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TREATMENT PLANNING FOR ENDOBRONCHIAL THERAPY

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Endobronchial therapy is only one of several considerations for managing patients with bronchogenic carcinoma, but is seldom a primary modality. Choosing any treatment rests first on establishing an accurate diagnosis, and distinguishing non-small cell from small cell lung cancer. For most patients with non-small cell cancer surgical resection remains preferable if margins are adequate, and performance status, pulmonary function, and cardiac reserve are satisfactory. All alternatives and combinations of therapy, with multidisciplinary consultations, should be available for optimal benefit to the lung cancer patient.

Therapeutic options include the following: 1) surgical resection, 2) radiation therapy, 3) systemic chemotherapy, 4) immunotherapy, 5) genetic manipulation, 6) local therapy, 7) palliation, and 8) hospice care. Local therapies, which are the focus of this presentation, include: 1) debridement, 2) laser, 3) electrocautery, 4) brachytherapy, 5) cryotherapy, and 6) photodynamic therapy.

MANAGEMENT

Simple debridement should not be overlooked as one becomes entranced with more sophisticated, and more expensive options. For a single bulky obstructive endobronchial tumor, significant symptomatic relief can often be achieved by using a large cup forceps through an open ventilating bronchoscope. Topical epinephrine may be applied initially to help constrict blood vessels and minimize bleeding. Often the lesion is sufficiently necrotic, that bleeding is minimal. Many endoscopists prefer general anesthesia for rigid bronchoscopy, but in experienced hands this can be accomplished with topical anesthesia and conscious intravenous sedation.

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LASERS

Medical use of lasers in bronchoscopy has generally employed CO_2 or Nd-YAG instrumentation. The CO_2 laser generates light energy with wavelength 10,600 nanometers. This energy is almost completely absorbed by tissue and has a shallow depth of penetration. Water in tissue is raised to 100ºC with resulting vaporization. Use of the CO_2 laser requires a combination of mirrors to focus and direct the beam, and thus is applicable around the larynx and in the proximal trachea through the open glottis. The Nd-YAG laser generates light energy at 1064 nanometers wavelength and can be transmitted through flexible quartz fibers with a rigid or fiberoptic bronchoscope. Turner and Wang reviewed many of the larger published series of laser treatment with bronchoscopy and summarized results of 20 papers. Several series also reported use in benign lesions, but overall results in 3892 patients with malignancy were described. Most papers reported symptomatic or endoscopic improvement, ranging from 53 to 100%, with the majority from 75 to 85% palliation. Complications were remarkably few, although at times serious. Contraindications to Nd-YAG therapy including extrinsic compression only, lesions greater than 4 cm. is length, obstruction and atelectasis longer than 4-6 weeks in duration, incursion into major vascular structures, invasion of the esophagus or mediastinum, and major coagulopathies.

ELECTROCAUTERY

Electrocautery had been employed in the gastrointestinal tract, and in a limited way in the respiratory tract in the 1920's and 1930's, but Hooper described the modern application in the bronchial tree in 1984. Since then interest is renewed, as a widely available and less expensive modality than Nd-YAG laser therapy. Alternating current is delivered via an insulated bronchoscope and specialized probe at high frequency, from 105 to 107 Hz. Depending on power setting (Watts) target tissue is heated, coagulated, and vaporized. Homasson in France reported results in 56 patients, with control of hemoptysis in 75%, and improvement of dyspnea in 67%. Sutedja's group in Amsterdam compared electrocautery with Nd-YAG in a series of patients with inoperable non-small cell lung cancers and symptomatic intraluminal tumors. They found the two techniques equally effective, and cautery less expensive on an individual case basis, and much less costly comparing initial capital costs. Mehta in Cleveland described experience with patients with

airways obstruction and found 89% benefit in 49 patients using endobronchial electrosurgery, and noted cost savings compared with laser therapy.

BRACHYTHERAPY

Brachytherapy refers to radiation delivered close to the target tissue, as opposed to external beam radiation where the source and target are more widely separated. Various radiation sources have been employed including radon seeds, Iodine125, Cobalt 60, and Iridium192. Iridium192 is most commonly used now, with either low dose rate (LDR) of less than 2 Gray (Gy) per hour over 24 to 48 hours, or high dose rate (HDR) of greater than 10 Gy per hour over 15 to 60 minutes at 1 to 2 week intervals, for 3 or 4 treatments. Either modality appears well tolerated with from 60 to 98 % palliative benefit in symptoms or endoscopic appearance. However, late complications can be a major concern. Schray and colleagues at the Mayo Clinic reported on 65 patients who had 93 LDR treatments, either following or concurrently with external beam therapy. Of those having follow-up bronchoscopy, 60% showed improvement. Eleven patients developed fistula and/or hemorrhage, of which seven (11 % of all patients) appeared to be treatment induced. Gollins and associates in Manchester, England reported a series of 406 patients with non-small cell cancer causing endobronchial obstructive symptoms, treated with HDR. Eighty percent of their patients were previously untreated, with the remainder having either prior or concurrent external beam therapy. Palliation was achieved in the majority, but they observed massive hemoptysis as a cause of sudden death in 32 patients (8%). Interestingly, the peak incidence of this complication was between 9 and 12 months post treatment, in contrast to peak deaths from other causes from 3 to 6 months. Macha et al. in Hemer, Germany, treated 365 patients with HDR, most of whom had prior maximal dose external beam radiation, and observed 66% palliation. However, fatal hemorrhage occurred in 21%, which they attributed to the selection of patients, rather than the sole effect of brachytherapy. The Lahey Clinic experience was reported by Lo and Beamis and colleagues in 1995. They initially used LDR in 110 patients, but changed to HDR for the next 59 patients. Most had previously received external beam radiation, and 1/4 to 1/3 had concurrent laser beam therapy. Both dose rates had similar effectiveness, and low complication rates, but they employ the HDR schedule exclusively now.

CRYOTHERAPY

Freezing can produce cellular damage which is enhanced by alternate freezing and thawing. A series of 28 patients was reported from the Mayo Clinic in1981, using a long insulated probe through a rigid bronchoscope, with half the patients showing some benefit. Maiwand in England has pioneered and promulgated the use of cryotherapy for advanced carcinoma in the trachea and main bronchi. Homasson in France has vast experience, and he and Maiwand reported experience in 1995 on 600 patients with symptomatic benefit, and minimal side effects. With development of semi-rigid and flexible probes additional access to the airway is available using the bronchofiberscope. Mathur, in Indianapolis, has used the flexible instruments to remove obstructing tumor from 18 of 20 patients, improved dyspnea and controlled hemoptysis in most of his patients. One must bear in mind that once the cryo-probe is applied and freezing occurs, it is firmly adherent until thawing takes place, whether spontaneous, or by re-heating the probe.

PHOTODYNAMIC THERAPY (PDT)

Hematoporphyrin was initially suggested to facilitate recognition of malignant tissue, by virtue of preferential uptake and fluorescence when illuminated by activating light. It was soon apparent that cellular injury could be induced by extended light exposure, mediated at least in part by production of singlet oxygen. Since the activating light does not penetrate deeply into the bronchial wall, PDT can be most effective for in situ or very superficial mucosal lesions. McCaughan reported a series of patients with early-stage squamous cell cancer who were not surgical candidates and found 69% of 16 patients disease free after 3 years. Cortese found similar benefit in 43% of 21 patients. Kato in Tokyo described a series of 95 patients with superficial central-type cancers seen over a 19 year period, and observed an 81% complete response. Moghissi and colleagues in England described experience with 100 patients with advanced inoperable lung cancer and endobronchial obstruction, with 82% having previous radiation and/or chemotherapy. Luminal obstruction generally improved and pulmonary function parameters documented benefit. The major side effect of HPD is the photo sensitization requiring avoidance of sun exposure for at least 3 to 4 weeks.

SUMMARY

Several options are available for treating malignant endobronchial lesions, in patients who are not surgical candidates, and for whom other conventional modalities have failed or are not indicated. The choices will depend on the experience and preferences of the medical and surgical team delivering care, and resources of the institution. Quality of life goals, safety, relative costs, and patient informed choice should all be considered in decision making.

REFERENCES

1. Banerjee A, and George J,Bronchoscopic photodynamic diagnosis and therapy for lung cancer. Current Opinion in Pulmonary Medicine 2000;6:378-383.
2. Cortese D. A. et al. Photodynamic therapy for early stage squamous cell carcinoma of the lung. Mayo Clin. Proc. 1997;72:595-602.
3. Coulter T D, and Mehta A C, The Heat is on: Impact of endobronchial Electrosurgery on the Need for Nd-YAG Laser Photoresection. Chest 2000;118:516-521.
4. Gollins S. W. et al. Massive haemoptysis death and other morbidity associated with high dose rate intraluminal radiotherapy for carcinoma of the bronchus. Radiotherapy and Oncology 1996; 39:105-116.
5. Hooper R. G. et al. Endobronchial electrocautery: a role in bronchogenic carcinoma. Endoscopy 1984;16:67-70.
6. Kato, H. Photodynamic therapy for lung cancer: a review of 19 year experience. J. Photochem. Photobiol B-Biol 1998;42:96-99.
7. Lo T C M. et al. Low dose rate versus high dose rate intraluminal brachytherapy for malignant endobronchial tumors. Radiotherapy and Oncology 1995;35:193-197.
8. Macha H.-N., et al. Endobronchial Radiation Therapy for Obstructing Malignancies: Ten Years' Experience with Iridium-192 High-Dose Radiation Brachytherapy Afterloading Technique in 365 Patients. Lung 1995;173:271-280.
9. Moghissi K, et al The place of bronchoscopic photodynamic therapy in advanced unresectable lung cancer: experience of 100 cases. European J of Cardio-thoracic Surg. 1999;15:1-6.
10. Sanderson, D. R., et al. Bronchoscopic Cryotherapy. Annals of Otol,Rhinol. and Laryngology 1991; 90:354-358.
11. Schray M F, et al Management of Malignant Airway Compromise with Laser and Low Dose Rate Brachytherapy. Chest 1988;93:264-269.
12. Sheski F D. and Mathur P N. Cryotherapy, Electrocautery, and Brachytherapy. Clinics in Chest Medicine 1999;20:123-138.
13. Van Boxem T, et al. Nd-YAG Laser vs Bronchoscopic Electrocautery for Palliation of Symptomatic Airway Obstruction. Chest 1999;116:1108-1112.
14. Verkindre C. et al. Morphological changes induced by extensive endobronchial electrocautery. Eur Respir J 1999;14:796-799.