The Ulster Medical Journal, Volume 74 No. 1, pp. 63-65, May 2005.

Case Report

Extra-pulmonary oat cell carcinoma: report of two cases

SA Badger, J Lee, H Vazir, T Diamond, KJS Panesar

Accepted 19 January 2005

Pulmonary oat cell carcinoma was first described in 1926 and constitutes around 25% of lung malignancy.[1] Dugoid *et al* reported the first case of extrapulmonary oat cell carcinoma, without any bronchial involvement, in 1930.[2] Primary extrapulmonary oat cell tumours have since been reported originating from different organs except the liver and the central nervous system. We report two cases of primary extrapulmonary oat cell carcinoma and have reviewed the literature of this rare condition with regard to prognosis and treatment.

The history of each patient was reviewed and a relevant summary made. A literature review was performed using Medline. The key words "oat cell carcinoma", "extrapulmonary" and "small cell carcimona" were used and the results of the search correlated. The current recommendations for treatment were also reviewed.

CASE 1 A 70-year-old man, who was a non-smoker, presented with a one-year history of passing dark stools and an eight-week history of anorexia, weight loss and early satiety. Physical examination revealed a palpable epigastric mass. He was anaemic (Hb level of 7.9g/dl and mean cell volume 83.8g/1), while liver function tests and carcinoembryonic antigen were normal.

Oesophagogastroduodenoscopy (OGD) showed an ulcerated polypoid lesion in the body of the stomach. Biopsy revealed a small round blue cell tumour. Further immunohistological studies showed a strong positive reaction for neuroendocrine marker PGP 9.5. An absence of staining was noted with vimentin, lymphoid and epithelial markers, which overall was suggestive of oat cell carcinoma.

CT scan of his chest and abdomen confirmed a mass lesion measuring 3 x 2 cm arising from the posterior wall of the stomach. No lymphadenopathy, metastatic disease or bronchial involvement was demonstrated, although not confirmed by bronchoscopy. At laparotomy, the tumour was unresectable due to extensive involvement with the left lobe of the liver and pancreas. The patient received two doses of adjuvant vincristine and etoposide but his general condition deteriorated and he died three months after surgery.

CASE 2 A 39-year-old female, who also was a non-smoker, presented with symptoms of gastric outlet obstruction. OGD revealed a necrotic ulcerating tumour in the duodenum, biopsies of which suggested a small cell carcinoma. A CT scan showed a 6 cm soft tissue mass in the second part of the duodenum, displacing the pancreas

Altnagelvin Area Hospital Glenshane Road, Londonderry, BT47 1SB.
Department of Surgery:
SA Badger, MRCS(Ed), Senior House Officer in General Surgery.
J Lee, MD, FRCS(Ed), Specialist Registrar in General Surgery.
KJS Panesar, FRCS, FRCSI, FRCSEd, OBE, Consultant Surgeon in General Surgery.
Department of Pathology:
H Vazir, MBBS, FRCPath, MA, Consultant Pathologist.
Mater Hospital Trust, Crimlin Road, Belfast BT14 6AB.
Department of Surgery:
T Diamond, BSc, MD, FRCS, FRCSI, Consultant Surgeon in General Surgery.
Correspondence to Mr Panesar.
E-mail: PanesarK@alt.n-i.nhs.uk

anteriorly. No lymphadenopathy or pulmonary or hepatic lesions were noted, although not confirmed by bronchoscopy.

At laparotomy the tumour was inoperable and a palliative gastrojejunostomy was fashioned and a stent inserted into the common bile duct. Histopathology of both the OGD biopsy and a lymph node obtained at the time of the laparotomy showed a poorly differentiated tumour with a small cell appearance. It stained positive for CD56 and P53 and PGP9.5, but stained negative for insulin and somatostatin. Chemotherapy was commenced using etoposide and cisplatin, but her condition deteriorated and she died three and a half months after surgery.

DISCUSSION

Oat cell carcinoma of the lung is very aggressive, metastasises widely and is rarely curable by surgery. This form of lung cancer occurs mostly in smokers and has a higher incidence in miners with previous exposure to uranium or radium. The prognosis of pulmonary oat cell cancer is poor with a median survival of about one year and a five-year survival of about 10% in spite of aggressive treatment.[3] Extra-pulmonary oat cell cancers originating from neuroendocrine cells are biologically aggressive and associated with a poor prognosis.[4] The two cases of extra-pulmonary oat cell cancer reported here represent neuroendocrine tumours of foregut origin.[5]

Gastric small cell carcinoma was first reported in 1976 with 66 cases reported since.[6] The presentation is usually at a late stage, as demonstrated in our case.[7] The tumour is usually polypoid in appearance at the early stage, progressing to crater-like ulceration due to rapid proliferation. The aggressive nature of the tumour and relative insensitivity to chemotherapy result in few long-term survivors and surgical efforts are generally palliative.[8]

Duodenal oat cell carcinoma is rare, with nine cases previously reported in the literature. Zamboni *et al* reported three cases of small cell carcinoma in the ampullary region of the duodenum.[9] The poor prognosis of oat cell tumours was again reflected in these three cases with a median survival period of ten months.

Histologically the cells grow in clusters that exhibit neither granular nor squamous organisation. It has been shown that the argentaffin (Kultchisky) cells in the gut closely resemble cells contained in normal bronchial mucosa.[5] Electron microscopy shows that these cells contain membrane-bound dense core granules characteristic of APUD (Amine Precursor Uptake and Decarboxylation) cells. Similar granules are found in bronchial carcinoids and oat cell carcinomas suggesting that they are of APUD cell origin. The APUD cell system is a family of cells with similar cytological and ultrastructural features derived from the neuroectoderm. During embryological neuralation, when the neural folds elevate and fuse together, cells at the lateral border of the neuroectoderm begin to dissociate from their neighbouring cells. This cell population will undergo epithelial to mesenchymal transition as it leaves the neuroectoderm by active migration and displacement to enter the underlying mesoderm. Among other places they enter the gastrointestinal tract. These APUD cells are responsible for the production of polypeptide hormones and biologically active amines. The presence of the neuroendocrine granules results in the positive staining of immunohistochemical cell stains for neuroendocrine markers.

Radical surgery does not have a primary role in managing extra-pulmonary oat cell cancer, as the benefit is limited.[10] Any additional benefit of radiotherapy is not adequate to justify its potential toxicity.[11] Multi-agent chemotherapy in different combinations has some success, achieving a complete response rate (defined as 50% or greater shrinkage of measurable disease) ranging between 21-91%.[11,12] However, these are non-comparative clinical studies with small numbers of patients and the median survival still remains poor at 18-51 weeks.[12] An analysis of the different chemotherapeutic regimens used suggests best results with a combination of cisplatin and etoposide with response rates reaching 70%, while doxorubicin-based regimens appear to be less active.[13, 14, 15] Complete response has been observed with cisplatin and etoposide based treatment in a patient with widespread metastatic disease.[16] The two patients reported by van der Gaast had extensive disease with a reported survival of 11 and 16 months after combination chemotherapy with cyclophosphamide, doxorubicin and etoposide.[17] Another patient with pancreatic oat cell carcinoma

reported by Wahid survived 14 months with combination chemotherapy and radiotherapy.[18]

In summary, primary extra-pulmonary oat cell carcinoma is rare and originates from neuroendocrine APUD cells. It is essential to obtain an early accurate diagnosis so that appropriate treatment can be commenced. Oat cell carcinoma may respond to chemotherapy and stay in remission for at least a few months. Despite this the prognosis is poor with an overall median survival of one year.[3] Our case reports demonstrate and reiterate the aggressive nature of extra-pulmonary oat cell cancer and the associated poor survival. Radical surgery has little role in the management of these patients and surgery is usually limited to palliation only.

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