Overview: The Changing Nature of Esophageal Cancer

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Squamous cell carcinomas of the esophagus, while still frequent in many locations throughout the world, now comprise a smaller percentage of esophageal cancers in the United States than was previously believed. Such tumors occur most often in black men and in association with tobacco and alcohol abuse. Adenocarcinomas of the distal esophagus represent an increasing proportion of esophageal tumors. These neoplasms arise in columnar epithelium (ie, Barrett's esophagus) or extend into the esophagus from their site of origin in the proximal stomach. Esophageal adenocarcinomas appear more often in white than black subjects and in men more than women. The clinical features and diagnostic approaches to squamous cell tumors and adenocarcinomas of the esophagus are similar.

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Incidence and Epidemiology

Esophageal cancer is a relatively uncommon yet highly lethal malignant disorder. It is estimated that the diagnosis will have been made in 11,000 Americans during 1992, resulting in 10,000 deaths. Elsewhere in the world, the incidence of cancer of the esophagus varies widely. The condition appears within a so-called esophageal cancer belt, extending from the Caspian Sea on the west, through Iran, Afghanistan, and Siberia before ending in China on the east. The disease also occurs in a higher-than-usual frequency in such disparate geographic sites as northwestern France, southeastern Africa, Finland, Iceland, and Curacao. In the United States, esophageal cancer occurs far more often in black than white subjects and in men more than women.

Anatomy and Pathology

Approximately 15% of esophageal cancers arise in the upper third of the esophagus ("cervical esophagus"), while 50% develop in the middle third and 35% in the lower third. The esophagus is surrounded by an especially rich lymphatic system, leading to frequent tumor spread to adjacent nodes. In the past, more than 75% of esophageal tumors were reported to be squamous cell carcinomas, arising from the squamous cell epithelium lining the tumor of the esophagus. Adenocarcinomas, while occurring less frequently, develop most commonly from columnar epithelium lining the distal esophagus. Data gathered during the past 20 years suggest a steady rise in the incidence of adenocarcinomas, while the rate for squamous cell carcinomas has remained relatively stable. In contrast to the higher incidence of squamous cell carcinoma of the esophagus in black than white subjects, the incidence of adenocarcinomas of the esophagus is greater in white than black subjects.

Esophageal cancer cannot be distinguished endoscopically or radiographically.

Etiologic Associations

In the United States, the vast majority of squamous cell carcinomas of the esophagus are thought to result from a long-standing history of cigarette smoking and/or excess consumption of alcohol. The risk of developing cancer increases with either the amount of tobacco smoked or alcohol consumed. Whiskey appears to act as a more potent causative factor than does beer or wine. The risk of developing squamous cell cancer of the esophagus has also been linked with mucosal irritation due to physical insults resulting from long-term exposure to extremely hot tea, radiation-induced strictures, the ingestion of silica particles contaminating millet bran, chronic achalasia, and bile ingestion as well as exposure to such potential carcinogens as smoked opiates, dietary nitrites, and fungal toxins in pickled vegetables. Furthermore, the appearance of esophageal cancer has been associated with nutritional deficiencies of zinc, vitamin A, and riboflavin, congenital hyperkeratosis and pitting of the palms and soles (ie, tylosis palmaris et plantaris), the presence of an esophageal web accompanied by glossitis and iron deficiency (ie, Plummer-Vinson or Paterson-Kelly syndrome), and possibly, celiac sprue.

The majority of adenocarcinomas of the esophagus develop in the lower third of the esophagus from columnar epithelium in the setting of chronic gastric reflux (ie, Barrett's esophagus). These tumors demonstrate the biologic behavior of gastric rather than esophageal malignancies and are morphologically indistinguishable from carcinomas of the gastric cardia. The difficulty in separating adenocarcinomas of the distal esophagus from those of the proximal stomach has led many investigators to consider the 2 tumor sites to represent a single entity, which has been termed adenocarcinoma of the gastroesophageal junction. Such a definition is of particular importance in view of the recently described shift of gastric cancers from the distal to the proximal stomach and the overall increase in the incidence of adenocarcinoma of the gastric cardia.

The relationship between Barrett's esophagus and esophageal adenocarcinoma has been the subject of several recent analyses. In contrast to squamous cell cancers, these tumors afflict white individuals far more commonly than black subjects, although the male predominance persists. Such adenocarcinomas appear to arise from dysplastic mucosa, which frequently contains aneuploid cells. The risk for the development of esophageal cancer in individuals having Barrett's esophagus is increased 30- to 125-fold above that for the general population but is still relatively small. Attempts at endoscopic and cytologic screening for patients with Barrett's esophagus, while effective as a means of detecting high-grade dysplasia, have not yet led to generally accepted guidelines regarding prophylactic surgi-
cal intervention and have not been shown to positively influence the prognosis in individuals found to have carcinoma. As such, the issue of surveillance endoscopy in patients with Barrett's esophagus should continue to be regarded as investigational.

CLINICAL FEATURES AND DIAGNOSIS

Progressive dysphagia and weight loss of relatively short duration represent the initial symptoms of esophageal cancer in the vast majority of patients. While these complaints are also consistent with achalasia or other motility disorders, they are particularly suggestive of the presence of a malignancy if accompanied by pain on swallowing (odynophagia). Generally, the dysphagia occurs initially with solid foods and gradually progresses to include semisolids and liquids. Dysphagia may also be accompanied by regurgitation and vomiting, aspiration pneumonia, pain radiating to the back, and hoarseness. Esophageal cancers most often spread to adjacent and supraclavicular lymph nodes, liver, and pleura. Tracheoesophageal fistulas and the superior vena cava syndrome may develop as the disease advances.

The low incidence of esophageal cancer in the United States makes population screening impractical. A variety of screening strategies, however, have been explored in high-risk areas in different regions of the world. These efforts have focused on obtaining cytologic material from the esophagus to identify asymptomatic individuals harboring malignant or highly dysplastic cells. Standard endoscopic brushing has been utilized in Iran and Italy, an expandable brush in a dissolvable capsule retrieved by a string has been employed in Japan, while a suction abrasive tube has been used in South Africa. By far the largest experience with screening has emerged from China, where an abrasive balloon technique has been developed to obtain cytologic samples. Approximately 500,000 individuals in China underwent such screening during a 20-year period, with those having abnormal cytologic preparations being subsequently examined radiographically and/or endoscopically. The technique has been reported to have 80% accuracy for cancer detection, with the majority of the identified tumors being early, surgically curable lesions.

Routine contrast radiographs are effective as a means of identifying esophageal lesions sufficiently large to cause symptoms. Esophageal carcinomas characteristically cause ragged, ulcerating changes in the mucosa, particularly when deeper infiltration is present, producing a picture similar to achalasia. Smaller, potentially resectable cancers are frequently poorly visualized despite technically adequate esopahograms. Consequently, esophagoscopy is indicated in all patients having an esophageal abnormality to visualize the tumor and obtain histopathologic confirmation of the diagnosis. Endoscopic biopsies of esophageal neoplasms occasionally fail to recover malignant tissue, because the biopsy forceps cannot penetrate deeply enough through normal mucosa which has been pushed in front of the malignancy. Cytologic examination of tumor brushing often complements standard biopsies and should be performed regularly. The extent of neoplasmic spread to the mediastinum, celiac, and para-aortic lymph nodes should be assessed by computed tomographic scans of the chest and abdomen. The roles of endoscopic ultrasonography and thoracoscopic visualization of paraesophageal lymph nodes on subsequent management strategies remain to be determined.

REFERENCES