PDT in early central lung cancer

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Lutz Freitag

Resources are needed to use the full potential of photodynamic therapy

In this issue of Thorax, Moghissi et al report their experience of treating a selected group of patients with porphyrin-based photodynamic therapy (PDT) (see p 391). These patients had localised early bronchogenic carcinomas without lymphadenopathy or distant metastases. They could not undergo surgery because of their overall clinical condition and half of them had been operated on before. Recognised as a world class thoracic surgeon, Mr Moghissi is certainly not questioning the value of surgery. Only after alternatives such as parenchymal-sparing bronchoplasty had been definitely excluded was PDT with curative intent offered. PDT was applied with a single laser light illumination using rigid bronchoscopy under general anaesthesia. Such a treatment usually takes less than 20 minutes, and at the Yorkshire Laser Centre it is performed as a day case procedure.
This is a solid and honest report from probably Europe’s most active PDT centre. At first sight the statement that “complete response was achieved in all of the 21 patients” builds a strong case for this type of treatment. However, the problem is hidden in the second part of the statement: “for variable duration”. As always, it depends on how you digest the data. Yes, these were patients with a poor prognosis and poor performance status, and complete response was achieved in all of them with a simple short endoscopic treatment. However, seven of the 21 patients had required a second or even a third treatment within 15 months because of tumour recurrence. Two patients had died by then from unrelated diseases.

PDT is not a magic cure. The results from the Yorkshire Laser Centre are in line with earlier findings from other groups who had treated comparable patients such as Okunaka et al who reported a 100% immediate response rate in 1991. However, all groups are struggling with the relatively high rate of tumour recurrences. Imamura et al could only achieve 64% long-term eradication of early cancers in 1994. It was soon recognised that the extent of the tumour is a key factor. Curing tumours with lengths <1 cm is obviously easy, but in larger tumours the response rate falls from 98% to 43%. New imaging techniques, especially fluorescence endoscopy, may prevent undertreatment as it visualises the tumour extension along the bronchial wall. However, prognostic factors which are probably more important in determining whether a tumour recurs are its thickness, degree of submucosal invasion and possible peribronchial extension. The chance of eradicating carcinomas in situ can be as high as 100%. In early but invasive tumours (T1A) recurrences must be expected, even if the cancer respects the bronchial wall. There are pathological and physical reasons for this. The chance of lymphatic and submucosal spread increases with tumour thickness. More important, all endoscopic treatments have a limited depth of penetration. Red light with a wavelength of 630 nm (as used in the current study) cannot penetrate much deeper than 4 mm into the bronchial tissue. Only truly superficial lesions can therefore be reliably cured with such surface treatment.

However, determining the depth of invasion is difficult with standard bronchoscopic or imaging techniques including high-resolution CT scanning. The most promising method for determining the true thickness of a tumour is endobronchial ultrasonography (EBUS). The pivotal studies of EBUS by Miyazuz et al and Takahashi et al showed that, in half the apparently superficial lesions, the tumour had extended beyond the cartilaginous layer; only in those where this had not occurred was long-term cancer eradication achieved. EBUS was not available for the current study but, in the future, it should be considered state of the art and be used as a selection criterion for PDT. Longer and thicker tumours should be treated with different approaches or combined treatments such as PDT plus brachytherapy.

However, this raises the question of cost-effectiveness. The authors point out that PDT is cheaper than surgery. It would be fairer to compare PDT with other local treatments. Brachytherapy has been proved to be equally effective but it is more expensive than PDT alone. Far cheaper but comparably successful treatments for eradicating early cancer are cryotherapy or electrocautery. Eradication rates of >85% have been reported in cases of superficial cancers. Cancers that are more invasive cannot be treated with these cheaper alternatives.

There is no doubt that more early cancers will be found in the future as a result of screening programmes, especially with autofluorescence or narrow band imaging. There will be a growing need for therapeutic strategies. PDT could be one of them. However, those of us who do PDT perform it with mixed feelings. In most countries the drug alone costs more than the reimbursement we receive. We can hardly justify it to our administrators. We know that photosensitisers exist that could be activated with infrared light which reaches deeper. This would probably increase the cure rate “for longer durations” but unfortunately these sensitisers are not approved for endobronchial treatment. The industry spends incredible amounts of money on chemotherapy drugs. It would be appropriate to spend some money on the development and approval of more sophisticated PDT drugs. A multicentre study using these new weapons together with EBUS is needed. The method deserves it and, more importantly, we owe it to our patients.

REFERENCES
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