THORAX

Editorials

Photodynamic therapy of lung cancer

Since 1980 photodynamic therapy (PDT) has been used both as an investigational tool and in the treatment of lung cancer around the world. PDT comprises the systemic administration of a tissue photosensitising drug such as porfimer sodium (Photofrin) and its local activation by visible light. The technique is relatively simple. It is generally performed under local anaesthesia in a similar manner to a standard fibreoptic bronchoscopy. Unlike surgery, the treatment does not result in loss of normal lung tissue so it can be performed even in patients with limited lung function such as those with coexisting chronic obstructive lung disease.

The most useful application of PDT is in patients with early stage lung cancer. Phase I–II clinical trials have shown that complete eradication of the tumour can be achieved in about 90% of these patients with disease free intervals of up to 11 years.[1–4] A phase III clinical trial completed recently in Japan showed similar results (H Kato, personal communication). In patients with superficial extension of the tumour to a central airway preoperative PDT can also convert an otherwise unresectable tumour to a resectable condition or reduce the extent of the surgery from a pneumonectomy to a sleeve lobectomy or bilobectomy.[5]

Despite the encouraging results, the effect of PDT on normal bronchial tissue has not been investigated. The most dreaded complication of PDT, although infrequent, is necrosis of the bronchial wall resulting in perforation, massive haemorrhage, or fistula formation. In this issue of *Thorax* (pp 474–480) Smith and colleagues have studied the effects of PDT on the rat trachea following intravenous administration of 5 mg/kg aluminium sulphonated phthalocyanine. With light doses of up to 80 J delivered by a 200 μm fibre onto the mucosal surface there was no apparent damage to the cartilage or reduction in the bursting pressure of the trachea, which suggests that PDT is unlikely to cause perforation or collapse of normal major airways. This finding supports the empirical observation by the group at Tokyo Medical College that light doses as high as 600 J/cm^2 and 2 mg/kg Photofrin were not associated with any serious complication.[1,2] One should be careful, however, not to extrapolate this observation to the membranous portion of the trachea or main bronchus or to the more peripheral airways where the cartilage support is absent or incomplete and the collagen content is different. Further investigation is necessary to clarify the effect of PDT in these sites. In addition, one should also be aware that excessive light treatment may cause oedema and mucous formation leading to airway obstruction, obstructive pneumonia, or respiratory failure which can be fatal. With healing of the airway injury, granulation tissue formation may also result in bronchostenosis.

Thermal ablation by the NdYAG laser is traditionally considered not to be safe for treating small bronchial cancers because of the risk of perforation. Indeed Smith and colleagues found that gross oedema occurred with tracheal obstruction leading to death in one rat following treatment with an energy of 100 J directed perpendicular to the tracheal wall. A study by Goodman and coworkers, however, showed that the injury can be confined to the mucosa and submucosa with energy not exceeding 50 J.[6] Successful vapourisation of centrally located early stage lung cancer has been reported by Koshiishi and coworkers.[7] A better understanding of the normal tissue response to PDT and to thermal ablation by studies such as the one reported here by Smith and coworkers and that of Goodman and coworkers[6] will help to clarify the relative role of these modalities.

Advances in imaging technology to detect and localise carcinoma in situ and even dysplasia[8] will probably result in a larger number of patients who will benefit from PDT as a curative treatment. Several factors have been identified that may account for an incomplete response to PDT in some patients such as extension of the tumour over two or more bronchi, invasion of the tumour beyond the cartilage layer, inability to visualise the entire lesion endoscopically, or inability to deliver sufficient light because of the anatomical location of the tumour.[1,2] The extent of the endobronchial spread of the tumour can be delineated by fluorescence bronchoscopy.[8] Light delivery to the tumour area can be improved with better fibreoptics. It is timely that studies are finally under way to define the dosimetry of PDT for early stage lung cancer to focus on curative applications of PDT, and to move away from palliating large invasive cancers which are better managed by other treatment methods such as endobronchial radiation or the NdYAG laser.

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