Primary Carcinoma of the Esophagus

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Laura R. Carucci and Robert A. Halvorsen, Jr.

Primary carcinoma of the esophagus includes squamous cell carcinoma and adenocarcinoma (typically arising in Barrett's esophagus). Carcinoma of the esophagus represents 7% of all cancers of the gastrointestinal tract (Levine and Halvorsen 2008). Historically, the majority of esophageal malignancies represented squamous cell carcinomas (90–95%); however, adenocarcinoma has increased in incidence dramatically in recent years, especially in the United States. Currently, less than 50% of esophageal cancers diagnosed in the United States are squamous cell carcinoma (Blot et al. 1993). However, worldwide 95% of esophageal cancers are squamous cell carcinomas. Although these neoplasms exhibit different pathologies and some differences in behavior; many of the imaging features are similar and they both have a poor prognosis with more than 50% of patients presenting with unresectable tumors and overall 5 year survival rates of only approximately 15% (Wang et al. 2005).

Primary carcinoma of the esophagus including squamous cell carcinoma and adenocarcinoma will be discussed in this chapter. Epidemiology, histopathology, imaging features, routes of spread, and staging will be reviewed. Benign esophageal neoplasms and other less common malignant neoplasms involving the esophagus will be discussed elsewhere in this section.

L.R. Carucci (✉) • R.A. Halvorsen, Jr.
Department of Radiology, Virginia Commonwealth University Medical Center, Richmond, VA, USA

Epidemiology

In the United States in 2010, the American Cancer Society estimated 16,640 new cases of esophageal cancer and 14,500 deaths due to esophageal cancer (American Cancer Society 2010). Esophageal cancer has a high fatality rate as demonstrated with a high ratio of fatalities to cases of 0.89 (Jemal et al. 2009). Esophageal cancer is the sixth leading cause of cancer death worldwide and the distribution of esophageal carcinoma is quite variable geographically. Esophageal cancer occurs most commonly in the sixth and seventh decades of life, and the disease becomes more common with advancing age. It is approximately 20 times more common in patients older than 65 years as compared with younger patients and less than 15% of cases are found in people younger than age 55. Overall, men have a more than three times greater rate of esophageal cancer as compared with women (Wang et al. 2005).

The epidemiology of esophageal carcinoma has changed markedly over the past several decades in the United States and western populations with a rapidly increasing incidence of adenocarcinoma of the esophagus. Until the 1970s, squamous cell carcinoma was the most common type of esophageal cancer, accounting for more than 90% of esophageal cancers (Shah and Kurtz 2010). Over the last three decades, the incidence of adenocarcinoma of the distal esophagus has risen sharply, increasing at a rate exceeding any other cancer. In fact, among white men, the incidence of adenocarcinoma of the esophagus has increased by more than 350% since the mid-1970s, surpassing squamous cell carcinoma of the esophagus by 1990 (Devesa et al. 1998). The rates of

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squamous cell carcinoma have remained essentially stable or have slowly declined. As a consequence, more than 50% of new cases of esophageal cancer are adenocarcinomas. By the early 1990s, adenocarcinoma became the most common type of esophageal cancer in white males, accounting for almost 60% of cases, although squamous cell carcinoma remains the predominant cancer type in African Americans. By 2003, overall there were more adenocarcinomas than squamous cell carcinomas of the esophagus diagnosed in the United States. This change in the epidemiology is most likely multifactorial and is likely at least in part due to the rising rate of Barrett's esophagus and gastroesophageal reflux disease (GERD) in the United States, as adenocarcinoma of the esophagus typically arises in Barrett's mucosa.

Clinical Presentation

Unfortunately, many of the symptoms experienced by patients with esophageal neoplasms occur late in the disease course and at an advanced stage, resulting in a very poor prognosis. Patients with early esophageal neoplasm tend to be asymptomatic.

The most common presenting symptom in patients with esophageal cancer is progressive dysphagia. Esophageal cancer patients tend to develop dysphagia only when the esophageal lumen becomes significantly narrowed and on average, patients experience dysphagia for 2–4 months prior to seeking medical attention (Mannell 1982; Martin et al. 1997; Layke and Lopez 2006; Levine and Halvorsen 2008). The esophagus can accommodate some degree of obstruction because it lacks a serosal layer and the smooth muscle can stretch. As a result, a patient may not experience dysphagia until the lumen is narrowed by more than 50–60%. At this point, invasion of the periesophageal lymph nodes or adjacent mediastinal structures has usually occurred (Lightdale and Winawer 1984). As a consequence, patients tend to present with advanced, unresectable tumors at initial diagnosis. The narrowed esophageal lumen leads first to solid food dysphagia followed by liquid dysphagia, and eventually to obstruction.

Odynophagia is the second most common presenting symptom of esophageal cancer. Patients may also present with substernal chest pain, anorexia, weight loss, gastrointestinal bleeding, hoarseness, and recurrent aspiration (Levine and Halvorsen 2008). Substernal chest pain may occur as a consequence of mediastinal invasion. Anorexia and weight loss are present in up to 75% of cases (Wang et al. 2005). Chronic subclinical gastrointestinal bleeding with Guaiac-positive stool or iron deficiency anemia is common; however, gross hematemesis due to esophageal neoplasm is rare (Mannell 1982; Levine et al. 1986). Hoarseness can occur due to direct invasion of the larynx or secondary to involvement of the recurrent laryngeal nerve. Patients may experience recurrent aspiration and chronic cough (Mannell 1982). A paroxysmal cough that occurs with swallowing may suggest a fistulous communication between the esophagus and the airway. Patients with esophageal adenocarcinoma arising in Barrett's esophagus may have a long-standing history of reflux symptoms prior to development of neoplasm.

Diagnosis

Double contrast esophagography is the best radiologic study for diagnosing early esophageal cancer. Early esophageal cancer has a relatively good prognosis with 5 year survival approaching 90% (Froelicher and Miller 1986; Bonavina 1995). However, as these patients are relatively asymptomatic, early cancers are most often diagnosed in areas with mass screening due to a high incidence of esophageal cancer (i.e., China) or as an incidental finding in a patient undergoing a workup for other indications. Double contrast esophagography has high sensitivity in the detection of subtle findings of early esophageal cancer; however, the specificity is relatively low and some degree of false-positive findings at esophagography should be accepted to maximize detection of early, treatable cancers (Moss et al. 1976). In patients with advanced esophageal carcinomas, the lesion is detected with double contrast esophagography in up to 98% of cases (Levine et al. 1997).

Because of the poor prognosis of esophageal cancer, any suspicious lesion at esophagography should undergo endoscopy with biopsy. Endoscopy with brushings and biopsy has an overall sensitivity of 95–100% for the diagnosis of esophageal carcinoma (Lal et al. 1992; Wang et al. 2005). Staging of a diagnosed esophageal neoplasm is best assessed with computed tomography, endoscopic ultrasound, and positron emission tomography (see Staging of Esophageal Carcinoma: Imaging Modalities below).

Squamous Cell Carcinoma

Although previously constituting the vast majority of primary esophageal carcinomas in the United States, squamous cell carcinoma (SCC) now makes up no more than 50% of esophageal cancers (Blot et al. 1993). Esophageal SCC tends to affect elderly men with a male to female ratio approaching 4:1 and a peak age of occurrence between ages 65 and 74 (Wang et al. 2005). As the normal esophagus is lined by squamous mucosa, this type of cancer can occur anywhere along the length of the esophagus.

Risk Factors and Predisposing Conditions

Risk Factors for Esophageal SCC

The development of esophageal SCC is associated with numerous risk factors including alcohol and tobacco use, obesity, dietary factors, vitamin and nutritional deficiencies, environmental carcinogen exposures, chronic esophageal irritation, and geographic location. Additional substances implicated in the development of esophageal cancer include tannin, betel leaves, and asbestos. Human papilloma virus has also been implicated in the pathogenesis of esophageal SCC.

In the United States, the two major risk factors for esophageal SCC are alcohol consumption and cigarette usage (Engel et al. 2003). The risk of esophageal carcinoma is directly related to the number of cigarettes smoked per day and the duration of smoking. In addition, combining smoking and drinking alcohol raises the risk of esophageal SCC much higher than using either substance alone (Mannell 1982). The risk is further increased by the overall poor health and nutritional deficiencies in alcoholic patients.

Geography plays an important role in esophageal SCC development with the highest incidences reported in Asia extending from eastern Turkey and northern Iran to India and northern China (Ribeiro et al. 1996). An increased incidence has also been reported in France and South Africa (Lightdale and Winawer 1984). The increased risk associated with geography appears largely due to environmental factors. Vitamin or microelement deficiencies may play a role. Riboflavin deficiency in China may contribute to a high incidence of esophageal cancer. In addition, low soil levels of molybdenum have been found from northern China to Iran and dietary molybdenum deficiency has been associated with an increased rate of esophageal cancer (Nouri et al. 2008). Molybdenum is an element required for metabolism of nitrites to ammonia, and its deficiency leads to an accumulation of nitrites and potentially carcinogenic nitrosamines in plants that may be subsequently consumed by humans (Mannell 1982). Nitrosamines and nitroso compounds have been found in the food and water supply in areas in northern China. Increased risk of esophageal SCC is also associated with a diet that favors starches and is deficient in fresh fruits and vegetables (Ribeiro et al. 1996).

There may also be a genetic component in high risk geographic areas. The BRCA2 gene was initially identified as a risk factor for breast cancer. The BRCA2 protein is believed to be important in facilitating repair of double stranded breaks in DNA. A BRCA2 anomaly has been associated with kindreds of squamous carcinoma in high risk areas in China and among the Turkmen population of Iran (Hu et al. 2004; Akbari et al. 2008). There also appears to be an increased risk for SCC in patients who frequently consume extremely hot beverages. The Turkmen population in the mountainous regions of Iran historically drinks scalding tea and has an extremely high incidence of SCC of the esophagus (Enzinger and Mayer 2003).

Predisposing Conditions

There are several conditions that may predispose to the development of esophageal SCC including head and neck tumors, achalasia, remote caustic ingestion, celiac disease, radiation exposure, Tylosis, and Plummer-Vinson syndrome. In these patients, periodic surveillance may be beneficial.

Patients with primary SCC of the head and neck have a significantly increased risk of developing separate synchronous or metachronous primary esophageal carcinomas, likely at least in part due to similar predisposing factors (i.e., smoking and alcohol use). Up to 8% of patients with oral, pharyngeal, or laryngeal neoplasm have synchronous esophageal cancers at endoscopy (Atkinson et al. 1982; McGuirt 1982).

Patients with long-standing achalasia (more than 17 years duration) have a risk of esophageal SCC that is at least 15 times normal. In patients with long-standing achalasia, the prevalence of esophageal cancer ranges from 2% to 8% (Carter and Brewer 1975). Malignant degeneration may occur in the setting of

chronic stasis esophagitis from retained food and debris within a dilated esophagus. Patients with chronic lye strictures have an increased risk of SCC as chronic inflammation and scarring are thought to predispose to SCC (Wychulis et al. 1971). Up to 5.5% of patients with chronic lye strictures will develop esophageal carcinoma (Leape et al. 1971; Appelqvist and Salmo 1980), with neoplasm developing more than 40 years after the caustic ingestion (Bigger and Vinson 1950; Appelqvist and Salmo 1980). Patients with long-standing celiac disease and malabsorption (35 years duration on average) also appear to have an increased risk of esophageal neoplasm, possibly due to the absorption of carcinogens through atrophic jejunal mucosa as well as likely genetic factors (Collins et al. 1978). Esophageal cancer may rarely occur as a consequence of chronic radiation injury, most often in the cervical or upper thoracic esophagus following radiation to the mediastinum or neck (Levine and Halvorsen 2008). Tylosis is an extremely rare autosomal-dominant hereditary disorder characterized by excess growth and thickening of the skin on the palms and soles and fissuring of the skin. This disorder has an extraordinarily high risk with as many as 95% of patients developing esophageal cancer by age 65 (Harper et al. 1970).

Pathology

Histology: The major distinction for an esophageal carcinoma at pathology is whether the lesion is "early" or "advanced." At diagnosis, most patients with SCC of the esophagus have "advanced" lesions that have already involved regional lymph nodes, invaded local structures, or spread to distant sites. Prognosis is poor with overall 5 year survival rates of only about 15% (Wang et al. 2005). However, "early" esophageal cancers are relatively curable with 5 year survival rates of more than 90% (Froelicher and Miller 1986; Bonavina 1995). Early cancers are most often diagnosed with mass screening of asymptomatic patients in areas with a high incidence of disease such as China (Moss et al. 1976).

Histologically, *"early"* esophageal cancer is cancer limited to the mucosa or submucosa without lymph node involvement (Japanese Society for Esophageal Diseases 1976). "Early" esophageal cancer is not synonymous with "superficial" or "small" esophageal cancers as these lesions can have histopathologic features that significantly change the disease prognosis. *Superficial* esophageal cancer is also confined to the mucosa or submucosa, but patients may have lymph node metastases (Japanese Society for Esophageal Diseases 1976). *Small* esophageal cancer indicates a tumor less than 3.5 cm, but this terminology does not take into account the depth of invasion or the presence or absence of lymph node metastases (Moss et al. 1976; Zornoza and Lindell 1980). Regional lymph node involvement markedly decreases the 5 year survival for esophageal cancer (Mannell 1982; Levine et al. 1986). Therefore, although superficial or small esophageal lesions can be "early" cancers histologically, involvement of regional nodes changes the prognosis such that it may be similar to that of advanced cancer despite the "superficial" or "small" terminology (Yamada 1979; Zornoza and Lindell 1980). Conversely, a lesion larger than 3.5 cm may still be classified histologically as an "early" cancer (Levine et al. 1986).

Gross Pathology: Esophageal SCC specimens may be infiltrative, polypoid, ulcerative, or superficially spreading. Esophageal SCC is most often infiltrative, resulting in an irregular lesion constricting the esophageal lumen. Polypoid lesions protrude into the lumen and can be lobulated or fungating. Ulcerative lesions are relatively flat masses with ulceration and necrosis within the tumor mass. Superficial spreading lesions extend longitudinally in the esophageal wall and can extend longitudinally for great distances without invading beyond the mucosa or submucosa. As a consequence, patients with superficial spreading carcinoma tend to have a better prognosis than patients with other forms of esophageal SCC.

Squamous Cell Carcinoma Location and Spread

Esophageal SCC can develop anywhere in the esophagus (Mannell 1982). Distal esophageal SCC almost never invades directly into the stomach (Levine and Halvorsen 2008). This is a key feature that can help distinguish distal esophageal SCC from adenocarcinoma arising in Barrett's mucosa, as distal esophageal adenocarcinoma has a tendency to invade contiguously into the proximal stomach.

SCC of the esophagus can invade locally, regionally, or distant structures through direct extension, lymphatic spread, and hematogenous metastases.

Direct Invasion: Esophageal cancer tends to quickly invade adjacent structures including the thyroid, larynx, trachea, bronchi, aorta, thoracic duct, lung, pericardium, and/or diaphragm. The esophagus lacks a serosal surface and is attached to neighboring structures via a loose adventitia. There is therefore no anatomic barrier to prevent rapid spread of tumor into the adjacent mediastinum. A common site of direct invasion is the tracheobronchial tree with tracheoesophageal or esophagobronchial fistulas developing in up to 5–10% of patients with esophageal cancer (Fitzgerald et al. 1981). Rarely, direct invasion can result in aortoesophageal or esophagopericardial fistulas.

Lymphatic Spread: Esophageal lymphatic drainage is longitudinal rather than segmental. Due to a large network of longitudinal interconnecting lymphatic channels along the esophagus, the site of lymphatic spread is often unpredictable and may occur at some distance from the primary tumor. Esophageal SCC metastases may be found in neck or mediastinal lymph nodes without lymph node involvement adjacent to the primary tumor. Spread to abdominal lymph nodes also occurs in 25–50% of patients and although more likely with distal esophageal primary lesions, spread to abdominal lymph nodes also occurs with upper or mid esophageal lesions (Mandard et al. 1981; Sannohe et al. 1981). Overall, lymphatic metastases are found in up to 75% of patients with esophageal cancer (Mandard et al. 1981).

Focal lymphatic metastasis can occur in the esophagus, producing a "satellite" or "skip" nodule separate from the primary lesion. Esophageal satellite nodules are associated with a very poor prognosis and are found at autopsy in up to 50% of patients with esophageal cancer (Mandard et al. 1981; Mannell 1982). This intramural metastasis may mimic a very rare second primary esophageal lesion. Tumor can also seed the gastric fundus via submucosal esophageal lymphatics extending below the diaphragm. Gastric submucosal metastases from esophageal SCC are found in up to 15% of esophageal cancer patients at autopsy (Glick et al. 1986). This does not represent contiguous spread and normal mucosa is found between the primary esophageal SCC and the gastric lesion.

Hematogenous metastases are often found in patients with advanced esophageal neoplasm. Metastatic disease from esophageal SCC may involve the lungs, liver, adrenal glands, pancreas kidneys, peritoneum, and/or the osseous structures.

Esophagography Findings

Early Esophageal Carcinoma

Double contrast esophagography is the radiologic study of choice for diagnosing esophageal cancer. Early esophageal cancers most often appear on double contrast studies as small (less than 3.5 cm in diameter) plaque-like lesions or sessile polyps with a smooth or slightly lobulated contour (Koehler et al. 1976; Moss et al. 1976; Levine et al. 1986). Alternatively, early cancers may appear as focal areas of irregularity, nodularity, or ulceration of the mucosa (Fig. 11.1). A confluent area of tiny, poorly defined nodules or plaques may indicate a superficial spreading carcinoma (Fig. 11.2) (Itai et al. 1978; Levine et al. 1986; Sato et al. 1986; Lee et al. 2005). Rarely, an intraluminal mass greater than 3.5 cm in diameter can still be classified histologically as an "early" lesion (see section "Pathology" above) (Levine et al. 1986; Ueyama et al. 1998). However, on esophagography, these lesions are indistinguishable from advanced carcinomas (Levine et al. 1986).

Advanced Esophageal Carcinoma

Advanced esophageal carcinomas appear on barium studies as infiltrative, polypoid, ulcerative, or varicoid lesions (Wiot and Felson 1973; Goldstein et al. 1981; Levine 1997). Infiltrative lesions are most common, followed by polypoid and ulcerative lesions. The least common appearance is varicoid. Lesions may demonstrate mixed or overlapping features.

Infiltrative carcinomas grow circumferentially to produce a malignant stricture with abrupt borders, eccentric luminal narrowing, and nodular, irregular, or ulcerated mucosa (Figs. 11.3, 11.4). Lesions may have an annular appearance with shelf-like, overhanging borders (Fig. 11.3) (Wiot and Felson 1973). Due to the luminal narrowing that occurs with infiltrating lesions, there may be an associated partial or complete esophageal obstruction with proximal dilatation.

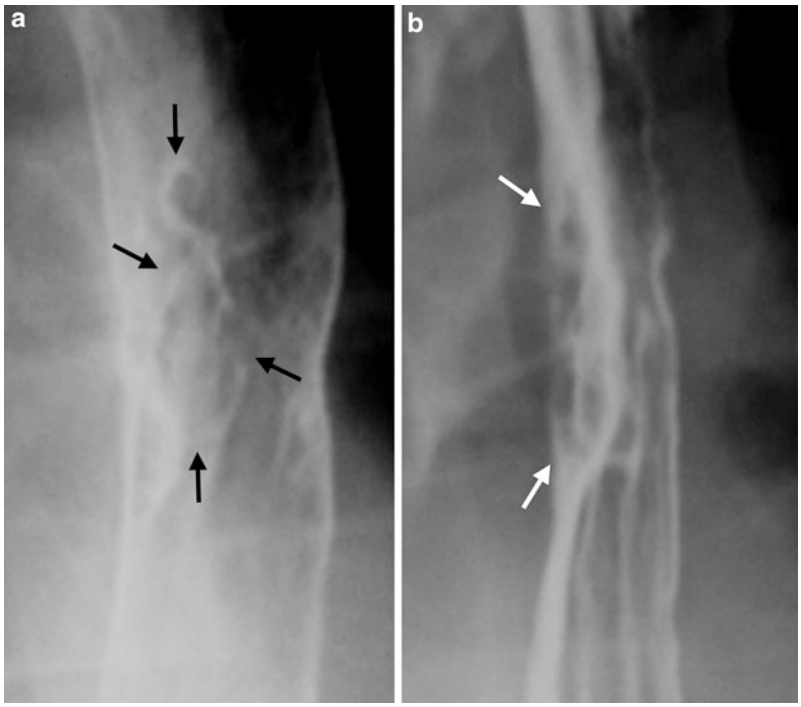

Fig. 11.1 Early esophageal cancer: SCC. (**a**) Upright left posterior oblique (LPO) double contrast image demonstrates a focal area of irregularity, nodularity, and ulceration of the mucosa in the mid thoracic esophagus (*arrows*). (**b**). A more collapsed, mucosal relief image better reveals the area of nodularity (*arrows*)

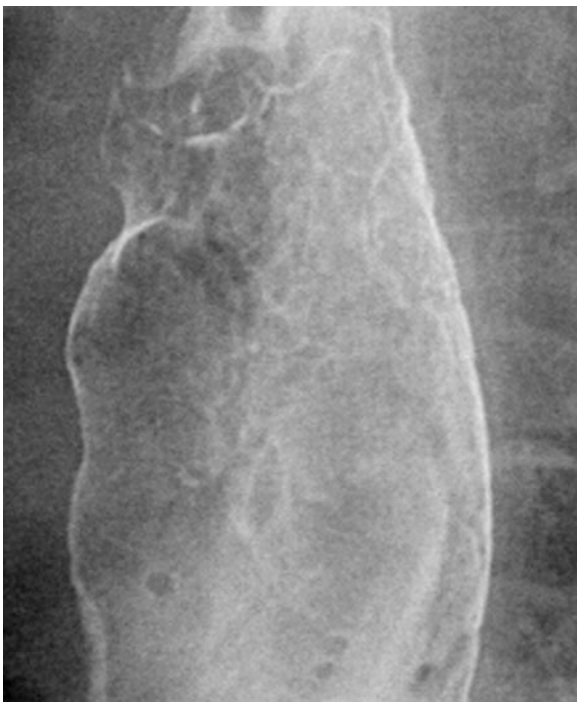

Fig. 11.2 Superficial spreading carcinoma. A double contrast right posterior oblique (RPO) image shows a focal area of confluent tiny, poorly defined nodules and plaques indicating a superficial spreading carcinoma. More focal wall thickening is noted superiorly

Polypoid carcinomas appear as lobulated intraluminal masses protruding into the lumen (Fig. 11.5) (Wiot and Felson 1973; Goldstein et al. 1981; Levine 1997). Polypoid lesions may be fungating and can contain areas of ulceration. Bulky lesions can cause luminal narrowing and obstruction.

Ulcerative carcinomas demonstrate ulceration and tissue necrosis within the tumor mass (Figs. 11.6, 11.7). In profile, these lesions appear as ill-defined ulcers with a thick radiolucent rim of tumor surrounding the ulcer (Fig. 11.6a). Ulceration occurs within a mass so that the ulcer may not protrude beyond the expected outer luminal contour (Figs. 11.6, 11.7). Visualization of the rim of tumor may require images obtained in multiple projections (Fig. 11.6).

Varicoid carcinoma represents submucosal spread of tumor. This submucosal spread results in thickened, tortuous longitudinal esophageal folds that may appear similar to esophageal varices (Fig. 11.8) (Sabedotti et al. 2006). However, unlike the variable appearance of esophageal varices at fluoroscopy, varicoid neoplasms have a fixed, rigid appearance with an abrupt transition to normal adjacent mucosa. Predominant varicoid carcinomas are uncommon, but a focal varicoid appearance can be seen adjacent to a predominantly infiltrative,

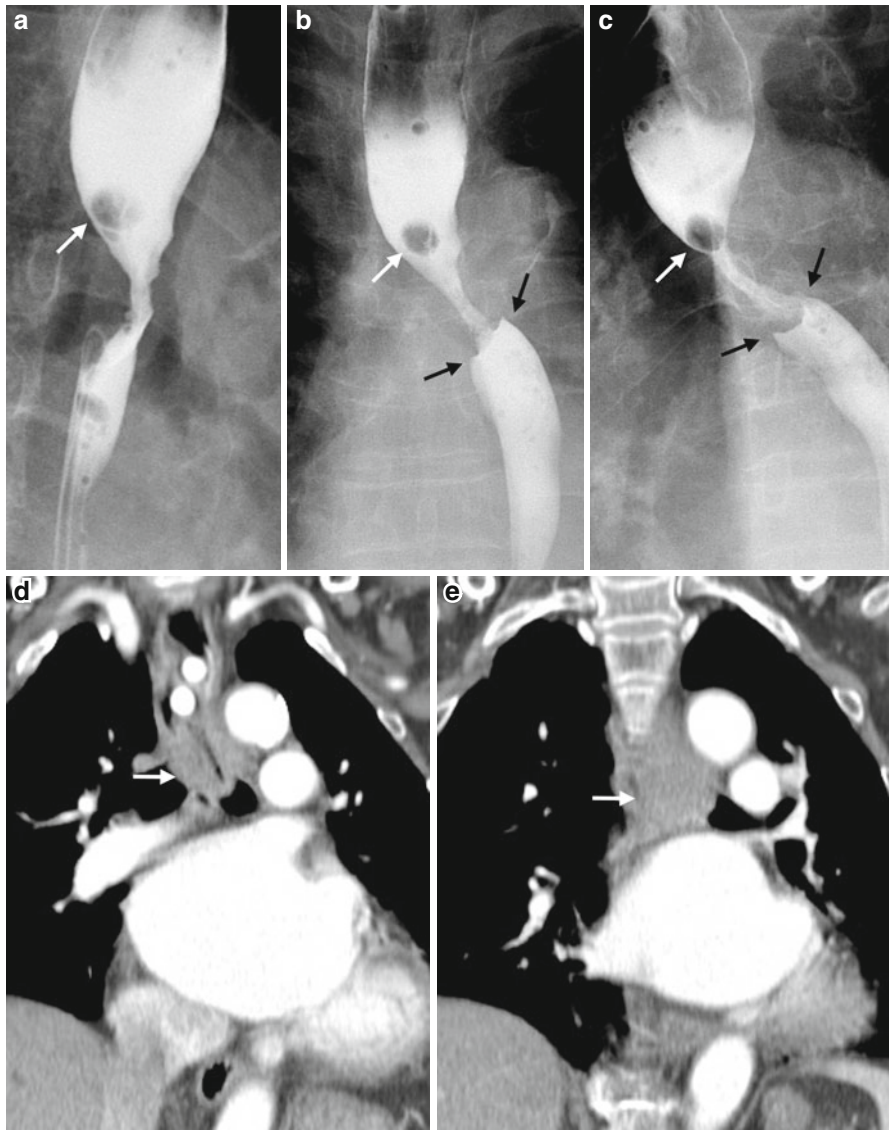

Fig. 11.3 Advanced esophageal cancer: Infiltrative SCC. (**a**) LPO, (**b**) anteroposterior (AP), and (**c**) RPO esophagram images show an infiltrative lesion in the mid esophagus just below the aortic arch. The lesion is circumferentially narrowing the lumen with proximal dilatation and partial obstruction. Note the retained pill above the lesion (*white arrows*). The lesion is annular with shelf-like overhanging margins most pronounced along its caudal extent (*black arrows*). (**d** and **e**) Coronal contrast-enhanced CT images show the soft tissue component of the infiltrative lesion (*arrow*). Also note two retained pills above the lesion (**d**)

polypoid, or ulcerative squamous cell carcinoma due to submucosal spread (Figs. 11.8, 11.9) (Cho et al. 1982).

Many esophageal cancers will exhibit more than one of the infiltrative, polypoid, ulcerative, and varicoid components (Figs. 11.10, 11.11).

Invasion and Spread at Esophagography

Direct Invasion: Up to 10% of esophageal cancer patients develop fistulous communication between the esophagus and the airway due to direct tumor invasion or tumor necrosis following radiation or chemotherapy (Fitzgerald et al. 1981; Levine and Halvorsen 2008). Most fistulas due to esophageal SCC extend to the trachea (Fig. 11.12) or left main stem bronchus. If fistulous communication with the airway is suspected, the diagnosis can be readily made at esophagography with contrast opacifying the distal trachea and/or bronchi. It is important to ensure that airway opacification is not due to aspiration. If fistula is suspected, the initial swallow should be observed in the lateral projection to exclude aspiration. At esophagography, the origin of the fistula may be visible in the vicinity of the invasive neoplasm (Fig. 11.12). Additional findings indicating invasive tumor include communication with the lung, filling of

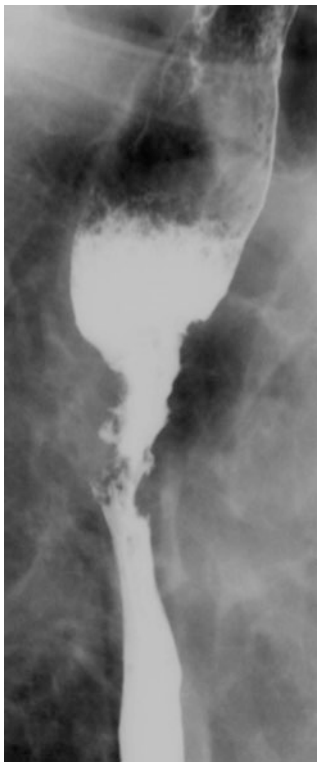

Fig. 11.4 Advanced esophageal cancer: Infiltrative SCC. An upright LPO esophagram image shows a circumferential infiltrative lesion with nodular and ulcerative mucosa. This lesion is resulting in partial obstruction with proximal dilatation

a necrotic cavity, or a mediastinal sinus track (Fig. 11.13) (Mannell 1982). Mediastinal involvement by advanced esophageal carcinoma can lead to extrinsic compression and displacement of the esophagus.

Lymphatic Spread: Lymphadenopathy due to esophageal carcinoma can also result in extrinsic compression and displacement of the esophagus. This can occur at a distance from the primary lesion and indicates an advanced tumor. On esophagography, this appears as a smooth extrinsic impression with obtuse borders rather than as a mucosal lesion (Figs. 11.10, 11.12). Occasionally, a second, discrete lesion can be seen in the esophagus, separated from the primary tumor by normal intervening mucosa and due to focal lymphatic metastasis (satellite nodule) (Fig. 11.14) (Mannell 1982). This appears as a small, polypoid, plaque-like, or ulcerative lesion, often indistinguishable from a rare second primary esophageal tumor.

Esophageal SCC can metastasize to the proximal stomach via submucosal lymphatic spread and can appear as a large submucosal mass in the gastric fundus (Glick et al. 1986). The gastric cardia and fundus should be carefully examined at esophagography in patients with esophageal cancer to assess for metastatic disease to the stomach. Areas of ulceration within the mass may simulate a gastrointestinal stromal tumor. Alternatively, the appearance can resemble a primary gastric carcinoma.

Diagnosis of Esophageal Carcinoma in Patients with Predisposing Conditions

As discussed earlier in this chapter, certain conditions may predispose to esophageal SCC and recognition of the secondary neoplasm may be difficult both clinically and at esophagography. Predisposing conditions may include long-standing achalasia, chronic lye ingestion, and Tylosis.

Patients with long-standing achalasia have a long-standing history of dysphagia and underlying significant esophageal dilatation. As a consequence, esophageal neoplasms tend to grow to become extremely large and unresectable before diagnosed (Carter and Brewer 1975; Hankins and McLaughlin 1975; Cho et al. 1982). On esophagography, a bulky intraluminal polypoid or fungating mass may be seen within a dilated esophagus, most often mid to distal in location (Hankins and McLaughlin 1975). Despite large size, these lesions may be obscured by retained fluid and debris in the esophagus.

Patients with chronic lye strictures have increased risk of SCC, likely due to chronic inflammation and scarring from caustic esophagitis (Bigger and Vinson 1950; Appelqvist and Salmo 1980). Patients present with sudden or worsening dysphasia many years following the caustic ingestion. Carcinomas arising in lye strictures tend to have a slightly better prognosis compared with most esophageal carcinomas with 5 year survival of 8–33%, likely due to surrounding scar tissue preventing early invasion of adjacent structures (Appelqvist and Salmo 1980). On barium studies, progressive stenosis, nodularity, or ulceration within a preexisting stricture may indicate cancer. Also, the presence of a fistulous communication with the airway is suspicious for a secondary neoplasm. Any change in the appearance of a chronic lye stricture should be evaluated with endoscopy.

Patients with Tylosis (an extremely rare hereditary disorder characterized by hyperkeratosis of the palms and soles) have an extraordinary high risk of esophageal cancer. Most patients present with advanced,

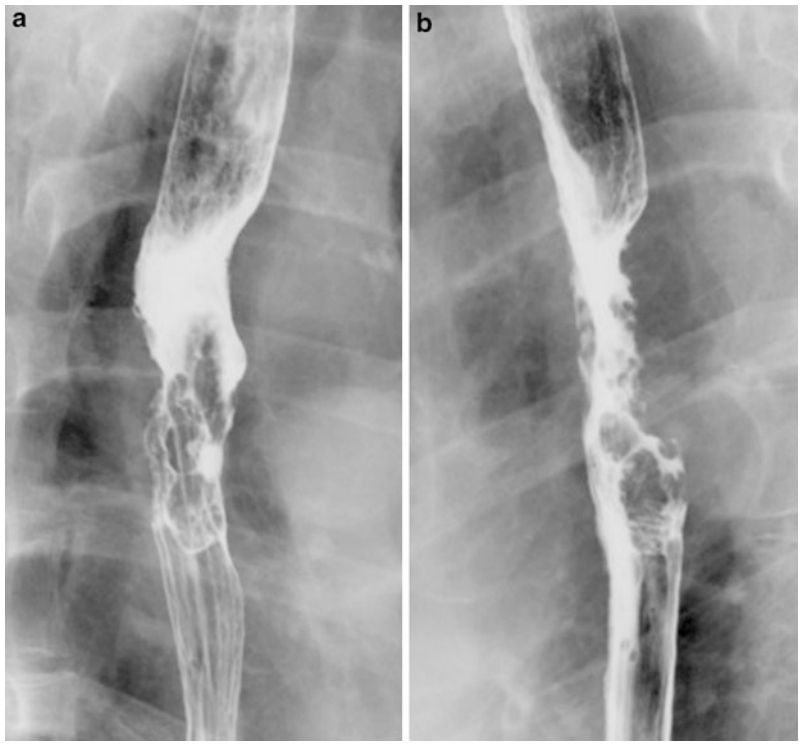

Fig. 11.5 Advanced esophageal cancer: Polypoid SCC. Upright LPO (**a**) and RPO (**b**) spot images from a double contrast esophagram in a patient undergoing workup for head and neck cancer reveal a simultaneous esophageal SCC. There is a polypoid lesion in the mid esophagus with lobulated intraluminal filling defects. There is mild luminal narrowing without obstruction

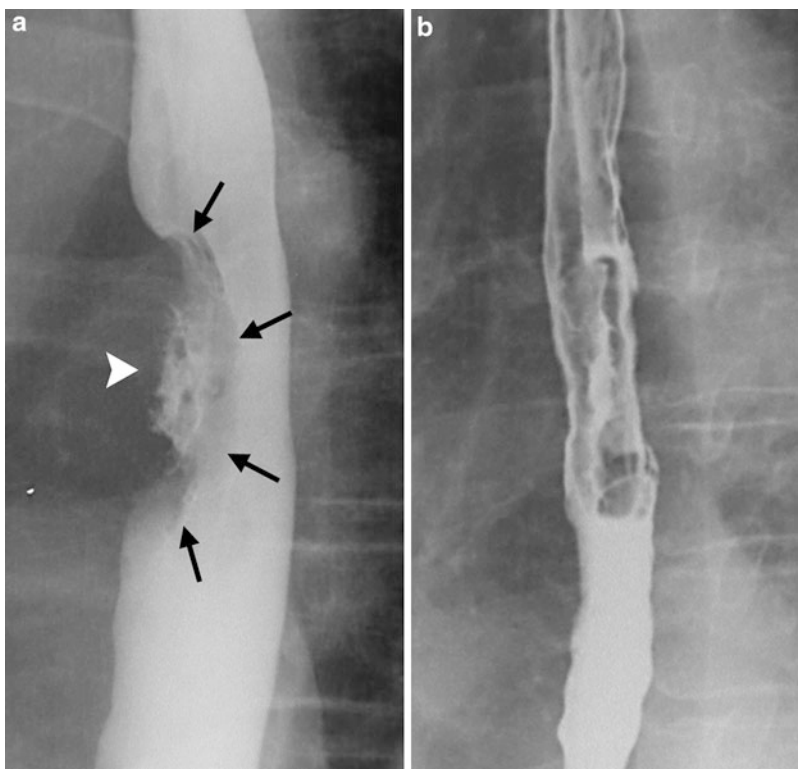

Fig. 11.6 Advanced esophageal cancer: Ulcerative SCC. (**a**) Prone right anterior oblique (RPO) image shows an ulcerative mass in the mid thoracic esophagus in profile with a thick, irregular radiolucent rim of tumor surrounding the ulcer (*arrows*). Contrast material is opacifying the irregular ulcer crater within the mass (*arrowhead*). The ulceration is within a soft tissue mass so that the ulcer does not protrude beyond the expected outer luminal contour. (**b**) When the lesion is viewed en face in the upright RPO position, it is difficult to appreciate its ulcerative nature and the thick rim of tumor. This shows the importance of obtaining images in multiple projections

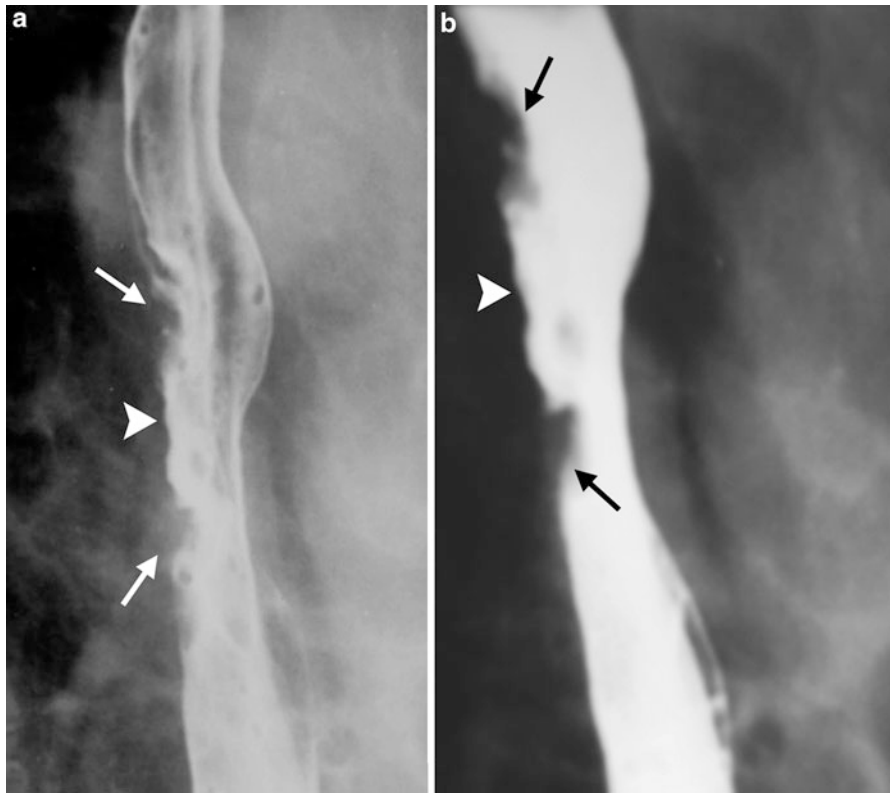

Fig. 11.7 Advanced esophageal cancer: Ulcerative SCC. There is an ulcerative mass in the mid esophagus seen in double contrast (**a**) and single contrast with luminal opacification. (**b**) The mass demonstrates nodular soft tissue components with filling defects (*arrows*) primarily along its margins as well as a central area of ulceration (*arrowhead*)

unresectable tumors. On barium studies, these lesions may appear annular, infiltrative, or plaque-like (Munyer and Margulis 1981).

Adenocarcinoma

Esophageal adenocarcinoma almost always arises in Barrett's esophagus and is most often located in the distal, or less frequently the middle third of the esophagus (Haggitt et al. 1978; Levine et al. 1984). At one time, these lesions were thought to be rare. However, in the past, many of the adenocarcinomas involving the gastroesophageal junction region or gastric fundus were thought to represent primary gastric carcinoma secondarily invading the distal esophagus. Currently, adenocarcinomas constitute at least 50% of all esophageal neoplasms in the United States and the incidence of esophageal adenocarcinoma in white men has increased by 350% in the past 30 years, such that adenocarcinoma is now the most common form of esophageal cancer in white men (Blot et al. 1993; Devesa et al. 1998). The increased incidence of esophageal adenocarcinoma is not solely due to reclassification of gastric cardia tumors as esophageal tumors, as the rates of gastric cardia tumors have not declined in a proportional manner (Devesa et al. 1998). The trend more likely reflects changes in the prevalence of risk factors, including gastroesophageal reflux disease and Barrett's esophagus. As with esophageal SCC, most patients with esophageal adenocarcinoma present with advanced disease and the prognosis is poor, with 5 year survival rates of less than 20% (Wang et al. 2005).

Risk Factors and Predisposing Conditions

Patients with gastroesophageal reflux disease (GERD) have an increased risk of adenocarcinoma of the esophagus, 2–16 times normal. The risk increases based on the duration and severity of reflux. The increased risk due to GERD appears due to the fact that GERD can cause Barrett's esophagus. Patients who are overweight or obese also have a higher chance of developing adenocarcinoma of the esophagus, and in recent

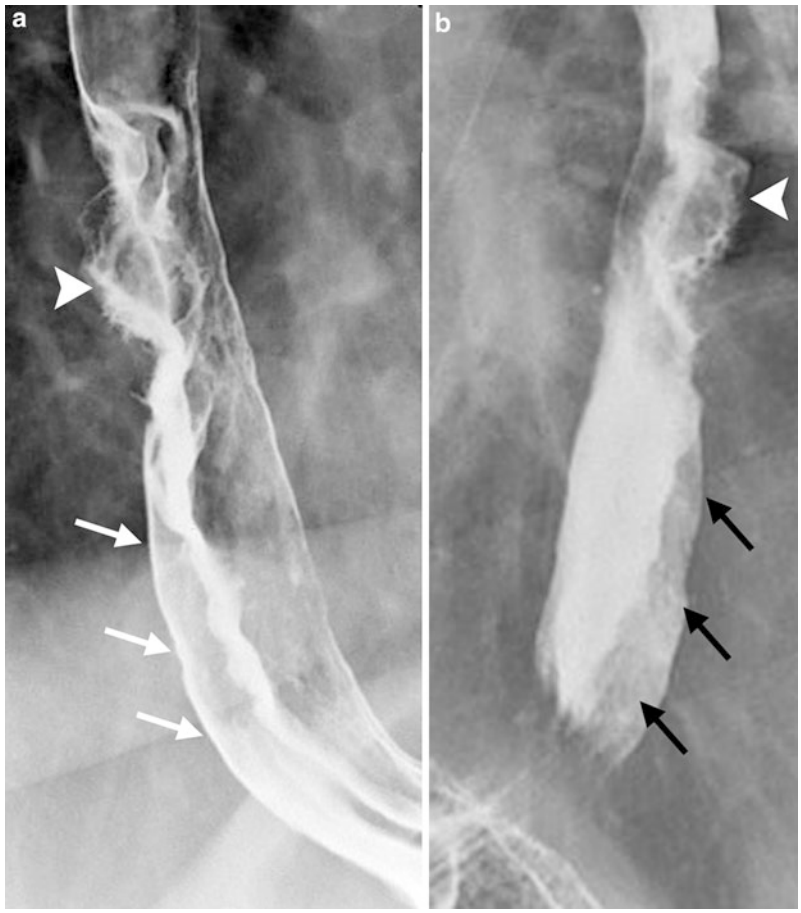

Fig. 11.8 Advanced esophageal cancer: Varicoid SCC. (**a**) Upright LPO and (**b**) prone RAO images from a double contrast esophagram show thickened, tortuous, lobulated folds in the distal esophagus (*arrows*) due to submucosal spread of tumor. Although the appearance is similar to esophageal varices, these folds are fixed and do not change in size of shape at fluoroscopy. Also note the ulcerative mass more cephalad (*arrowhead*). There is a large ulcerative mass with lobulated fold thickening and nodularity

years, obesity has emerged as a major risk factor for esophageal adenocarcinoma. This is at least in part due to increased intra-abdominal pressure and associated gastroesophageal reflux as well as due to dietary factors (Devesa et al. 1998). Barrett's esophagus and scleroderma may be considered predisposing conditions in the development of esophageal adenocarcinoma. Adenocarcinoma has also been found in Barrett's esophagus in patients with Zollinger-Ellison syndrome and achalasia, especially following esophagomyotomy (Keen et al. 1984; Lightdale and Winawer 1984; Chen and Frederick 1994). While some authors have found no association between alcohol consumption and the development of adenocarcinoma in the esophagus (Wu et al. 2001; Lindblad et al. 2005; Freedman et al. 2007), others have found a strong association (Kabat et al. 1993; Vaughan et al. 1995).

While traditionally believed to be an acquired condition, Barrett's esophagus is now thought to represent two groups of patients: those with acquired disease and others with a genetic predisposition to develop the disease (Drovdlic et al. 2003; Chak et al. 2004; Sappati Biyyani et al. 2007). Of interest, *Helicobacter pylori* (*H. pylori*) infection may be protective against esophageal adenocarcinoma, while increasing the risk of gastric cancer (Whiteman et al. 2010). In a meta-analysis of *H. pylori* and esophageal cancer risk, Islami and Kamangar found an inverse association between *H. pylori* infection and the risk of esophageal adenocarcinoma (Islami and Kamangar 2008). They propose that a decline of *H. pylori* infections in the past few decades may at least partially explain the recent increase in esophageal adenocarcinomas in Western countries.

Barrett's Esophagus

The vast majority of adenocarcinomas of the esophagus occur due to malignant degeneration in Barrett's esophagus. Barrett's esophagus occurs most often as

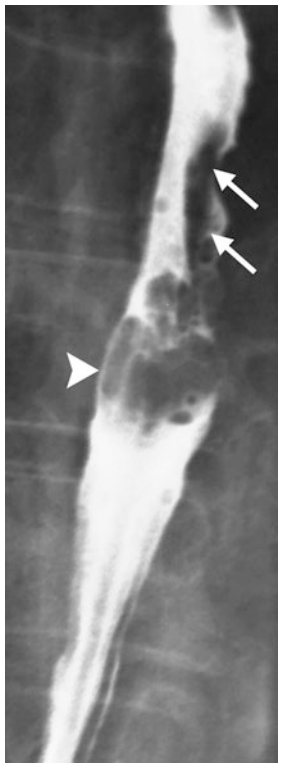

Fig. 11.9 Advanced esophageal cancer: Varicoid SCC adjacent to a polypoid lesion. A single contrast spot image of the mid esophagus shows a lobulated, polypoid intraluminal filling defect due to SCC (*arrowhead*). A focal varicoid appearance is seen adjacent to the lesion due to submucosal spread (*arrows*)

a consequence of long-standing gastroesophageal reflux and reflux esophagitis. There is progressive columnar metaplasia of the squamous epithelium in the distal esophagus (Agha 1985; Spechler and Goyal 1986; Levine et al. 1995). This is considered a premalignant condition with increased risk of esophageal adenocarcinoma through a sequence of progressive dysplasia (Levine et al. 1995). The prevalence of Barrett's esophagus in patients with reflux esophagitis ranges from 5% to 15% (Thompson et al. 1983a; Sarr et al. 1985; Levine et al. 1995; Csendes et al. 2000). Barrett's esophagus occurs primarily in older patients with a mean age of 65 years at diagnosis and a male to female ratio of 3:1 (Wang et al. 2005).

Several types of columnar epithelium have been described in the distal esophagus including junctional, gastric fundic, and intestinal-type (specialized columnar epithelium). Intestinal-type metaplasia (with characteristic crypts and villi lined by mucus-secreting columnar cells and goblet cells) is the key component for a pathologic diagnosis of Barrett's esophagus and the type of epithelium that predisposes to subsequent development of adenocarcinoma (Haggitt et al. 1978; Chen and Frederick 1994; Hirota et al. 1999; American Gastroenterological Association 2011). The reported prevalence of adenocarcinoma in patients with Barrett's esophagus ranges from 2% to 46% with an overall prevalence of approximately 10% (Levine et al. 1984; Sarr et al. 1985; Spechler and Goyal 1986). Prevalence data may overestimate the risk due to selection bias, as many patients with Barrett's esophagus are asymptomatic until cancer develops. The incidence of adenocarcinoma in patients with Barrett's esophagus is more than 30–40 times greater than the general population and adenocarcinoma develops in approximately 0.5% of patients with Barrett's esophagus each year (Cameron et al. 1985; Shaheen et al. 2000; American Gastroenterological Association 2011).

Barrett's esophagus may be classified as long or short segment disease based on the vertical extent of intestinal metaplasia and the distance from the gastroesophageal junction (more or less than 3 cm respectively). Short segment Barrett's esophagus is more common than long segment (Hirota et al. 1999).

Development of Neoplasm in Barrett's Esophagus

Dysplasia-Carcinoma Sequence: Esophageal adenocarcinoma arises in Barrett's esophagus through a sequence of progressive epithelial dysplasia, carcinoma in situ, and invasive adenocarcinoma in preexisting columnar metaplasia (Berenson et al. 1978; Hamilton and Smith 1987; Hameeteman et al. 1989). Dysplasia can occur in all types of Barrett's mucosa but is most likely to occur with intestinal metaplasia (Hirota et al. 1999). Patients with long segment disease appear more likely to develop dysplasia than those with short segment disease (Weston et al. 1997). Dysplastic changes can be detected on endoscopic biopsy specimens and can be classified as low or high grade histologically. High grade dysplasia may progress to invasive adenocarcinoma and in patients with high grade dysplasia in Barrett's esophagus, progression to cancer has been found in 22% of patients within 7 years (Wang et al. 2005). The prevalence of high grade dysplasia in patients with esophageal adenocarcinoma ranges from 68% to 100% (Skinner et al. 1983; Spechler and Goyal 1986).

Adenoma-Carcinoma Sequence: Much less frequently, adenocarcinoma may develop from neoplastic change in an adenoma similar to the process that occurs in the colon. Benign adenomatous polyps have been found in Barrett's mucosa in the esophagus and these polyps can contain foci of invasive

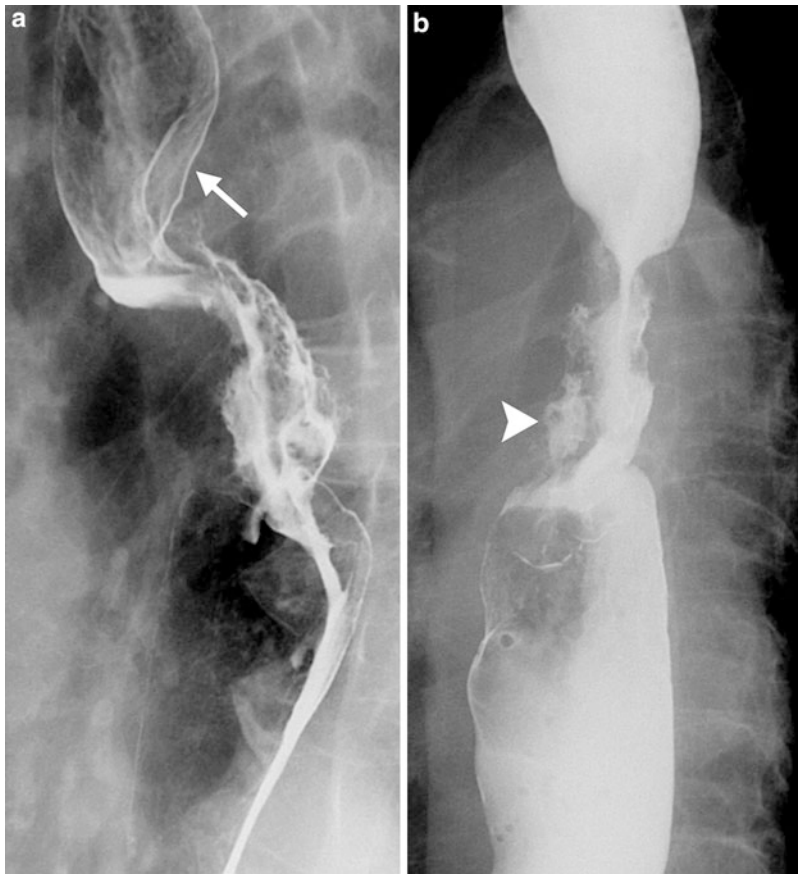

Fig. 11.10 Advanced esophageal cancer: Infiltrative, polypoid, and ulcerative components. (**a**) Double contrast upright RPO and (**b**) single contrast prone RAO images show a partially obstructing esophageal cancer with infiltrative components most pronounced proximally, polypoid components in the mid lesion, and ulceration (*arrowhead*) best seen with single contrast technique (**b**). Also note the smooth extrinsic impression upon the esophagus just cephalad to the mass (*arrow*) (**a**) due to mediastinal lymphadenopathy

adenocarcinoma (Levine et al. 1984). Adenomatous polyps in Barrett's esophagus should be endoscopically resected to decrease the risk of malignant degeneration and development of adenocarcinoma.

Endoscopic Surveillance and Management in Patients with Barrett's Esophagus

Due to the increased risk of cancer in patients with Barrett's esophagus, endoscopic surveillance is advocated. Although surveillance with endoscopy in Barrett's esophagus has not been proven to improve mortality from esophageal adenocarcinoma (Sharma et al. 2004), evidence suggests that endoscopic surveillance can reduce mortality from esophageal adenocarcinoma through early detection of treatable cancers in Barrett's esophagus when recommended biopsy techniques are utilized (American Gastroenterological Association 2011). Biopsies should be obtained from all quadrants of the lower esophagus at 1–2-cm intervals starting at the GE junction to detect and treat dysplastic changes prior to the development of invasive carcinoma (Berenson et al. 1978; Haggitt et al. 1978; Spechler and Goyal 1986; Hameeteman et al. 1989; Wang et al. 2005; American Gastroenterological Association 2011). In addition, specific biopsies should be obtained in areas of mucosal irregularity (American Gastroenterological Association 2011). Methylene blue–directed endoscopic biopsies may also be an accurate and more cost-effective method of diagnosing Barrett's esophagus and detecting dysplasia or cancer (Canto et al. 2000).

In patients with non-dysplastic Barrett's esophagus, the American Gastrointestinal Association recommends surveillance endoscopy at 3–5 year intervals. In patients with low grade dysplasia, endoscopy is recommended every 6–12 months. In patients with high grade dysplasia, the risk of developing cancer is so great that endoscopic eradication therapy or definitive surgical treatment (esophagectomy) is recommended (Wang et al. 2005; American Gastroenterological Association 2011). Endoscopic eradication therapy may include radiofrequency ablation,

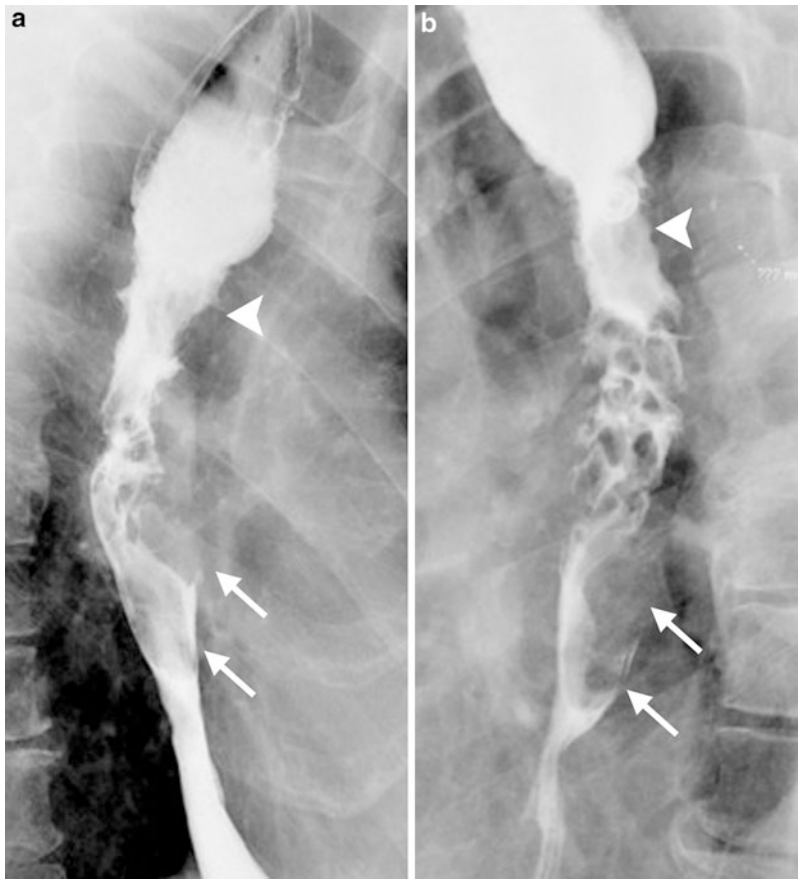

Fig. 11.11 Advanced esophageal cancer: Infiltrative, polypoid, and varicoid components. (**a**) LPO and (**b**) RPO spot images from an esophagram show a partially obstructing lesion demonstrating an infiltrative component most pronounced proximally (*arrowhead*), followed by a large polypoid component in its mid portion. A varicoid component is seen inferiorly (*arrows*) with lobulated filling defects

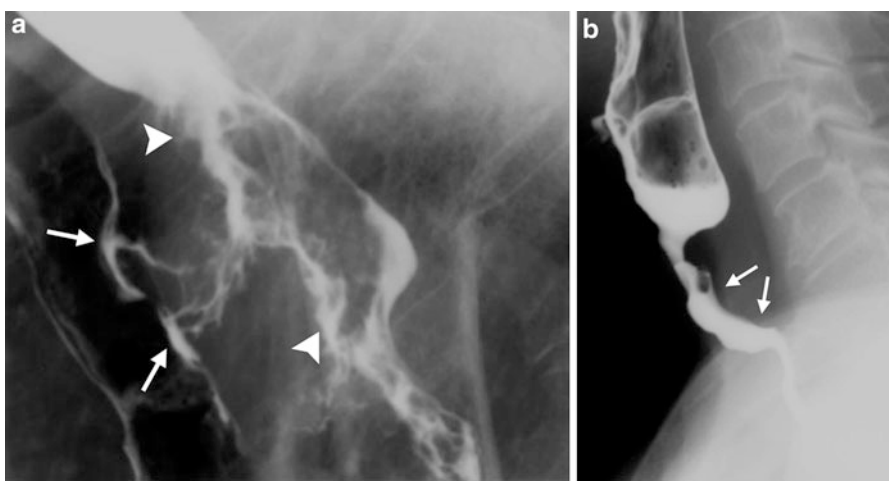

Fig. 11.12 Proximal esophageal SCC with fistula to the trachea. (**a**) A fluoroscopic spot image acquired in the lateral position shows a large polypoid and ulcerative mass in the proximal esophagus (*arrowheads*). There is fistulous communication with the trachea. Note barium coating the posterior wall of the trachea (*arrows*). (**b**) A lateral image more superiorly shows smooth mass effect on the posterior cervical esophagus due to lymphadenopathy (*arrows*)

photodynamic therapy, or endoscopic mucosal resection. The goal of eradication therapy is to permanently eliminate all intestinal metaplasia with reversal to squamous epithelium. Up to 80% of patients with high grade dysplasia can be successfully treated with endoscopic eradication (American Gastroenterological Association 2011). Patients with high grade dysplasia without eradication therapy should undergo endoscopic surveillance every 3 months (American Gastroenterological Association 2011).

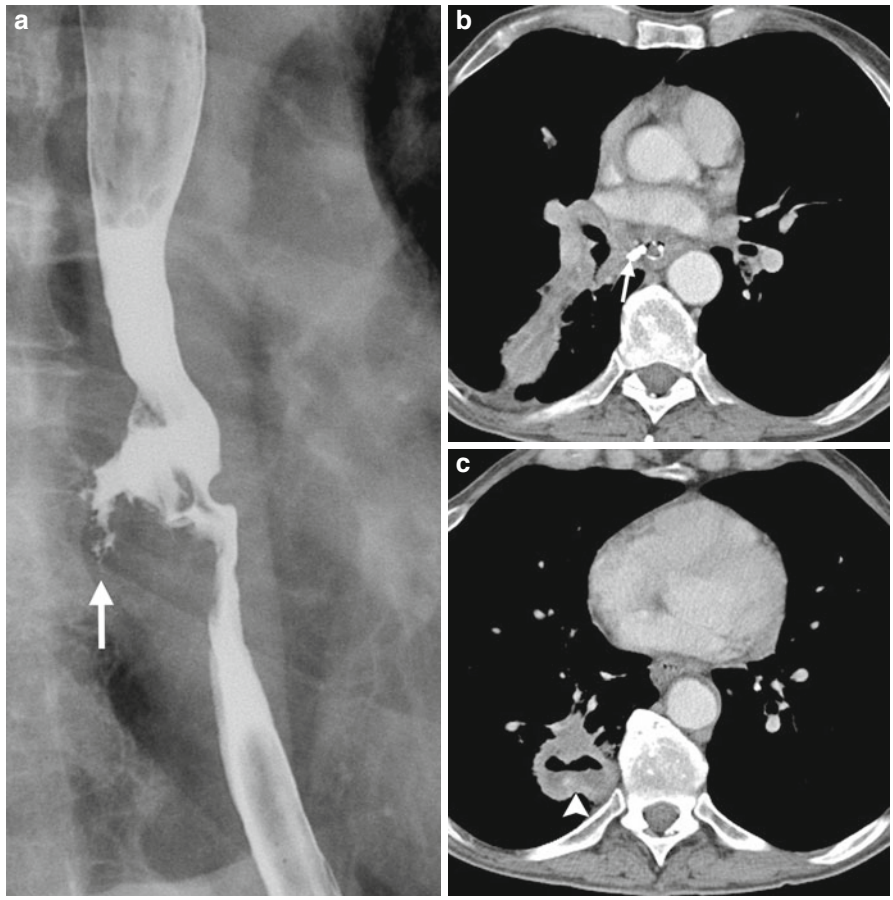

Fig. 11.13 Advanced esophageal cancer invading the mediastinum and communicating with a necrotic cavity. (**a**) Upright LPO double contrast image shows an annular and ulcerative lesion in the mid esophagus. There is barium tracking posterolaterally into the soft tissues (*arrow*). Axial contrast-enhanced CT images show the esophageal mass with contrast extending into the adjacent soft tissues (*arrow*) (**b**). (**c**) A cavity with an air-fluid level is noted in the right posterior lung (*arrowhead*) and containing minimal dependent contrast material

Scleroderma

Scleroderma, a connective tissue disorder affecting smooth muscle, involves the esophagus in 75% of patients and can result in an incompetent lower esophageal sphincter with marked gastroesophageal reflux. There is also significantly decreased esophageal peristalsis with poor clearance of contents, including refluxed gastric acid. Because of the severity of associated reflux esophagitis, scleroderma patients have an increased risk of Barrett's esophagus, greater than patients with gastroesophageal reflux disease alone (Agha and Dabich 1985). Up to 37% of scleroderma patients undergoing endoscopy for reflux symptoms were found to have Barrett's esophagus (Recht et al. 1988). Because of the increased risk of Barrett's esophagus, patients with scleroderma have an increased risk of esophageal adenocarcinoma (Halpert et al. 1983; Recht et al. 1988).

Pathology

Histologic Features: As with esophageal SCC, most esophageal adenocarcinomas are advanced, unresectable tumors at diagnosis. Early, potentially curable, lesions may be detected with imaging or endoscopic studies in patients undergoing surveillance for known Barrett's esophagus or due to underlying reflux disease (Levine et al. 1986; Reid et al. 1988).

Gross Pathology: Adenocarcinoma of the esophagus may be infiltrating, polypoid, ulcerative, or varicoid lesions.

Adenocarcinoma Location and Spread

Esophageal adenocarcinoma is most often located in the distal esophagus or less commonly the middle third

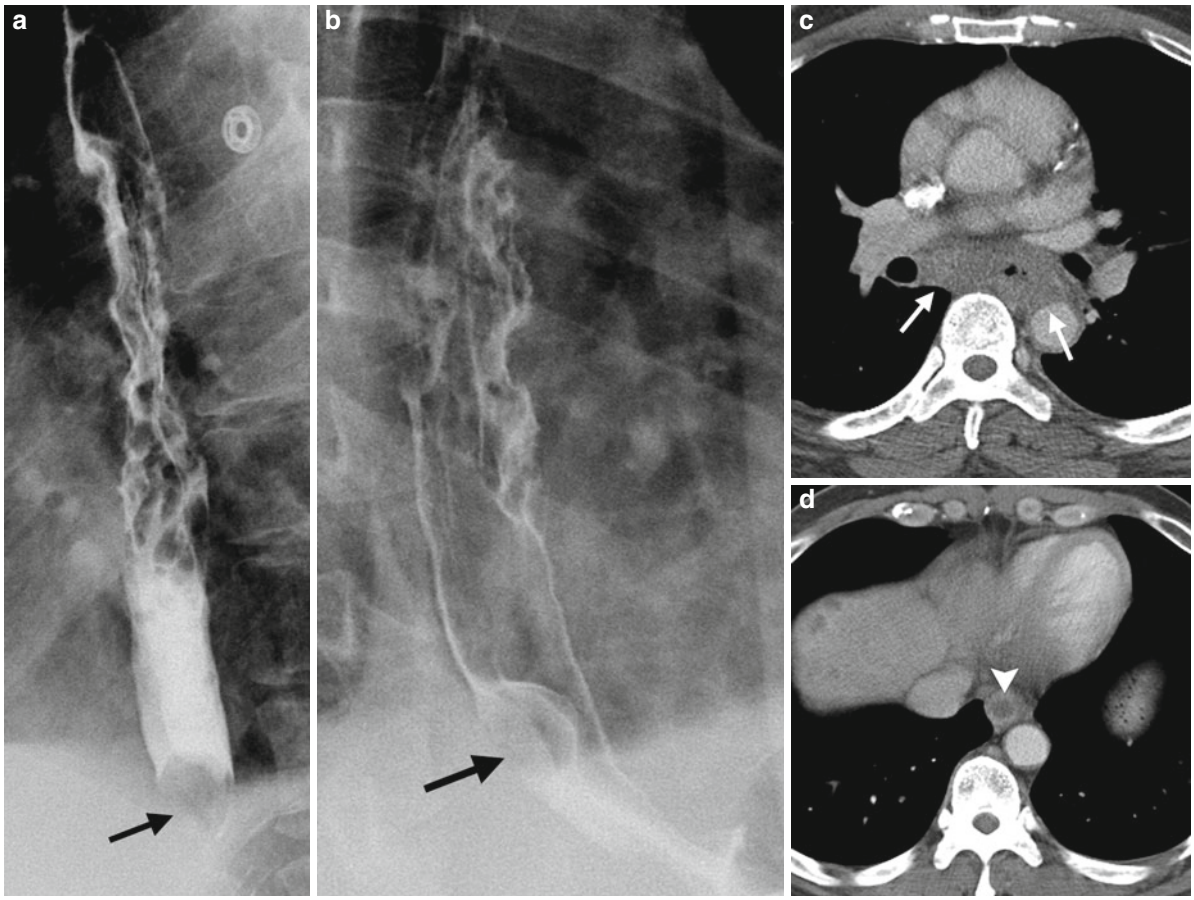

Fig. 11.14 Advanced esophageal cancer with a satellite nodule. Upright RPO (**a**) and LPO (**b**) esophagram images show a large infiltrative and polypoid mass in the mid esophagus. There is a discrete, polypoid lesion in the distal esophagus (*arrow*), separated from the primary tumor by normal intervening mucosa. This is a satellite nodule due to focal lymphatic metastasis. Contrast-enhanced axial CT images show the mass in the mid esophagus (*arrows*) and partially surrounding the aorta (**c**). (**d**) More inferiorly, the small nodule is seen (*arrowhead*). Also note liver metastases at the hepatic dome

of the esophagus. As opposed to esophageal SCC, adenocarcinoma of the distal esophagus frequently spreads across the diaphragm to involve the gastric cardia or fundus, occurring in 35–50% of patients (Fig. 11.15) (Thompson et al. 1983a; Keen et al. 1984; Levine et al. 1984; Agha 1985). Adenocarcinoma arising in Barrett's esophagus represents up to 50% of all adenocarcinomas involving the gastroesophageal junction region (Keen et al. 1984; Levine et al. 1984; Agha 1985). Alternatively, primary carcinoma of the gastric cardia or fundus can invade into the distal esophagus. Adenocarcinomas arising from the distal esophagus or the stomach will exhibit similar features in terms of growth, differentiation, and invasion (Kalish et al. 1984). The important distinction is the presence of underlying Barrett's esophagus, as definitive therapy may necessitate treatment of all of the Barrett's mucosa in addition to the primary tumor.

As with esophageal SCC, adenocarcinoma of the esophagus can invade local, regional, or distant structures by direct extension, lymphatic spread, or through hematogenous metastases. With the exception of the propensity for adenocarcinoma to directly invade the proximal stomach, the mechanisms of spread are similar to that of esophageal SCC.

Esophagography Findings

Early Adenocarcinoma

Early adenocarcinoma arising in Barrett's esophagus may appear on double contrast esophagography as

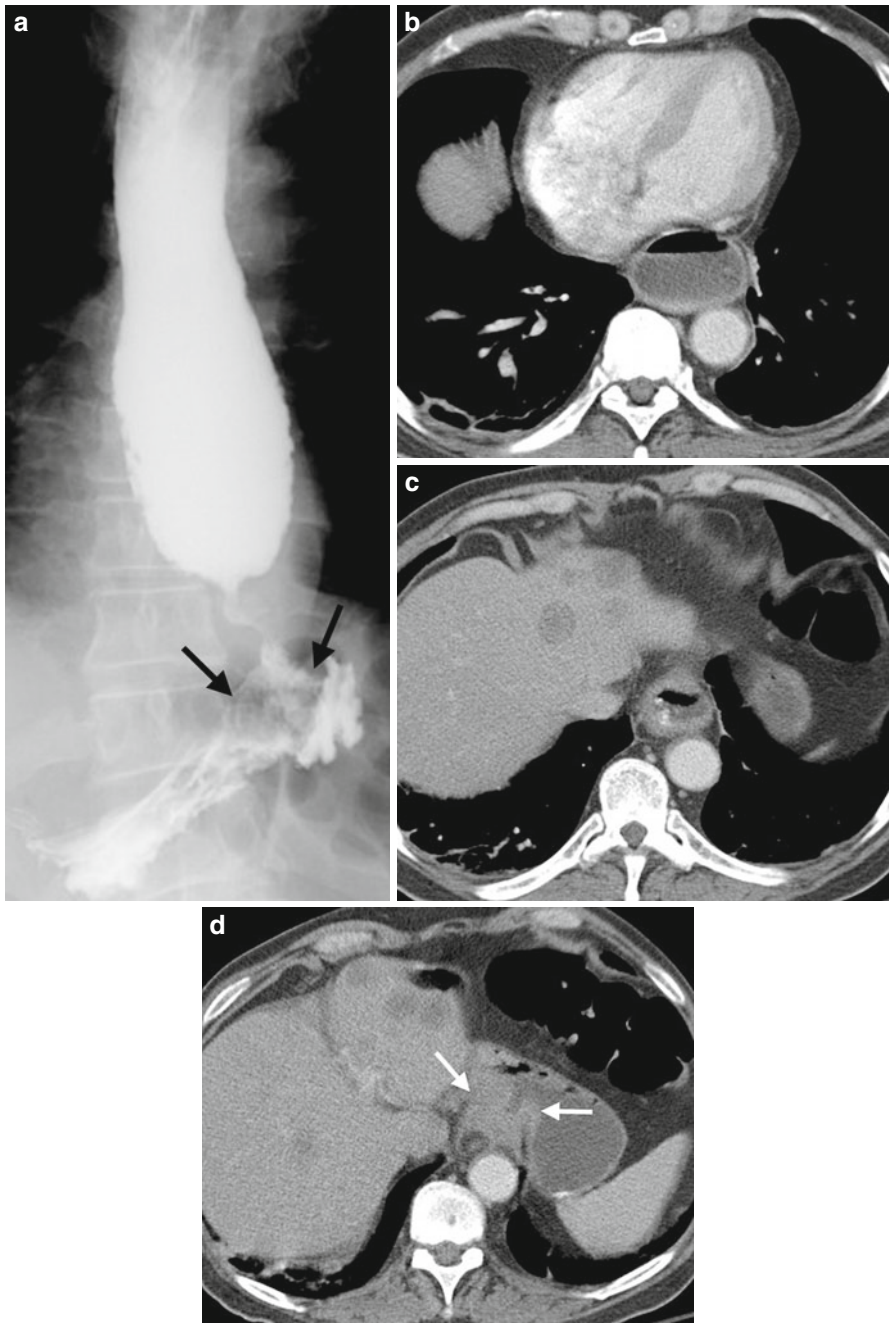

Fig. 11.15 Adenocarcinoma of the distal esophagus crossing the diaphragm to involve the gastric cardia. (**a**) An upright AP image from an esophagram shows a significantly dilated esophagus due to an infiltrating, annular lesion in the distal esophagus. The neoplasm crosses the gastroesophageal junction to involve the proximal stomach (*arrows*). Axial contrast-enhanced CT images show (**b**) a dilated esophagus with an air-fluid level, (**c**) circumferential soft tissue density wall thickening of the distal esophagus, and (**d**) tumor extension into the proximal stomach (*arrows*). Note the hepatic metastases

a small plaque-like or sessile polypoid lesion, similar to early esophageal SCC. A small polypoid lesion in the distal esophagus could also represent an adenomatous polyp arising in Barrett's mucosa, possibly containing foci of invasive carcinoma (Levine et al. 1984; Keeffe et al. 1986). Superficial spreading cancers may appear as confluent areas of nodularity or granularity of the mucosa and a discrete mass may not be visible (Levine et al. 1986). As in SCC, early adenocarcinoma can appear as a larger polypoid mass (>3.5 cm) indistinguishable from advanced esophageal carcinoma on esophagography

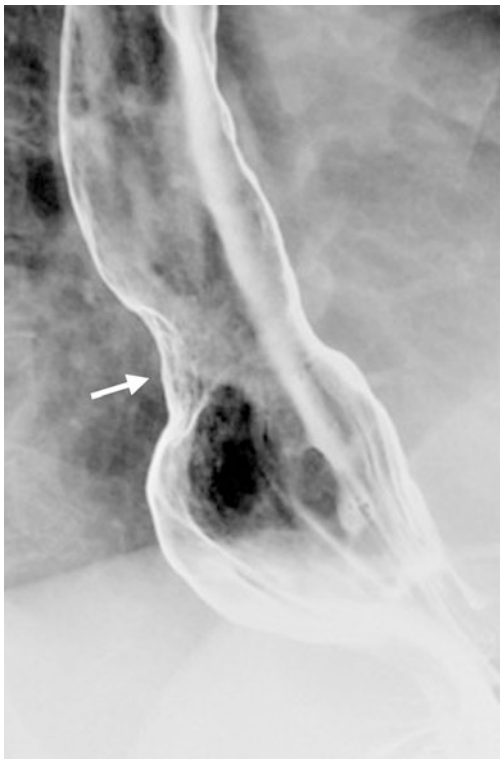

Fig. 11.16 Early adenocarcinoma arising in Barrett's mucosa. A double contrast upright LPO spot image shows a small hiatal hernia with stiffening of the walls of the distal esophagus and fine nodularity. There is a more focal area of confluent nodularity and decreased distensibility with flattening of the esophageal wall due to an early adenocarcinoma (*arrow*)

(Levine et al. 1986). A localized area of flattening or stiffening in the wall of a peptic stricture could be an indicator of early adenocarcinoma (Fig. 11.16) (Levine et al. 1984, 1986; Agha 1985).

Advanced Adenocarcinoma

Overall, esophageal SCC and adenocarcinoma may appear similar on barium studies, making it difficult to distinguish these pathologic entities. However, adenocarcinomas are more likely to involve the distal esophagus and invade the proximal stomach and esophageal adenocarcinomas tend to involve a longer segment of the esophagus as compared with SCC. A distal esophageal lesion crossing the gastroesophageal junction should be considered adenocarcinoma, either arising from the distal esophagus (Fig. 11.17) or the stomach, as esophageal SCC very rarely extends to involve the stomach (Keen et al. 1984; Levine et al. 1984; Agha 1985). Also, many patients with adenocarcinoma arising in Barrett's mucosa will have associated findings of reflux disease on esophagography including hiatal hernias, gastroesophageal reflux, reflux esophagitis, and/or peptic strictures (Levine et al. 1984; Agha 1985). These findings in combination with an esophageal malignancy may favor a pathologic diagnosis of adenocarcinoma over SCC; however, endoscopy and biopsy should be obtained for definitive diagnosis.

Advanced esophageal adenocarcinomas appear as infiltrative lesions with irregular luminal narrowing, nodularity of the mucosa, and abrupt asymmetric borders (Keen et al. 1984; Levine et al. 1984; Agha 1985). As in the case of SCC, advanced adenocarcinoma less often appears as a polypoid intraluminal mass or as a primary ulcerative mass. Submucosal spread of tumor may have a varicoid appearance, as in SCC (Odes et al. 1980; Levine et al. 1984; Agha 1985).

Unlike the discontinuous involvement of the proximal stomach that may be found in esophageal SCC due to submucosal lymphatic spread, adenocarcinomas in the distal esophagus have a tendency to directly invade the gastric cardia or fundus with contiguous involvement. Irregular luminal narrowing may be seen extending from the distal esophagus into the proximal stomach. Involvement of the proximal stomach may be manifest on barium studies as distortion or obliteration of normal anatomic landmarks in the gastric cardia or as a polypoid or ulcerative mass (Fig. 11.18) (Keen et al. 1984; Levine et al. 1984; Agha 1985). Optimal double contrast technique including views of the gastric cardia may be necessary to demonstrate the extent of disease. It is not typically possible to distinguish esophageal adenocarcinoma invading the proximal stomach from gastric carcinoma invading the distal esophagus on esophagography. However, esophageal adenocarcinoma tends to have more esophageal involvement than gastric involvement and gastric carcinomas tend to have a greater degree of proximal gastric involvement in relation to esophageal involvement.

Differential Diagnosis

Early esophageal SCC and adenocarcinoma can appear on double contrast studies as small plaque-like or polypoid lesions. Benign squamous papillomas may also appear as small, sessile, and slightly lobulated polyps

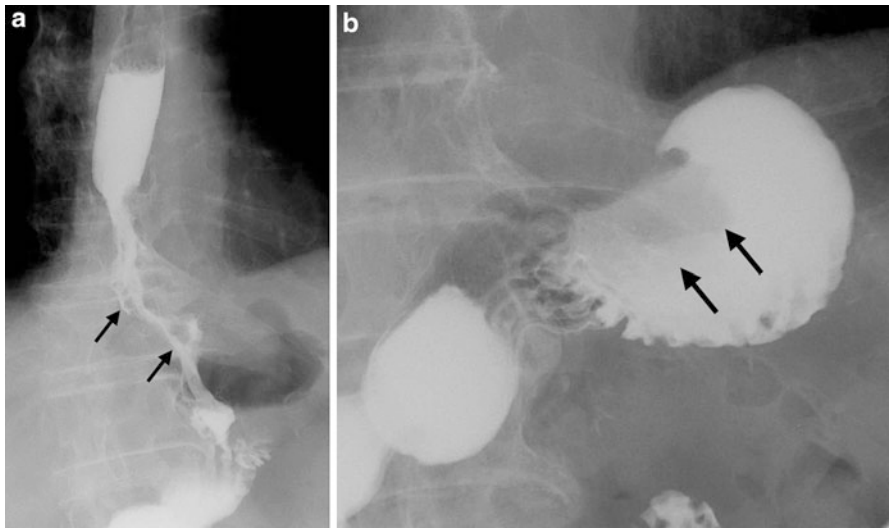

Fig. 11.17 Advanced esophageal cancer: Infiltrative adenocarcinoma. (**a**) An upright AP image from an esophagram shows a long infiltrative lesion narrowing the lumen of the distal esophagus. Luminal narrowing and irregularity extend across the diaphragm and into the proximal stomach (*arrows*). (**b**) A supine AP image shows a lobulated mass-like filling defect in the proximal stomach (*arrows*)

that may be indistinguishable from an early cancer. Candida esophagitis and glycogenic acanthosis can appear as plaque-like filling defects and nodularity. When focal, these entities could mimic neoplasm, especially superficial spreading carcinoma. However, candidal plaques and glycogenic acanthosis tend to appear as discrete nodules with normal intervening mucosa. Nodules and plaques of superficial spreading carcinoma are more ill defined and coalescent with contiguous disease. Changes from severe reflux esophagitis can appear plaque-like and raise concern for Barrett's esophagus or early adenocarcinoma. When radiographic findings are equivocal or suspicious, endoscopy and biopsy should be recommended for definite diagnosis.

An advanced infiltrating esophageal neoplasm may rarely demonstrate relatively tapered borders and could be mistaken for a benign stricture (Goldstein et al. 1981; Levine and Halvorsen 2008). However, focal irregularity, nodularity, or stiffening of even one wall of a stricture should suggest the possibility of malignancy. Also, malignant strictures tend to be more asymmetric and irregular as compared with benign strictures. Rarely, esophageal cancer can cause beak-like narrowing of the distal esophagus, similar to primary achalasia (Agha 1985). Asymmetry, nodularity, or ulceration of the mucosa of the narrowed segment should suggest malignancy.

Esophageal SCC or adenocarcinoma can appear as a polypoid, intraluminal mass, often with associated obstruction. However, a very large, bulky intraluminal mass expanding the esophageal lumen should suggest the possibility of other rare tumors of the esophagus including spindle cell carcinoma and primary melanoma of the esophagus. An impacted food bolus in the esophagus could be confused with a polypoid neoplasm (Fig. 11.19). The patient's history (sudden onset of dysphasia while eating) or the presence of a stricture below the filling defect should suggest the possibility of food impaction.

An ulcerative carcinoma could be mistaken for a benign ulcer if the adjacent neoplastic soft tissue is subtle or overlooked. Alternatively, a large benign ulcer can have excessive surrounding edema and could be mistaken for an ulcerative neoplasm. Endoscopy and biopsy should be performed for these lesions. Varicoid carcinoma (SCC or adenocarcinoma) is a result of submucosal spread. This should not be mistaken for esophageal varices, as varicoid tumors demonstrate a fixed, rigid appearance and an abrupt transition to adjacent normal mucosa. Esophageal varices change in size and shape at fluoroscopy. On occasion, however, varices that have been sclerosed may mimic varicoid carcinoma.

Cancer Staging

Multiple imaging modalities are currently available for the staging of esophageal carcinoma. While traditionally computed tomography (CT) has been the mainstay

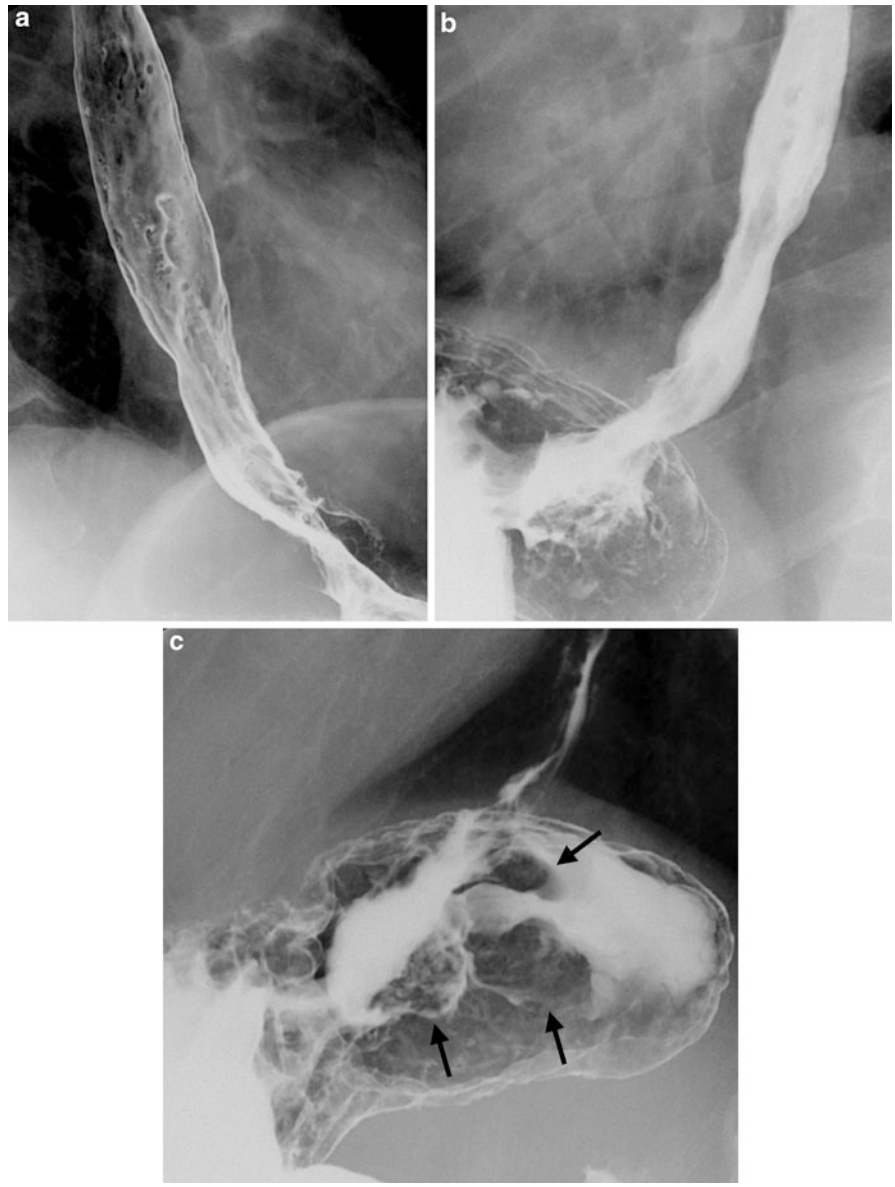

Fig. 11.18 Advanced esophageal cancer: Adenocarcinoma invading the stomach. (**a**) A double contrast upright LPO image shows decreased distensibility of the distal esophagus with associated irregular nodularity of the mucosa. (**b**) In the prone RAO position, irregular mild luminal narrowing is seen. (**c**) A double contrast right lateral image of the gastric cardia shows distortion and obliteration of normal anatomic landmarks with polypoid filling defects (*arrows*) due to tumor involvement

in staging of esophageal carcinoma, endoscopic ultrasound (EUS) and positron emission tomography (PET) are alternative and potentially complementary imaging modalities for tumor staging. Cancer staging is especially efficacious when it can help guide therapy. With esophageal carcinoma, the decision is often whether to initiate therapy with surgery, preoperative adjuvant chemoradiation therapy, or palliative therapy. As with any carcinoma, staging is dependent upon accurate detection of local invasion, regional lymph node involvement, and/or distant metastases. The different imaging modalities have relative strengths and weaknesses in the detection of these findings.

TNM Staging

Commonly, esophageal cancers are staged using the TNM staging classification system. Local invasion (T) is divided into four categories (T1–T4). T1 and T2 tumors are contained within the esophageal wall, T3 tumors have spread through the wall into

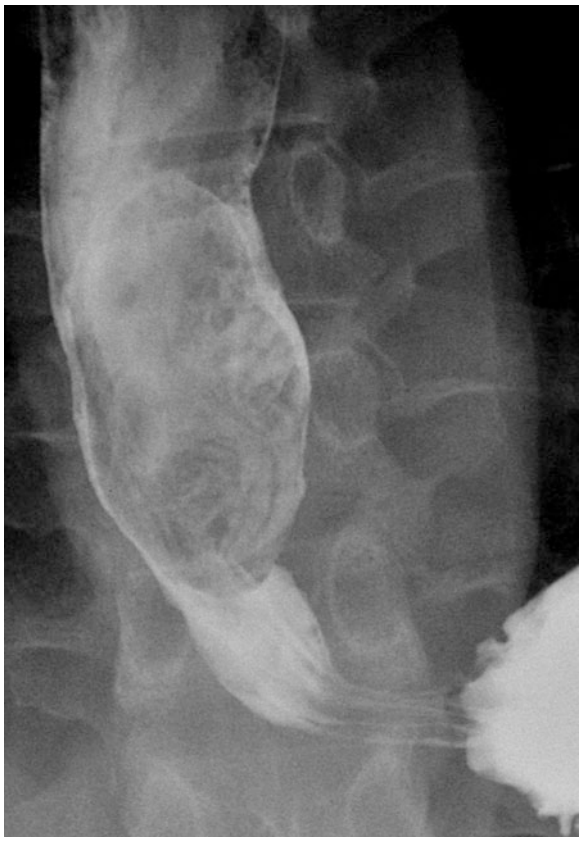

Fig. 11.19 Impacted food bolus/bezoar in the distal esophagus. LPO esophagram image shows expansion of the distal esophagus with a large, mass-like filling defect. Barium can be seen in the interstices of the mass indicating a conglomerate of food and debris rather than neoplasm. This occurred above a focal stricture

periesophageal fat, and T4 tumors have invaded adjacent structures such as the trachea, bronchus, aorta, heart, or spine.

TNM Staging of Esophageal Cancer: The American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) revised the TNM staging system for esophageal cancer in 2010. The major change from the prior 2002 TNM system was the development of different stage groupings according to histology. The alteration in the TNM system was based upon analysis of worldwide data of 4,627 patients with cancer of the esophagus or GE junction who underwent surgery alone (Saltzman and Gibson 2011). This review demonstrated that among patients with lymph node negative tumors, prognosis was dependent upon T stage as well as histologic grade and tumor location.

In addition to separating stage groupings for squamous cell carcinoma and adenocarcinoma, other changes from the 2002 classification system include:

- Subclassification of T4 lesions based on potential resectability of adjacent involved organs or structures. T4 is divided into T4a with resectable tumor invading pleura, pericardium, or diaphragm versus T4b with unresectable tumor invading adjacent structures such as aorta, vertebral body, trachea, etc.
- Subclassification of nodal status according to the number of regional nodes containing metastases.
- The anatomical boundaries of the components of the esophagus have been modified slightly to make them more specific. For instance, the esophagus is divided into four components: (1) cervical esophagus, (2) upper thoracic, (3) middle thoracic, and (4) lower thoracic and abdominal esophagus including the GE junction. The cervical esophagus extends from the lower border of the cricoid cartilage to the thoracic inlet as determined by the sternal notch. The upper third of the esophagus extends from the sternal notch to the carina. The middle thoracic esophagus extends from the carina to the inferior margin of the inferior pulmonary vein or endoscopically 32 cm from the incisors. The lower thoracic and abdominal esophagus extends to the GE junction, approximately 40 cm from the incisors (Saltzman and Gibson 2011).
- The definitions of the primary tumor (T), regional lymph nodes (N), and distant metastases (M) are identical for squamous cell and adenocarcinomas. Histologic grade is also identical. The location of the tumor affects the staging only in stages 0–2, but not in stages 3 and 4.

Lymph Node Metastases (N): The esophagus differs from the rest of the gastrointestinal tract with lymphatic channels in the lamina propria and muscularis mucosa inside the mucosal layer (Tachibana et al. 2008). In the remainder of the GI tract, lymphatics are first encountered in the submucosa, a deeper layer. Esophageal lymphatics run longitudinally upward into cervical nodes and downward into the abdominal nodes. With esophageal cancer, lymphatic metastases can follow three routes: (1) longitudinal: along the submucosal plexus to regional or more distant nodes, (2) perpendicular: into periesophageal nodes, or (3) into the thoracic duct, and then into the systemic venous circulation.

Detection of metastatic lymph nodes is important for staging. The short axis diameter exceeding 1 cm is considered pathologic for lymph nodes in the mediastinum. While mediastinal nodes are considered regional nodes for esophageal cancer, pathologic nodes in the neck or abdomen are considered distant metastases. Lymph node enlargement may also occur with inflammatory or infectious etiologies (Halvorsen and Thompson 1984) so that based upon size criteria alone, imaging cannot distinguish between benign and malignant causes of lymph node enlargement. Also, lymph nodes may contain metastatic disease and still be normal in size. Micrometastases in normal size lymph nodes may occur in up to 50% of esophageal cancers at the time of diagnosis (Izbicki et al. 1997; Natsugoe et al. 1998). Another problem in staging esophageal cancers is that lymph node metastases can "skip." "Skip" lymph node spread of disease occurs when abdominal lymph nodes contain cancer, but mediastinal nodes do not. In a study of 143 patients, Schröder et al. found an overall rate of skip metastases to abdominal nodes of 55% (Schröder et al. 2007).

The number of lymph node metastases influences cancer staging. With the 2010 TNM system N1 is defined as one or two positive regional nodes, N2 as three to six positive nodes and N3 as seven or more positive regional lymph nodes.

Distant Metastases (M): Lymph node metastases are the most common form of distant metastases with esophageal cancer. In a review of 838 patients with metastatic esophageal cancer, Quint et al. found the most common site of metastases to abdominal lymph nodes (45%) followed by the liver (35%), cervical or supraclavicular nodes (18%), bone (9%), and adrenal glands (5%) (Quint et al. 1995). Lung metastases are uncommon at the time of diagnosis but are increasingly common during terminal phases of the disease. Margolis et al. in a series of 116 patients found that a solitary lung nodule at the time of diagnosis is more likely to represent a benign lesion or primary lung carcinoma than a metastatic lesion (Margolis et al. 1998).

Staging of Esophageal Carcinoma: Imaging Modalities

Many institutions routinely perform chest and abdominal CT, EUS of the esophagus and PET imaging prior to referral to a thoracic surgeon (Keswani et al. 2009). Each of these imaging modalities has advantages.

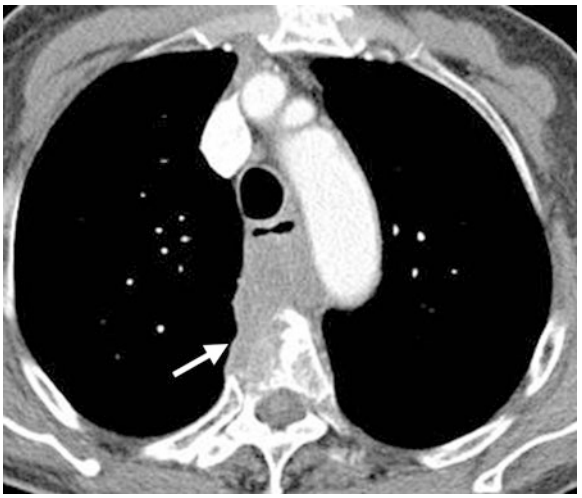

Fig. 11.20 Direct invasion: Axial contrast-enhanced CT. Obvious direct invasion of esophageal cancer into the right side of a thoracic vertebral body (*arrow*)

Computed Tomography

CT is typically performed during a preoperative staging evaluation for a known esophageal carcinoma. CT is useful to assess tumor size, including wall thickening and extraesophageal extent, as well as invasion of periesophageal tissues, the tracheobronchial tree and aorta, mediastinal or abdominal lymphadenopathy, and distant metastases.

Direct Invasion: CT has been demonstrated in the past to be highly accurate in the detection of T4 tumors and differentiating them from T3. T4 indicates local invasion of adjacent structures such as the trachea, bronchus, pericardium, or aorta (Thompson et al. 1983b). Direct invasion may occasionally be obvious, with visible tumor directly invading and destroying an adjacent structure, such as a vertebral body (Fig. 11.20). Often, tumor invasion by esophageal cancer can only be recognized by more subtle, but specific findings.

CT appears superior in the detection of direct invasion by esophageal carcinomas as compared with other tumors of the GI tract. This superiority of CT staging with esophageal cancers may be due to the fact that the mediastinum is a contained space and direct invasion can be predicted by mass effect criteria that are not useful elsewhere. CT criteria for local invasion include loss of a detectable fat plane between the esophageal tumor and the adjacent structure as well as displacement or indentation of the adjacent structure.

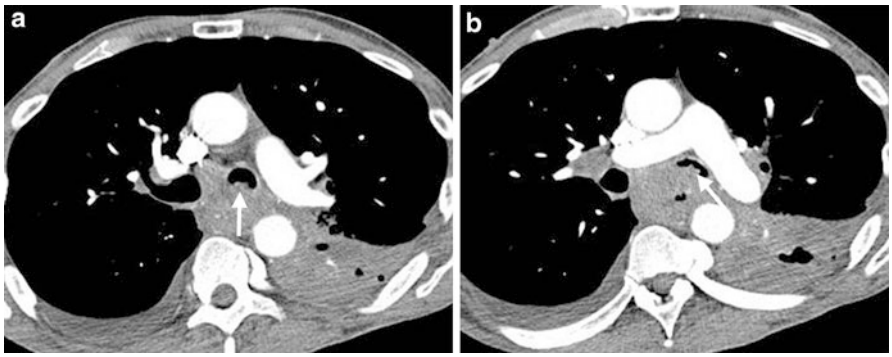

Fig. 11.21 Left bronchial invasion: Obvious extension of esophageal tumor to the left main stem bronchus, displacing and indenting the bronchus but also extending into bronchus. CT images demonstrate (**a**) displacement and indentation of left posterior bronchial wall (*arrow*) and (**b**) extension of tumor into the bronchial lumen (*arrow*), indicating direct bronchial invasion

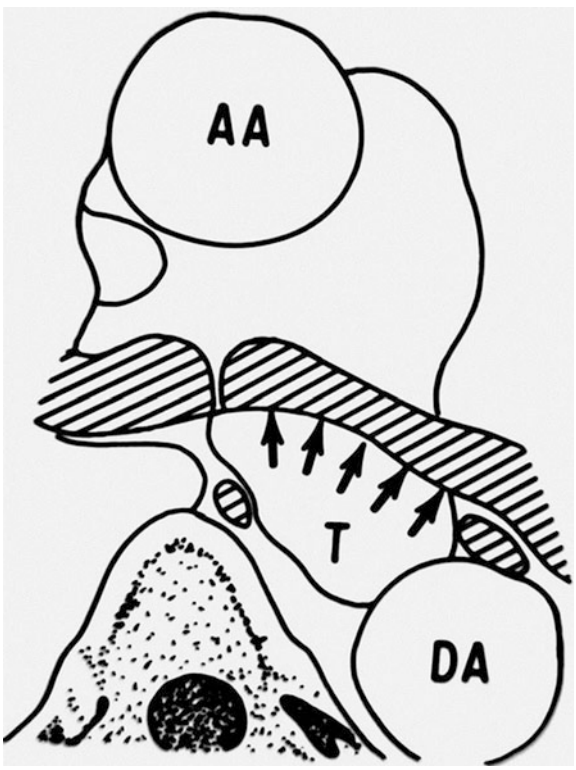

Fig. 11.22 Diagram demonstrating criteria for predicting bronchial invasion: Tumor (T) extends to and displaces the posterior wall of left main bronchus (*arrows*), a specific finding for direct local invasion. (AA) Ascending aorta. (DA) Descending aorta (From Halvorsen RA, Thompson WM: CT of esophageal neoplasms. Radiol Clin North Am 27:673, 1989. With permission from Elsevier.)

The CT finding required to predict direct invasion of the trachea or bronchi is displacement or indentation of the posterior wall of the trachea or bronchus by the tumor mass (Figs. 11.21–11.23). This mass effect criterion has been found to have a high accuracy rate. Combined data from six studies obtained from the pre-helical CT era correlating CT findings of tracheal invasion with operative and histological findings have demonstrated excellent results. Combined results demonstrated a sensitivity for the CT prediction of tracheal or bronchial invasion of 93% with a specificity of 98% and an overall accuracy of 97% (Halvorsen and Thompson 1989). Fistulization to the airway is also an accurate indicator of invasion.

Pericardial invasion from an esophageal carcinoma is also based upon mass effect criteria. Pericardial invasion can be predicted with a high level of accuracy when an esophageal tumor extends to the posterior surface of the heart with no intervening fat plane and bulges into the lumen of the left atrium either on CT or MR (Fig. 11.24). The sensitivity, specificity, and accuracy rate for prediction of pericardial invasion may approach 94% (Halvorsen and Thompson 1989).

The prediction of local invasion of the aorta is more difficult. The problem arises because the normal esophagus contacts the normal aorta with no intervening fat plane. Criteria have been developed to determine invasion based on the amount of contact between the esophageal tumor and the aorta (Picus et al. 1983). If the circumference of the normal aorta is equated to a compass with a circumference of 360°, then if an esophageal tumor obliterates the periaortic fat for more than 90° (one quarter of the circumference of the aorta), then the tumor can be considered invasive of the aorta (Figs. 11.25, 11.26). If there is less than 45° of direct contact between the tumor and the aorta, then there is no evidence of aortic invasion (Fig. 11.27). Between 45° and 90° of direct contact is considered indeterminate for

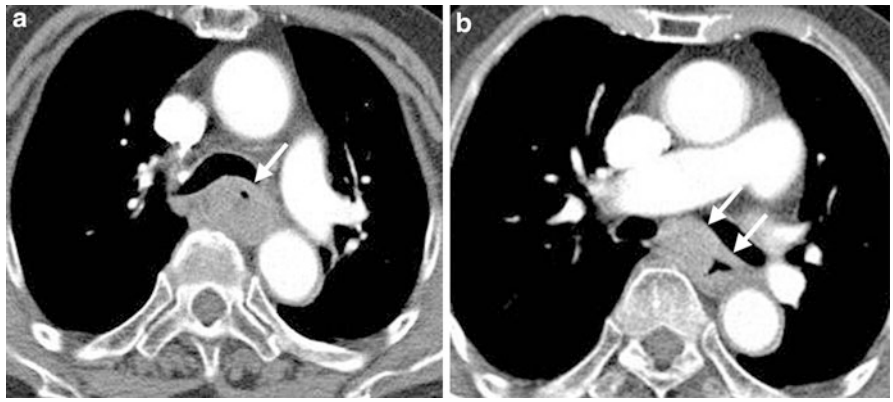

Fig. 11.23 Direct bronchial invasion: (**a** and **b**) CT images contrast enhanced. An esophageal tumor is displacing and indenting the posterior wall of left main stem bronchus (*arrows*). This is diagnostic of direct bronchial invasion with a high specificity (96%)

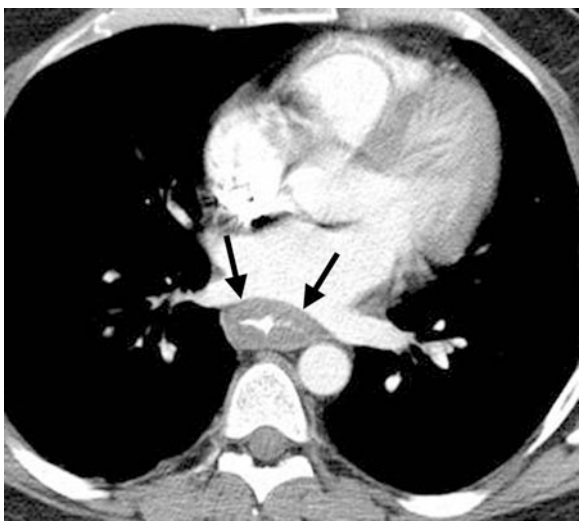

Fig. 11.24 Pericardial invasion: Esophageal tumor extends to the posterior surface of the heart without intervening fat plane and indents the posterior surface of the left atrium (*arrows*), diagnostic of direct local invasion

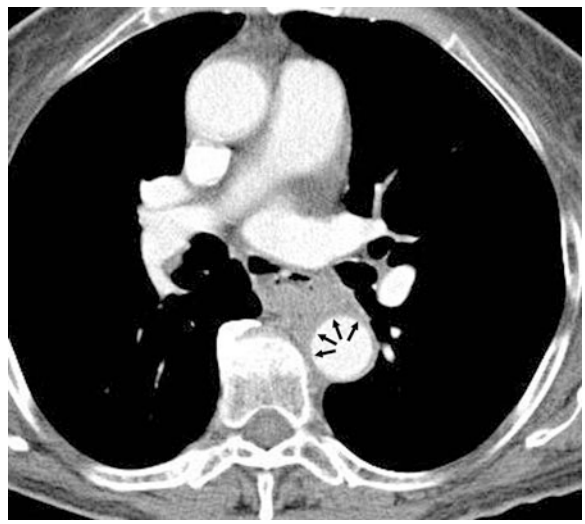

Fig. 11.25 Aortic invasion: Esophageal tumor is seen to extend to the aorta without intervening fat plane and obliterates the periaortic fat plane for more than 90° or one quarter of the circumference (*arrows*)

aortic invasion. Based upon this criterion, the combined results of the six studies with surgical proof suggested a sensitivity of 88%, a specificity of 96%, and an accuracy rate of 94% (Halvorsen and Thompson 1989).

Lymph Node Metastases: Regional lymph nodes serve as the primary method of systemic spread of esophageal cancer (Dhar et al. 2002). CT detection of cancer involvement of the regional lymph nodes is based upon size criteria. Current clinical practice is to consider any mediastinal lymph node with a short axis greater than 1 cm as a "positive" node. Short axis is obtained by determining the longest axis of a node, then measuring the maximal diameter of the node perpendicular to the long axis. The concept of size reflecting malignancy is compromised by two problems: namely, a normal size node may contain cancer, and an enlarged lymph node may not. Nodal enlargement may also reflect local inflammation rather than malignant involvement (Thompson et al. 1983b). In a study of 187 patients with squamous cell cancers who had undergone surgery, Dhar et al. measured the long axis of lymph nodes on histopathologic specimens and found that metastatic lymph nodes ranged in size from 3 to 30 mm with an average of 12.6 mm (Fig. 11.28) (Dhar et al. 2002). They found that node size was related to prognosis, and recommended using 10-mm long axis on histopathologic analysis. They also reported that the number of positive nodes had a significant effect on

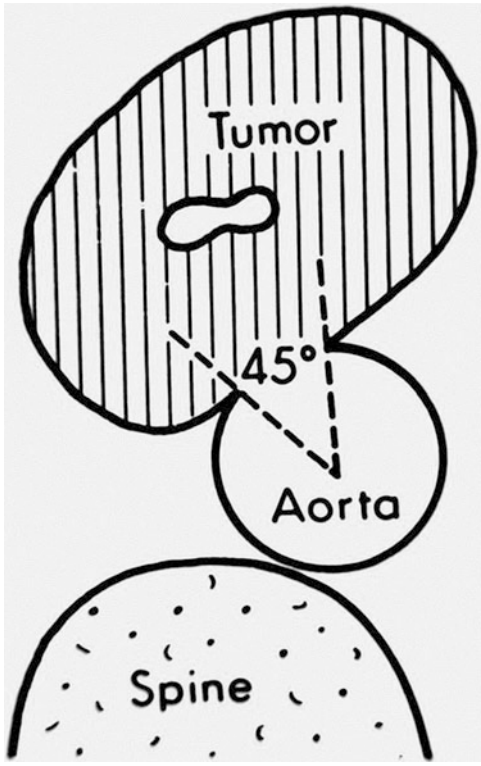

Fig. 11.26 Aortic invasion diagram: Esophageal tumor is seen to directly contact the descending thoracic aorta over a 45° angle. Tumors contacting the aorta in less than 45° of aortic circumference are considered noninvasive, between 45° and 90° indeterminate, and greater than 90° invasive of the aorta

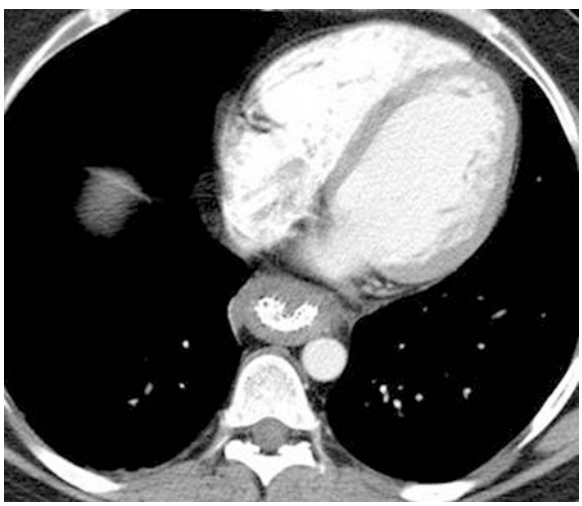

Fig. 11.27 Aorta free of invasion: CT demonstrates circumferential esophageal tumor that barely contacts the aorta. If contact of the tumor and aorta is less than 45°, then no invasion is predicted

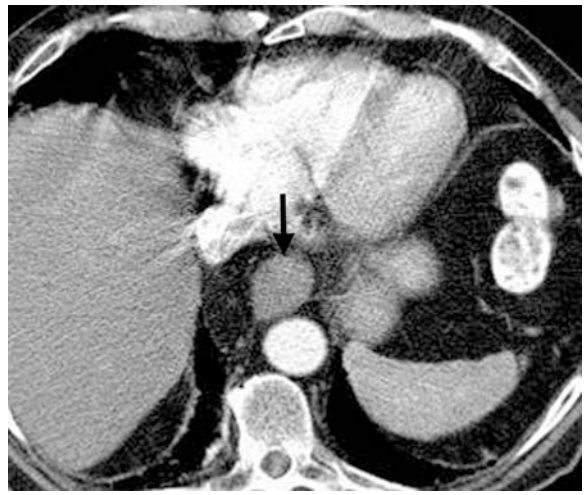

Fig. 11.28 Large mediastinal node (*arrow*) posterior to heart and anterior to aorta in a patient with squamous cell carcinoma of the esophagus

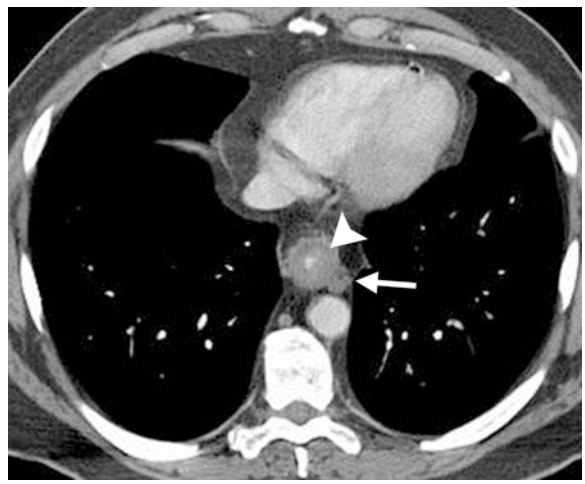

Fig. 11.29 Mediastinal lymph node metastasis (*arrow*) adjacent to primary esophageal tumor (*arrowhead*)

survival. In patients with three or fewer positive nodes, the 5 year cancer specific survival (CSS) was 82% for patients with nodes less or equal to 1.0 cm (long axis) and 30% with nodes greater than 1.0 cm. While their work uses long axis measurements at histopathology, the concepts should hold true with CT, namely that larger nodes and an increased number of large nodes correlate with a worse prognosis.

A potential limitation of CT in the diagnosis of mediastinal lymph node involvement occurs when a lymph node is not identified because it is inseparable from the primary tumor (Fig. 11.29). This is more

likely encountered in cachectic patients. No known data exist regarding the frequency of this problem.

Distant Metastases: CT is an excellent tool for the detection of lung metastases and has been the standard test utilized to detect distant metastases to the liver, adrenal glands, and upper abdominal lymph nodes (Fig. 11.30). Upper abdominal lymph nodes are frequently encountered in the gastrohepatic ligament (in the fat between the liver and stomach) and may be more easily detectable than enlarged mediastinal lymph nodes (Figs. 11.31, 11.32).

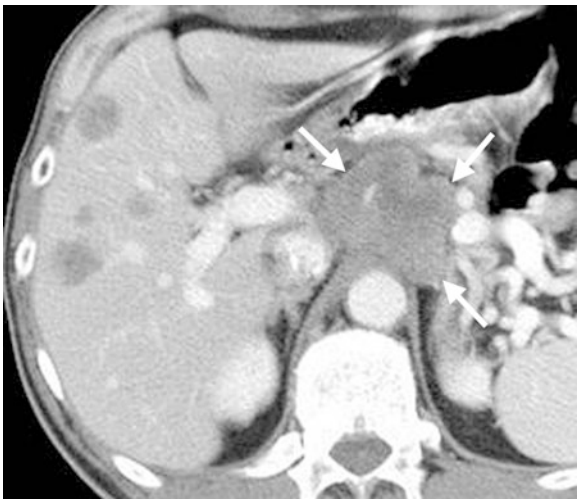

Fig. 11.30 Liver and abdominal lymph node metastases: CT demonstrates multiple liver metastases and large bulky lymph node metastases between the stomach and abdominal aorta (*arrows*)

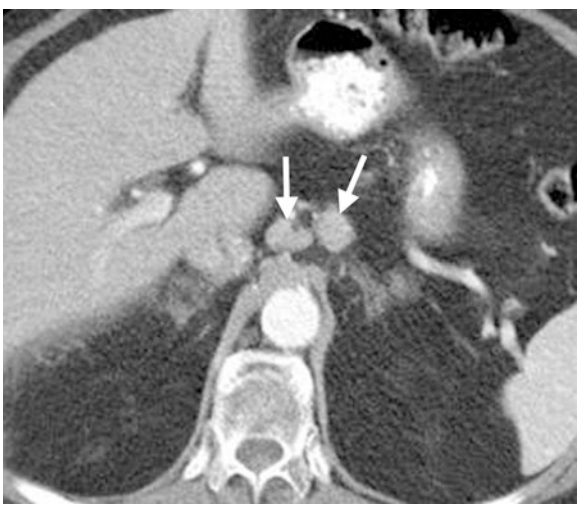

Fig. 11.31 Abdominal lymph node metastases from esophageal cancer in gastrohepatic ligament (*arrows*); a typical location for lymph node metastases from esophageal cancer

Endoscopic Ultrasound (EUS)

The EUS device is typically built into the tip of a fiberoptic endoscope specifically designed for endoscopic ultrasound. There is an inflatable balloon at the tip of the probe that can be filled with water to produce an acoustic interface between the esophageal wall and the transducer. EUS devices are typically stand-alone devices separate from a standard upper endoscope. The ultrasound probes are similar in size to standard endoscopes and often cannot pass through a stenotic esophageal cancer. Miniaturized ultrasound catheter probes have been developed that can be passed through the biopsy channel of a standard upper gastrointestinal endoscope (Koch et al. 1993; Hünerbein et al. 1998; Menzel and Domschke 2000). These smaller probes utilize very high frequency, typically 12.5 MHz. The higher the frequency of ultrasound waves, the lower the depth of the penetration. Therefore, these miniprobes have a more limited field of view than a standard EUS device. However, these smaller probes may be available at the time of the initial diagnostic endoscopy and can pass through more stenotic esophageal cancers than the standard EUS probe.

Direct Invasion: Endoscopic ultrasound is the best available test for determining depth of tumor invasion within the esophageal wall. In a study comparing EUS with pathologic findings from surgical resection, EUS was reported as 87% accurate, 82% sensitive, and 91% specific for the differentiation of tumors confined to the esophagus ($\leq$T2) or invading beyond the esophagus ($>$T2). As the esophagus is the sole portion of the gastrointestinal tract that lacks a serosa, invasion of the adventitial fat is considered to be a T3 lesion (Rice et al. 2003).

The major advantage of EUS is that it can provide excellent visualization of the layers of the esophageal wall. Typically five layers can be identified in the esophagus with EUS with the layers appearing as alternating increased and decreased echogenicity and producing five separate rings (Fig. 11.33). Fat is echogenic on ultrasound and the central echogenic line seen on EUS represents submucosal fat. The inner echogenic line represents the mucosal interface

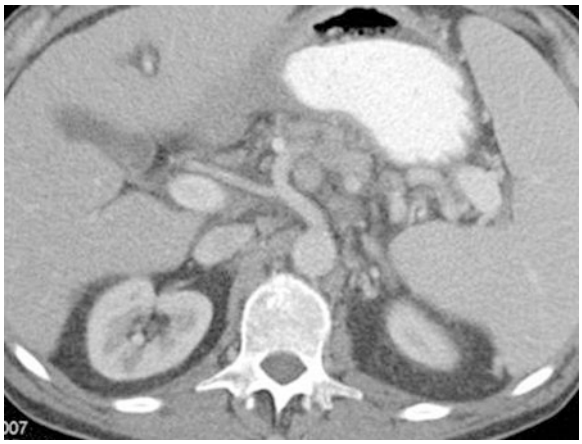

Fig. 11.32 Multiple enlarged nodes adjacent to celiac artery in patient with adenocarcinoma of the esophagus

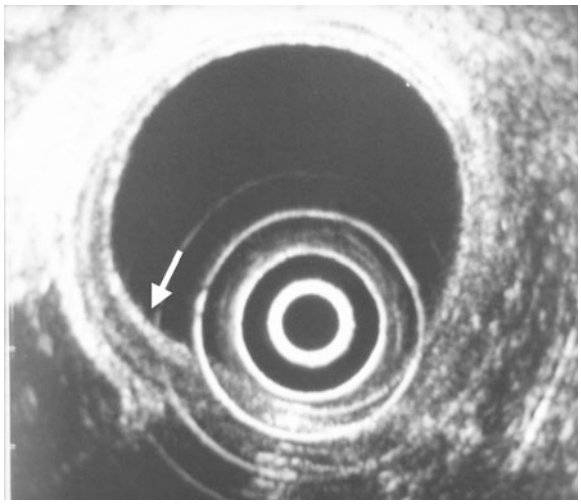

Fig. 11.33 Normal endoscopic ultrasound: EUS image of the esophagus demonstrates five layers (*arrow*). The central echogenic stripe is submucosal fat, an important landmark for T staging of esophageal tumors (From Gore RM, Levine MS (eds): Textbook of Gastrointestinal Radiology, 3rd ed. Philadelphia, Saunders, 2008. With permission from Elsevier.)

with the transducer and the outer echogenic line represents adventitial fat. With EUS, tumors are identified as a hypoechoic mass that disrupts or widens these esophageal rings (Fig. 11.34).

EUS can predict invasion within the esophageal wall and can often identify tumor spread beyond the esophageal wall into the periesophageal fat. This allows EUS to differentiate between T2 tumors and T3 tumors with extension into the periesophageal fat.

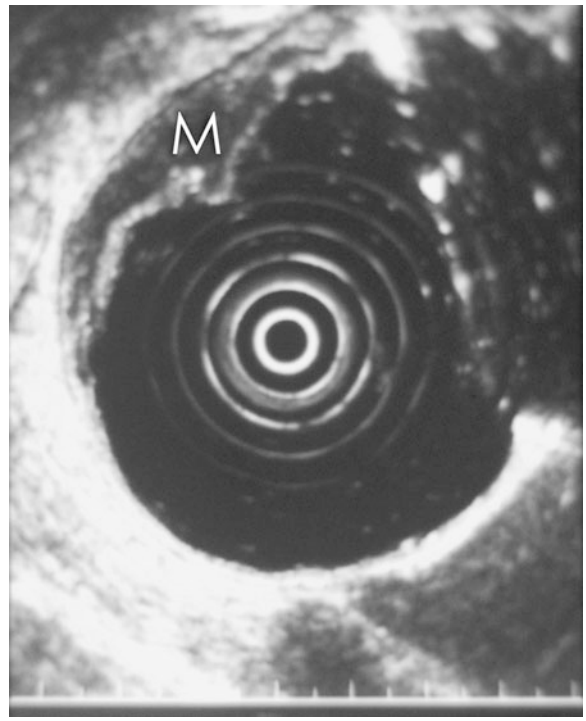

Fig. 11.34 EUS of esophageal squamous cell carcinoma with the tumor identifiable as a mass (*M*) disrupting the layers of the esophageal wall (From Gore RM, Levine MS (eds): Textbook of Gastrointestinal Radiology, 3rd ed. Philadelphia, Saunders, 2008. With permission from Elsevier.)

The ability of endoscopic ultrasound to predict T4 lesions or invasion of adjacent structures is somewhat limited due to the inability of EUS to determine whether a tumor abuts or invades an adjacent structure. Differentiation of T2 from T3 tumors is important, as in many institutions, patients with tumors invading the adventitial fat undergo multimodality therapy including preoperative chemotherapy and radiation therapy while tumors restricted to the esophageal wall with no lymph node or distant metastases will go directly to surgery (Rice et al. 2003). In a study of 209 patients undergoing esophagectomy for esophageal cancer and 128 patients undergoing induction therapy followed by esophagectomy, Rice et al. found that EUS was 87% accurate, 82% sensitive, and 91% specific in distinguishing between tumors confined to or invading beyond the esophageal wall. In their patient population, down-staging by induction preoperative chemoradiation therapy was beneficial only if tumors invaded beyond the esophageal wall ($P = 0.003$) (Rice et al. 2003).

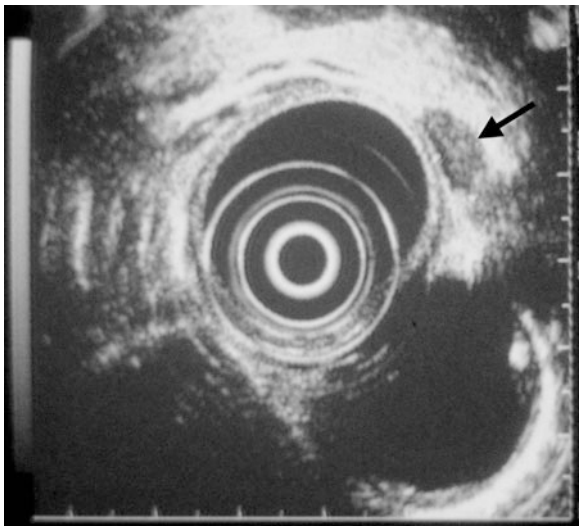

Fig. 11.35 EUS of metastatic lymph node (*arrow*) in a patient with esophageal squamous cell carcinoma (From Gore RM, Levine MS (eds): Textbook of Gastrointestinal Radiology, 3rd ed. Philadelphia, Saunders, 2008. With permission from Elsevier.)

Lymph Node Metastases: EUS uses relatively subjective criteria for the prediction of lymph node metastases. During EUS, a lymph node is considered to have a malignant appearance if it is round or oval, sharply demarcated, and hypoechoic (Fig. 11.35) (Catalano et al. 1994). Strict criteria for lymph node size are not used, but size greater than 10 mm is considered suggestive of involvement. EUS is limited in its ability to stage esophageal cancers when the tumor is stenotic and will not allow passage of the endoscope through the tumor. Therefore, potentially involved lymph nodes may go undetected. Standard EUS is unable to traverse an esophageal cancer in up to 20–45% of cases (Heidemann et al. 2000; Kelly et al. 2001).

An additional limitation of EUS in the detection of lymph node metastases is that only nodes in close proximity to the esophageal or gastric wall can be visualized as EUS has a penetration depth of only approximately 5 cm. CT can readily identify more distant nodes.

EUS Versus CT: In a meta-analysis of 13 studies that evaluated the ability of EUS to stage esophageal cancers, the accuracy rate for T staging was found to be 89% and the accuracy for detection of lymph node metastases 79% (Lightdale and Kulkarni 2005). Early studies of EUS suggested that it was superior to CT for esophageal cancer staging. In a meta-analysis performed by Kelly et al. and published in 2001, they found that EUS was superior to CT (Kelly et al. 2001). Today, most institutions consider EUS as complementary rather than competitive with CT. A combination of the two tests is often useful as they provide different information. For instance, EUS is superior to CT in detecting the extent of tumor spread through the esophageal wall, but CT may be superior in the detection of T4 lesions directly invasive of adjacent mediastinal structures. EUS appears to be superior to CT in the detection of mediastinal lymph node involvement, but CT is superior in the detection of distant metastases.

Positron Emission Tomography

The availability of PET using (18F) fluorodeoxyglucose (FDG) has improved in the United States in the last 10 years. It is becoming more widely available and more frequently utilized in the staging of esophageal cancer. One limitation continues to be the high cost of the examination approximating $930 per patient (Medicare reimbursement rate, 2011). PET using FDG is useful for esophageal cancers because they are relatively FDG avid (Fig. 11.36) (Kato et al. 2002). The role of PET-CT is to detect metastases that are not seen on a routine CT of the chest and abdomen or on EUS. A number of studies have reported that PET can detect metastases not visible on CT of the chest and abdomen in up to 15–20% of patients (Imdahl et al. 2004; Kato et al. 2005). In a study by Kato et al. of 149 untreated esophageal cancer patients who had undergone both CT and PET, the incremental value of PET compared to CT was 14%, 20 of 149 patients had detectable metastases that had been overlooked by CT (Kato et al. 2005). In another study, the metastases detected by PET and missed by CT were most frequently cervical lymph node metastases, representing 38% of the total, followed by bone metastases (23%), and hepatic metastases (15%) (Imdahl et al. 2004).

PET or PET-CT has not been evaluated for the detection of local invasion. Often PET-CT scans are obtained without intravenous contrast and without breath holding. This limits the spatial resolution and may limit the ability of the CT component of the study to detect local invasion.

PET uses increased activity, indicating increased glucose metabolism, within a lymph node to predict malignant lymph node involvement and metastatic disease.

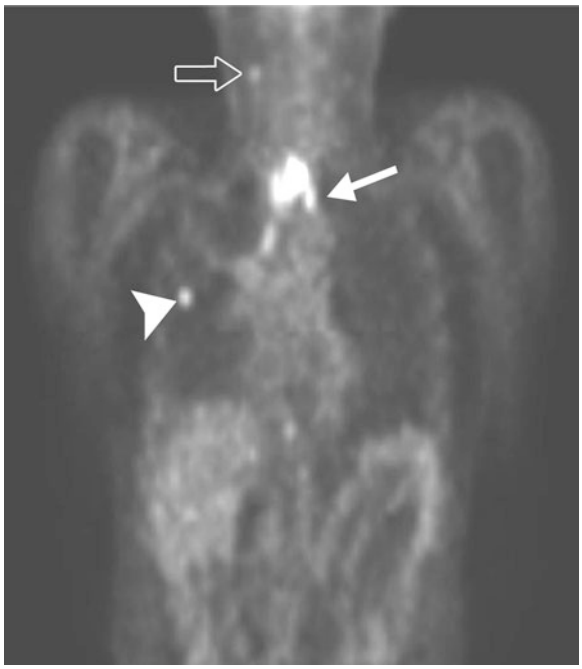

Fig. 11.36 PET image: Metastatic disease. Squamous cell carcinoma involving the proximal thoracic esophagus demonstrates increased activity. There is also increased activity in an adjacent mediastinal node (*arrow*), lung metastasis (*arrowhead*), and cervical lymph node metastasis (*open arrow*) (From Gore RM, Levine MS (eds): Textbook of Gastrointestinal Radiology, 3rd ed. Philadelphia, Saunders, 2008. With permission from Elsevier.)

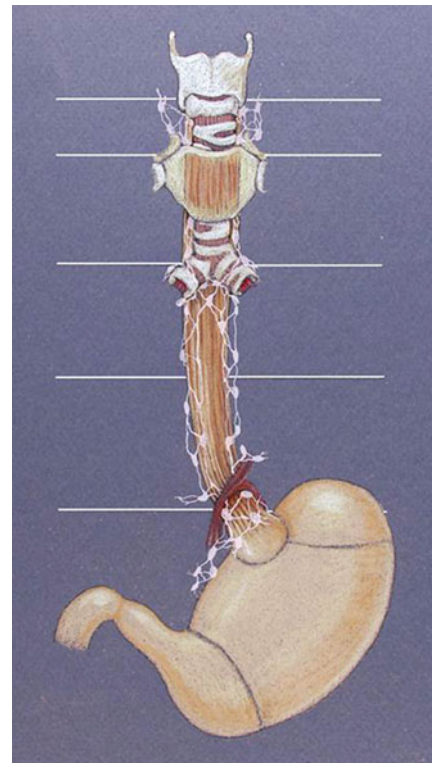

Fig. 11.37 Drawing of longitudinal orientation of lymphatics of the esophagus with direct communication of lymphatic channels from the mediastinum into the neck and below the diaphragm

As with CT, mediastinal lymph node metastases adjacent to the primary tumor may be inseparable from the tumor and the tumor may therefore be understaged.

Anatomical Considerations

The esophagus is drained by multiple interconnecting longitudinal lymph node chains (Fig. 11.37). This is in contrast to the colon where the lymphatics run in a circumferential fashion contributing to the development of circumferential colon cancers (apple core lesions). Typically with esophageal cancers, lymph node metastases can occur before there is significant stenosis.

Traditionally, evaluation of upper abdominal lymph nodes has been thought to be of paramount importance in the proper staging of esophageal cancer. A typical surgical approach was to perform a laparotomy to first evaluate the celiac lymph nodes and if these were negative on frozen section, then proceed with resection of the esophageal cancer either via a transhiatal esophagectomy or via a thoracotomy. More recently, the importance of cervical lymph nodes has been described. In one surgical study, one third of patients who underwent esophagectomy with lymph node dissection of the neck for a "curable" cancer of the thoracic esophagus had lymph node metastases in the neck (Altorki and Skinner 1997). They also reported that cervical lymph node metastases were as frequent as mediastinal lymph node metastases. In another study, Griffith et al. reported that the higher the esophageal cancers were in the mediastinum, the more likely were positive cervical lymph nodes (Griffith et al. 2000). In their series, patients with primary cervical esophageal cancer had an 80% probability of cervical lymph node metastases (Fig. 11.38). With tumors in the upper third of the mediastinum, 52% had nodal metastases in the neck while 29% of those with middle third

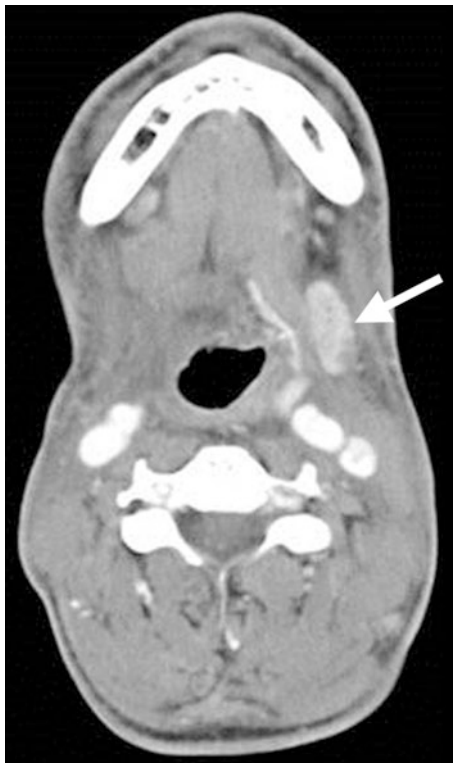

Fig. 11.38 Cervical lymph node metastasis (*arrow*) from primary esophageal squamous cell carcinoma in the upper third of the mediastinum

carcinomas had cervical lymph node metastases. Lower third mediastinal esophageal cancers had a rate of only 9% of cervical lymph node metastases.

Additional imaging of the neck to detect cervical lymph node metastases has been recommended by a number of authors. This may be accomplished with sonography or CT of the neck. A benefit of sonography is that it allows for fine needle aspiration of suspicious nodes (van Overhagen et al. 1991; Tachimori et al. 1994). Neck sonography is usually performed with a high frequency transducer (7.5–10 MHz). Nodes are considered suspicious for malignancy with either a size greater than five mm or with a short to long axis ratio measurement of over 50% (Doldi et al. 1998). The cervical nodes of interest in esophageal neoplasm are within 3 cm of the skin surface and are readily assessed with sonography. Natsugoe reported a sensitivity of 88%, specificity of 59%, and an accuracy of 78% for the prediction of positive lymph node involvement with neck US in esophageal cancer patients (Natsugoe et al. 1999). Alternatively, CT of the neck can be performed in addition to the staging CT of the chest and abdomen in esophageal cancer patients (Fig. 11.38). In a study of 40 patients with head and neck cancer undergoing CT followed by lymphadenectomy and pathologic confirmation, the CT accuracy was 95% in predicting cervical lymph node involvement (Stevens et al. 1985). However, the utility of routine neck CT to detect cervical lymph node metastases in esophageal cancer patients has not yet been reported.

Therapeutic Options and Imaging Following Treatment

Despite differences in pathology and risk factors for development of adenocarcinoma and squamous cell carcinoma, the therapy is relatively similar, with patients receiving the same surgical procedures and radiation therapy options. Chemotherapy regimens may be modified depending upon the tumor histology. In addition to attempted curative surgical resection, esophageal neoplasms may be treated with radiation therapy, chemotherapy, laser therapy, endoscopic resection, and investigational therapies.

Traditionally, surgical resection has been the mainstay of treatment for esophageal carcinoma. Overall 5 year survival in patients with esophageal adenocarcinoma ranges from 10% to 30% with surgical resection alone (Muller et al. 1990; Hulscher et al. 2002). However, in patients with unresectable tumors and metastatic disease, chemotherapy produces response rates of only 20–40% of patients and median survival time of 8–10 months (Enzinger and Mayer 2003). Preoperative chemotherapy or preoperative radiation therapy alone has not been demonstrated to consistently improve survival. More recently, combined preoperative chemoradiation therapy has been proposed. In a recent meta-analysis, preoperative chemoradiation therapy appeared superior to preoperative chemotherapy alone (Gebski et al. 2007). The hazard ratio of all-cause mortality was 0.81 with preoperative chemoradiation therapy versus surgery alone, resulting in a 13% absolute difference in mortality at 2 years. The hazard ratio with preoperative chemotherapy was 0.9 compared with surgery alone resulting in a 2 year absolute survival benefit of only 7%.

In those institutions that have adopted routine use of preoperative chemoradiation therapy, staging is often performed at the time of diagnosis and restaging is performed following neoadjuvant therapy and

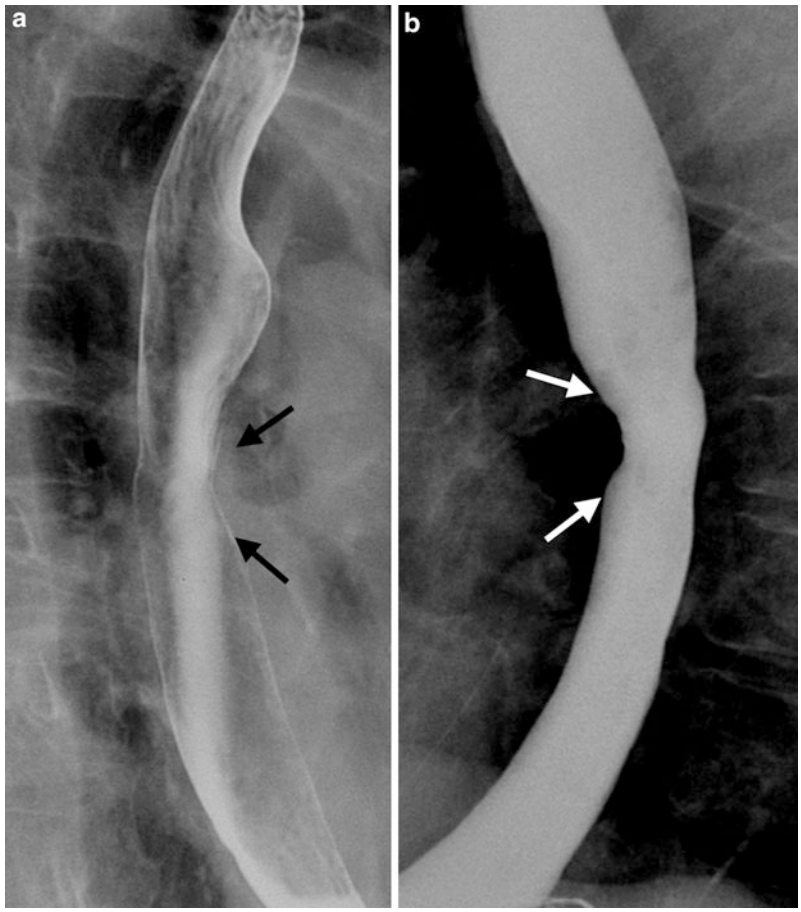

Fig. 11.39 Tumor regression after chemotherapy and radiation therapy. (**a**) Upright LPO and (**b**) prone RAO spot images from a double contrast study show mild, smooth focal luminal narrowing with minimal deformity at the site previous esophageal cancer (*arrows*). Endoscopy revealed no residual tumor

prior to surgery. In those institutions that still operate without chemoradiation therapy, preoperative staging is used to help determine which patients will likely benefit from attempted curative resection.

Radiation therapy as a sole treatment option is more often palliative than curative and esophageal SCC tends to be more radiosensitive than adenocarcinoma. The esophagram may be used to assess for disease response following radiation therapy. Following treatment, there may be noticeable tumor regression with a decrease in size of the lesion or with a smooth stricture at the site of the previous lesion (Fig. 11.39) (Levine et al. 1987). Absence of a visible tumor in the esophagus does not indicate a cure, as these patients often succumb to distant metastases. Local esophageal tumor recurrence often presents with new ulceration, infiltration, or a polypoid mass. The esophagram may be used to distinguish recurrent tumor from other pathologies and to diagnose radiation-induced fistulas to the trachea, bronchi, or mediastinum (Levine et al. 1987). Barium studies can also be used to assess the postsurgical anatomy following resection and to assess for postoperative strictures and other complications (Fig. 11.40).

Algorithmic Approach

Based upon the above findings, a staging algorithm may be suggested (Halvorsen 2007). Patients with an esophageal cancer diagnosed by biopsy can be initially studied with CT of the chest and abdomen. If there is no evidence of direct local invasion or metastases, then the patient is still potentially resectable. The next step would be to proceed to EUS with nodal biopsy if suspicious nodes are encountered. If EUS demonstrates no evidence of invasion beyond the esophageal wall or lymph node involvement, then PET or PET-CT could be obtained to assess for distant metastases.

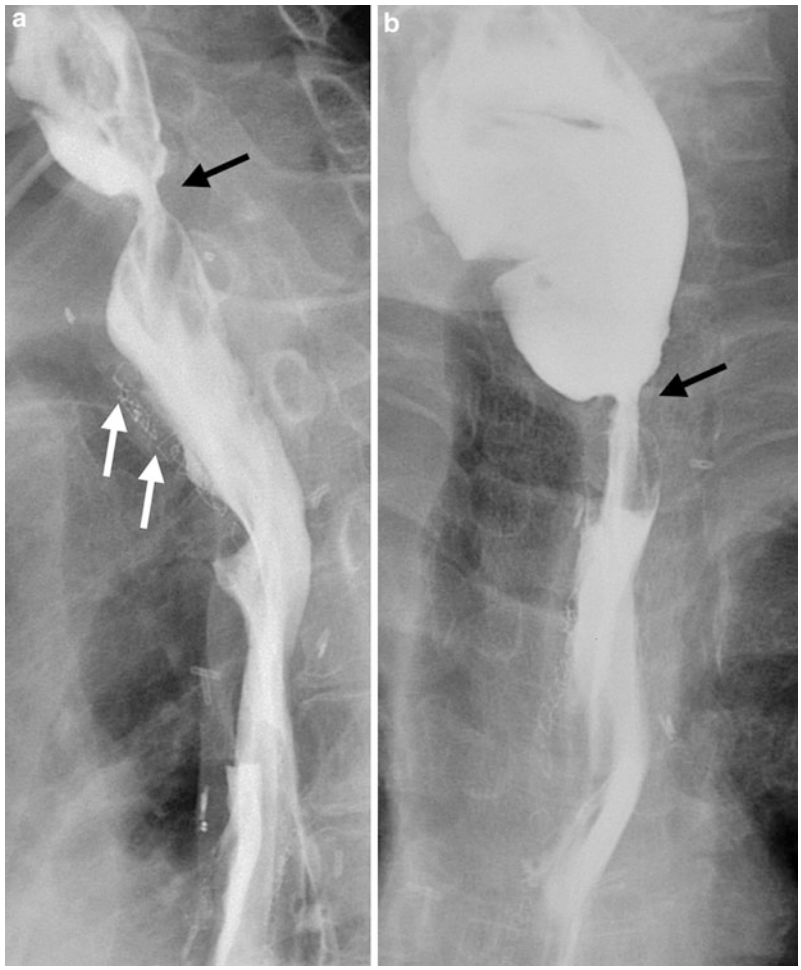

Fig. 11.40 Status post esophagectomy with gastric pull-through: anastomotic stricture. (**a**) RPO and (**b**) AP images from an esophagram show that the patient is status post esophagectomy with an intrathoracic stomach. Note the suture lines (*white arrows*). There is an anastomotic stricture (*black arrow*) with proximal dilatation

If these studies demonstrate no metastases, lymphadenopathy, or evidence of direct invasion, then the patient can be considered for surgical treatment. If there is invasion into the periesophageal fat or positive lymph nodes, then the patient should undergo preoperative chemoradiation therapy following by restaging. An imaging controversy that is not yet resolved is whether patients with esophageal cancer should undergo routine neck US or CT.

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