

CASE REPORTS

Treatment of a malignant bronchial carcinoid affecting the mediastinum and left atrium by radical two stage resection with cardiopulmonary bypass and somatostatin infusion

C Darby, M Sinclair, S Westaby

Abstract

At operation a malignant bronchial carcinoid that had invaded the left atrium produced a carcinoid crisis in a 63 year old woman. A somatostatin infusion was required to resuscitate the heart and circulation and to allow subsequent resection of the carcinoid under cardiopulmonary bypass.

The malignant carcinoid syndrome has excited clinical interest and posed a therapeutic challenge since its description 30 years ago. The disorder is usually associated with carcinoid tumours of the small bowel that are metastatic to the liver. It may less often be seen in association with primary carcinoid in other sites such as the lung or stomach or, more rarely, with non-carcinoid tumours such as small cell carcinoma of the lung. Bronchial carcinoids are of fore-gut origin unlike the more commonly found ileal tumours which are of mid-gut origin. Fore-gut carcinoids usually do not possess the decarboxylase enzyme required for generation of serotonin (5-HT) from its precursor 5-hydroxytryptophan.¹ Therefore 5-hydroxyindole acetic acid, which is usually present in the urine as a marker of the carcinoid syndrome, will often not be found. Peripheral conversion of precursor to serotonin can often occur in the liver, intestine, and kidney. Methyldopa may also block the decarboxylase enzyme.

Bronchial carcinoid tumours rarely cause symptoms though "atypical" pulmonary carcinoids with more aggressive cell type and clinical behaviour have been recognised.² Radical surgical excision is recommended for these tumours.³ We describe a patient with a primary lesion which directly invaded the left atrium and with a large solitary metastasis in the posterior mediastinum. A two stage approach was required for excision.

Case report

A 63 year old white female non-smoker presented with a nine month history of persistent

distressing cough. For a month she had also had epigastric pain and flushing of the face. She was not taking methyldopa. There had been no diarrhoea or weight loss or other features of the carcinoid syndrome. Physical examination showed no abnormality. There were no cardiac murmurs. A chest radiograph (figure) showed a 5 cm diameter mass at the right hilum with a further large paratracheal mass in the mediastinum above the azygos vein. A computerised tomogram suggested that this was a solitary enlarged lymph gland. A provisional diagnosis of bronchogenic carcinoma was made based on these findings.

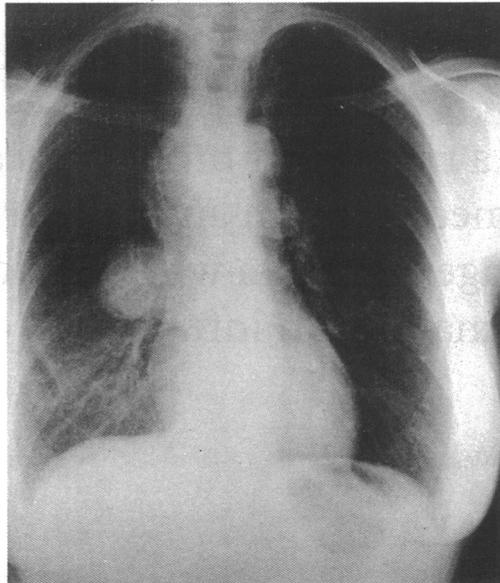
Bronchoscopy, with the rigid Storz scope, showed external compression of the lateral wall of the right bronchus intermedius and of the right tracheal wall but no intraluminal tumour. Mediastinoscopy was performed to obtain a histological diagnosis. The smooth tumour was easily located and a biopsy specimen was taken without event. Histology showed this to be a metastatic bronchial carcinoid; however, despite a history suggestive of hormone secretion, urinary hydroxyindole acetic acid estimations proved negative. Biochemical and haematological screening tests were normal. Liver ultrasound and bone scans were unremarkable.

Because there was no evidence of extra-thoracic spread surgical resection was considered to be the treatment of choice. The first approach was by right thoracotomy which confirmed the preoperative findings. The mediastinal deposit measuring 10 cm by 8 cm was first mobilised and then excised without difficulty from the mediastinum. No other signs of tumour spread were seen and there were no adverse haemodynamic consequences. However, the pulmonary mass was situated centrally, between the superior and inferior pulmonary veins and seemed to invade through the pericardium at this point. Involvement of the hilum including the right main pulmonary artery above the fissure meant that pneumonectomy was required. However, an attempt to mobilise the lesion provoked profound hypotension (systolic < 30 mm Hg) and there was no response to transfusion or massive doses of adrenaline. Interestingly, there was no concomitant tachycardia. The tumour was highly

John Radcliffe
Hospital, Oxford
C Darby
M Sinclair
S Westaby

Correspondence to
Mr C Darby, FRCS,
Department of
Cardiothoracic Surgery,
John Radcliffe Hospital,
Headington, Oxford
OX3 9DU.

Posterior-anterior chest radiograph showing the right hilar bronchial carcinoid primary and azygos nodal metastasis.



vascular and invaded directly into the cavity of the left atrium. At this stage we did not have somatostatin; this was obtained some 30 minutes later. During this time the blood pressure remained below 50 mm Hg and the operation was abandoned despite persistent bleeding. An intravenous bolus (250 µg) of somatostatin increased the blood pressure immediately to normal (140/90 mm Hg). A continuous infusion of 250 µg/h was started but because the tumour secretion was so high supplies of somatostatin were exhausted in two hours and the blood pressure again fell to 30 mm Hg. The patient remained moribund for a further two hours despite transfusion of 6 l of blood and intravenous hydrocortisone. When further supplies of somatostatin were obtained, blood pressure again returned to normal and she made a satisfactory recovery in the intensive care unit. 5 Hydroxyindole acetic acid estimations were repeated but were again negative.

Three days later she returned to the operating room for right pneumonectomy. A somatostatin infusion was started at a rate of 250 µg/h before anaesthesia and was maintained throughout the operation. Median sternotomy was performed and a clotted right haemothorax was evacuated. Cardiopulmonary bypass was established before the tumour was touched. Exploration of the lung hilum confirmed that the tumour invaded directly into the cavity of the left atrium between the pulmonary veins. Pneumonectomy was performed with excision of the wall of the left atrium. This provided good tumour clearance. The mitral valve seemed normal and there was no haemodynamic instability. Perfusion pressure during cardiopulmonary bypass was 60–70 mm Hg. The defect was closed by direct suture and cardiopulmonary bypass was discontinued without difficulty. Somatostatin infusion was stopped eight hours after operation and the patient made a satisfactory recovery.

Histology of the primary lesion confirmed that it was an “atypical” carcinoid tumour, though the hormone was not identified. Eighteen months after the operation the patient remains well.

Discussion

Two types of carcinoid tumour are recognised by histology and by clinical behaviour. So called “typical” carcinoid has a characteristic histological appearance and patients with this tumour have a five year survival in excess of 80%. “Atypical” carcinoids (10–20% of all bronchial carcinoids) show greater mitotic activity, nuclear atypia, and metastasis to lymph nodes. Five year survival when node involvement is found at presentation is only 25%.^{2,4}

The diagnosis of carcinoid syndrome, with primary bronchial carcinoids, usually requires either extensive intrathoracic spread or hepatic secondary deposits. The patient described had neither but the tumour was able to secrete directly into the cavity of the left atrium and systemic circulation. The bronchial carcinoid syndrome has a characteristic pattern. The flush is prolonged, up to 24 hours, and may affect the entire body; there may be lacrimation, hypotension, periorbital oedema, and facial and salivary gland swelling.¹ The absence of 5-hydroxyindole acetic acid in the urine should not have surprised us because these tumours commonly lack the decarboxylase enzyme to convert precursor (5-HTP) to serotonin. More than twenty different mediators have been recognised and in our patient the clinical findings were more in keeping with the release of bradykinin, histamine, or substance P. Indeed, substance P has been shown to be 100 times more potent a vasodilator than bradykinin and it causes flushing, bradycardia, and hypotension.⁵ Direct secretion of such a substance into the left atrium avoids the usual detoxifying action of liver or lung found with carcinoids at other sites.

Somatostatin, discovered in hypothalamic tissue 13 years ago, is a naturally occurring hormone with pronounced inhibitory effects on the secretion of many endogenous peptides such as growth hormone, insulin, glucagon, and gastrointestinal peptides. Native somatostatin has been reported to be effective in blocking the carcinoid flush induced by pentagastrin, in reducing circulating concentrations of serotonin, and in controlling other symptoms associated with the carcinoid syndrome. However, it has a limited therapeutic application because its short half life necessitates continuous intravenous infusion. Hypertensive crises can also occur during anaesthesia in patients with carcinoid tumours that secrete serotonin. Somatostatin was reported to reverse a potentially lethal carcinoid crisis during induction of anaesthesia.⁶ Certainly in our patient somatostatin dramatically and repeatedly reversed circulatory collapse in a carcinoid crisis in which 5-hydroxyindole acetic acid was not found. Excision of the tumour with cardiopulmonary bypass would have been impossible without continuous somatostatin infusion because sudden profound vasodilatation would have emptied the bypass circuit and brought the extracorporeal circuit to a halt. The circulation was completely unaffected by adrenaline infusion during the carcinoid crisis.

Recently a somatostatin analogue, SMS 201-995 (Sandoz, East Hanover, NJ) was used on a long term basis by subcutaneous injection to control symptoms of the carcinoid syndrome.⁷ It has been associated with decreased concentrations of urinary 5-hydroxyindole acetic acid and with regression of hepatic metastases. It is apparent that somatostatin or its analogue should be available when operations are undertaken in patients with the carcinoid syndrome whether or not this is positive for hydroxyindole acetic acid.

1 Strickman N, Hall R. Carcinoid heart disease. In: Kapoor

- AS, ed. *Cancer and the heart*. New York: Springer-Verlag, 1986:135-56.
- 2 Goodner JT, Berg JW, Watson WL. The non-benign nature of bronchial carcinoids and cylindromas. *Cancer* 1961; **14**:539-46.
- 3 Wilkins EW, Grillo HC, Moncure AC, Scannell JG. Changing times in surgical management of bronchopulmonary carcinoid tumour. *Ann Thorac Surg* 1984;**38**:339-44.
- 4 Arrigoni MG, Woolner LB, Bernatz PE. Atypical carcinoid tumours of the lung. *J Thorac Cardiovasc Surg* 1972;**64**: 413-21.
- 5 Zinner MJ, Yeo CJ, Jaffe BM. The effects of carcinoid levels of serotonin and substance P on haemodynamics. *Ann Surg* 1984;**199**:197-204.
- 6 Roy RC, Carter RF, Wright PD. Somatostatin, anaesthesia and the carcinoid syndrome. *Anaesthesia* 1987;**42**:627-32.
- 7 Kvols LK, Moertle CG, O'Connell MJ, Schutt AJ. Treatment of the malignant carcinoid syndrome. Evaluation of a long acting somatostatin analogue. *N Engl J Med* 1986; **315**:663-6.