in younger patients, are more common in women, are poorly differentiated, and are locally advanced but without significant lymph node spread.

Diagnosis

Screening for colorectal cancer is an important public health tool. Screening methods include fecal occult blood testing, imaging (barium enema, CT-guided colonography), and endoscopy (flexible sigmoidoscopy, colonoscopy). The resource setting, patient preference, and risk assessment (personal and family medical history) should guide the choice of screening method. Colonoscopy is the "gold standard" for visual confirmation and histologic diagnosis. In addition, colonoscopy aids in cancer prevention because it allows removal of adenomatous polyps that could progress to cancer if left untreated. Once a cancer diagnosis is established, staging is performed with the use of CT scans to evaluate for distant disease.

Treatment

For patients with resectable disease, surgical resection is the treatment of choice. Removal of the involved segment of the colon, along with the associated mesentery containing all draining lymph nodes, is recommended. Such procedures are being increasingly performed with the use of laparoscopic techniques, resulting in decreased perioperative morbidity. Decisions regarding chemotherapy after surgery (i.e., adjuvant chemotherapy) are based on the pathologic findings. For stage I disease (T1 or T2, N0), no chemotherapy is recommended. For stage III disease (any T, N+), chemotherapy is strongly recommended. A combination of a fluoropyrimidine (5-FU, capecitabine) with oxaliplatin, administered for 6 months, is the standard of care. For stage II disease (T3 or T4, N0), data are controversial. A careful risk-benefit evaluation for each patient is recommended to determine whether adjuvant chemotherapy is appropriate. Rectal cancer is associated with a high rate of local recurrence that can lead to significant morbidity. To improve outcomes, preoperative chemotherapy and radiation therapy are used, and surgery should include total mesorectal excision.

For metastatic colorectal cancer, treatment options include chemotherapy agents such as fluoropyrimidines, oxaliplatin, and irinotecan. The advent of targeted therapies has improved clinical outcomes. These therapies include anti-angiogenic agents (bevacizumab, ziv-aflibercept), anti–epidermal growth factor receptor antibodies (cetuximab, panitumumab), and multikinase inhibitors (regorafenib). Colon cancer is one of the few malignancies in which some cases of metastatic disease can also be cured with aggressive systemic therapy and surgery. Therefore, close surveillance after treatment of the initial cancer is recommended to detect recurrences early. Surveillance should include regular physical evaluation, CT scanning, and measurement of serum levels of carcinoembryonic antigen (CEA), a protein synthesized disproportionately by malignant epithelial cells. Increased physical activity and dietary modifications (reduced red meat and fat; increased fruits, vegetables, and fiber) have been associated with improved outcomes. Another important component of colorectal cancer care is family risk assessment, because this is a common disease, with up to 7500 cases each year in the United States being attributable to heritable syndromes. Referral for genetic counseling should be made if such a syndrome is suspected.

Prognosis

Among gastrointestinal cancers, colorectal cancer has the best overall prognosis. For nonmetastatic disease, the 5-year survival rate ranges from 50% to 95%, depending on the extent of lymph node involvement. For metastatic disease, newer therapies, given in succession, can achieve a median overall survival time of more than 2 years. The key remains early detection by screening, which can improve population-level outcomes.

ANAL CANCER

Epidemiology

Anal cancer is an uncommon malignancy, with about 7000 cases reported annually in the United States. It is strongly associated with human papillomavirus (HPV) infection. It is also more common in patients with human immunodeficiency virus (HIV) infection and in those who engage in anal-receptive sexual intercourse, most likely because of poor host immunity and increased transmission of HPV, respectively. Condyloma acuminata are precursor lesions for this cancer.

Pathology

The histology is typical of a squamous cell carcinoma, with sheets of hyperproliferative keratinized cells. HPV, especially types 16 and 18, causes inactivation of the tumor suppressor genes *TP53* and *RB1* via the viral proteins E6 and E7, predisposing to eventual development of carcinoma. Chronic local inflammation due to inflammatory bowel disease or recurrent anal fissures and fistulas can also lead to anal cancer.

Clinical Presentation

Local symptoms, such as perianal pruritus or pain, bleeding, discharge, and a mass-like sensation, are common presentations. In cases of chronic underlying disease such as Crohn's disease, the presence of a nonhealing anal or perianal lesion despite good disease control elsewhere should raise suspicion for malignancy.

Diagnosis

Physical examination is adequate to identify suspicious lesions. A biopsy should be obtained to confirm the diagnosis. Evaluation for distant spread should include CT scans of the chest, abdomen, and pelvis. Special attention should be paid to examination of inguinal lymph nodes, because they are common sites of early spread.

Treatment

Anal cancer is one of the few solid tumor malignancies that are curable without surgical resection. For very small, early lesions, complete excision may suffice. However, for most cases, combined chemotherapy with 5-FU and mitomycin, together with radiation therapy, is the standard curative modality. This regimen has significant short-term toxicities that should be managed carefully. This treatment can obviate the need for a large operation that would result in a permanent colostomy.