Photodynamic Therapy in Lung Cancer

As a practicing physician, Dr. Ost’s perspective on the use of photodynamic therapy (PDT) in the treatment of lung cancer is informative and helpful, particularly regarding its application in the multimodality setting. My comments represent the viewpoint of a scientist involved in the clinical use of PDT in an academic tertiary referral institution.

Integrating PDT Into the Overall Treatment Plan

This brings up an important point: In general, PDT can be used effectively even after other treatments. However, given a choice, how would PDT best be integrated into the overall treatment plan for nonsurgical patients with non–small-cell lung cancer? Would it be best to first administer radiation therapy or possibly chemotherapy followed by PDT? Or, would the reverse sequence of administration be superior?

The clinical trial conducted by Lam et al,[reference 57 in Dr. Ost’s article] which compared PDT followed by radiation therapy to radiation therapy alone, reported that radiation therapy following PDT produced superior results to radiation alone. However, Lam et al did not evaluate the reverse sequence of therapies; namely, PDT followed by radiation. In their study, radiation therapy alone often opened the airway (as determined by chest x-ray), but residual tumor was generally found during endoscopy.

From a theoretical standpoint, the use of PDT to debulk the tumor prior to radiation therapy makes sense. Unlike PDT, radiation or chemotherapy kills cells exponentially; ie, each dose destroys a given fraction of the remaining cells. Therefore, the fewer cells present at the start of radiation therapy or chemotherapy, the greater the chance for a good outcome.

PDT and the LIFE System for Detecting Early-Stage Lung Cancer

With respect to early-stage lung cancer, Dr. Ost alludes to an approach that takes advantage of the natural fluorescence (ie, without the addition of a fluorescing agent) of the normal endobronchial mucosa vs that of dysplasia or early-stage cancer to aid in the early detection of lung cancer. We have been evaluating this approach for about 2 years, selecting patients with a prior history of lung cancer. This so-called LIFE (light-induced fluorescence endoscopy) system incorporates white light and fluorescence bronchoscopy in a single unit. The data presented to the Food and Drug Administration (FDA) that led to the approval of the LIFE system[1] indicated its greatly enhanced ability to detect lung cancer at an early stage when the two methods (white light and fluorescence bronchoscopy) were used together, compared to the use of white light bronchoscopy alone.

With about 70 patients evaluated to date, we have detected seven cases, most of which were not indicated on chest x-ray or white light bronchoscopy alone. This result appears to confirm, in a preliminary way, the results of the larger study reported by Lam et al. The LIFE system, combined with PDT when appropriate, has the potential to have a major impact on the outcome of patients with lung cancer.

It is important to examine the studies that led to health agency approvals of PDT in the United States, Germany, France, and elsewhere for early-stage lung cancer. These studies, unlike most phase III clinical trials, were open-label, noncomparative investigations conducted in four institutions using similar, but not identical, methodologies. The studies were based largely on much earlier work...
carried out by Edell and Cortese, Kato et al, and Sutedja et al.[references 46, 47, and 49 in the Ost paper] The point to be emphasized is that numerous investigators in various countries using somewhat different methodologies have arrived at similar results; ie, that PDT is effective and safe for this group of lung cancer patients.

**PDT in Late-Stage Lung Cancer**

Much of the early work that examined PDT in advanced lung cancer was carried out by Balchum et al.[2] Balchum was the first to devise dosimetry for these patients, to apply an interstitial means of light delivery, and, very importantly, to emphasize the absolute need to perform toilet bronchoscopy in all patients within 2 days of PDT.

The necessity for this last measure was brought home to us in the early 1980s, when a patient treated for an obstructive tumor near the carina developed a plug of mucosa and tumor debris that ultimately blocked both mainstem airways, resulting in asphyxiation.[3] By the time the patient was in distress, the material had become too hard to be removed with the biopsy forceps. Since that time, we routinely subject all patients—both those with early- and late-stage lung cancers—to toilet bronchoscopy 2 days following PDT, or sooner, if indicated. In some cases, especially in patients with large tumors, multiple clean-out bronchoscopies over several days are required.

Thus, although PDT is generally safe and easily performed, care must be taken in the immediate few days following treatment, especially in this group of debilitated patients.

**References:**


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