

PHOTOFRIN® (porfimer sodium) for Injection

CASE STUDY: Roentgenologically Occult Squamous Cell Carcinomas of the Lung

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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 1-877-370-1142.

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 67-year-old male with a long-standing history of cough and dyspnea on exertion presented with hemoptysis for 4 days. The hemoptysis was non-massive, but expectoration was approximately 5 mL, 3 times per day. After resolving spontaneously, he denied any other symptoms, such as weight loss or fatigue. His past medical history included diabetes, hypertension, and Chronic Obstructive Pulmonary Disease (COPD).

EXAMINATION

Physical examination revealed a healthy-appearing male in no distress, although he had distant breath sounds bilaterally. Chest CT suggested emphysema but did not reveal any specific findings to account for the patients' hemoptysis. Pulmonary Function Tests (PFTs) confirmed a severe obstruction with GOLD Stage III COPD.

DIAGNOSTIC EVALUATION

Fiber optic bronchoscopy was performed to inspect the airway and identify the cause of the patient's hemoptysis. Results were within normal limits except for mucosal irregularity (approximately 8 mm in diameter) at the proximal end of the left lower lobe bronchus, above the origin of the superior segment (Figure 1). The mucosal irregularity was more prominent on narrow band imaging (Figure 2). Endobronchial biopsies were performed from the lesion and were consistent with squamous cell carcinoma in situ, without any evidence of involvement of deeper layers.

BRONCHOSCOPIES



Figure 1

Figure 1 Mucosal abnormality at the proximal end of left main bronchus.

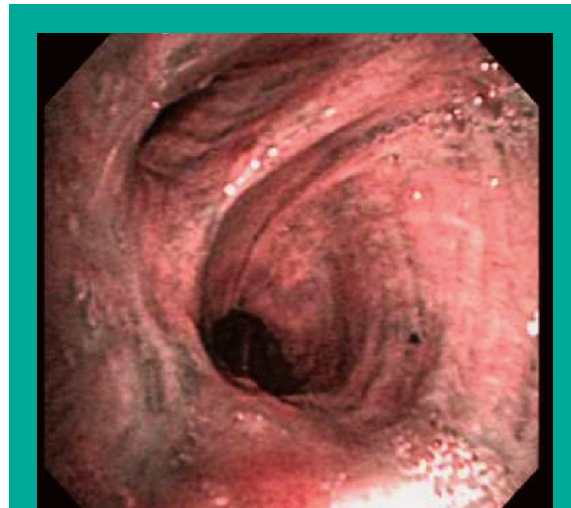


Figure 2

Figure 2 Left lower lobe lesion with narrow band imaging.

COURSE OF TREATMENT

The patient's case was reviewed at the multidisciplinary chest tumor board. Due to his poor functional capacity, surgery was not an option, so he was presented with options of photodynamic therapy (PDT) with PHOTOFRIN® (porfimer sodium) versus continued bronchoscopic surveillance. Argon plasma coagulation (APC) was also pursued as an alternative approach, however was not strongly considered due to lack of evidence for treatment of squamous cell carcinoma in situ with APC. The patient and his family chose PDT.

The patient received the standard 2 mg/kg of PHOTOFRIN® (porfimer sodium) intravenously, with sunlight precautions initiated. Subsequent bronchoscopy was performed under moderate sedation. Under direct visualization, a 25-mm cylindrical fiber was advanced adjacent to the lesion at the energy setting of 200 Joules/cm for 8 minutes and 20 seconds with a nominal wavelength of 630 nm \pm 3nm (Figure 3).

Forty-eight hours later, a second session using a similar technique was performed. A third bronchoscopy was performed revealing necrotic debris along the treatment site and suggesting a positive treatment effect (Figure 4). The debris was suctioned and debulked. All PDT sessions were performed on an outpatient basis.

BRONCHOSCOPY



Figure 3

Figure 3 Laser fiber placed adjacent to the lesion.



Figure 4

Figure 4 Necrotic debris post-PDT suggesting positive treatment response.



CLINICAL OUTCOMES

For surveillance, the patient received bronchoscopy every 6 months for 2 years with narrow band imaging. Each time, endobronchial biopsies were also performed at the treatment site, which were concluded to be negative for malignancy. Accordingly, the patient was considered cured of his squamous cell carcinoma in situ and surveillance was discontinued.

DISCUSSION

While surgical resection is an effective treatment modality for roentgenologically occult bronchogenic carcinomas, there are many patients for whom surgery and radiotherapy are not indicated. PDT with PHOTOFRIN® (porfimer sodium) is not only minimally invasive, but it is also associated with low treatment related morbidity and has a high initial complete response rate to therapy.¹⁻⁵ Therefore, in our experience, PDT may be considered a treatment modality for patients with roentgenologically occult squamous cell carcinomas of the lung that are:

- bronchoscopically visible
- have tumor lengths of ≤ 1 cm
- have no radiologic findings on computed tomography imaging

Patients undergoing PDT should be carefully monitored. Most recurrences of carcinoma in situ following PDT can be adequately treated with surgery, radiation therapy, and repeat administration of PDT.

References

1. Endo C, Miyamoto A, Sakurada A et. al. Results of long-term follow-up of photodynamic therapy for roentgenographically occult bronchogenic squamous cell carcinoma. *Chest*. 2009 Aug;136(2):369-75. 2. Furuse K, Fukuoka M, Kato H, et al. A prospective phase II study on photodynamic therapy with photofrin II for centrally located early-stage lung cancer: The Japan Lung Cancer Photodynamic Therapy Study Group. *J Clin Oncol*. 1993;11:1852-1857. 3. Edell ES, Cortese DA. Photodynamic therapy in the management of early superficial squamous cell carcinoma as an alternative to surgical resection. *Chest*. 1992;102:1319-1322. 4. Kato H, Okunaka T, Shimatani H. Photodynamic therapy for early stage bronchogenic carcinoma. *J Clin Laser Med Surg*. 1996;14:235-238. 5. Moghissi K, Dixon K, Thorpe JA, et al. Photodynamic therapy (PDT) in early central lung cancer: a treatment option for patients ineligible for surgical resection. *Thorax*. 2007;62:391-395.

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Please see accompanying Important Safety Information within sales aid and full Prescribing Information for PHOTOFRIN® (porfimer sodium).

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