Primary oat cell carcinoma of the oesophagus

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ABSTRACT Three cases of oat cell carcinoma of the oesophagus are presented and published reports reviewed. This is mainly a disease of older age with a 3:2 predominance of men. Of all published cases, 43 (47.3%) occurred in the middle third, 41 (45.1%) in the lower third, and four (4.4%) in the upper third. In one case it was multifocal and in two the location was not stated. Dysphagia was the most common symptom and was found in 82.5% of cases. Overall survival was 4.7 months. The longest survival in a patient treated by resection was 24 months and in a patient treated by chemotherapy 11 months. All but one of the patients had widely disseminated metastatic disease at death. It is concluded that surgery, possibly with adjuvant chemotherapy, holds out the best prospect for such patients.

Since the original description of this condition by McKeown in 1952, 88 cases of oat cell carcinoma have been reported. These cases had both the clinical and histologic characteristics of oat cell lung cancer, with a rapidly fatal course when untreated. The pathology is characteristic and has been well described in pathology journals, where most of the cases have been reported. The purpose of this paper is to review the available clinical information on this entity and to present three cases of our own.

Patients and findings

The present cases

Case 1
A 74 year old woman presented in December 1978 with a two month history of dysphagia and lower retrosternal pain radiating to the back. A barium swallow showed an irregular filling defect in the lower end of the oesophagus. Physical findings, laboratory results, and chest radiograph appearances were all within normal limits. Oesophagoscopy showed a tumour arising 34 cm from the incisors. A biopsy showed that the subepithelial tissues were infiltrated by an oat cell carcinoma. The patient underwent distal oesophagectomy with oesophagogastrectomy. At operation the tumour was found in the lower third of the oesophagus. There was also a small nodule in the parietal pleura overlying the aorta and some enlarged glands along the left gastric vessels. All obvious tumour was excised at operation. The patient was discharged on the 12th postoperative day after an uneventful recovery. Microscopic examination of the specimen showed oat cell carcinoma of the oesophagus infiltrating the whole of the oesophageal wall. The pleural nodule and left gastric lymph nodes contained metastatic tumour.

The patient died three months later; postmortem examination showed widespread metastatic disease in the liver, peritoneum, and left adrenal gland.

Case 2
A 78 year old woman with four week history of dysphagia was found to have an irregular filling defect in the mid oesophagus on barium swallow examination in December 1980. An ulcerating lesion was found 28 cm from the incisors on oesophagoscopy and the biopsy showed oat cell carcinoma. A chest radiograph was normal and there was no evidence of metastases on clinical examination or on isotope scans of liver and bone. Because of her poor general condition she was referred for palliative radiotherapy. She had subjective improvement of her dysphagia, but died at home six weeks after diagnosis; permission for post-mortem examination was refused.

Case 3
A 55 year old woman presented in May 1985 with a three week history of retrosternal pain on eating, which radiated to the back, and dysphagia. Clinical
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Barium swallow from case 3 showing a polypoid filling in the mid oesophagus.

examination showed nothing abnormal. A barium swallow examination showed a polypoid mass in the mid thoracic oesophagus (figure). Oesophagoscopy showed tumour arising 30 cm from the incisors. Histological examination of the biopsy specimen showed oat cell carcinoma. Chest radiography, bronchoscopy, and isotope scanning of the liver showed nothing abnormal. The patient underwent an Ivor-Lewis oesophagectomy and oesophagogastronomy. Recovery was uneventful and at follow up three months later the patient was doing well. The resected specimen contained a polypoid mass 6.25 cm in diameter, which on microscopic examination proved to be an oat cell carcinoma with small areas of squamous differentiation. It had not infiltrated the muscle and the attached lymph nodes were tumour free.

Published cases

Clinical features

In the present series of 91 cases (which include our own) there were 54 men (59.3%) and 37 women (40.7%). Ages ranged from 29 to 88 years, with a mean of 64.5. Most cases (73.6%) were diagnosed in the sixth, seventh, and eighth decades. The reported incidence varies from 0.05% to 7.6% of all carcinomas of the oesophagus. Briggs and Ibrahim, who have published the largest series, gave an incidence of 23 out of 955 cases (2.4%).

Dysphagia was the most common symptom and was found in 82.5% of cases. The duration of symptoms varied from two weeks to two years (mean 3.2 months). Ectopic endocrine syndromes were noted in two cases. One patient had inappropriate anti-diuretic hormone secretion and the other presented with hypercalcaemia, which resolved after radiotherapy but recurred with tumour recurrence.

Pathology

Forty three oat cell carcinomas of the oesophagus (47.3% of the total) occurred in the middle third, 41 (45.1%) in the lower third, and four (4.4%) in the upper third. The location was not stated in two cases. An apparent multifocal origin was reported in one case. Macroscopically, oat cell carcinomas were either polypoid (47.5%), fugating (15%), ulcerating (15%), or stenotic (22.5%). Mircoscopically, 67 (73.6%) were pure oat cell carcinomas and the rest

Results of treatment

<table>
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<th>Treatment</th>
<th>No of patients</th>
<th>Post operative deaths</th>
<th>Survival not stated</th>
<th>Survival 1 y</th>
<th>2 y</th>
<th>Mean (range) (months)</th>
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<tr>
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<td>3</td>
<td>4</td>
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<td>7.3 (1-24)</td>
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<tr>
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<td>0</td>
<td>0</td>
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<td>1</td>
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<td>0</td>
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<tr>
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<td>0</td>
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<td>2.3 (6 d-6 m)</td>
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<tr>
<td>Treatment or survival not stated</td>
<td>3</td>
<td></td>
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</table>
mixed, oat cell being combined with squamous or glandular components or both. Of the mixed tumours, 17 had areas of squamous differentiation and three glandular elements, and in three there was carcinoid differentiation. One patient showed squamous, glandular, and oat cell differentiation. The characteristic electron dense granules have been demonstrated ultrastructurally.

Treatment and prognosis (table)

No long term survival has been reported in patients with oat cell carcinoma of the oesophagus. Overall survival has been 4.7 (range 0–24) months. Forty patients have undergone oesophagectomy. There were nine postoperative deaths. Of the patients who left hospital after surgery, 82% have died within one year of diagnosis, the most (18 out of 23) dying within six months. The longest survival among the seven patients treated with chemotherapy alone was 11 months. Radiotherapy alone was used in nine patients. One patient was treated with chemotherapy followed by surgery and another was treated by a combination of chemotherapy, radiotherapy, and surgery. All but one of the patients had widespread lymphogenous and haematogenous metastases at death. Levenson et al.17 reported a patient with supraclavicular lymph node metastases who was treated with multiagent chemotherapy and achieved a complete remission, confirmed at autopsy 11 months later, when he died in an accident.

Discussion

Small cell undifferentiated (oat cell) carcinoma of the oesophagus rarely occurs as a primary lesion. Although this tumour was described by McKeown1 33 years ago, it has only recently been studied in detail. Careful light and electron microscopic examination has indicated morphological and histochemical characteristics indistinguishable from those of small cell carcinoma of the lung.7,8,10,12,14,19,21,23,25,27,29

The clinical presentation of these oesophageal tumours appears to be similar to those of the more frequent squamous carcinomas and adenocarcinomas. As with other oesophageal carcinomas,10,19 there was a preponderance of men (60%).

The histogenesis of oat cell carcinoma remains to be elucidated. Two cases of oat cell carcinoma of the oesophagus were associated with ectopic endocrine syndromes13,27; tissue analysis has revealed the presence of adrenocorticotropic hormone in five15,9,26 and calcitonin in one,18 without any clinical evidence of systemic endocrine hyperfunction. Oat cell carcinomas are therefore widely believed to be derived from the APUD (amine precursor uptake and decarboxylation) cells.5,9,12,15,18,21,26,30 The embryogenesis of these cells has been a subject of controversy. Initially Pearse31 proposed a “neural crest” origin for these cells, but later work30,32–34 has shown that APUD cells are in fact derived from endoderm. An origin of oat cell carcinoma from “basal” cells with pluripotentiality, or multipotential cells, has been suggested by some authors8,13,21,23,29 to explain the mixed type of tumour.

The clinical behaviour of oat cell carcinoma of the oesophagus is similar to that of oat cell carcinoma of the lung with rapid and widespread dissemination. Published reports strongly imply that occult metastases are present at the time of diagnosis in most patients.1–29 Despite this four (10%) of the operated patients lived for more than one year, while with other modes of treatment there were no survivors by one year. Complete remission confirmed by necropsy at 11 months in one patient treated by multiagent chemotherapy17 is encouraging. Resection, if feasible, appears to be the treatment of choice. Because of the possibility of occult metastases adjacent chemother- apy might be worthwhile, although the small number of cases will make controlled trials difficult. In view of the radiosensitivity of small cell carcinoma, radiotherapy should be considered for palliation of inoperable lesions.

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