Photodynamic therapy for bronchial carcinoid tumours: complete response over a 10-year follow-up

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Abstract

A 63-year old woman diagnosed in September 2001 with a typical bronchial carcinoid of the left upper lobe bronchus extending into the left main stem bronchus is presented. The patient was unsuitable for standard surgical treatment, and the topography was not amenable for a parenchyma-saving bronchoplastic procedure. Two cycles of bronchoscopic photodynamic therapy (PDT) were undertaken at 6 monthly intervals. The patient has now been followed up regularly for over 10 years without signs of recurrence bronchoscopically or radiologically. To our knowledge, this is the first case of a carcinoid tumour treated solely by PDT.

Keywords: PDT in bronchial carcinoid tumour • 10-year follow-up

INTRODUCTION

Bronchopulmonary carcinoids (BPC) are an uncommon group of tumours originating from the Kulchitzky stem cells of the bronchial epithelium and are classified within the diffuse neuro-endocrine system tumours. They account for 5% of all primary neoplasms of the lung [1]. The bronchial carcinoid subtype as opposed to the peripheral one presents with symptoms related to endobronchial obstruction characterized by cough, dyspnoea and chest infection. They are generally diagnosed bronchoscopically; the tumour is either pedunculated or sessile. In 1954, Thorson et al. [2] described the carcinoid syndrome characterized by episodes of flushing, tachycardia, abdominal pain and diarrhoea and valvular disease of the heart attributed to 5-hydroxytryptamine (serotonin) and its precursor 5-hydroxytryptophane and their various breakdown products secreted by the tumour.

Pathologically and behaviourally, there are two variants of broncho-pulmonary carcinoids; typical and atypical. Atypical carcinoids are histo-pathologically and behaviourally malignant tumours. Typical carcinoids behave like benign tumours, are nevertheless locally invasive and have malignant potential for spread to a distance.

Current standard resection and parenchyma-saving bronchoplastic procedures are considered to be the treatments of choice. For patients unsuitable for surgery, endoscopic intervention using diathermy or laser fulguration/ablation have been advocated [3, 4]. We present a case of typical bronchial carcinoid treated successfully with photodynamic therapy (PDT). To our knowledge, PDT has not been used as a sole treatment modality previously.

CASE REPORT

A 63-year old woman consulted her General Practitioner in June 2001 with a 2-week history of asthma-like symptoms and chest infection. With no improvement after a course of antibiotics, she was referred for a chest X-ray, indicating collapse of the upper lobe of the left lung (LUL) (Fig. 1A). CT scan of the chest and abdomen followed, showing a mass 2 cm in diameter totally obstructing the LUL bronchus into the left main stem bronchus with no enlarged lymphadenopathy (Fig. 1B). The liver contained a small lesion 2.8 × 2.1 cm, which on sonographically guided biopsy showed a nonmalignant cyst. Bronchoscopy demonstrated a polyploid tumour with a broad base totally obstructing the lumen of the LUL bronchus (Fig. 1C). The biopsy of the tumour, on standard histology and specific immuno-histo chemistry confirmed the diagnosis of a typical carcinoid.

The case was discussed in the multi-disciplinary team and the topography of the lesion was judged to be unsuitable for a parenchyma-saving bronchoplastic operation. Considering that the pulmonary function was insufficient for pneumonectomy, after discussion the patient was referred to the Yorkshire Laser Centre (YLC) to be considered for PDT.

In November 2001, the patient was bronchoscopically re-assessed at the YLC (by the senior author K.M.) using white light (WLB) and autofluorescence bronchoscopy (AFB). WLB revealed a strawberry-like tumour obstructing the LUL bronchus. AFB demonstrated an extension of the growth into the mainstem bronchus in addition to the LUL bronchus tumour toward the carina. The tumour had in fact a broad base. Biopsies from both areas confirmed the involvement by a carcinoid. Further CT scan of the thorax showed no pulmonary parenchyma involvement and no lymphadenopathy.
The bronchoscopic PDT method consisted of intravenous administration of Photofrin (Porfimer Sodium Axcan Pharma) 2 mg/kg of body weight; followed 48 h later by illumination with a laser light of 630 nm. The light was delivered to two areas:

(i) First, the optical fibre with a 1-cm diffuser tip passed through the biopsy channel of the fibropic bronchoscope was inserted into the tumour mass within the LUL bronchus delivering 200 J/cm (400 mW for 500 s).

(ii) Secondly, a microlens fibre with a forward firing projection was directed to the superficial part of the tumour in the left main bronchus delivering 150 Joules/cm (400 mW × 375 s).

In April 2002, chest X-ray, CT scan and bronchoscopy showed complete clearance. However, although there was no abnormality on WLB, there was an area of intense positive fluorescence in the left main bronchus on AFB. Biopsy of this area revealed carcinoid recurrence.

Figure 1: Preoperative chest X-ray (A), CT scan (B) and bronchoscopic image (C) showing complete obstruction of the left upper lobe by the tumour (see arrow).

Figure 2: Postoperative chest X-ray (A), CT scan (B), white light bronchoscopic image showing total opening of the left upper lobe orifice (C) and autofluorescence bronchoscopic image showing no evidence of positive fluorescence (D).
A second bronchoscopic PDT was undertaken on 27 May 2002 using 150 J/cm by the surface application to the fluorescent positive areas.

Four months later, the patient was reviewed clinically, endoscopically and radiologically. She was asymptomatic, with a clear chest X-ray. WLB and AFB showed no abnormality of the bronchial tree. Regular 6–9 monthly reviews with chest X-ray and 2 yearly CT scans have shown no evidence of recurrence and clear chest X-ray. At the last review in August 2012, the patient was clinically asymptomatic, with a clear chest X-ray and bronchoscopy (WLB and AFB) (Fig. 2A–D). Thus, the patient has been in complete response for over 10 years.

**DISCUSSION**

Carcinoids are currently classified as neuro-endocrine tumours within lung cancer [5], which have a number of subtypes and variants according to differentiation and malignant propensities. At one end is the typical benign carcinoid and, at the other, atypical ones that are undifferentiated with malignant behaviour of its subtypes approaching that of small cell lung cancer.

Bronchoscopic excision of tumours began in the 1930s. Since then, a variety of endoscopic therapies have been used such as electro-cautery, argon plasma coagulation, cryotherapy and Neodymium:Yttrium Aluminium Garnet (Nd:YAG) laser. Currently, the standard treatment for bronchial carcinoid is resectional surgery with parenchyma-saving broncho-plastic operation when possible. In unresectable cases, Nd:YAG laser has been extensively used both for malignant, including carcinoid and benign tumours [3, 4]. However, in our experience when NdYAG laser is used for malignant lesions or potentially malignant lesions such as typical carcinoid, the procedure usually needs to be repeated every 6–8 weeks to achieve continued long-term clearance, and the rate of failure and complication can be near 20%.

PDT has been extensively used for malignant endobronchial lesions since 1986. The only drawback with PDT is potential skin photosensitivity reaction, which is totally avoidable with thorough counselling. In the authors’ experience of over 500 patients and well documented in the literature, there has been no haemorrhage, stenosis or perforation. As a sole treatment modality, PDT appears not to have been used for endobronchial carcinoids. The lesson learnt here is that PDT can be used in this pathology with the expectation of a long period of complete response.

**Conflict of interest:** none declared.

**REFERENCES**