have shown modest activity, and combination cisplatin-based regimens are typically used owing to the insufficient activity of single agents.

Up to 20% of gastric cancers and 30% of gastroesophageal junction adenocarcinomas recently have been found to overexpress the *HER2* growth factor receptor, which is a target for the anti-*HER2* monoclonal antibody trastuzumab. Therefore, evaluation of all metastatic gastroesophageal carcinomas for *HER2* is performed, and trastuzumab is added to chemotherapy regimens in patients whose tumors express *HER2*.

KEY POINTS

- Patients with local and locoregional gastroesophageal cancer (American Joint Committee on Cancer stages I, II, and III) are typically treated surgically.
- Treatment of metastatic gastroesophageal cancer is palliative and usually consists of cisplatin-based therapy or cisplatin-based therapy plus trastuzumab in patients with *HER2* tumor expression.

Neuroendocrine Tumors

Neuroendocrine tumors (NETs) are rare in incidence, but because of their often relatively indolent course, the prevalence of NETs in the population is disproportionately higher than the incidence. NETs arising from the endocrine cells of the pancreas are called pancreatic NETs, whereas those arising from all other neuroendocrine tissues of the aerodigestive tract are called carcinoid tumors. Although older literature categorized pancreatic NETs (previously called islet cell tumors) and carcinoids together, these two entities clearly behave differently, with several anticancer agents showing activity against pancreatic NETS but not against carcinoid tumors. Typically, NETs of the gastrointestinal tract are well to moderately differentiated and indolent in growth pattern. However, NETs may be poorly differentiated, in which case they typically exhibit a very aggressive growth pattern and are treated like small cell lung cancer. Most NETs are hormonally nonfunctioning, but about 25% are hormone producing. For example, carcinoid tumors typically produce serotonin, which can cause the classic carcinoid syndrome of diarrhea and facial flushing. Pancreatic NETs, when hormonally active, may produce any of the pancreatic endocrine hormones, including insulin, gastrin, glucagon, somatostatin, or vasoactive intestinal peptide, with resulting hormonal syndromes based on the type of hormone elaborated.

Although patients with hormonally functioning tumors may present with hormonal symptoms, those with nonfunctioning tumors may be asymptomatic and have metastatic disease for many years before diagnosis. The liver is overwhelmingly the most common site of metastasis, and diagnosis is often established through an incidental finding of hepatomegaly.

Because well-differentiated NETs are so indolent, patients often can be effectively managed with expectant observation and serial imaging. Triple-phase contrast-enhanced CT scanning or MRI with gadolinium are the preferred imaging modalities. Indium 111 pentetreotide scanning can be used to establish the presence of somatostatin receptors, which are commonly expressed on these tumors. Tumors that have demonstrated somatostatin receptors and are hormonally symptomatic or show clear growth under observation may be treated with the somatostatin analogues octreotide or lanreotide. Mechanical interventions, such as hepatic arterial embolization, radiofrequency ablation, or surgical debulking, may be used to reduce symptomatic tumor bulk in the liver or to decrease hormone production.

In pancreatic NETs, the small-molecule inhibitors sunitinib (an anti-VEGF agent) and everolimus (an anti–mammalian target of rapamycin [mTOR] agent), and the oral cytotoxic combination of capecitabine and temozolomide, are active. However, these agents have not demonstrated the same activity in carcinoid tumors. Chemotherapy is minimally effective in carcinoid tumors, and no specific agents are FDA approved for this indication.

KEY POINTS

- Most neuroendocrine tumors are hormonally nonfunctioning, but about 25% that manifest are hormone producing.
- Because well-differentiated neuroendocrine tumors are so indolent, patients often can be effectively managed with expectant observation and serial imaging using triple-phase contrast-enhanced CT scanning or MRI with gadolinium.
- In pancreatic neuroendocrine tumors, the small-molecule inhibitors sunitinib and everolimus and combination capecitabine and temozolomide are active.

Gastrointestinal Stromal Tumors

Although gastrointestinal stromal tumors (GISTs) were once considered rare, significant improvements in molecular diagnostics and therapy have led to increased recognition of these tumors. GISTs are the most common tumor of mesenchymal origin, or sarcoma, of the gastrointestinal tract, representing 1% to 3% of all gastrointestinal tumors, and are derived from the precursors of the intestinal cells of Cajal. Almost all GISTs have an activating mutation in the c-*kit* proto-oncogene, leading to constitutive activation of the KIT receptor tyrosine kinase. CD-117, the immunohistochemical marker for the KIT protein, is the hallmark of most GISTs. GISTs may also present with mutations in the platelet-derived growth factor-α receptor.

Localized GISTs typically appear as isolated, discrete masses anywhere along the digestive tract. Localized GISTs

are managed with surgical resection. For patients undergoing a potentially curative resection of a localized GIST, tumors with favorable risk factors require no further treatment, whereas patients with higher-risk tumors are treated with an extended course of the small-molecule receptor tyrosine kinase inhibitor imatinib, which blocks c-*kit* tyrosine kinase phosphorylation. In such patients, recurrence-free survival and overall survival are superior in patients who receive 3 years of imatinib therapy versus 1 year of therapy.

Metastatic disease is extremely refractory to standard cytotoxic chemotherapy agents; however, imatinib is remarkably effective in this setting, and lifelong treatment with this drug typically is recommended until disease progresses or treatment toxicity becomes unacceptable. However, despite its outstanding efficacy, imatinib is not curative. More recently, other agents such as sunitinib and dasatinib have shown activity in the treatment of GISTs that have become refractory to imatinib.

KEY POINTS

- Patients with localized gastrointestinal stromal tumors are managed with surgical resection.
- Following surgery, patients with localized gastrointestinal stromal tumors and tumors with favorable risk factors require no further treatment, whereas those with higher-risk tumors are treated with an extended course of imatinib.
- Patients with metastatic gastrointestinal stromal tumors are treated with lifelong imatinib until disease progresses or treatment toxicity is no longer tolerable.

Lung Cancer

This section will focus on treatment and follow-up of patients with lung cancer. See MKSAP 17 Pulmonary and Critical Care Medicine for discussion of epidemiology, risk factors, screening, diagnosis, and staging.

The initial step in developing a therapeutic plan for lung cancer is to obtain a tissue diagnosis to determine whether the tumor is non–small cell lung cancer (NSCLC) or small cell lung cancer (SCLC) and to exclude metastatic disease from another site. It is important to obtain an adequate biopsy sample (with at least a core biopsy) to allow for additional molecular studies that may be helpful in guiding therapy in some patients.

NSCLC constitutes 80% to 90% of cases, SCLC is responsible for approximately 10% of cases, and the management of these two forms of lung cancer differs significantly. Unfortunately, most patients with lung cancer have advanced, and often incurable, disease at diagnosis, reflecting the relatively asymptomatic nature of early-stage disease. Nonetheless, lung cancer research efforts have led the way in improving therapy through molecular targeting, resulting in multiple targeted therapies that are now readily available to patients and have dramatically affected treatment efficacy and tolerability.

KEY POINTS

- The initial step in developing a therapeutic plan for lung cancer is to obtain a tissue diagnosis to determine whether the tumor is non–small cell lung cancer or small cell lung cancer and to exclude metastatic disease from another site.
- Most patients with lung cancer have advanced, and often incurable, disease at diagnosis, reflecting the relatively asymptomatic nature of early-stage disease.

Non-Small Cell Lung Cancer

Diagnosis and Staging

The clinical manifestations and diagnosis of lung tumors are discussed in MKSAP 17 Pulmonary and Critical Care Medicine.

NSCLC includes several different histologic types, including squamous cell carcinoma, adenocarcinoma, large cell carcinoma, and other less commonly occurring tumors. It may also be characterized by various paraneoplastic syndromes, including hypercalcemia due to secretion of parathyroid hormone–related protein, hypertrophic pulmonary osteoarthropathy, and inflammatory myopathies. Adenocarcinoma is the most common subtype, accounting for about 50% of cases. Correct assignment of subtype, especially adenocarcinoma versus squamous cell carcinoma, is important to allow for proper treatment in patients with metastatic disease. Additionally, adenocarcinoma can be associated with genetic mutations that help predict the response to tyrosine kinase inhibitors.

The histologic subtypes of NSCLC are all staged similarly; selection of therapy is based primarily on disease stage. Stage I disease is characterized by a solitary tumor without regional (peribronchial-or hilar) or mediastinal lymph node involvement. Stage IA disease consists of tumors measuring less than 3 cm, whereas stage IB disease consists of tumors measuring greater than 3 cm but less than 5 cm. Patients with stage II disease have tumors greater than 5 cm; regional lymph node involvement; tumor invasion into local structures, such as the pleura or chest wall; or tumors that are located near the carina. Most patients with stage III disease have mediastinal lymph node involvement. Patients with stage IV disease have metastatic disease or an ipsilateral malignant pleural effusion.

KEY POINTS

- Non–small cell lung cancer may be characterized by various paraneoplastic syndromes, including hypercalcemia due to secretion of parathyroid hormone–related protein, hypertrophic pulmonary osteoarthropathy, and inflammatory myopathies.

(Continued)

KEY POINTS *(continued)*

- Correct assignment of subtype, especially adenocarcinoma versus squamous cell carcinoma, is important to allow for proper treatment in patients with metastatic disease.

Treatment

Lung cancer treatment varies significantly based on cancer stage, as noted below. A vital component of treatment, regardless of stage, is smoking cessation. Continued smoking has been shown to increase the risk of complications associated with treatment as well as reducing the potential efficacy of treatment. Furthermore, it is associated with higher risks of secondary cancers in patients with lung cancer.

Surgery with curative intent is recommended for patients with stage I or II NSCLC. Because many patients with lung cancer have concomitant chronic obstructive pulmonary disease, evaluating baseline pulmonary function with measurement of DLCO and spirometry in all potential surgical candidates is necessary. Depending on results of baseline pulmonary function testing, further evaluation to assess predicted postoperative pulmonary function and exercise capacity may be indicated. Some patients are considered to have unresectable disease based on poor pulmonary function or the presence of extensive medical comorbidities rather than disease stage. In these patients or those of advanced age, stereotactic ablative radiation therapy may be an alternative treatment option, as phase II trials have found it can result in tumor control rates similar to surgery. Patients with stage III disease with mediastinal lymph node involvement and those with metastatic disease or an ipsilateral malignant pleural effusion (stage IV) are not typically treated with surgery.

Although adjuvant chemotherapy is not usually recommended following surgery for stage I disease, it may be beneficial in patients with high-risk tumors (poorly differentiated histology, vascular invasion, need for wedge resections, tumors greater than 4 cm, visceral pleural involvement, and incomplete lymph node sampling). Adjuvant chemotherapy has a proven role in patients with resected stage II and resected stage III disease. Cisplatin-based combination therapy has demonstrated a clear survival advantage in these settings.

Adjuvant radiotherapy has been shown to decrease the risk of locoregional recurrence, although its effect on overall survival in patients with stage I and II NSCLC has not been established. Consequently, radiotherapy is not typically given to patients with negative tumor resection margins but may be considered for those with an incompletely resected tumor.

For most patients with stage III NSCLC, combined chemoradiation therapy given with curative intent is the preferred treatment approach. There is no single standard chemotherapy regimen used, but treatment with cisplatin- or carboplatin-based chemotherapy can be given. Adjuvant chemotherapy does not improve survival following definitive chemoradiation. In highly selected patients with stage III disease, surgery may be considered an appropriate therapeutic option. For patients with T3N1 disease, surgery can be done as initial therapy, although the procedure should include mediastinal lymph node dissection. If mediastinal lymph nodes are negative, adjuvant chemotherapy should be given. In patients with positive mediastinal lymph nodes, sequential chemotherapy and radiation is recommended. For patients with limited mediastinal lymph node involvement, chemotherapy or chemoradiation can be given initially, followed by surgery in patients without disease progression. However, no data indicate that this approach is superior to definitive chemoradiation therapy. Following surgery, patients with positive margins or multistage mediastinal lymph node involvement who were treated with chemotherapy only before surgery should be offered adjuvant radiotherapy.

Metastatic disease (stage IV) is not curable, and treatment in these patients is, by definition, palliative. Proper assessment of performance status using a validated measure is vital, as the benefit of chemotherapy in this patient population is confined to those with an adequate performance status (see Issues in Oncology for discussion of performance status scales). In addition, it is important to address issues surrounding goals of care and provision of palliative care in patients with metastatic NSCLC (see Issues in Oncology for discussion of palliative care goals and benefits).

Selected patients with a single site of metastasis can be treated with resection of the metastatic lesion and aggressive treatment of the primary tumor. However, most patients who present with metastatic disease have multiple sites of metastasis and are treated with systemic therapy. Recommended treatments for patients with metastatic disease are based on the pattern of metastatic spread and the results of histologic and molecular assessment. Recent evidence has indicated that squamous cell carcinoma and adenocarcinoma each respond differently to certain chemotherapeutic agents. Additionally, mutations in the epidermal growth factor receptor (EGFR), translocation of the *ALK* and *EML-4* genes, or mutation of the *ROS1* gene have been identified in a few non-squamous cell lung cancers, usually adenocarcinomas. Patients with EGFR mutations have been found to derive significant benefit from treatment with erlotinib, whereas those with *ALK* translocations and *ROS1* mutations derive similar benefit from crizotinib; these agents are recommended as initial therapy in these patients when mutation status is known before treatment is initiated. In patients who must start treatment before mutation test results are available, these agents can be used later in treatment.

Patients without an activating mutation are treated with chemotherapy. Platinum-containing doublet regimens are widely used in the first-line treatment of metastatic NSCLC and are typically combined with pemetrexed for patients with adenocarcinoma or gemcitabine for squamous cell tumors. For patients in whom the histologic subtype is uncertain, paclitaxel or docetaxel can be used. Bevacizumab, a monoclonal antibody directed against vascular endothelial growth factor, can be combined with chemotherapy for patients with non-squamous cell histology. Patients receiving platinum-based chemotherapy are typically treated for an initial four to six cycles because more than six cycles has not been shown to be beneficial.

Following the initial course of therapy, management options include observation and maintenance chemotherapy. Maintenance therapy is typically given until the patient experiences disease progression or an unacceptable level of toxicity. In such cases, the platinum-containing drug is stopped, and patients continue to receive the same drug that was used in combination with the platinum-based agent (continuation maintenance) or a different drug (switch maintenance). Bevacizumab should be continued along with maintenance therapy in patients receiving this agent, as it has been shown to improve progression-free survival. Patients with an activating mutation detected after initial platinum-based chemotherapy is started should receive the appropriate tyrosine kinase inhibitor as maintenance therapy if it was not used sooner. Maintenance chemotherapy results in improved progression-free survival and is therefore considered an accepted treatment option in patients with responsive or stable disease following four to six cycles of a platinum-based treatment. If disease progression occurs while on or after first-line chemotherapy, patients are often treated with single-agent chemotherapy consisting of docetaxel or pemetrexed (for non-squamous cell cancers). However, response rates in patients receiving second-line therapy are low, and median survival is relatively short following progression after first-line treatment. Patients with an EGFR mutation or *ALK* translocation can be treated with erlotinib or crizotinib, respectively, as maintenance therapy if they were initially treated with chemotherapy. It is especially important to address goals of care and symptom management in patients whose disease progresses after they receive first-line chemotherapy.

Following curative-intent treatment for NSCLC, patients should undergo follow-up monitoring with a periodic history, physical examination, and CT of the chest. Follow-up monitoring is important in the detection of recurrence and new primary lung cancers, which occur at a rate of approximately 3% per year. In addition, smoking cessation counseling is important in the care of lung cancer survivors.

Despite these treatment interventions, the 5-year survival rate for patients with NSCLC is only 10% to 15%. This low survival rate is largely attributable to the finding that 70% of patients present with stage III or IV disease. However, 5-year survival rates for patients with stage IA disease is only 73%, decreasing to 36% for those with stage IIB disease, and lower for those with stage III disease.

KEY POINTS

- Surgery is recommended for patients with stage I or stage II non-small cell lung cancer.
- Adjuvant chemotherapy is appropriate for patients with resected stage II and stage III non-small cell lung cancer.
- For patients with stage III non-small cell lung cancer, the preferred treatment is combined chemotherapy and radiation.
- Metastatic non-small cell lung cancer (stage IV) is not curable and treatment is palliative; the benefit of systemic therapy in this patient population is confined to those with adequate performance status. **HVC**
- Patients with metastatic non-small cell lung cancer and adequate performance status should be treated with systemic therapy selected based on the pattern of metastatic spread and the results of histologic and molecular assessment. **HVC**

Small Cell Lung Cancer

Diagnosis and Staging

SCLC is a neuroendocrine tumor that is seen almost exclusively in smokers. Large cell neuroendocrine carcinoma is a form of lung cancer that is distinct from small cell carcinoma histologically but behaves and is treated similarly to SCLC. SCLC is characterized by rapid growth, with most patients presenting with locally advanced or metastatic disease. Like NSCLC, SCLC can be associated with several paraneoplastic syndromes, including hyponatremia due to the syndrome of inappropriate antidiuretic hormone secretion, hypertrophic pulmonary osteoarthropathy, inflammatory myopathies, Cushing syndrome caused by ectopic adrenocorticotropic hormone deficiency, and other various hematologic and neurologic syndromes. SCLC is also associated with superior vena cava syndrome (see Oncologic Urgencies and Emergencies).

Staging of SCLC involves a two-stage system that was first used in early clinical trials conducted by the Veterans Administration Lung Study Group. Limited-stage disease is defined as cancer confined to a single hemithorax, which could include ipsilateral supraclavicular lymph node disease, and requires that all disease be encompassed by a single radiation portal. Extensive disease refers to disease that extends beyond a single hemithorax. Typically performed staging studies include CT of the chest, abdomen, and pelvis; whole-body bone scintigraphy; and MRI of the brain. The most recent update of lung cancer staging has recommended that SCLC be staged with the TNM system used for staging NSCLC; however, because most patients with SCLC present with locally advanced or metastatic disease, the use of the TNM staging system does not alter treatment decisions in most patients.

KEY POINTS

- Limited-stage small cell lung cancer is defined as cancer confined to a single hemithorax, which could include ipsilateral supraclavicular lymph node disease, and requires that all disease be encompassed by a single radiation portal.
- Extensive-stage small cell lung cancer refers to disease that extends beyond a single hemithorax.

Treatment

The role of surgery in the management of patients with SCLC is limited to those with very early-stage disease (<10% of patients). Although no firm criteria can be used to identify patients for surgery, eligible patients should optimally have single, small primary tumors without associated lymph node involvement (T1-2 and N0). Patients require extensive preoperative evaluation to exclude occult disease, including invasive staging of the mediastinum with endobronchial ultrasonography or mediastinoscopy. Although no prospective data are available to guide clinical decision making, retrospective data indicate 5-year survival rates of 15% to 48% following resection depending on disease stage. Patients treated with surgery typically receive adjuvant chemotherapy, as currently available data indicate that surgery alone is suboptimal.

Limited-stage SCLC that is too advanced for surgical resection is potentially curable, but treatment outcomes are poor, with 5-year survival rates of only 10% to 15%. The mainstay of treatment is combined chemotherapy and radiation therapy. The addition of radiation to chemotherapy in patients with limited-stage disease has been shown to improve survival compared with chemotherapy alone, which is associated with a high risk of local recurrence. Radiation is typically started with cycle 1 or cycle 2 of chemotherapy. Cisplatin or carboplatin can be used in combination with etoposide. Patients who experience a complete response or a significant partial response to primary chemoradiation should be offered treatment with prophylactic cranial irradiation to reduce the incidence of brain metastases and improve overall survival.

Extensive-stage SCLC is treated with chemotherapy usually consisting of cisplatin or carboplatin combined with etoposide or irinotecan and given for four to six cycles. Although response rates to chemotherapy are high, overall treatment outcomes remain poor. Nonetheless, survival in patients with extensive-stage SCLC who receive chemotherapy is superior to those who do not receive chemotherapy. As with limited-stage disease, cisplatin or carboplatin is used as initial therapy, but carboplatin is most commonly used owing to its more favorable side effect profile. Patients with extensive-stage disease who respond to initial chemotherapy also should be offered prophylactic cranial irradiation.

Unfortunately, even in the setting of significant tumor response, patients with extensive-stage SCLC will likely experience recurrent disease. The median survival following relapse of extensive disease is 4 months, but patients can still benefit from treatment depending on the timing and extent of the relapse and response to initial therapy. Patients with a good performance status who had a good response to initial therapy and whose disease progresses more than 90 days after initial treatment are most likely to benefit from second-line chemotherapy. Conversely, patients who experience relapse less than 90 days after completion of first-line chemotherapy, whose disease progresses while being treated with first-line chemotherapy, or who have a poor performance status are less likely to benefit from second-line chemotherapy. Although second-line chemotherapy can be offered, best supportive care is often more appropriate for these patients. In particular, patients with a poor performance status should not be treated with additional chemotherapy. Except in patients with extensive-stage SCLC who have experienced a late relapse following first-line therapy, combination chemotherapy is not used in the second-line setting because it provides no benefit compared with single-agent chemotherapy, and single-agent chemotherapy confers a reduced risk for side effects.

KEY POINTS

- Patients with small cell lung cancer who are considered eligible for surgery optimally have single, small primary tumors without associated lymph node involvement (T1-2 and N0) and require invasive staging of the mediastinum with endobronchial ultrasonography or mediastinoscopy to exclude occult disease.
- The mainstay of treatment for patients with limited-stage small cell lung cancer that is too advanced for surgical resection is combined chemotherapy and radiation therapy.
- Extensive-stage small cell lung cancer is treated with chemotherapy usually consisting of a platinum-containing doublet.

Head and Neck Cancer

Cancers arising in the oral cavity, nasopharynx, oropharynx, hypopharynx, larynx, paranasal sinuses, thyroid, and salivary glands are grouped together as head and neck cancer. Squamous cell carcinoma, which arises from the mucosa, constitutes 90% to 95% of cases of head and neck cancer and will be the focus of this chapter. Thyroid cancer is discussed in MKSAP 17 Endocrinology and Metabolism.

Risk Factors

Head and neck cancer constitutes approximately 3% of cancer diagnoses in the United States and is more common among men than women. Tobacco and alcohol use are well-described and potent risk factors that also can cause global mucosal

alterations, markedly increasing the risk for second primary cancers involving other head and neck subsites. More recently, human papillomavirus (HPV) infection has emerged as an important risk factor for head and neck cancer, particularly for oropharyngeal cancer. HPV-associated oropharyngeal cancer has dramatically increased in incidence in North America over the past 30 to 40 years, accounting for 70% to 80% of oropharyngeal cancers diagnosed in the United States. This is mostly related to oral sexual contact. While not yet definitively proved, it is hoped that use of the HPV vaccine will be able to reduce the incidence of HPV-associated oropharyngeal cancers.

HPV-associated tumors differ markedly from conventional squamous cell carcinoma of the head and neck. These tumors occur almost exclusively within the oropharynx, develop in younger individuals, and are associated with a significantly improved prognosis, even when diagnosed at an advanced stage. However, despite the improved prognosis of patients with HPV-associated oropharyngeal cancer, HPV status does not currently factor into treatment decisions. Other risk factors for head and neck cancer include Epstein-Barr virus infection, HIV infection, various occupational exposures, and betel nut chewing. Persons with occupations placing them at risk for head and neck cancer include painters, wood workers, textile workers, farmers, and construction workers.

KEY POINTS

- Tobacco, alcohol, and human papillomavirus infection are important risk factors in the development of head and neck cancer.
- Human papillomavirus tumors differ markedly from squamous cell carcinoma of the head and neck as they occur almost exclusively within the oropharynx, develop in younger individuals, and are associated with a significantly improved prognosis.

Clinical Manifestations

Head and neck cancer is characterized by various presenting symptoms, many of which are nonspecific and therefore important for physicians to recognize to avoid unnecessary delays in diagnosis. An isolated neck mass is a common presentation prompting further evaluation. Other symptoms and signs suggestive of head and neck cancer are less obvious and include hearing loss (often unilateral), tinnitus, ear pain, nonhealing oral ulcers, loosening of teeth, ill-fitting dentures, throat pain, dysphagia, hoarseness, bleeding, and unilateral nasal obstruction. Weight loss also occurs in patients with more advanced disease at diagnosis.

KEY POINT

- An isolated neck mass is a common symptom in head and neck cancer and should prompt further evaluation.

Evaluation and Staging

Patients with suspected head and neck cancer require prompt referral to an otolaryngologist. The basis of diagnosis is the history and physical examination, which includes flexible fiberoptic laryngoscopy to facilitate direct visualization of the mucosa of the entire pharynx and larynx. Examination under anesthesia with diagnostic panendoscopy (laryngoscopy, bronchoscopy, and esophagoscopy) is done to obtain a biopsy, better characterize the anatomic extent of disease, and identify second primary cancers. Imaging studies, particularly CT and MRI, are important in evaluating the primary site and regional lymph nodes. PET and PET/CT are especially effective in detecting metastatic disease, and they can also help to clarify the results of MRI and CT imaging.

Staging of head and neck cancer follows the TNM staging system (**Table 59**). Although tumors arising from different anatomic locations are staged differently with regard to T stage, staging of cervical lymph node metastases is similar for all the different anatomic sites. Generally, patients with stage I and II disease have clinically negative lymph nodes, whereas patients with stage III to IVb disease have varying degrees of lymph node involvement. Stage IVc disease is typically limited to patients with distant metastatic disease. Patients with stages I and II disease are generally considered to have localized disease, whereas those with stages III and IVa disease are considered to have locally advanced disease. Although it occurs infrequently, metastatic disease must be excluded, particularly in patients with locally advanced head and neck cancer.

KEY POINTS

- The basis of diagnosis of head and neck cancer is the history and physical examination, which includes flexible fiberoptic laryngoscopy to facilitate direct visualization of the mucosa of the entire pharynx and larynx.
- In patients with head and neck cancer, imaging studies, including CT and MRI, are important in evaluating the primary site and lymph nodes, and PET and PET/CT detect metastatic disease and clarify results of CT and MRI.

Treatment

Treatment of clinical early-stage (typically stage I and II) head and neck cancer consists of surgical resection or definitive radiotherapy. One exception to this is nasopharyngeal cancer, which is treated with radiation alone for stage I disease and combined chemotherapy and radiation for stage II and higher (nonmetastatic) disease. Recurrence rates are generally similar for patients treated surgically or with radiation, and the selected modality most commonly is chosen based on expected morbidity and functional outcomes. For patients treated with surgery, the use of adjuvant radiation or combined chemotherapy and radiation is recommended based on findings at surgery. Factors indicating a need for adjuvant therapy include

(Text continued on page 100)