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Cause of Death in Carcinoma of the Esophagus

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Carcinoma of the esophagus continues to carry a very poor prognosis. Previous studies have rarely reported the exact cause of death in these patients. Twenty-five autopsies were retrospectively reviewed in patients with the diagnosis of carcinoma of the esophagus, noting the cause of death. Two-thirds of all patients with unresected middle-third lesions ultimately died as a result of direct extension of the tumor into the aorta or tracheobronchial tree. Other findings included a high incidence of second neoplasms (12%) and the lack of an antemortem diagnosis of esophageal cancer in three of four females in the series.

INTRODUCTION

Although carcinoma of the esophagus accounts for 4% of deaths due to malignant neoplasms in the United States' population, it represents only 1% of all diagnoses of cancer (1, 2). This is a result of the relatively short survival of most patients with this tumor. Overall, 5-yr survival rates are less than 5%, and 70% of patients are dead within 1 yr of diagnosis (1, 3). Reasons for the dismal prognosis seem to be related more to anatomic considerations unique to the esophagus than to the particularly aggressive nature of the cancer itself. Diagnosis is usually made late in the course of the disease and treatment is rarely curative. This paper investigates the relationship between the levels of the primary lesion within the esophagus and the ultimate cause of death.

METHODS

Over a 10-yr period, 25 autopsies were performed at Temple University Hospital on patients with carcinoma of the esophagus. The final autopsy reports on these 25 patients were reviewed in detail. Specific attention was paid to the level of the lesion as it was described at autopsy or, in the case of the four resected tumors, from the preoperative radiologic or endoscopic localization of the lesion. In addition, the cause of death, as surmised from clinical assessment, laboratory data, and autopsy findings, was recorded on all patients. Other data included age, sex, race, treatment, length of survival from diagnosis to death, histological type of tumor, and pertinent associated conditions.

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RESULTS

The results of this review are summarized in Table 1. Twenty-five patients were included in this study, whose mean age was 63 yr. The male:female ratio was 6:1. The mean survival time from diagnosis was 6.5 months, with a median survival time of 3.5 months. The level of the lesion was the upper third of the esophagus in four patients, the middle third in 17 patients, and the lower third in four patients. The histology of the lesion was squamous cell carcinoma in 23 patients, anaplastic squamous cell carcinoma in one patient, and small cell carcinoma in one patient. Eleven of 25 (44%) patients had undergone operation. Seven of these procedures bypassed the cancer; four cancers were resected. Nine patients were treated with colonic interposition alone or combined with resection and/or radiation treatment. Esophagectomy with thoracic esophagogastrostomy was performed in two patients. Five patients received radiation treatment alone. Six patients who were diagnosed antemortem received no treatment. In three patients, the diagnosis was made postmortem at the time of autopsy.

Upper-third lesions

Death occurred as a result of surgical complications (bypass necrosis, anastomotic dehiscence) in both patients with upper third lesions in whom operative procedures were performed. Both died of overwhelming sepsis postoperatively. One patient exsanguinated from his ulcerating carcinoma. No apparent communication with a major vessel was found at autopsy. Another patient who died of tuberculous pneumonia was found to have an esophageal carcinoma at autopsy.

Middle-third lesions

Among 17 patients with middle-third lesions, three died catastrophically from exsanguination due to tumor erosion into the thoracic aorta. Seven patients died secondary to necrotizing pneumonia and overwhelming

TABLE 1
Summary of Findings in 25 Autopsied Patients with Carcinoma of the Esophagus

Age	Sex	Survival*	Level†	Treatment‡	Cause of Death
56	M	3 wk	U	BI	Bypass necrosis, pneumonia
71§	M	1 mo	U	Res BI	Anastomotic dehiscence, sepsis, pneumonia
57	F	No dx	U		Pulmonary tuberculosis, bronchopneumonia
45	M	2 wk	U	NT	Ulcerating lesion with exsanguination
57	M	3 mo	M	BI	Esophagobronchial fistula, bronchopneumonia
61	M	8 mo	M	NT	Esophagopleural fistula, empyema, bronchopneumonia
43	M	3 mo	M	Rad BI	Peritoneal carcinomatosis, necrotizing pneumonia
60	M	1 wk	M	NT	Hypercalcemia, abscess pneumonia
71	M	14 mo	M	BI	Esophagobronchial fistula, abscess pneumonia
63	M	1 mo	M	NT	Esophago-aortic fistula, exsanguination
79	M	1 mo	M	NT	Esophago-aortic fistula, exsanguination
74§	M	1 mo	M	NT	Esophagotracheal fistula, abscess pneumonia
47	M		M	NT	Esophago-aortic fistula, exsanguination
72	M	4 mo	M	Rad	Abscess pneumonia, carcinomatosis
48	M	4 mo	M	Rad BI	Esophagobronchial fistula, pneumonia
66	M	2 mo	M	Rad	Esophagobronchial fistula, pneumonia
51	M	20 mo	M	Rad BI Res	Carcinomatosis peritonitis, pneumonia
72	M	9 mo	M	Rad	Carcinomatosis
62	M	7 mo	M	Rad	Esophagobronchial, bronchopleural fistula
56	F	9 mo	M	EG	Bronchopneumonia
67§	F	No dx	M		Liver failure, hepatorenal syndrome
80	M	4 mo	L	BI	Widepsread metastases, bronchopneumonia
74	M	2 mo	L	EG	Peritonitis, secondary to anastomotic leak
59	M	2 mo	L	BI	Widespread metastases, bronchopneumonia
83	F	No dx	L		Bronchopneumonia, empyema

* Survival, from date of diagnosis to date of death; no dx, undiagnosed in life.

† Level of lesion in esophagus: U, upper third; M, middle third; L, lower third.

‡ Treatment: BI, bowel interposition; Res, resection of primary lesion; NT, not treated or feeding gastrostomy only; Rad, radiation; EG, esophagectomy with esophagogastrostomy.

§ Other neoplasms present.

sepsis as a result of the direct extension of their tumors into the tracheobronchial tree or pleural space. Of the remaining six patients in whom the diagnosis was made antemortem, diffuse carcinomatosis was present in four. Three of these patients died of necrotizing pneumonia, and in one 72-yr-old male, the cause of death was impossible to determine. Two others died of pneumonia without fistula formation. One patient with alcoholic cirrhosis died of hepatorenal syndrome, and a squamous cell carcinoma of the esophagus was found at autopsy.

Lower-third lesions

One patient died of peritonitis after esophagogastrectomy. Two patients in whom palliative bowel interposition was performed developed wide-spread metastases and succumbed to pneumonia. One elderly female who died of pneumonia was found to have an esophageal tumor at autopsy.

DISCUSSION

The autopsy population reported in this study is typical of other autopsy populations with esophageal cancer that have been reported (2–6). The male-to-female ratios and location of the tumors from several studies are presented in Table 2. Differences among geographic areas are well recognized. In particular, U.S. studies show male-to-female ratios of 6:1; 50% to 65% of lesions are located in the middle third of the esophagus. Any autopsy study deals with a select population and will be skewed to represent patients with more unusual or dramatic causes of death in whom an autopsy is more likely to be performed. Few studies have actually addressed the immediate cause of death in patients with carcinoma of the esophagus. Isono *et al.* (7) was able to determine the cause of death in 192 operative survivors of 638 patients who underwent esophoectomy for carcinoma of the esophagus. Most (79%) survived less than 5 yr, of whom four-fifths died of "recurrent disease." The actual cause of death in patients with recurrent disease is not specified. Mandard *et al.* (8) attributed death to pulmonary complications in more than one-half of 111 patients autopsied with esophageal cancer. Eighteen had esophago-tracheobronchial fistulas. Four had aortic fistulas. Sixty percent showed local invasion into continguous organs.

TABLE 2
Comparison of Studies of Patients with Carcinoma of the Esophagus

	Cases	Males %	Females %	Level of Lesion (%)		
				Upper third	Middle third	Lower third
Cilley	25	84	16	16	68	16
Bosch (Wisconsin)	82	85	15	15	63	22
Schuchmann (VA study)	214	81	19	13	42	42
Ming (worldwide)	2663			16	52	32
Griffith (England)	211	57	43	03	21	76
Cedarquvist (Denmark)	1002	67	33	15	46	39

Primary lesions and cause of death

In the four cases of upper-third lesions, survival was uniformly poor (2 wk, 3 wk, 1 month, undiagnosed). Surgical treatment was not helpful. This is consistent with the findings of others that patients with upper-third lesions may not be good candidates for surgical procedures. (3, 5, 9)

Ten of 17 (59%) of the middle-third lesions resulted in deaths that were attributable to direct extension of the tumor into either the aorta or tracheobronchial tree. This appears to confirm the intuitively obvious conclusion that the tumor will invade organs to which it is adjacent. A more important observation is that local growth and extension of the primary lesion was directly responsible for the terminal event in more than one-half of middle-third lesions. In the two cases of middle-third lesions in which the primary tumor was resected, fistula formation did not occur.

It would thus appear that the catastrophic terminal event of fistula formation can be anticipated in most patients with middle-third lesions in whom the primary tumor is not resected. In this study, 15 middle-third lesions were not resected, and 10 eventually formed fistulas resulting in death from exsanguination or necrotizing pneumonia.

Some have found that when a neoplastic esophagotracheobronchial fistula is present, early diagnosis and aggressive management can increase both length and quality of life (10, 11). Optimally, early endoscopic and radiologic diagnosis will allow detection of esophageal tumors prior to extension into surrounding structures. Operative management that removes the primary tumor and effectively separates the respiratory and alimentary tracts may then prevent fistula formation (12).

Multiple neoplasms

As reported by Ming (3) and reviewed by Fogel *et al.* (13), neoplasms occur in other organs in 3–12% of patients with esophageal carcinoma. The preponderance of second neoplasms occur in the oral cavity. In this study, three of 25 patients had other neoplasms (12%), including one case of carcinoma of the tonsil. The other two patients had several different neoplasms. One patient had five neoplasms, two malignant, and the second patient had three neoplasms, one malignant. This occurrence probably represents individuals with a predisposition and/or extraordinary environmental insult resulting in neoplasia.

Underdiagnosis of esophageal carcinoma in females

Of the 25 patients reported in this study, a premortem diagnosis was not made in three cases. All three of these patients were females. Medical conditions that may have obscured the diagnosis include carcinoma of the left tonsil with multiple metastases and cirrhosis in one patient, and tuberculosis and cirrhosis in another. In the other patient, progressive dysphagia was part of the chief complaint. It may be that because of the infrequency of esophageal carcinoma in females, clinical suspicion for this disease is low and diagnoses are thus more often missed in females than in males.

Conclusion

Few data appear in the literature concerning the immediate cause of death in patients with carcinoma of the esophagus. From this autopsy review, we conclude that middle-third lesions that are not surgically resected will result in death in the majority of patients from direct extension of the primary lesion into the aorta or tracheo-bronchial tree.

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