Malignant carcinoid tumour of the oesophagus

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ABSTRACT A patient with a carcinoid tumour of the oesophagus developed widespread metastases within three years of a successful local resection. Of the seven patients with oesophageal carcinoid tumours so far reported, four have died with widespread metastases.

The documented follow up¹⁻⁶ of patients with carcinoid tumour of the oesophagus has been insufficient to establish the behaviour of this rare tumour. Our inquiries about the long term fate of these patients, initiated as a result of our own case, now suggest that oesophageal carcinoids may be highly malignant.

Case report

In September 1981 a 67 year old woman presented with progressive dysphagia. Barium studies suggested a malignant obstruction of the oesophagus and oesophagoscopy confirmed the presence of a tumour 27 cm from the incisor teeth. Biopsy suggested an adenocarcinoma. At operation a mobile tumour was found at the level of the inferior pulmonary vein, with no macroscopic evidence of spread. A subtotal oesophagectomy with cervical oesophagogastric anastomosis was performed and the patient made an uneventful recovery.

Pathological examination of the excised specimen showed a 5 × 2 cm ulcerated tumour 2 cm proximal to the oesophagogastric junction, which infiltrated all the coats of the oesophageal wall. Although the tumour had arisen in a squamous lined oesophagus, the histological features were those of a carcinoid tumour with solid cell nests of acinar, and occasionally tubular cells, surrounded by a fibrous stroma of variable density. The cells were of medium size with a scanty to moderate amount of eosinophilic cytoplasm and at the periphery the nests had a palisaded appearance (fig). Mitoses were frequent (about 35/10 high power fields) and minimal necrosis was present. No areas of undifferentiation were encountered. Intercellular bridge formation and keratin production were not observed and mucin, argyrophil, and argentaffin staining was negative. Immunoperoxidase staining for neurone specific enolase was positive, supporting a neuroendocrine origin.⁶ Electron microscopy was not performed. Associated lymph nodes were tumour free, as were the resection lines.

After discharge the patient remained well until her readmission in February 1984 with gross increasing dyspnoea, bilateral pitting oedema, and a right pleural effusion, which was treated by intercostal drainage. Shortly afterwards she developed renal and hepatic failure, from which she died. At necropsy there was evidence of widespread malignancy with tumour deposits on the pleural surfaces of the ribs, pericardium, and both diaphragmatic leaflets and in both lungs. The remaining oesophagus and the anastomosis were free of tumour but the serosa of the intrathoracic stomach was covered with tumour deposits. The liver was invaded by tumour from the right hemidiaphragm and also contained discrete metastases. The largest of these was 10 cm in diameter and encircled the inferior vena cava, producing thrombosis in the inferior vena cava that extended distally to affect the left renal and both iliac veins. All other organs, including the appendix and small bowel, were normal. Histological examination of the metastases showed features similar to those in the oesophagectomy specimen.

*Cell nests with acinar formation and peripheral palisading.
(Haematoxylin and eosin.)*

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Clinical and pathological features of the seven known cases of oesophageal carcinoid

Authors	Site	Pathological features					Clinical features	
		Histological appearance	Mitoses	Necrosis	Silver staining	EM findings	Nodal metastases	Outcome
Brenner <i>et al</i> 1969	Lower third	Carcinoid	NR	NR	Argent - ve Argyro NR	NR	Yes	Died at 6 months; myocardial infarction
Watanabe <i>et al</i> 1974	Mid-third	Carcinoid	NR	NR	Argent NR Argyro + ve	Neurosecretory granules	Yes	Died at 11 months; disseminated metastases
Chong <i>et al</i> 1979	Upper third	Carcinoid and adenocarcinoma	"Considerable"	NR	Argent + ve Argyro + ve	NR	No	Died of metastases; survival time NR
Rankin <i>et al</i> 1980	Lower third	Carcinoid	NR	NR	Argent - ve Argyro NR	Neurosecretory granules	Yes	Died 6 months; complications of radiotherapy to mediastinal metastases
Siegal and Schwartz 1986	Mid and lower third	Carcinoid	"Abundant"	Absent	Argent - ve Argyro - ve	Neurosecretory granules	Yes	Alive and recurrence free at 2 years
Nawroz 1987	Lower third	Carcinoid	NR	NR	Argyro + ve Argent NR	Neurosecretory granules	No	Died postoperatively
Ready <i>et al</i> 1989	Lower third	Carcinoid	"Frequent" 35/10 hp fields	Present but minimal	Argent - ve Argyro - ve	NR	No	Died 2 years 5 months; disseminated metastases

NR—not reported; argent—argentaffin; argyro—argyrophil; - ve—negative; + ve—positive.

Discussion

Carcinoid tumours arise from cells of the amine precursor uptake and decarboxylation (APUD) system and are classically defined by silver stains as either argyrophilic or argentaffinic. Foregut carcinoids are generally argyrophil and the oesophagus, particularly near the oesophagogastric junction,⁸ contains many argyrophilic cells. These probably originate from local, endoderm derived epithelium⁹ and represent the precursors of oesophageal carcinoid tumours.¹⁰ Despite their presence oesophageal carcinoids are rare and only six isolated case reports exist.¹⁻⁶ The features of these are summarised in the table. The tumours occurred at sites throughout the oesophagus and none was accompanied by the carcinoid syndrome. At presentation all had invaded the oesophageal wall and four had regional lymph node metastases.^{1,2,4,5} None had evidence of distant dissemination.

The diagnosis of carcinoid was based on typical histological appearances, although one tumour³ showed both carcinoid and adenocarcinomatous components and was classified as a mucin secreting carcinoid. A wide variation in reactivity was reported with silver stains, while verification of neuroendocrine origin by other histochemical techniques was largely omitted. In four cases^{2,4,5,6} the presence of neurosecretory granules in tumour cells was, however, confirmed using electron microscopy. Although necrosis and an increase in mitotic figures suggests a more aggressive "atypical carcinoid" than the more indolent "classical" type,¹¹ these features were not reported in most of these cases. The absence of necrosis was specifically noted in only one case,⁵ and increased mitoses were inferred in two.^{3,5} In our own case abundant mitoses and the presence of necrosis was associated with aggressive behaviour of the tumour subsequently.

From the documented follow up of the patients in the published reports, all of whom underwent oesophagectomy,

we know that one patient died of a postoperative chest infection,⁶ one from metastases 11 months after resection² and one from a myocardial infarction after six months.¹ Follow up was too short to establish the character of the tumour in the remaining three cases. Inquiries by letter disclosed that one patient⁴ died of respiratory complications after radiotherapy for residual mediastinal nodes and another died from disseminated metastases.³ Only one patient⁵ remains well, with no clinical or investigative sign of recurrence two years after resection (despite initial nodal metastases). Four of the seven documented patients with an oesophageal carcinoid tumour have therefore died directly or indirectly from metastases.

It is likely that carcinoids of the oesophagus, as elsewhere,¹¹ may form a spectrum of malignancy ranging from relatively benign classical carcinoids through atypical types to aggressive anaplastic tumours. Although it is difficult from the histological information available to assess where along this spectrum each documented case lies it is apparent from the revised follow up data and the fate of our patient, whose tumour appears to have been of the atypical type, that oesophageal carcinoids do have the potential to be as lethal as more common forms of oesophageal cancer.

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