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Communication

Intratumoural chemotherapy with 5-fluorouracil for palliation of bronchial cancer in patients with severe airway obstruction

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Abstract

Patients with tracheal or major airway obstruction owing to inoperable carcinomas are at risk of developing respiratory failure or postobstructive pneumonia. In such cases, there is an urgency to restore the airway. Bronchoscopic interventional procedures for palliation of malignant airway obstruction are becoming more common in clinical practice. However, as current interventional methods may be unavailable or are contraindicated, we have investigated the use of direct intratumoural injection with 5-fluorouracil for tumour regression to open the airway. In this study, 65 patients who presented with greater than 50% obstruction of at least one major airway were treated with 5-fluorouracil injection directly into the endobronchial tumour or area of infiltrated bronchial mucosa through a flexible fiber-optic bronchoscope. The pretreatment luminal opening for this cohort of 65 patients ranged from 0% (totally obstructed) to 40%, with an overall mean luminal opening of 22% (78% occlusion). There was a positive response to intratumoural injection in 56 of 65 patients, and a large reduction in the size of tumours by endoscopic evaluation in the majority of cases. Overall, the mean pretreatment luminal opening of 22.0% was significantly improved to a mean post-treatment luminal opening of 58.5%, an increase in the opening of the airways of 36.5%. The increase in the diameter of the airway lumen was more than 50% for 34 of 65 patients, and 23 showed a 25–50% improvement. The results were of obvious immediate clinical benefit. Statistical analysis of all patient data by a Wilcoxon matched-pairs/sign-ranked test confirmed the significant benefit achieved ($P < 0.001$). The therapy was well tolerated, with no systemic side-effects or any serious complications. The results of this study suggest that in patients with life-threatening airway obstruction, intratumoural injection of anticancer drugs should be regarded as an important new therapeutic approach and an integral part of interventional bronchoscopic management. This study further encourages more general consideration of intratumoural drug injection as a minimally invasive therapeutic method for the treatment of lung cancer and various inoperable cancers.

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Introduction

Endobronchial obstruction by a tumour is a common and potentially life-threatening complication both on initial presentation and in patients with recurrent or metastatic disease. According to one estimate, 20–30% of newly diagnosed malignant lung neoplasms will present with atelectasis and pneumonia owing to endobronchial obstruction (Minna et al 1985). In patients with inoperable disease, most therapeutic approaches result in a high incidence of local failure with malignant airway occlusion.

In patients with life-threatening central airway obstruction, there is an urgent need for rapid re-canalization of the obstructed airway, which can be life-saving. In these cases, surgical resection is often impossible owing to the advanced stage of the tumour, and systemic chemotherapy or radiotherapy is, for most patients, either ineffective or the response is brief. Therefore additional treatment strategies are necessary.

Interventional bronchoscopic procedures could be successful in re-establishing patency of the airway as an alternative treatment method. These techniques can be divided into four main groups (Minna et al 1985; Freitag et al 2001): (i) mechanical procedures for re-canalization, such as removing the tumour bulk by forceps and

dilatation techniques using angioplasty balloon catheters; (ii) thermic procedures using extreme heat or cold, such as cryotherapy, electrocautery, or laser resection; (iii) endobronchial radiation therapy using highly active radioisotopes, so-called "brachytherapy"; and (iv) endobronchial prostheses (stent insertion).

When these techniques were unavailable or were contraindicated, we proceeded to use a new technique for which we had promising preliminary clinical results: direct intratumoural injection with chemotherapeutic agents. We reported the results of the initial endobronchial drug therapy study for 93 patients who presented with over 50% obstruction of at least one major airway (Celikoglu et al 1997). In that study, all patients were treated with a mixed regimen of various drugs (5-fluorouracil (5-FU), mitomycin, methotrexate, bleomycin and mitoxantrone) injected directly into the tumour. Of 35 patients presenting with complete obstruction of one lung, 18 showed complete re-expansion, six had partial re-expansion, and for 11 there was no effect. Overall, 39 of the 93 patients showed an increase in the luminal diameter of more than 50%, and 42 showed a 25–50% improvement.

Since 1992, partly owing to rising drug costs, instead of the several anticancer drugs noted above, we have used higher doses of 5-FU alone for intratumoural injection. This report details the short-term results of intratumoural injection of 5-FU in 65 patients with malignant airway obstruction.

Materials and Methods

Patient selection

Between 1 August 1992 and 30 August 2001, we enrolled 65 patients (eight women, 57 men), aged 28–82 years (mean age 52 years), with nearly complete (> 50%) obstruction of at least one major airway. Patients with isolated lobar obstruction were included only if it was felt to contribute to respiratory insufficiency, atelectasis or postobstructive pneumonia. Patients with obstruction of a more peripheral bronchus were not included in this study.

All patients were initially classified according to their health status and the status of their tumours (i.e. inoperable, localized, extent of disease, poor overall general health). Patients entered with inoperable tumours were either unable to receive primary external beam radiation therapy or had a recurrence after such therapy. Patients were also eligible if they did not respond or relapsed after systemic chemotherapy. Newly diagnosed patients were given intratumoural drug injection as a primary treatment if there was an urgent obstructive condition. We only included patients with metastatic disease when dyspnoea was the dominant symptom. There was no age limit and all tumour cell types were accepted.

Informed consent was obtained from each patient before initiation of treatment. The ethical committee of Cerrahpaşa Medical School of Istanbul University gave approval for this study. Preliminary studies included a complete medical history and physical examination, posteroanterior and lateral chest X-rays, full blood cell count, prothrombin time, platelet count, spirometry and flow volume loops, and arterial blood gas analysis. The protocol of symptom scores, X-ray examinations, physiological tests and blood examinations was repeated every week following initial treatment and before all subsequent bronchoscopic examinations.

The size and extent of the tumour burden seen at bronchoscopy was recorded on charts of the bronchial tree, and video documentation was obtained before and after all treatments for further comparative assessment. Computed tomography (CT) of the chest and abdomen with contrast infusion and rapid sequence imaging was employed to display the relationship between the involved bronchus and the surrounding structures, particularly the large intrathoracic blood vessels.

Histology identified 43 squamous cell carcinomas, three small cell carcinomas, 14 adenocarcinomas, and two adenocystic carcinomas, as well as three other types of carcinoma (metastatic adenocarcinoma from the gastrointestinal tract).

Intratumoural injections: procedure and instrumentation

After intravenous injection of 3–5 mg midazolam, 2% xylocaine spray was used to numb the pharynx and larynx. Oxygen, 5–7 L min^{-1} was administered nasally.

All injections of intratumoural chemotherapy were performed through a flexible bronchoscope. With the patient in the sitting position, the flexible bronchoscope was inserted transnasally into the trachea. Direct intratumoural injection was performed with a flexible 23-gauge needle manufactured for transbronchial needle aspiration biopsy. To prevent damage to the working channel of the flexible bronchoscope, all needles should be of retractable design.

The needle device is advanced through the bronchoscope channel in the retracted position. Once the tip of the device is 2 cm above the area to be injected, the needle can be advanced from its sheath. At this point, it is usually helpful to withdraw the needle's sheath into the bronchoscope channel so that only the needle remains exposed. This manoeuvre allows the sheath to be supported by the bronchoscope channel and gives the operator greater control over the exact placement and advancement of the needle.

If the tumour was bronchoscopically visible as a polypoid mass, the needle was then inserted directly into the tumour mass (Figure 1A). When an infiltrating tumoural lesion on the bronchial wall was present, the needle was inserted at an oblique angle into the submucosal tumoural infiltration. In the case of extraluminal tumoural disease (either a mass or metastatic lymph nodes), the needle was inserted perpendicular to the wall of the airway (Figure 1D). To inject the drug into an extraluminal cancerous lesion, a 21-gauge, 15 mm long needle, with a wider and stiffer catheter should be used. Once the needle is embedded in the tissue, the drug is injected. Of course it is important to withdraw the needle into its sheath before removing it from the bronchoscope.

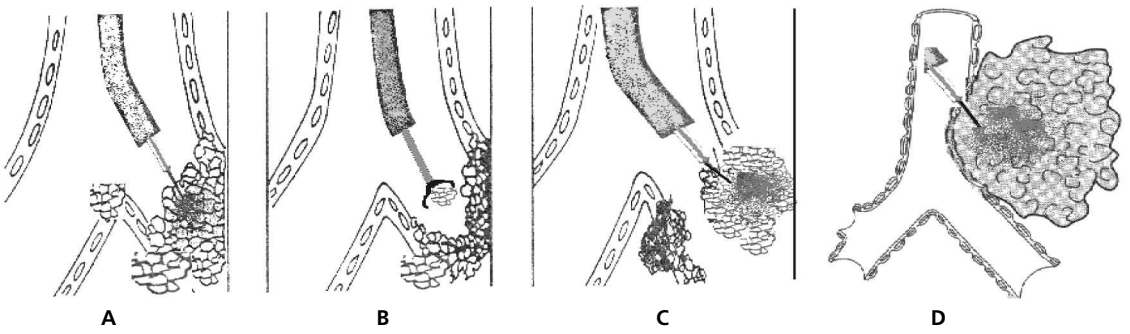

Figure 1 A. Intratumoural injections of anticancer drug directly into intraluminal tumour mass. B. Necrotic tumour debridement with forceps. C. In cases with mixed obstruction, after removal of intraluminal necrotic tumour debris, injection of drug into both the intramural and extraluminal components. D. Injection of anticancer drug into extraluminal tumour.

Drugs that do not induce local necrotic changes in the normal mucosa, that have a pH of approximately 7.4, and that exhibit direct antineoplastic activity should be selected for this type of intratumoural chemotherapy. Drugs that require activation by hepatic microsomes before antineoplastic activity is present (e.g. cyclophosphamide) were considered unsuitable for direct injection. In this study, 5-FU was selected because it fulfils the above conditions and because it is inexpensive.

At every session of intratumoural injection, according to the size of the tumour, 0.5–1 g of 5-FU solution (at a concentration of 50 mg mL^{-1}) was injected into the tumour. Injections were made in a fanning manner to disperse the drug throughout the tumour and maximize tumour perfusion of the drug.

In this study, the success of therapeutic intervention was determined not only by symptomatic relief, but also by the increase in the diameter of the lumen observed on bronchoscopic evaluation at the end of 2 weeks of intratumoural treatment.

Semi-quantitative bronchoscopic evaluation of therapeutic effects were as follows: (i) good response: > 50% increase in the diameter of the lumen; (ii) moderate response: 25–50% increase in the diameter of the lumen; and (iii) small response: < 25% increase in the diameter of the lumen.

Statistical analysis

Two methods of analysis were applied to the clinical results: Mann-Whitney/Wilcoxon rank sum and Wilcoxon matched pairs.

The Mann-Whitney rank sum test is designed for comparison of data that are categorical/ordinal, rather than truly continuous or numerical. No assumption of a particular distribution function is required, therefore the data do not need to be normally distributed. The data for 65 patients were summarized in clinical categories that numerically reflected the degree of efficacy (i.e. the increase in lumen diameter). Values of 1, 2 and 3 for increase in lumen diameter were assigned to reflect the increasing degrees of efficacy for the purpose of this analysis (see Table 1). Table 2 summarizes the data numerically according to the different tumour locations and outcomes using the numerical assignments from Table 1.

No controls could be evaluated in parallel-arm fashion because of ethical considerations (i.e. every patient had to be treated). The arbitrary control group of 20 was therefore created based on clinical experience, since it is known that without treatment, the chance of spontaneous reduction of the tumour mass and therefore an increase in lumen diameter is not likely. The assignment of a value of < 25% increase in lumen diameter for each control was very conservative, since it allows for not only the normal growth of the tumour (a negative increase in lumen diameter), but also encompasses no change or even spontaneous regressions up to 24%. A SigmaStat 2.0 program was used to obtain the data summarized in Table 3. Overall results as well as data comparing individual tumour locations show highly significant effects for the intratumoural 5-FU treatment.

Wilcoxon matched-pairs signed-rank analysis required no arbitrary control group assignment and was made possible by analysis of raw clinical data (pretreatment vs post-treatment) for all 65 patients. This analysis is designed to detect differences between two treatment groups, or between baseline and treatment values of the response variable. We regard this analysis as more appropriate than the rank sum test, since it is designed to analyse differences between individual pretreatment and post-treatment results, and allows each patient to serve as their own control rather than requiring a representative control group as was done for the rank sum test. This

Table 1 Numerical value assignment based on reported categories.

Category	Value
> 50% increase in lumen diameter	3
25–50% increase in lumen diameter	2
< 25% increase in lumen diameter	1

Table 2 Categorized data for Mann-Whitney rank sum statistical analysis.

Tumour location	> 50% increase in lumen diameter	25–50% increase in lumen diameter	< 25% increase in lumen diameter	Total
Trachea	5	3	0	8
Carina + main bronchus	1	3	1	5
Main bronchus or bronchus intermedius	18	11	3	32
Lobar bronchus	10	6	4	20
Total	34	23	8	65

Table 3 Summary of statistical findings using data from Table 2 and Mann-Whitney rank sum test.

Tumour location	n	*P* value (vs control)
Trachea	8	< 0.001
Carina + main bronchus	5	0.007
Main bronchus or bronchus intermedius	32	< 0.001
Lobar bronchus	20	< 0.001
Control[a]	20	< 0.001
Total	65	< 0.001

[a]A reasonable but arbitrary control group was assigned for this analysis, with controls assigned highly conservative values of < 25% increase in lumen diameter.

analysis was run using the MiniTab Release 12 program. Table 4 summarizes the results.

Overall, statistical analysis demonstrated a significant treatment benefit comparing pretreatment percentage luminal opening with post-treatment percentage luminal opening. Even subgroups showed statistical significance at the 0.05 level, with the exception of those in the carina + main bronchus subgroup. This is likely owing to the small number of patients in this subgroup and the variability of changes in percentage luminal opening for this group.

Results

After intratumoural injection with 5-FU, there was an endoscopically visible effect. Tumours were reduced in size and infiltrative changes improved. In subsequent bronchoscopies, a white/yellowish gel-like substance consisting of fibrin plugs and necrotic cell debris of the tumour tissue was observed attached to the surface of the injected portion of the tumour or infiltrated mucosa.

Injection of the chemotherapeutic agent into the tumour kills the cancerous cells but leaves tumour cell debris. Therefore, dead cells and tissues were removed mechanically by forceps (piecemeal resection), irrigated and aspirated by suction, or sometimes coughed up. It was observed that one important added benefit of intratumoural injection of 5-FU was to provide a haemostatic effect on tumour tissue, thus allowing the debridement of the cell debris by piecemeal resection with forceps and suction, even during the initial therapy (Figure 1B). The intraluminal necrotic tumour debridement also allowed injection of 5-FU more deeply into any remaining tumour mass attached to the bronchial wall in the mixed obstruction (Figure 1C).

Initially, intratumoural injections were given weekly until airway patency was restored with relief of symptoms. With further clinical experience, an average of three sessions of intratumoural injection was used to achieve symptomatic response over a 2-week period in 57 patients for whom airway patency was completely or partially restored.

In patients with recurrent malignancies who showed an initial favourable response to this treatment, direct injection of 5-FU was carried out weekly (for a maximum of 2 months) until complete clearing of the tumour tissue. If patency of the airways was maintained, bronchoscopy was repeated at intervals of 1–3-months and treatment was repeated for recurrent tumour tissue.

Table 4 Summary of statistical findings using raw data from individual patient examinations comparing lumen opening before and after treatment with 5-fluorouracil.

Tumour location	n	*P* value
Trachea	8	0.014
Carina + main bronchus	5	0.225
Main bronchus or bronchus intermedius	32	< 0.001
Lobar bronchus	20	< 0.001
Total	65	< 0.001

Intratumoural chemotherapy was abandoned if patency of the airways could not be established with a maximum of four successive sessions of injections and debridement, or when the severity of metastatic disease outweighed the potential benefits of continued treatment. Because the long-term systemic effects of intratumoural therapy are unclear, initiation of radiation and/or systemic chemotherapy may be appropriate within a short time, perhaps 2 weeks, following relief of bronchial obstruction by intratumoural injection.

In six patients with obstruction of the trachea or carina plus one main bronchus, dyspnoea worsened 1–6 h after intratumoural 5-FU injection owing to accumulation of necrotic tumour coagulum and secretions. For these patients, dexamethasone (4 mg) was administered systematically and a clean up bronchoscopy was performed immediately, with removal of necrotic material and accumulated secretions by piecemeal resection with forceps and suction. In these patients, the cleaning procedure immediately restored the patency of the airway, with alleviation of dyspnoea.

Clinical observations

Representative bronchoscopic images are presented in Figure 2. On initial bronchoscopic examination for eight of 65 patients, there was >50% obstruction of the trachea. In five patients there was involvement of the carina, with complete obstruction in one of the main bronchi and partial obstruction in the other. There were 32 patients with obstruction in one of the main bronchi or bronchus intermedius, and 20 patients had an obstruction in one of the lobar bronchi (see Table 5 for the results according to endobronchial localization).

Of the 65 patients with airway obstruction entered into this study, 41 were cases of recurrent carcinomas that had been previously treated with external beam radiation therapy and/or systemic chemotherapy, and 24 were newly diagnosed without any previous therapy.

There were 45 patients with exophytic intraluminal (intrinsic) malignant obstruction, five patients with extraluminal (extrinsic) compression, and 15 patients with extraluminal and intraluminal (mixed) stenosis treated with intratumoural 5-FU injection.

For 41 of 45 patients in whom the tumour was visible as a polypoid mass by bronchoscopy, there was a reduction in size of the tumour and improvement in atelectasis or obstructive pneumonia within 2 weeks after intratumoural chemotherapy.

For 13 of 15 patients in whom only a small part of an extraluminal tumour was visible by bronchoscopy (mixed obstruction), intratumoural chemotherapy was useful not just for the bronchoscopically visible tumour, but also for the extraluminal component seen on CT. This suggests that injected 5-FU infiltrated and diffused deeply into the tumour mass.

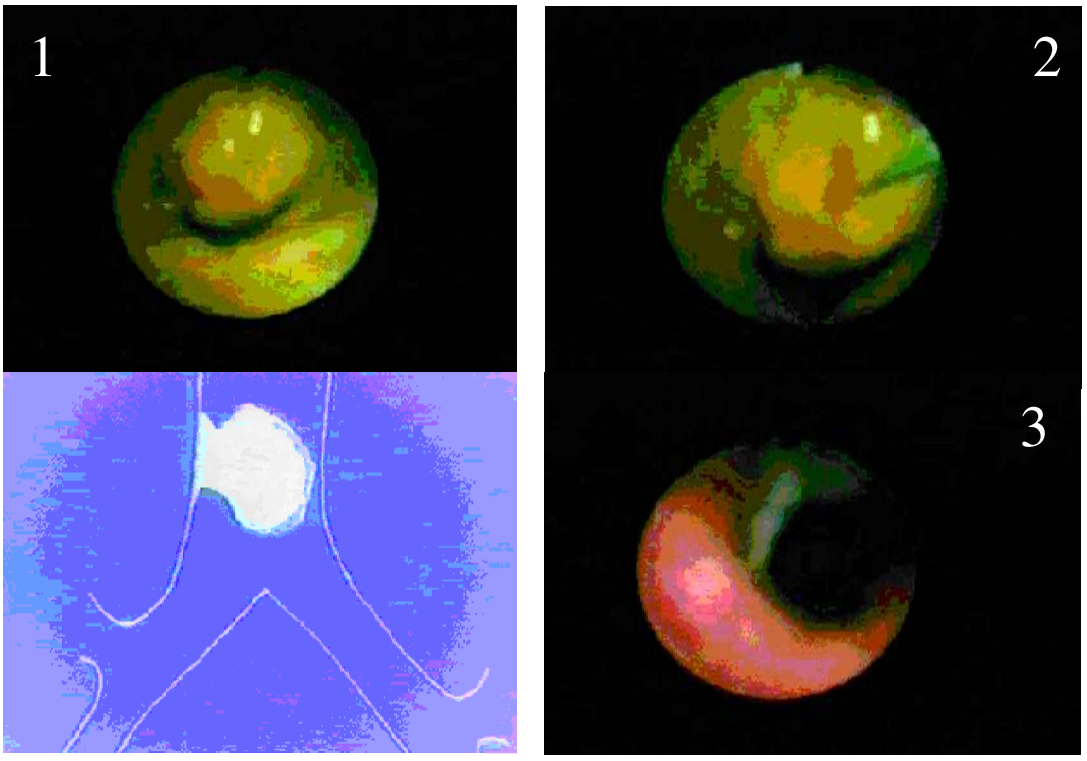

Figure 2 A 51-year-old male patient with adenocystic carcinoma in the trachea. 1. Pretreatment: lumen of the trachea 80% obstructed. 2. Insertion of the needle. 3. Following four weekly intratumoural injections of 5-fluorouracil, the lumen of the trachea is completely re-canalized; bronchoscopically, only a yellow cicatricial lesion on the wall of the trachea was seen.

Table 5 The increase in lumen diameter in response to 5-fluorouracil injection.

Tumour location in airway	Good response	Partial response	No response	Total
Trachea	5	3	–	8
Carina + main bronchus	1	3	1	5
Main bronchus or bronchus intermedius	18	11	3	32
Lobar bronchus	10	6	4	20
Total	34	23	8	65

Furthermore, in five patients with obstruction owing to extraluminal (extrinsic) compression, after three sessions of 5-FU injections into the extramural mass, the size of the tumours was reduced and airway patency was improved for three patients within 2 weeks.

Overall, during a 2-week period of treatment, 34 of 65 patients showed an increase in the airway lumen diameter of more than 50%, and 23 patients showed an improvement of 23–50%. By radiologic examination, 2 weeks of treatment for 20 patients having complete luminal obstruction plus total collapse of one lung, resulted in complete relief of obstruction in 10 cases and full re-expansion of the collapsed lung. In four cases, partial lung re-expansion occurred. There was no change for six of 20 cases. Even a single session of intratumoural drug injection with extensive debridement improved airway patency for 14 of 65 patients. After intratumoural chemotherapy, stridor or dyspnoea, postobstructive pneumonia and haemoptysis were either relieved or completely disappeared in the patients who responded to the treatment.

Spirometry was performed before and after intratumoural chemotherapy in 22 patients with main bronchus obstruction. Forced vital capacity (FVC) improved in 18 of 22 patients (mean improvement of FVC = 342 mL, range 50–1200 mL). Forced expiratory volume in 1 s (FEV_1) improved in 17 of 22 patients (mean improvement of FEV_1 = 250 mL, range 30–850 mL). Spirometric values improved in eight of the 14 patients with lobar bronchus obstruction in whom measurements could be obtained before and after treatment (mean improvement of FVC = 330 mL, range 25–950 mL; mean improvement of FEV_1 = 290 mL, range 18–800 mL).

Adverse events for intratumoural injections of 5-FU were minimal. No toxicity and no haemoptysis were observed. The most common adverse systemic effect was mild fever in 20 patients occurring 6–24 h after injection. No patients suffered from nausea, interstitial pneumonitis, bone-marrow suppression, worsening of inflammatory findings or hair loss. There was no pain or discomfort during intralesional injection of the 5-FU. These results indicate the safety and efficacy of repeated doses of 5-FU; clinical benefits were not accompanied by toxic complications.

Discussion

Bronchoscopic interventional procedures for palliation of malignant airway obstruction are becoming standard clinical practice in many large clinical centres (Minna et al 1985; Torre et al 2000; Freitag et al 2001). Tumour obstruction of the trachea and main bronchia, with comparable degrees of narrowing of the lumen, can be separated into three main types: intraluminal, extraluminal and mixed types. Intraluminal exophytic tumours in the trachea or main bronchia are usually removed with cutting techniques such as Nd-YAG laser photoresection, electrocautery or cryotherapy. However, these cutting methods are not useful for extraluminal tumours, with or without metastatic lymph nodes, with extrinsic compression of the airway lumen. Endoscopically, they are treated most efficiently using brachytherapy or stent insertion. Although several techniques for re-canalization are interchangeable in many cases, best results may be achieved by combination therapies and it is often advisable to apply them sequentially (e.g. brachytherapy or stent insertion following laser surgery).

Unfortunately, not all medical centres are suitably equipped for interventional bronchoscopy and methods of treatment may vary widely depending on facilities available for bronchoscopy. There is, therefore, an important role for newer, simpler and less costly bronchoscopic interventional methods to provide immediate airway relief with low morbidity and mortality. Intratumoural injection of anticancer drugs fulfils these criteria and should prove to be of increasing clinical importance as a method for palliation of malignant airway obstructions.

Intratumoural therapy

Intratumoural injection by bronchoscopy was first developed in the early 1970s (Hayata et al 1978). In that study, the direct injection of BCG immunotherapy and some anticancer drugs into endobronchial tumours or infiltrated mucosa was used to manage endobronchial exophytic tumours and to relieve obstruction.

There has been a proliferation of intratumoural chemotherapy and immunotherapy research during the past decade. High local drug concentrations with minimal systemic toxicity is a key potential benefit of intratumoural therapy (Goldberg et al 2002). Clinical and experimental studies consistently report significantly higher drug concentrations in injected target tissues (e.g. 6–10 times higher), with greatly reduced systemic toxicity compared with conventional intravenous chemotherapy. In general, significant tumour regression has been reported. Studies suggest that patients may be first treated by intratumoural injection

weekly and then at intervals of 4–5 weeks as regression is observed (Brincker 1993), or treated preoperatively as a local neo-adjuvant therapy (Goldberg et al 2002).

Direct injection of several anticancer drugs into endobronchial tumours has been successfully tested and used by us since 1986 with various mixed drugs regimens. The present study demonstrates that injection of high doses of a single drug, 5-FU, produces the same effect as the injection of several mixed anticancer drugs used previously (e.g. mitoxantrone, mitomycin, bleomycin, methotrexate, 5-FU). This regimen, using only 5-FU, also greatly reduces the drug cost for intratumoural chemotherapy. The total intratumoural dose of 0.5–1.0 g was administered as a 50 mg mL^{-1} solution (5–10 mL^{-1}) and was dependent on the size of the tumour mass. The large drug solution volumes used were well absorbed by the spongy tumour mass. For reference, the local intratumoural 5-FU dose was in the same range as often given by conventional systemic bolus intravenous injection for the treatment of various cancers (e.g. 500 mg m^{-2} per day).

Following direct drug injection into the tumour, the size of the intraluminal mass was significantly reduced, most likely owing to the very high concentration of cytotoxic material around the tumour cells, with an immediate effect leading to tumour cell death and shrinkage of the tumour. The intratumoural chemotherapy treatment appears to concentrate the cytotoxic drug in the injected tumour mass and thus spares the sensitive normal surrounding tissue structures. 5-FU injections also exhibit a haemostatic effect, probably owing to constriction of small vessels in or around the tumour mass. This haemostatic effect facilitates mechanical removal of necrotic tumour residue by forceps. In cases where collapse of a lung accompanied severe airway obstruction, partial or complete re-filling of the collapsed lung was often observed with opening of the airway.

In this study, there were 24 newly diagnosed patients with bronchogenic carcinoma that produced severe dyspnoea and clinical evidence of severe airflow obstruction or obstructive pneumonia. These patients had not previously received radiation therapy or systemic chemotherapy. They were given intratumoural injections of 5-FU as a primary therapy because of the urgency of their condition. Their treatment plan was to first open the airway by intratumoural chemotherapy. This was to be followed by radiation therapy and/or chemotherapy, or other interventional bronchoscopic procedures such as brachytherapy or stent insertion. The opening of an atelectatic or poststenotic airway, enabling the removal of retained secretion and pus from the obstructed bronchial system, was expected to improve the general condition of the patient. Patients with symptomatic relief would then be more likely to benefit from conventional radiotherapy or systemic chemotherapy, or both (Mathisen & Grillo et al 1989; Macha & Loddenkemper 1995; Yapp et al 1998).

For a tumour mass, $<25\%$ of which is growing endobronchially as imaged by CT, endobronchial treatment with laser photoresection, electrocautery or cryotherapy is unlikely to be helpful (Bolliger et al 2002). However, intratumoural chemotherapy could be successfully used in such cases. Moreover, intratumoural injection of 5-FU into extramural carcinomas does not run the risk of creating fistulas or damage to the stabilizing cartilage as has been observed in thermal resections with high-power laser or electrocautery.

Conclusions

Treatment of obstructive bronchoesophageal cancer by intratumoural injection of 5-FU has been shown to be simple and safe. It is an extremely easy procedure to perform. Although very high local doses are used, it is accompanied by no significant adverse reactions or systemic toxicity. Haemostasis is another important and unexpected benefit. The low cost of treatment using 5-FU is also a considerable advantage.

In this report, we have presented only short-term results for the palliation of obstructive tumours, results obtained over a period of only a few weeks after intratumoural treatment. However, although the acute life-threatening airway obstructions of patients was relieved, whether long-term patient survival is significantly improved is difficult to answer because the severity of symptoms in these patients did not allow placebo-controlled or double-blind clinical trials and follow-up. Such long-term controlled clinical studies remain to be done, with the hope that intratumoural chemotherapy or immunotherapy may ultimately be designed to achieve improved quality of life, greatly prolonged survival, and perhaps even remission of disseminated disease. In the meantime, we recommend that intratumoural injection of anticancer drugs such as 5-FU be an integral part of interventional bronchoscopic management for patients presenting with life-threatening cancerous airway obstruction.

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