Endoscopic treatment of lung cancer invading the airway before induction chemotherapy and surgical resection

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Abstract

Objective: Many patients with advanced lung cancer invading the airway require only palliation; however, induction chemotherapy and surgery may sometimes be considered. Preliminary endoscopic palliation may improve quality of life and functional status, allows better evaluation of tumor extension and contributes to prevent infectious complications. We reviewed our experience with preliminary laser treatment, induction chemotherapy and surgical resection in patients with lung cancer invading the airway.

Methods: Twenty-one patients with stage IIIA and IIIB lung cancer presenting with an 80% unilateral airway obstruction were treated with laser resection, induction chemotherapy and surgery. Spirometry, arterial blood gas analysis, quality of life (QLQ-C30 score) and performance status were recorded before and after laser treatment and after chemotherapy. Complications during chemotherapy, surgical morbidity and mortality, and survival were also recorded.

Results: No complications were observed after endoscopic treatment. FEV1 significantly improved from 1.4 ± 0.4 l/s to 2.2 ± 0.7 l/s, as well as FVC (from 2 ± 0.5 to 3.1 ± 0.8 l), and remained stable after chemotherapy. The QLQ-C30 score significantly improved after laser treatment (from 45 ± 4.8 to 31 ± 2.5) as well as the Karnofsky status (from 76 ± 5 to 90). One patient developed pneumonia during induction chemotherapy. Three patients were not operated on. We performed five pneumonectomies (one right tracheal sleeve pneumonectomy) and 13 lobectomies (five associated to a bronchial sleeve resection). One patient (5.5%) died after the operation. Four patients experienced minor postoperative complications. Three-year survival after the operation was 52%.

Conclusions: Preliminary endoscopic palliation of lung cancer invading the airway is feasible, improves evaluation and staging, helps to reduce the incidence of complications during induction chemotherapy without increasing surgical morbidity and mortality.

Keywords: Lung cancer; Laser treatment; Induction chemotherapy

1. Introduction

Primary surgical resection is actually considered, whenever feasible, the gold standard for lung cancer treatment; however, only 30–40% of patients survive more than 5 years and almost 95% of the whole population requires palliative treatment at a certain point of their disease history. Thirty percent of lung cancers cause partial or complete obstruction of the airway with consequent respiratory distress, bleeding and infection [1]. Many patients require palliation only; however, in selected cases, induction chemotherapy and surgery may be considered. Endoscopic management should play an important role since conventional treatment with chemotherapy/radiotherapy alone as performed in the past [2,3] yielded unsatisfactory immediate restoration of a viable airway; Nd:YAG laser, intraluminal brachitherapy and stenting allow better results in terms of patency of the airway and immediate palliation of symptoms [4]. Preliminary endoscopic laser resection contributes to improve quality of life and functional status, allows better evaluation of tumor extension and staging, and contributes to prevent infectious complications, especially when chemotherapy is to be administered.

We reviewed our experience with preliminary endoscopic laser treatment, induction chemotherapy and surgical resection in patients with lung cancer invading the airway.

2. Patients and methods

Twenty-one patients with stage IIIA and IIIB lung cancer
presenting with an 80% unilateral airway obstruction where initially treated with Nd:YAG laser resection of the endobronchial component of the tumor. Fifteen patients were males and six were females; the mean age was 59 ± 13 years (45–75 years). At presentation hemoptysis was present in ten patients (48%), cough in 11 (52%), fever and signs of infection in seven (33%), dyspnea under effort in six (29%), dyspnea at rest in three (14%) and pain in four (19%). Histology of the tumor was obtained by direct biopsy during endoscopy in all patients. Fourteen patients had squamous cell carcinoma (67%) and seven (33%) had adenocarcinoma. In 15 patients the primary tumor was located in the upper lobe, in five in the inferior lobe and in one in the middle lobe. Six patients had complete atelectasis and seven had lobar atelectasis; all the other patients had an 80% obstruction of the airway without atelectasis. After laser treatment and restoration of a viable airway induction chemotherapy and subsequent surgical resection were considered. Mediastinoscopy was performed in all patients to stage the mediastinal lymph nodes before induction chemotherapy. Before chemotherapy three patients (14%) had T₂N₂ lung cancer, 9 (43%) T₃N₂, 2 (9.5%) T₃N₀, 2 (9.5%) T₂N₁, 5 (24%) T₂N₂. A cisplatin based induction regimen was administered and patients were subsequently reassessed. Spirometry, arterial blood gasanalysis and Karnofsky performance status were recorded before and after laser treatment and after chemotherapy. Also quality of life was measured at the three different steps using the EORTC QLQ-C30 questionnaire [5]; this is a 30-item questionnaire composed of multi-item scales and single items that reflect the multidimensionality of the quality of life construct [6,7]. It incorporates five functional scales (physical, role, cognitive, emotional and social), three symptom scales (fatigue, pain, and nausea and vomiting) and a global health and quality-of-life scale. The remaining single items assess additional symptoms commonly reported by cancer patients as well as the perceived financial impact of the disease and treatment.

Complications during chemotherapy, type of surgical resection, morbidity and mortality after surgery, and survival were also recorded. The statistical analysis was performed with the Student t-test.

3. Results

No complications were observed during and after endoscopic Nd:YAG laser resection. FEV₁ significantly improved after laser treatment and remained stable after chemotherapy (1.2 ± 0.7 l pre laser, 2.2 ± 0.7 l post laser, 2.2 ± 0.9 post chemio; P < 0.001), as well as FVC (2 ± 0.5 l pre laser, 3.1 ± 0.8 l post laser, 3 ± 0.6 l post chemio; P < 0.001) and PaO₂ (69 ± 8 mmHg pre laser, 82 ± 5 mmHg post laser, 81 ± 5 mmHg post chemio; P < 0.001). Two patients requiring supplemental O₂ before laser resection were completely weaned after the endoscopic procedure. Preliminary laser resection contributed to palliate hemoptysis, dyspnea, cough and infection in all patients presenting with these symptoms. The Karnofsky status (76 ± 5, 90 ± 5 and 92 ± 5 respectively; P < 0.001) and the global QLQ-C30 score (45 ± 5, 31 ± 2.5 and 30 ± 3 respectively; P < 0.001) significantly improved after laser treatment and remained stable after chemotherapy. Also the functional scales and the symptoms scales were significantly improved after laser treatment, as well as the dyspnea and global quality of life scales (Table 1).

One patient developed pneumonia during induction chemotherapy. Three patients were not operated on since they showed a progression of the disease during induction chemotherapy with distant metastases (M₁) and N₂ disease.

At operation we performed five pneumonectomies (one tracheal sleeve resection) and 13 lobectomies (five associated to a bronchial sleeve resection); one patient (5.5%) was staged T₀N₀ (T₄N₁ pre chemio) nine (50%) T₂N₁, three (17%) T₁N₁, two (11%) T₁N₂, two (11%) T₁N₂, one (5.5%) T₃N₀. One patient (5.5%) died after right tracheal sleeve pneumonectomy; the postoperative course was complicated by a dehiscence of the tracheal anastomosis, sepsis and multiple organ failure. Four patients experienced minor postoperative complications (arrhythmia: one; wound infection: one; prolonged air leaks: two). Survival at one and three years for all patients included in the study was 71 and 46% respectively; the 1 and 3 year survival for patients receiving surgical resection was 83 and 52% (Fig. 1).

4. Discussion

Stage IIIA and IIIB lung cancer may present with symptoms of airway obstruction due to either direct infiltration or extrinsic compression; at this stage, primary surgery is often not feasible both for technical and oncological reasons; however, several studies demonstrated that preoperative chemotherapy alone or in combination with radiotherapy may improve resectability and survival [8–11]. Partial or complete airway obstruction may contribute to deteriorate the functional and clinical status of the patient and also

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<th>Table 1</th>
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<tr>
<td>Functional scales and symptoms scales of the EORTC QLQ-C30 score before and after endoscopic laser resection and after induction chemotherapy*</td>
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<table>
<thead>
<tr>
<th>Score</th>
<th>Pre laser</th>
<th>Post laser</th>
<th>Post chemio</th>
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<tr>
<td>Physical</td>
<td>7 ± 0.8</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Emotional</td>
<td>9.7 ± 1.3</td>
<td>5.8 ± 1.2</td>
<td>5.7 ± 1.1</td>
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<tr>
<td>Social</td>
<td>3.8 ± 0.7</td>
<td>2.1 ± 0.3</td>
<td>2 ± 0.2</td>
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<tr>
<td>Fatigue</td>
<td>6.3 ± 1.3</td>
<td>3.8 ± 0.8</td>
<td>3.7 ± 0.5</td>
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<tr>
<td>Pain</td>
<td>2.8 ± 0.5</td>
<td>2.2 ± 0.4</td>
<td>2.1 ± 0.2</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>2.5 ± 0.7</td>
<td>1.1 ± 0.3</td>
<td>1.1 ± 0.1</td>
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<tr>
<td>Global Q. of L</td>
<td>6.2 ± 1.1</td>
<td>10 ± 0.7</td>
<td>10.1 ± 0.7</td>
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* The P value was extremely significant for all the variables (<0.001) when comparing values measured before vs. after laser resection.
staging may be difficult due to lung atelectasis. Restoration of a viable airway is mandatory to improve functional parameters, stage the tumor and establish which patient is really unresectable or could undergo either primary surgery or be included in an induction therapy protocol. In this setting, endoscopic treatment is obviously palliative and is sometimes required in emergency [12–14]; it may be of particular value to provide time to assess the disease and allow subsequent treatment to be given electively [15–17]. Only few reports stress the importance of a combined approach [15–19]; this has been proposed for low grade malignant tracheal and bronchial tumors or for primary carcinoma of the central airway (trachea, carina, origin of the main stem bronchi) [16,17] in this setting surgery can be performed immediately after laser therapy, when the potential life threatening situation has been treated and the patient is stable. Lung cancer implies different considerations; in this setting, endobronchial management may play an important role; in fact, conventional treatment with chemo-radiotherapy was usually administered in the past [2,3] with unsatisfactory results on airway patency and also mechanical resection [20] allows less stable results [4]. Laser resection enables an immediate restoration of a viable airway with better medium term palliation, probably in relation to the cytocide effect deeply within the tumor.

In case induction chemotherapy and surgery are deemed possible after laser treatment, computed tomography of the chest should be repeated for a reliable assessment of the extension of the primary tumor and ilo-mediastinal lymph nodes. Invasive staging for N2–N3 disease (mediastinoscopy) is mandatory and also thoracoscopy may be considered to evaluate T3–T4 parameters [21]. The tumor could be downstaged by aeration of the atelectatic lung and consequent better definition of tumor size and local invasion; it could also be assessed correctly the site of origin of endobronchial invasion; the latter is usually more distal than first glance preoperative evaluation since the endobronchial component tend to migrate proximally towards the carina. All our patients were considered inoperable at other centers either for functional reasons or because extension of the primary tumor and mediastinal involvement or a combination of those situations. In many cases pneumonectomy was considered the only possible resection and it was deemed unfeasible for functional or technical reasons; after laser resection and induction chemotherapy a simple lobectomy or a bronchial sleeve resection could often be performed [22] with lower operative risk, better early and long term functional results and similar radicality from the oncological stand point.

Preliminary laser resection ameliorates the performance status and quality of life with a consequent improved tolerance of induction chemotherapy; almost all our patients could complete the protocol without major complications; their performance status, functional parameters and quality of life improved after endoscopic palliation and remained stable during chemotherapy. Pulmonary rehabilitation and an adequate medical treatment should be enclosed in the schedule.

Preliminary endoscopic laser treatment and restoration of a viable airway is feasible, improves the clinical status and allows accurate staging of patients with lung cancer without increasing postoperative morbidity and mortality. The potentiality of the combined approach should be considered to enlarge the group of patients to be treated with induction chemotherapy.

References

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Appendix A. Conference discussion

Dr K. Moghissi (Yorkshire Laser Centre, UK): I think this is a very good idea, and I have pursued that idea but without chemotherapy. I want to ask you, what contribution specifically do you think chemotherapy has made? Is that to reduce the mass of the tumor, or the nodal part, because from the mass of tumor, as you showed on the picture, it’s very difficult to say whether it was obstruction of the bronchus which had caused that collapse or really tumor, in the lung substance.

Dr Venuta: Induction chemotherapy played certainly an important role in the multimodality treatment of patients with N2 disease; in fact, most of these patients were reversed to either N1 or even N0. The T4 parameter is difficult to evaluate before induction chemotherapy. For this reason, most of the protocols evaluate this parameter only on the base of clinical signs and symptoms and CT scan evaluation. However, it is certainly difficult to confirm that a specific lung cancer can be classified as a T4. We have a number of CT parameters that can tell us if the mediastinum or the vessels are involved; we rely on these parameters but sometimes we can try to help our staging with additional invasive manoeuvres. We have performed in some patients that are not included in the present series thoracoscopic and anterior mediastinotomy or mediastinoscopy. However, even with these additional invasive manoeuvres, it can be difficult to assess mediastinal invasion and confirm it histologically. In most of the cases we have to rely on preoperative radiological evaluation and consider how the tumor diameter and relationship with other organs changes after induction chemotherapy, and compare it to what we found at thoracotomy.

Dr W. Klepetko (Vienna, Austria): I have two questions. How many sessions of laser therapy were necessary to completely open the airways in the patients? Secondly, what period of time do you take until you start chemotherapy after reopening the airway?

Dr Venuta: We performed only one laser resection in all the patients included in this study. It was obviously a temporary palliation; we generally perform a second treatment when the first one was unsatisfactory or when we intend to go more deeply within the tumor to obtain long lasting results. In these cases the bronchus needed to be open until chemotherapy was performed. Chemotherapy was started after 2–3 weeks from laser resection, just the time required to clean completely the airway from secretions. If there was any sign of infection, antibiotics were given on the base of the cultures performed at the time of endoscopic treatment.

Dr O. Levang (Trondheim, Norway): I just have one question. How did you confirm the lymph node situation prechemo and postchemo?

Dr Venuta: All the patients underwent mediastinoscopy before induction chemotherapy.

Dr Levang: And after chemo?

Dr Venuta: After induction chemotherapy the mediastinum was evaluated at thoracotomy. We performed mediastinoscopy in a very small number of patients that are not included in the present study.

Dr F. Rea (Padova, Italy): I have a question about the invasion of the carina or the tracheobronchial angle. I believe that there is no way to perform carinal resection in N2 disease because it’s a very complicated operation with a very high complication rate. In your case you performed the induction chemotherapy because there was N2 disease or just to assess exactly the extension of the airway invasion?

Dr Venuta: In that case we performed induction chemotherapy because at that time the multimodality protocol was considered for all T4 tumors. It was a huge lesion and we had the feeling that other structures beyond the trachea were involved.

Dr Y.T. Kim (Seoul, South Korea): What was the limitation of the length of the involved tracheal or bronchial segment in which you will not perform the laser treatment?

Dr Venuta: Patients reported in this series did not have a long involvement of the airway; in fact most of them received a simple lobectomy or a sleeve lobectomy; in fact only the segment of the airway that was above or below the bronchus was involved. We perform laser section also for other indications, and when only palliation is intended the airway can be cleaned also for longer segments.