PHOTOFRIN® (porfimer sodium) for Injection

CASE STUDY: Endobronchial Low-Grade Neuroendocrine Tumor (Bronchial Carcinoid)

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PHOTOFRIN® (porfimer sodium) IS INDICATED FOR

Palliation of patients with completely obstructing esophageal cancer, or of patients with partially obstructing esophageal cancer who, in the opinion of their physician, cannot be satisfactorily treated with Nd:YAG laser therapy.

Treatment of microinvasive endobronchial non–small cell lung cancer (NSCLC) in patients for whom surgery and radiotherapy are not indicated.

Reduction of obstruction and palliation of symptoms in patients with completely or partially obstructing endobronchial NSCLC.

PHOTOFRIN® (porfimer sodium) is indicated for the ablation of high-grade dysplasia (HGD) in Barrett's esophagus patients who do not undergo esophagectomy.

IMPORTANT SAFETY INFORMATION ABOUT PHOTOFRIN FOR INJECTION

Photodynamic therapy (PDT) with PHOTOFRIN is a two-stage process requiring administration of both drug and light in a properly equipped facility. Refer to the OPTIGUIDE™ instructions for use for complete instructions concerning the fiber optic diffuser.

PHOTOFRIN is contraindicated in patients with porphyria. PDT is contraindicated in patients with an existing tracheoesophageal or bronchoesophageal fistula and patients with tumors eroding into a major blood vessel. PDT is not suitable for emergency treatment of patients with severe acute respiratory distress caused by an obstructing endobronchial lesion because 40 to 50 hours are required between injection with PHOTOFRIN and laser light treatment. PDT is not suitable for patients with esophageal or gastric varices, or patients with esophageal ulcers >1 cm in diameter.

Tracheoesophageal or bronchoesophageal fistula can occur if esophageal tumor is eroding into trachea or bronchial tree. Gastrointestinal perforation can occur. There is a high risk of bleeding in patients with esophageal varices and for fatal massive hemoptysis with endobronchial tumors that are: large, centrally located; cavitating; extensive, extrinsic to the bronchus. After treatment of high-grade dysplasia (HGD) in Barrett's esophagus (BE), monitor endoscopic biopsy every three months, until four consecutive negative evaluations for HGD have been recorded. Photosensitivity can be expected; ocular sensitivity is possible. Allow 2-4 weeks between PDT and subsequent radiotherapy. Substernal chest pain may occur after treatment. Treatment-induced inflammation can cause airway obstruction. Administer with caution to patients with tumors in locations where treatment-induced inflammation can obstruct the main airway. Esophageal stenosis occurs frequently after treatment of HGD in BE. Patients with hepatic or renal impairment may need longer precautionary measures for photosensitivity (possibly more than 90 days). Thromboembolic events can occur following photodynamic therapy with PHOTOFRIN.

MOST COMMON ADVERSE REACTIONS reported during clinical trials are:

Esophageal Cancer: Anemia, pleural effusion, pyrexia, constipation, nausea, chest pain, pain, abdominal pain, dyspnea, photosensitivity reaction, pneumonia, vomiting, insomnia, back pain, pharyngitis.

Obstructing Endobronchial Cancer: Dyspnea, photosensitivity reaction, hemoptysis, pyrexia, cough, pneumonia.

Superficial Endobronchial Tumors: Exudate, photosensitivity reaction, bronchial obstruction, edema, bronchostenosis.

High-Grade Dysplasia in Barrett's Esophagus: Photosensitivity reaction, esophageal stenosis, vomiting, chest pain, nausea, pyrexia, constipation, dysphagia, abdominal pain, pleural effusion, dehydration.

Inform patients to report adverse reactions. All patients who receive PHOTOFRIN will be photosensitive for at least 30 days and should be warned about this and counselled to take appropriate precautions. Laser treatment should not be given if an overdose of PHOTOFRIN is administered.

FOR MORE INFORMATION ABOUT PHOTOFRIN visit www.Photofrin.com or call Concordia Laboratories Inc. at 1-866-248-2039. at 1-866-248-2039.You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see full prescribing information for PHOTOFRIN.

PATIENT HISTORY

This 83-year-old male farmer and former smoker presented with worsening paroxysmal cough and recurrent hemoptysis. His past medical history was remarkable for coronary artery disease, but negative for prior pulmonary disease.

EXAMINATION

Physical exam revealed focal wheezes over the right anterior chest, and the patient exhibited paroxysmal cough with deep inspiration. CT imaging revealed evidence of obstruction of the right mainstem bronchus, without evidence of adenopathy (Figure 1). No distal atelectasis was present, and the distal airways appeared to be patent.

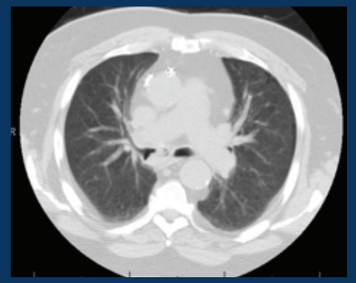

Figure 1

Figure 1 CT imaging of obstruction without adenopathy.

DIAGNOSTIC EVALUATION

The patient underwent fiberoptic bronchoscopy, which confirmed the presence of a large, smooth, friable fungating endobronchial tumor that originated from the proximal right mainstem bronchus less than 1 cm from the main carina (Figure 2).

The right mainstem bronchus was 80% occluded by a fungating, smooth, erythematous, and extremely friable endobronchial tumor emanating from the medial wall.

Advancing the bronchoscope past the tumor allowed visualization of the right upper lobe, right middle lobe, and right lower lobe, which were all patent and normal in configuration. Photographs were obtained. Minimal suction resulted in oozing from the tumor, which was treated with 3 cc of 1:20,000 epinephrine topically. Endobronchial biopsies were obtained from the tumor without complication.

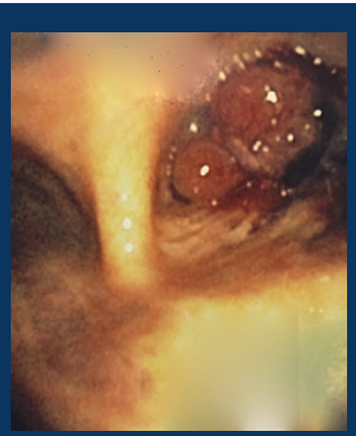

Figure 2

Figure 2 Bronchoscopy confirming endobronchial tumor.

Pathologic review of biopsies confirmed the diagnosis of low-grade neuroendocrine carcinoma (bronchial carcinoid). H & E stains revealed neoplasm composed of nested cells with neuroendocrine-like features morphologically. Immunohistochemical stains further confirmed that the tumor was a neuroendocrine carcinoma (bronchial cardinoid).

COURSE OF TREATMENT

The patient's case was reviewed at the multidisciplinary chest tumor board. Thoracic surgery members felt that carinal resection was technically feasible, but would not be tolerated by this elderly patient. The patient was unwilling to consider surgery, so photodynamic therapy (PDT) with PHOTOFRIN® (porfimer sodium) was proposed as an alternative therapeutic option. Chemoradiotherapy was proposed as an alternative if an incomplete response to PDT was observed. The option of PDT was proposed to the patient and his family, and they agreed.

The patient received 2.0 mg/kg of PHOTOFRIN IV, and sunlight precautions were initiated. Forty-eight hours later, bronchoscopy was performed under general anesthesia. Under direct guidance, a 25-mm cylindrical fiber was advanced directly into the tumor at the 6 o'clock position and light at 630 nm was administered to a total dose of 200 Joules/cm^2. The fiber was then withdrawn and replaced into the 10 o'clock position, and the procedure was repeated. An additional dosage of 200 Joules/cm^2 was administered.

Finally, the fiber was withdrawn and impaled into the tumor at the 3 o'clock position. A third dose of 200 Joules/cm^2 was administered. After withdrawal of the third laser fiber, the tumor appeared to be less vascular, and bleeding had stopped (Figure 3).

Clean-out debridement bronchoscopy was performed 48 hours later. After the induction of general anesthesia, the bronchoscope was advanced with the swivel adapter into the endotracheal tube. The right mainstem bronchus was completely obstructed with white necrotic debris, which was removed with 2.7-mm forceps, allowing visualization of the right upper lobe. Upon further tumor removal, visualization of the middle lobe and lower lobe was possible without difficulty. Large amounts of purulent secretions were present in the lower lobe, which were removed with irrigation and suction.

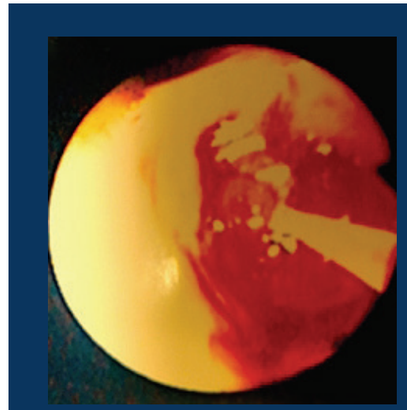

Figure 3

Figure 3 A 25-mm cylindrical fiber impaling the tumor at the 10 o'clock position.

An excellent response to PDT with PHOTOFRIN was observed at the proximal right mainstem bronchus, and patency was restored. Some friability of the deeper aspect of the tumor was encountered at the medial bronchus intermedius. It was determined that this represented a persistent viable tumor that was distal to the area of initial treatment. Since PHOTOFRIN was still present, re-treatment was initiated with a 1-cm fiber advanced into the posterior aspect of the bronchus intermedius, impaling the remaining tumor, and red light at 630 nm was administered to a light dose of 200 Joules/cm^2. The fiber was then removed.

A second clean-out debridement bronchoscopy was performed 48 hours later. The right mainstem bronchus was once again completely obstructed with necrotic debris. The debris was avascular and was mechanically removed with 2.7-mm forceps. The right upper lobe was easily exposed, revealing moderate purulent secretions, which were removed with suction. The distal bronchus intermedius was also obstructed with devascularized tumor, which was debrided. Moderate purulent secretions were present in this area, and they were also cleared with suction and irrigation.

CLINICAL OUTCOMES

PDT with PHOTOFRIN® (porfimer sodium) resulted in complete restoration of airway patency, with a visible complete response (Figure 4). Afterward, the patient reported resolution of hemoptysis and dyspnea. Repeat bronchoscopy 1 year later revealed no evidence of tumor at the main carina or right mainstem bronchus (Figure 5).

One year following therapy, the patient experienced continued resolution of hemoptysis and dyspnea. His performance status improved, as did his cough-related symptoms. PDT with PHOTOFRIN resulted in tumor necrosis and complete pathologic response that was durable and averted the need for surgery.

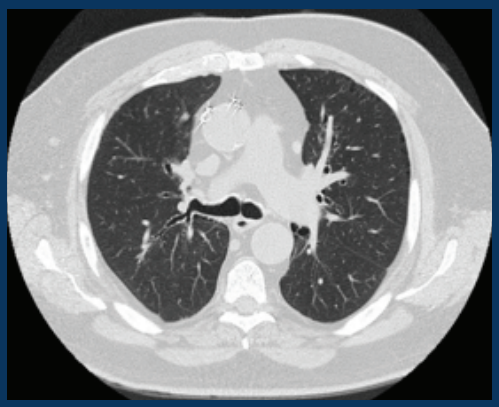

Figure 4

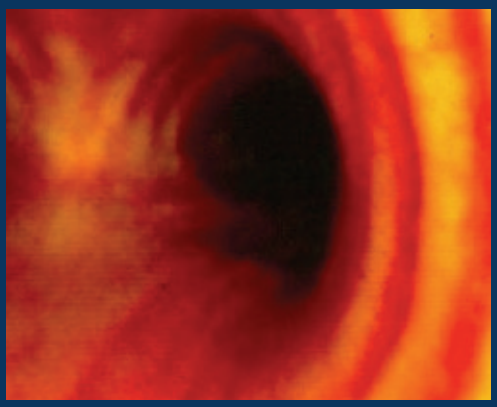

Figure 5

Figure 4 CT shows no evidence of recurrent disease at the right main bronchus, 1 year post-treatment.

Figure 5 Bronchoscopy demonstrates no evidence of recurrent disease at the right main bronchus, 1 year post-treatment.

DISCUSSION

PDT with PHOTOFRIN is an established endobronchial therapy for non–small cell lung cancer (NSCLC). Advantages of PDT include the selective photochemical mechanism of action and downstream therapeutic effects, which include immunologic mechanisms that contribute to therapeutic efficacy.[1] Bronchial carcinoid is now classified as low-grade neuroendocrine carcinoma, and represents an on-label application for PDT in the treatment of NSCLC.[2] PDT has shown effectiveness for the treatment of endobronchial neuroendocrine carcinoma, with frequent complete pathologic responses, averting the need for surgical resection of the endobronchial obstruction.[3] PDT should be considered in the management of endobronchial neuroendocrine carcinoma.

References: 1. Loewen GM, Pandey R, Bellnier D, Henderson B, Dougherty T. Endobronchial photodynamic therapy for lung cancer. *Lasers Surg Med.* 2006;38(5):364-370. **2.** Klimstra DS, Modlin IR, Coppola D, Lloyd RV, Suster S. The pathologic classification of neuroendocrine tumors: a review of nomenclature, grading, and staging systems. *Pancreas.* 2010;39(6):707-712. **3.** Downie GH, Qureshi A, Loewen G, Cuenca R, Allison R, Sibata C. Endobronchial ablation of typical carcinoid tumor with photodynamic therapy. *J Bronchol.* 2007;14(1):10-14.

The information contained in this case study has been supplied by the medical professional whose name appears here. The advice, opinion, statements, materials and other information expressed and contained in this case study are from the authors and reflect their personal experience with the specific patient. Results may vary. Pinnacle Biologics, Inc. makes no claim that similar treatment will result in a similar outcome.

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