated the risk that fertility will be damaged.

Adjuvant Treatment of Early-Stage Germ Cell Testicular Tumors



Also, there are long-term risks of chemotherapy, such as cardiovascular disease and second malignancies," Dr. Pagliaro said. "Therefore, the burden of these risks becomes the paramount consideration in selecting adjuvant intervention or observation for selected patients."

Seminomas

The standard adjuvant therapy for stage I seminoma is radiation therapy. In recent years, treatment fields have been refined to limit the side effects of radiation therapy. While the chance of affecting fertility is low with radiation, there is still a higher risk of second malignancies as compared to the normal population. Two main approaches have been developed as alternatives to radiation therapy after orchidectomy for seminomas:

Chemotherapy. Patients receive one dose of carboplatin chemotherapy. This approach kills micrometastases or isolated cancer cells throughout the body but there is limited knowledge about the long-term risks.

Observation. This approach decreases the likelihood of unnecessary adjuvant therapy through the careful monitoring of selected patients. Only if metastasis is clinically detected will therapy be given.

The disadvantage of observation is that patients must adhere to a rigorous, long-term follow-up schedule—and failure to do so can ultimately result in unchecked disease progression.

The data comparing observation and chemotherapy have evolved slowly, since a follow-up period of 20–30 years is needed to accurately assess recurrence rates, rates of second malignancies, and the cardiovascular effects of therapy.

Clinical trials have supported the use of platinum-based chemotherapy agents such as carboplatin, said Dr. Pagliaro. For example, he cited a recent European study¹ of patients randomly assigned to receive adjuvant carboplatin or radiation therapy after orchidectomy for stage I seminoma. The study found that each group experienced similar recurrence rates. Long-term follow-up is needed, but based on the results of this study and others like it, adjuvant carboplatin is now sometimes given for one or two cycles instead of radiation therapy to treat stage I seminoma.

"The role of platinum-based chemotherapy has been well established, and the high cure rates for seminoma suggest that we are doing well with the treatments we have available," Dr. Pagliaro said. "But there continues to be vigorous debate about how much

chemotherapy is appropriate and whether it might be better for some patients to be carefully observed for recurrence before receiving further treatment after orchiectomy. What we are really trying to determine is which approach will produce the best outcome for each patient in terms of limiting both recurrence and effects of therapy.”

Non-seminomas

The standard adjuvant therapy for stage I non-seminoma testicular cancer is actually a second surgery—prophylactic retroperitoneal lymph node dissection (RLND). In this surgery, the lymph nodes most likely to be the initial sites of metastasis are removed. The advantage of RLND is that metastasis can be completely removed if it is confined to the retroperitoneal lymph nodes, increasing the chance of a cure; the disadvantage is that RLND can result in damage to nerves that control ejaculation and fertility.

To reduce risk to fertility, surgeons at M. D. Anderson perform nerve-sparing RLND, a procedure that is available at only a handful of centers. This surgery attempts to preserve the sympathetic nerve trunks responsible for maintaining ejaculation and fertility, and the techniques have been improved in recent years. “We have developed a better understanding of the retroperitoneal pattern of spread and where the sympathetic nerve trunks are. This helps us properly select patients in a way that doesn’t appear to be reducing the cure rate,” said Louis L. Pisters, M.D., a professor in the Department of Urology. The nerve-sparing approach has increased the likelihood that normal ejaculation will be preserved following surgery.

RLND is performed for patients who have early-stage non-seminoma with no clinical signs of spread (i.e., those with apparently confined tumors who might have micrometastases in the lymph nodes). For patients with lymphovascular invasion in the primary tumor or other histologic characteristics of high-risk disease, the surgery is not considered appropriate or feasible because the amount of metastatic tumor is likely too great, Dr. Pisters said. Likewise, radiation therapy is not appropri-

“We have developed a better understanding of the retroperitoneal pattern of spread and where the sympathetic nerve trunks are.”

– Dr. Louis Pisters

ate for high-risk stage I non-seminoma since this tumor is not as sensitive to radiation as seminoma.

Instead of RLND or radiation therapy, patients at M. D. Anderson who have high-risk early-stage non-seminoma usually receive adjuvant chemotherapy or are carefully observed for metastasis before receiving any therapy. The standard chemotherapy is two courses of combined bleomycin-etoposide-cisplatin (BEP), a regimen that lowers the risk of recurrence from 50% in high-risk non-seminoma to about 2% but increases the risk of second malignancies and cardiovascular disease.

Separate European studies^{2,3} have found that one course of BEP instead of two may result in a similar reduction of recurrence risk with less toxicity, but no randomized study comparing one versus two courses has been conducted. A study of 745 men in Sweden and Norway compared one course of BEP to observation (with patients assigned to therapy in a risk-adaptive fashion)

and showed that the chemotherapy significantly reduced risk of recurrence³. “These data have prompted a re-evaluation of combination chemotherapy involving platinum-based agents as a preferred option over RLND for adjuvant intervention in patients who are known to be at high risk for recurrence,” Dr. Pagliaro said.

Following adjuvant therapy

After initial treatment, non-seminoma germ cell tumors are most likely to recur in the 2 to 3 years following initial therapy. Seminomas can recur much later, and patients should be evaluated regularly for at least 10 years, Dr. Pagliaro said. Most patients, however, will never experience a recurrence. ●

For more information, call Dr. Pagliaro at 713-792-2830 or visit www.mdanderson.org and navigate to the Genitourinary Cancer Center page.

¹ Oliver RT, Mason MD, Mead GM, et al. Radiotherapy versus single-dose carboplatin in adjuvant treatment of stage I seminoma: a randomised trial. *Lancet*. 2005;366(9482):293-300.

² Albers P, Siener R, Krega S, et al. Randomized phase III trial comparing retroperitoneal lymph node dissection with one course of bleomycin and etoposide plus cisplatin chemotherapy in the adjuvant treatment of clinical stage I nonseminomatous testicular germ cell tumors: AUO trial AH 01/94 by the German Testicular Cancer Study Group. *J Clin Oncol*. 2008;26(18):2966-2972.

³ Tandstad T, Dahl O, Cohn-Cedermark G, et al. Risk-adapted treatment in clinical stage I non-seminomatous germ cell testicular cancer: the SWENOTECA management program. *J Clin Oncol*. 2009;27(13):2122-2128.

Clinical Trials in Testicular Cancer

High-Dose Chemotherapy for Poor-Prognosis Relapsed Germ-Cell Tumors (2008-0378). Principal investigator (PI): Yago Nieto, M.D., Ph.D. The goal of this phase II clinical research study is to learn whether bevacizumab, when given in combination with 2 cycles of high-dose chemotherapy, can help to control germ-cell tumors. The first cycle of chemotherapy will include the drugs gemcitabine, docetaxel, melphalan, and carboplatin. The second cycle of chemotherapy will include the drugs ifosfamide, carboplatin, and etoposide. The safety of these drug

combinations will also be studied.

Phase II Study of Sunitinib Malate in Refractory Germ Cell Tumors (2006-0685). PI: Lance Pagliaro, M.D. The primary goal of this clinical trial is to define the 12-week progression-free survival rate in refractory germ cell tumors treated with sunitinib malate. Secondary goals are to determine the objective response rate to therapy, tumor marker outcomes, qualitative and quantitative toxicity, and putative biomarkers of response to therapy in refractory germ cell tumors. ●

Metastatic Rectal Cancer

First-Line Treatment Options That Prioritize Cure Over Palliation

Introduction

According to the American Joint Committee on Cancer tumor-node-metastasis staging system, stage IV rectal cancer is defined as a tumor that has spread to at least one distant site, commonly the lung and liver. The National Comprehensive Cancer Network (NCCN) notes that for 75%–90% of rectal cancer patients who present with liver metastases at diagnosis, the disease is considered unresectable; nearly all will eventually die of the disease if they cannot undergo surgery.

Those sobering statistics mean that patients with metastatic rectal cancer are often treated with a strictly palliative intent, whereby surgery is deferred and chemotherapy is provided not for cure but to prolong overall survival. Recently, the approach has changed for some patients: treatment advances have allowed initially unresectable disease to be “downsized” to resectable status with neoadjuvant chemotherapy and/or combined chemotherapy and radiation therapy (chemoradiation). Owing to those advances, patients diagnosed with metastatic rectal cancer at The University of Texas M. D. Anderson Cancer Center are now considered for curative treatment.

The key is the timing and sequence of treatments, which are based on a thorough evaluation before any treatment is given and on continual monitoring and re-evaluation. The individual patient factors that determine the treatment plan are so varied that there is no typical sequence. The plan is a delicate and carefully orchestrated one, and it must be devised and carried out in real-time collaboration among specialists from multiple disciplines.

Initial evaluation

When a patient is diagnosed with stage IV rectal cancer, a comprehensive treatment plan should be developed before any treatment begins—and the decisions that shape the plan are vital to the patient’s potential survival. “Long-term survival may be possible even if the patient has 10 or more liver metastases,” said Eddie K. Abdalla, M.D., an associate professor in the Department of Surgical Oncology. “The patient’s best hope is a careful initial evaluation and an exquisitely timed and managed treatment sequence.”

The first decision is whether a curative approach is possible. To answer that question, the initial evaluation must be thorough and multidisciplinary: the patient should be directly examined by all of the physicians who might be involved in the treatment plan. According to George Chang, M.D., an assis-

tant professor in the Department of Surgical Oncology, the initial evaluation should include a pretreatment proctoscopic examination by the surgeon who will perform the rectal surgery. At M. D. Anderson, the evaluation might also include computed tomography, positron emission tomography, magnetic resonance imaging, and endorectal ultrasonography studies—all of which yield different but complementary information.

Among the more important questions to be addressed in the initial evaluation are whether the primary tumor is likely to grow and, if it is, whether it would then become unresectable or symptomatic. “At M. D. Anderson, the treating physicians review each patient’s case individually to determine the optimum sequence of treatment, including the need for surgical or endoscopic intervention.”

Treatment modalities

Rectal surgery

For advanced rectal cancer to be cured, the primary and metastatic tumors must be completely surgically resected. In the past, surgical resection of the primary tumor was often performed without consideration of the overall treatment plan. Today, the timing of resection of the primary tumor in relation to resection of the metastasis and to chemoradiation administration is carefully considered for each individual patient. The goal is to ensure that optimal treatment can be performed with each modality, which may mean that the first step is not resection of the primary tumor, Dr. Chang said.

When surgical resection of the primary tumor is performed, it is important to consider whether the goal of treatment is curative or palliative. It is also important to involve a hepatobiliary specialist to determine whether curative resection of any liver tumors can be performed. Depending on the extent of rectal and liver surgery needed, it may be possible to perform both surgeries at the same time and avoid the need for multiple anesthetics, hospitalizations, and recovery periods. The goal should be complete resection of the primary tumor.

Following surgery, the colorectal surgeons review the resection specimens face-to-face with the gastrointestinal pathologist, Dr. Chang said. “The advantage for the patient is that there is never a question about the specimen because of confusion about the operative or pathologic findings, for example, and therefore we all have a clearer understanding going forward. This also allows for the best chance for restoring intestinal continuity without a permanent colostomy and without compromising oncologic outcome.” Similar pathology consultations are

also valuable when physicians are evaluating tumor response to chemotherapy.

Dr. Chang, who specializes in colorectal tumors, said local recurrences of rectal cancer can be very difficult to treat. Unfortunately, local recurrence is a common type of rectal cancer progression after palliative surgical therapy. Therefore, it is critical that the treatment sequence be devised to yield the optimal conditions for a complete resection of the primary tumor and metastatic disease. This may include neoadjuvant chemoradiation, particularly for large or bulky tumors in the pelvis. “When we operate with the intent to cure, we want to have confidence that the cancer will not recur,” Dr. Chang said. “In addition, as these tumors often respond to chemotherapy and radiation therapy, resulting in tumor downsizing, the adjacent tissue becomes more accessible and we can more readily remove all tumor-bearing tissue and prevent local recurrence.” Based on the group’s experience, the risk for local recurrence after primary resection should be less than 10%—well under the risk for systemic recurrence.

Liver surgery

One factor that determines resectability of liver metastases is whether there would remain sufficient functional liver tissue to sustain life after the diseased tissue is removed. Today, staged surgeries and innovative techniques such as portal vein embolization (PVE) capitalize on the fact that the liver has the ability to regenerate, even when disease is extensive and both lobes are affected.

PVE is an outpatient procedure performed by a highly skilled interventional radiologist. The procedure blocks blood flow to the part of the liver that contains tumor and will be removed. As a result of PVE, blood flow to the liver is diverted to the disease-free side of the liver, and the diseased side atrophies. The healthy side then grows (hypertrophies), creating additional vital liver tissue—enough to enable the surgeon to remove the disease and leave behind adequate liver reserve.

When both lobes have metastases, the surgery is done in stages: one liver surgery is done to remove lesions from the lobe that will ultimately remain, and following PVE, a second surgery to is done to remove the remaining liver containing tumors (if needed). This two-stage approach to bilateral liver metastases has raised the overall survival rate from nearly 0% to more than 80% 3 years after surgery.

Dr. Abdalla, who specializes in hepatobiliary surgery, said decisions about the intent of treatment for patients with liver metastases should take into account the improved survival rate. “We do see patients who have had incomplete rectal surgery—treatment that was approached as palliative rather than curative—after which they might receive chemotherapy and even

liver surgery but later have a recurrence from the primary site,” Dr. Abdalla explained. “Patients with a primary local tumor recurrence don’t have a long-term survival benefit from the resection of metastases.” For such patients, involvement of the colorectal specialist for “completion” rectal surgery is sometimes considered at the time of liver surgery to ensure the best possible patient outcome.

Chemotherapy

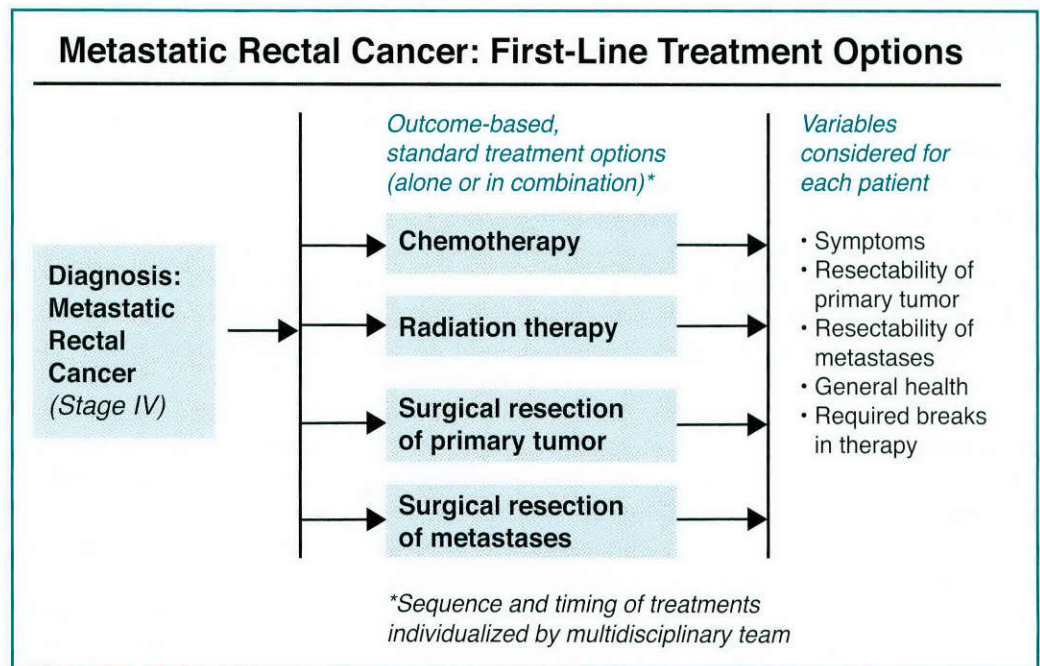
Chemotherapy is used both before surgery (neoadjuvantly) and after surgery (adjuvantly) for metastatic rectal cancer. But it is response to neoadjuvant chemotherapy that best determines whether a patient may benefit from surgery, according to Cathy Eng, M.D., an associate professor in the Department of Gastrointestinal Medical Oncology.

The goal of neoadjuvant chemotherapy is to decrease tumor burden—or downsize the tumor—to make successful surgical removal of both the primary and metastatic tumors more likely. In effect, this approach can convert disease initially deemed “unresectable” to “resectable.” Conversion is successful in 10%–15% of cases, Dr. Eng said. “Although the percentage seems small, those patients have dramatically better outcomes,” she said. The 5-year overall survival rate for patients with surgically unresectable disease is about 10%, compared with 25%–65% for patients with metastatic but resectable disease.

If the patient is a candidate for surgery, chemotherapy must be delivered carefully to avoid chemotherapy-induced liver toxicity, since the liver may be compromised by cancer and chemotherapy toxicity could compromise surgical candidacy. “We treat until the disease is resectable,” Dr. Eng said, “not until the limits of tolerance are reached.”

Surgical recovery is another consideration, and chemotherapy agents likely to compromise wound healing are avoided for a specified period of time. Timing is a factor—for example, if antiangiogenic agents (which inhibit blood vessel growth) are used, at least 5–6 weeks must elapse between the end of

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chemotherapy and when surgery is done. For each patient, the risk of disease progression during breaks in therapy must be weighed against the potential benefit of the agent.

There is an additional benefit to neoadjuvant chemotherapy: it gives the medical oncologist the opportunity to directly observe the response of the cancer to the agents used, and thus it helps better determine which agents are to be used in the adjuvant setting.

Chemoradiation

Chemoradiation is most effective and safest when it is used immediately before surgery in rectal cancer patients. The goals of neoadjuvant chemoradiation in this setting are to improve the local tumor control rate and to increase the probability of sphincter-preserving surgery. "Since surgery for metastatic rectal disease has become so successful, radiation therapy must be considered in the treatment plan if the intent is cure," said Christopher Crane, M.D., a professor in the Department of Radiation Oncology. "Neoadjuvant chemoradiation increases the likelihood of complete, curative resection of the primary tumor, which is critical because when the primary tumor recurs, it is usually too late for a curative approach."

Factors in the treatment sequence

In the past, a common approach to the treatment of metastatic rectal cancer was to surgically resect the primary tumor, and then perform surgery to address metastases and to give chemotherapy before and/or after surgery. Today, there is no typical treatment plan. The initial treatment might be the first stage of liver surgery, or it might be combination chemotherapy and radiation therapy. Choreographing the treatment plan for an individual patient requires careful evaluation, monitoring and collaboration among specialists, including the medical and radiation oncologists, the surgical oncologists who will operate on the primary tumor and the metastases, and the pathologist.

Symptoms

A major consideration for the timing of rectal surgery is whether the patient is experiencing symptoms—such as bleeding or obstruction—from the primary tumor. A significant obstruction requires treatment, and in the past, immediate rectal surgery would have been the first intervention. But in many instances today, temporary mitigative measures—for example, a stent or a colostomy—may be appropriate. Such less-radical measures can allow the patient to proceed to neoadjuvant therapies that may ultimately make the rectal surgery more successful.

Tumor resectability

Only in the rare case in which both the primary tumor and the metastases are considered completely resectable would surgery for both be considered as a first treatment; in such cases, the resections can be done during the same

surgery. However, in most cases, the primary and metastatic tumor sites must be prepared with neoadjuvant therapy to achieve tumor resectability or to maximize oncologic benefit. In fact, even when the tumors do appear to be resectable, neoadjuvant therapy is often the first treatment because it enhances the probability of complete resection and lowers the chance of local or further systemic recurrence.

The size and location of the primary tumor obviously have consequences for whether it is likely to be resectable, whether it will be amenable to radiation, and what type and severity of symptoms the patient experiences. The metastatic tumor burden likewise is a factor in the treatment sequence—dictating, for example, whether more than one liver surgery will be necessary.

Resectability is monitored and re-evaluated as the treatment plan unfolds and the response to therapy is observed. The course of neoadjuvant chemotherapy is calibrated to achieve a response while limiting liver effects. The initial response to chemotherapy is also an important indicator of prognosis and therefore is helpful in the very careful selection of patients who will benefit from further surgery. For example, when disease is seen to progress instead of diminish after chemotherapy and the first stage of PVE, the treatment team might re-evaluate whether further liver surgery will be potentially curative or therapeutic. "However, when there is a disease response to chemotherapy and first-stage PVE, the 3-year overall survival rate after surgery is 86%—almost double that of other approaches," Dr. Abdalla said. Based on published experience from their group, he estimates that about two-thirds of patients are able to proceed to second-stage surgery and potentially experience a survival benefit, while those who would not benefit are spared unnecessary surgery.

Patient health and habitus

The patient's performance status is a consideration for any treatment. For each patient, the treatment team must ask: Is the patient well enough to tolerate surgery? Will fragile health or co-morbidities necessitate long treatment breaks during which the disease might progress? Does the patient have physical limitations or characteristics (such as obesity) that might preclude successful radiation therapy or need to be considered prior to surgical therapy?

Required breaks in therapy

Regardless of sequence, the course of treatment is likely to stretch over many months. Chemotherapy is often given for a period of several weeks neoadjuvantly and perhaps several months adjuvantly. Radiation therapy typically is given over the course of 5 1/2 weeks. More than one liver surgery may be needed.

A break or recovery time of several weeks between treatments must be allowed—between chemoradiation and surgery to allow for local tissue inflammation and swelling to

(Continued on page 8)



What Is Pancreatic Cancer?

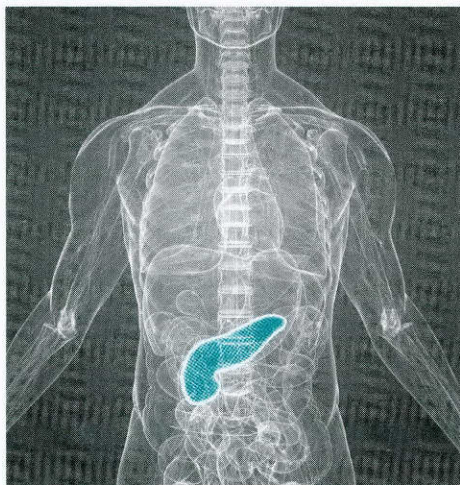
You might not know much about pancreatic cancer, but chances are you've heard of it. Public awareness of the disease has increased in recent years as well-known people including Steve Jobs, Luciano Pavoratti, Patrick Swayze, and Gene Upshaw were diagnosed with various forms of pancreatic cancer. According to the American Cancer Society, more than 35,000 Americans are expected to die from pancreatic cancer during 2009.

Risk factors

Scientists don't know exactly what causes cancer of the pancreas, an organ in the abdomen that produces insulin and digestive enzymes. However, several factors are thought to increase the risk of pancreatic cancer. These include cigarette smoking, chronic pancreatitis (inflammation of the pancreas), obesity, and diabetes. People with a family history of pancreatic, ovarian, or colon cancer and those who are age 50 years or older, male, or African-American also have a higher risk of developing the disease. Having one or all of these risk factors does not mean a person will develop pancreatic cancer, and some people with the disease have no known risk factors.

Symptoms

Unfortunately, most symptoms of pancreatic cancer occur only when the cancer has progressed to an advanced stage, said Gauri Varadhachary, M.D., an associate professor in the Department of Gastrointestinal Medical Oncology at The University of Texas M. D. Anderson Cancer Center. As the tumor grows, various symptoms may be caused by its interference with other organs of the digestive system. These symptoms can in-



The pancreas is a digestive and endocrine organ located in the abdomen. Cancer that starts in the pancreas can be difficult to detect and treat.

clude jaundice (yellowing of the eyes and skin), a change in the color of urine or stool, pain, nausea, loss of appetite, and weight loss. Symptoms like indigestion or a sudden change in blood sugar levels may occur because the pancreas is unable to perform its normal functions. Having one or all of these symptoms does not necessarily mean a person has cancer, but it does mean he or she should see a physician to find the cause.

Diagnosis

Because the symptoms of pancreatic cancer are vague and could be caused by numerous other diseases, it is often difficult for doctors to diagnose pancreatic cancer. There is no blood test that can screen for pancreatic cancer, although increased levels of certain substances in the blood can indicate the need for further testing. When doctors suspect pancreatic cancer, they will usually order imaging tests, first to confirm the presence of the cancer and then to determine whether it has spread to other parts of the body. These tests may include computed tomography (CT), ultrasonography, positron emission tomography (PET), and magnetic resonance imaging (MRI).

If imaging tests show a tumor, the next step usually is biopsy, which involves the removal of tumor tissue so

it can be examined for cancer under a microscope. Pancreas biopsy is commonly done using a thin needle, which is guided into the tumor by CT or ultrasonography. Tissue samples can also be taken during a procedure known as endoscopic retrograde cholangiopancreatography, or ERCP, which is done to drain blocked bile ducts by inserting plastic or metal stents. Laparoscopic examination through tubes inserted in the abdomen is sometimes done to see whether the tumor has spread. A patient's treatment options are determined largely by the stage of the tumor and whether it has spread.

Treatment

If the tumor has not spread beyond the pancreas, it may be possible for doctors to surgically remove the entire tumor. Unfortunately, because pancreatic cancer often has spread in microscopic form beyond the pancreas before being detected, only about 20%–25% of patients can be cured by surgery. Typically, chemotherapy, radiation therapy, or both are used in combination with surgery. While chemotherapy and radiation therapy alone will not cure pancreatic cancer, they are often used to relieve symptoms and prolong life in patients for whom surgery is not an option because their cancer has spread.

In those patients, different surgical procedures or medication may relieve symptoms. "Optimal pain control can be achieved in most patients," Dr. Varadhachary said. Because treatment options are fewer as the disease progresses, people with the symptoms listed above should share their concerns with their physician. ●

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subside, between chemotherapy or chemoradiation and surgery to allow for the fullest possible tumor downsizing to occur, or between surgery and adjuvant chemotherapy to allow postoperative recovery. These breaks in treatment must be very carefully managed, as they could also give the disease an opportunity to progress. In rare cases, liver surgery is chosen as the first intervention (after neoadjuvant chemotherapy), since the patient can move to chemoradiation in preparation for rectal surgery shortly thereafter. "When we're able to do the liver surgery first, it limits the duration of treatment-free intervals," Dr. Abdalla said.

Communication between surgery, medical oncology, and radiation oncology specialists is imperative, and the risks and benefits of each treatment modality and how each impacts the others must be considered. For example, it is often preferable for chemotherapy to precede chemoradiation and for rectal surgery to be done shortly after chemoradiation, since the scarring that develops 3–6 months after chemoradiation makes the surgery more difficult and the tumor could grow if surgery is delayed. However, an ideal course for each patient can be developed depending on the factors detailed above. "The use and sequencing of all modalities must be individualized in order to reach the optimal outcome," Dr. Crane said. ●

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