Diathermy resection and radioactive gold grains for palliation of obstruction due to recurrence of bronchial carcinoma after external irradiation

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ABSTRACT   During 1985–7 15 patients previously treated by external radiotherapy for inoperable carcinoma of the lower trachea and major bronchi underwent endobronchial insertion of radioactive gold grains as a palliative procedure for relief of symptoms. Four patients had undergone three or more endobronchial laser treatments before being referred. Under general anaesthesia diathermy was used to resect obstructing tumour before the insertion of the gold grains into the tumour and the compressed endobronchial wall. Four patients died within one month. The remaining 11 patients were symptomatically and objectively improved when assessed at one month. Both collapsed lungs and three out of six collapsed lobes had re-expanded. Fourteen of the 15 patients died within 13 months (median survival 2·5 months); one patient with recurrent symptoms after 10 months underwent a further implantation and is alive after two years.

Introduction

Tracheal and bronchial obstruction due to local recurrence of tumour after external radiotherapy for inoperable carcinoma of the lung presents a clinical problem, causing stridor, dyspnoea at rest or with minor exertion, and frequently collapse of a lobe or lung. In a review of 5000 necropsies on patients with lung cancer, 40% of the deaths were judged to be the direct result of failure to control local disease.[1] There are various methods of palliation of the patient's symptoms. They are principally aimed at removing the obstructing endobronchial tumour and include curettage, diathermy, cryoresection, and laser treatment. Often, however, a major component of the obstruction is extrabronchial, caused by tumour or affected lymph nodes. This component can be overcome only by stenting or by further radiotherapy. When external radiation is limited either by normal tissue tolerance or by its relative ineffectiveness when fibrous tissue surrounds the airways, further radiotherapy can be given directly to the tumour by interstitial implantation of a radioactive source.[2-6] We have for

some years been using radioactive gold grains in these circumstances.

The properties of radioactive gold (^{198}Au) for interstitial use were described by Sinclair[2] and Henschke.[3] The isotope emits gamma radiation and has a half life of 2·7 days. In keeping with the law of inverse squares, the dose of radiation falls off steeply with increasing distance from the source. The maximum range of therapeutically effective radiation is limited to tissue within about 5 mm of each source, so normal lung is not subjected to radiation and total body irradiation is negligible. The exact dose received by the tumour in any one patient is difficult to calculate as it is related to the spatial arrangement of the gold grains. Calculations have been based on theoretical models. Sufficient grains are implanted with the object of delivering about 60 Gy (6000 rad) to complete decay (a radical dose of external radiotherapy may administer 35–50 Gy over three to five weeks). Tissue immediately adjacent to a gold grain might receive 100 Gy. This should swing the therapeutic equation, the balance between toxicity and response, in the patient's favour.

Patients and methods

From 1985 to 1987 15 patients previously treated by external radiotherapy for inoperable carcinoma of the lower trachea and major bronchi presented with

symptoms of stridor or dyspnoea 4–36 months after radical deep x ray treatment. Thirteen were male; the age range was 37–73 (mean 58) years. Fourteen patients had squamous cell carcinomas and one an adenocarcinoma. Tumour or external compression or both affected the lower trachea, carina, and both major bronchi in three patients; the lower trachea and a major bronchus in five patients; and major bronchus alone in seven patients. Collapse of a lung was present in two patients and collapse of a lobe in six. Four patients had undergone three or more endoscopic laser resections before being referred.

Insertion of the gold grains was performed under general anaesthesia with a rigid bronchoscope. This facilitates the removal of large pieces of tumour and the control of resultant bleeding while the airway is maintained in a still field so that safe and accurate positioning of the gold grains is possible. After the induction of anaesthesia an exploratory bronchoscopy was undertaken initially to assess the extent of the tumour. Where indicated, obstructing tumour was resected with the Stortz diathermy resection loop. Sufficient tumour was removed from the trachea to relieve stridor and from the main bronchi to relieve dyspnoea.

The radioactive gold grains (Amersham International) are supplied in the form of cylinders, 2·5 mm long and 0·8 mm in diameter, in lead cartridges containing 14 grains each. The cartridge is taken from its protective container and loaded into the Royal Marsden implantation gun, which is fitted with an extended introducing needle.[7] A fine trocar displaces the grains into the shaft of the needle and with each pull of the trigger a single grain is expelled from its tip. The aim is to insert the gold grains into the tumour and compressed endobronchial wall with a uniform distribution. Ideally, one quarter of the total dose should be placed centrally in the tumour and three quarters around its perimeter. This was attempted by starting at the centre of the area to be treated and spiralling outwards, grains being placed 5–10 mm apart. At the time they are used each grain has an activity of 110 Mbq. Around 17 grains were generally implanted.

The procedure was performed in accordance with the local code of practice laid down by the radiation protection officer of the Brompton Hospital. All grains were accounted for and checks were made of the room and suction circuits with a scintillation counter. The whole procedure generally took about 45 minutes. When patients returned to the ward they were nursed in an isolated room for one week while the activity of the grains decayed to a safe level. The radiation protection officer advised the staff of the maximum time that could be spent close (within 2 feet) to the patient and this increased daily. Radiation badges were worn by all staff going into the room, though negligible amounts of radiation were detected. All sputum was checked with a scintillation counter for expectorated grains, but none was detected during the period in hospital in this series of patients.

Results

All patients were discharged home or back to their referring hospitals one week after the insertion of gold grains. One month later they returned to the outpatient clinic to be assessed. This was at a time when the effect of the radiotherapy was thought to be at a maximum and before tumour regrowth was likely. By this time, however, only 11 of the 15 patients were alive.

FAILURE TO IMPROVE
Four patients had died in their referring hospitals two to four weeks after insertion. One patient died of a pulmonary artery to bronchus fistula four weeks after treatment. He had previously received two courses of deep x ray treatment and a course of chemotherapy overseas. With the addition of gold grains he had probably received a total dose of 150 Gy. Some re-expansion of a collapsed right upper lobe had been achieved before necrosis of the pulmonary artery wall developed.

A second patient died of a tracheo-oesophageal fistula two weeks after the insertion of gold grains. He had previously received a radical course of external radiotherapy and laser therapy but now had a frozen mediastinum due to recurrent tumour with external compression of the lower trachea and both main bronchi. The diathermy was used to resect obstructing tumour and gold grains were inserted. One week later he had experienced no improvement so the procedure was repeated but with a smaller number of grains. One week after this he developed the tracheo-oesophageal fistula.

One patient died of disseminated disease three weeks after treatment. A further patient, with recurrent tumour of the lower trachea and right main bronchus, died of pneumonia after two weeks.

SYMPTOMATIC IMPROVEMENT
All the 11 patients who were alive one month after insertion of the gold grains had improved symptomatically. Improvement in FEV_1 ranged from 30% to 120% (mean 69%). Both the collapsed lungs and three of the six collapsed lobes had re-expanded.

SURVIVAL
Fourteen of the 15 patients had died within 13 months of insertion of the radioactive gold grains, with a median survival of 2·5 months. Ten patients died

without recurrence of their symptoms. These patients had been reviewed at regular intervals at their referring hospitals. One patient is alive at two years, having undergone a further insertion of gold grains at 10 months when her symptoms recurred. She has recently been reviewed and remains symptom free.

Discussion

Patients with advanced neoplastic disease and critical airway narrowing are often extremely ill and have a limited life expectancy. Previous treatment, including deep x ray treatment and steroid treatment, and superimposed infection make them difficult to treat. In these circumstances palliation of the patient's symptoms is all that can be expected, and this is reflected in the median survival of 2·5 months for this series. All patients who were alive one month after insertion of radioactive gold grains were symptomatically improved, and this response was maintained until death. Objective improvement of FEV_1 was also recorded, particularly in those patients with radiological improvement. Four patients died within one month of insertion and their brief survival indicates the severity of their disease. The deaths of two patients, however, were accelerated by necrosis of vital structures caused by excessive radiation.

In an earlier series[8] we reported greater difficulty in maintaining a response with radioactive gold grains in patients with bulky tumour extending into the trachea. We suggested that cryotherapy or laser treatment may be beneficial in these circumstances. At that time the bronchoscopic diathermy resection equipment was not available to us but we have since used it to remove large pieces of tumour quickly. This has an immediate effect on the endobronchial component of the obstruction. The gold grains are then inserted into the residual tumour and compressed wall, where their limited range of radiation can be more effective. The diathermy loop can adequately resect tumour from the trachea and main and lower lobe bronchi, but tumour within upper lobe bronchi is not reached so easily.

There are various techniques for dealing with endobronchial disease, of which laser treatment is the most popular.[9-11] The advantage of this technique is that it is performed through the flexible bronchoscope under local anaesthesia, produces an immediate response, and can be repeated when necessary. It takes a long time, however, to vaporise large quantities of tumour and frequent sessions are often necessary. George *et al*[12] have recently reviewed a series of 97 patients comparing treatment under general anaesthesia and under local anaesthesia, using a rigid bronchoscope through which the flexible bronchoscope and laser is passed. Under general anaesthesia there was better control of the airway and the

laser could be used more effectively. Under local anaesthesia the mean number of sessions required for achieving a response to treatment was almost two, compared with only one with general anaesthesia. Two operative deaths occurred under local anaesthesia and none under general anaesthesia. Patients in both groups spent an average of one week in hospital. The experience of these authors was consistent with that of others,[13] and they now recommend the use of general anaesthesia and rigid bronchoscopy for laser treatment.

In the laser series referred to above 21 out of 97 patients and in another series 25 out of 70 patients[14] with incomplete obstruction of the bronchus underwent additional courses of treatment. Four patients in our series had been referred after three or more laser treatments. Whether these were performed under general anaesthesia is unknown but the results reflect the limitation of laser treatment in removing large amounts of tumour and dealing with extrabronchial disease. A recent presentation described increased relief of obstruction when laser therapy was followed by endobronchial radiation from an "afterloaded" radioactive gold chain or iridium wire.[15] Schray[16] and Fish[17] had previously reported success with similar techniques using "conventional" radioactive sources that have dose rates of 10 cGy/h–50 cGy/min and have to remain in the airway for one or several days. Yet more powerful high dose rate sources are now available. Cobalt-60 and iridium-192 can be afterloaded into prepositioned conduits (for example, a transnasal catheter) to treat tumours locally and their use in endobronchial irradiation has been reported by Seagren.[18 19] The principle advantages of this technique are the exceptionally short time (less than 30 minutes) required to administer the total dose of radiation prescribed, the better radiobiological efficiency of high dose rate radiation (a given dose achieves a greater effect[20]), and the possibility of using the technique in outpatients. The radiation received by the tumour is more predictable than with gold grain treatment and there is no risk of radiation to others. Normal tissue, however, may receive more irradiation and its efficacy in comparison with that of gold grains is at present unknown.

For the palliation of recurrent endobronchial tumour we have found that diathermy and radioactive gold grains offer a single treatment that provides rapid symptomatic relief to most patients.

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