Intraoperative Photodynamic Therapy: A Description of a New Adjuvant Technique for Patients with Nonmelanoma Skin Cancer

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atients undergoing Mohs surgery for the clearance of nonmelanoma skin cancer (NMSC) could benefit from a combination therapy of Mohs and intraoperative photodynamic therapy (PDT) to reduce the risk of tumor recurrence and development of new adjacent tumors. Approximately 80 patients have received this new adjuvant treatment in our practice in the past 2 years. Based on our experience, intraoperative PDT seems to be well tolerated, does not impair wound healing, and may impart a lower risk of recurrence. This new combination therapy may help to lower recurrences of basal (BCC) and squamous cell carcinomas (SCC) while also treating small neoplasms that are not clinically evident to avoid future surgeries. Although our study is still ongoing, it is our goal to determine whether this modality may serve as an effective adjunct to Mohs surgery in patients with prominent sun damage and extensive NMSC lesions. We present herein a brief description of our technique.

Methods

Candidates for this combination therapy of Mohs surgery plus intraoperative PDT are selected in two

ways. First, patients having Mohs surgery who have extensive sun damage, a history of NMSC, and multiple precancerous lesions are candidates for intraoperative PDT (Figure 1). Second, patients undergoing Mohs surgery whose frozen sections reveal actinic keratoses (AK) or in situ disease, especially in the setting of severe solar elastosis and field cancerization, are included as candidates for this new therapy. Patients are excluded if they have a photosensitivity disorder or any known contraindications to 5-aminolevulinic acid (ALA).

First, the borders of the tumor (BCC or SCC) are excised in a classic Mohs layer with 1- to 3-mm margins. Immediately after this first Mohs stage, for patients who have a history of multiple NMSC and have multiple AK in the surgical field, a topical application of 20% ALA solution is applied to the wound bed and surrounding tissue (Figure 1). Alternatively, ALA is applied after stage 1 or 2 for patients with histopathologic evidence of AK on the tissue margins and clinical AK in the surgical field. The extent of the treatment area where the ALA is applied is tailored to each patient. Typically, the ALA is applied within the lesion (open defect and particularly the epidermal–dermal

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Figure 1. During intraoperative photodynamic therapy (PDT). Patient has multiple actinic keratoses, photodamage, and squamous cell carcinoma in left temple. PDT applied to entire face.

margins that are exposed) and in a 2- to 3-cm radius outside the perimeter of the lesion (generally the subunit of the face in which the lesion is located such as the forehead or nose). For patients with very severe sun damage and multiple AK in areas far away from the primary lesion, the patient has ALA applied to the entire face. The solution is allowed to incubate for approximately 1 to 3 h. Most patients receive a 3-h incubation period for theoretically stronger treatment. Patients with time constraints or very sensitive skin receive a 1-h incubation time. In our patients, the incubation time selected is typically 3 h for treatment on the extremities. Stages continue as necessary during the incubation time. When all margins are tumor free (clear of BCC or invasive SCC, not AK), the area is then exposed to blue light (Figure 2) for 16 min and 40 s before closure. Finally, the wound is reconstructed.

The side effects of this regimen are similar to standard treatment with PDT (3–7 days of erythema), but the PDT is immediately more tolerable because the patient has residual lidocaine from the Mohs procedure (Figure 3). Also, many of the side effects related to photosensitivity after PDT are reduced



Figure 2. Patient is exposed to blue light therapy after 5-aminolevulinic acid application and incubation.

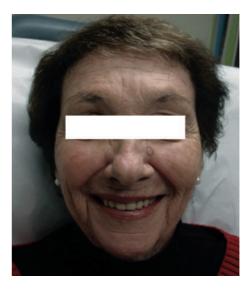


Figure 3. Two weeks after intraoperative photodynamic therapy.

because the majority of the treated area is covered with a bandage after surgery. This technique also allows for incubation of ALA between Mohs stages and therefore helps to use the downtime between stages, which benefits patients and physicians. Ideally, the patient should subsequently receive cyclic PDT two to three times annually for 1 to

2 years before reassessment. These later sessions usually encompass the entire facial field to prevent development of additional skin cancers. Intraoperative PDT can be readily incorporated into any Mohs practice with an appropriate light source for activation. Some studies show that ambient light can also activate the ALA, but this is outside the scope of this study.

Discussion

PDT is used to eradicate premalignant and earlystage cancer and reduce tumor size in end-stage cancers. It works through three key components: a photosensitizer, light, and tissue oxygen.¹

PDT has proven to be an effective modality in treating superficial NMSC. Numerous studies have shown excellent outcomes for PDT when used to treat AK, Bowen's disease, and superficial and nodular BCC. PDT also has proven efficacy in the prevention of AK, BCC, and SCC in immunosuppressed individuals.¹

Although there is extensive literature on the use of PDT, this is the first description, to our knowledge, of PDT used intraoperatively in conjunction with Mohs for the treatment of NMSC, although in 1996, Biel and colleagues reported on the use of intraoperative PDT with porfimer sodium for the treatment of extensive, recurrent head and neck SCC.² This study showed that adjuvant intraoperative PDT improved cure rates and survival in patients with these extensive malignancies.

Several authors have also written about the use of intraoperative PDT as a treatment for noncutaneous carcinomas. It has been investigated as a treatment for tumors arising in the brain, liver, trectum, and muscle. Although most of these studies were conducted in animal models, they showed success in the use of PDT to eradicate cancer cells in the wound bed and to delay and prevent tumor recurrence.

A possible concern regarding the use of intraoperative PDT is damage to vital tissue structures. A 1996 study in rats showed delayed wound healing with myocutaneous skin flaps after PDT, but the technique described in this study varies significantly from our technique in that the rats were given 5 mg/kg of photofrin with 630-nm light of different dosages delivered using an argon dye laser at light doses of 50 and 75 J/cm². A more-recent study of intraoperative PDT in animal models found that, even with a maximal treatment protocol (very high doses of photosensitizing agents and short drug-light intervals), no clinical symptoms were seen, although there were histologic effects such as small-vessel damage.8 We have no evidence of wound healing inhibition due to intraoperative PDT with ALA and blue light.

The intraoperative PDT technique described combines Mohs surgery with immediate PDT (Figure 4). Using PDT intraoperatively allows the photosensitizer to bypass the epidermal barrier for more-effective absorption, eliminating one of the main limitations of conventional PDT: the inability to deliver blue light with ALA beyond approximately 1 to 2 mm into the tumor bed. Intraoperative PDT expands the utility of PDT, a modality typically used only for superficial tumors.¹

In addition, it has been proposed that intraoperative PDT eliminates new tumor foci in areas of AK



Figure 4. Patient receiving intraoperative photodynamic therapy for a basal cell carcinoma on the nose.



Figure 5. Patient at 2-year follow-up with complete healing and no tumor recurrence.

and field cancerization (Figure 5). Furthermore, it is our hope that intraoperative PDT may destroy the residual undetectable microscopic disease near the tumor bed after surgical tumor resection to prevent local tumor recurrence. This may decrease morbidity in patients with multifocal disease and high-risk patients. Although further study is needed to determine the utility of intraoperative PDT in the role of treatment and prevention of NMSC, it seems to be a promising new modality using combination therapy that we hope may help prevent additional primary tumors and reduce recurrence rates.

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