Cutaneous Consequences of Photodynamic Therapy

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Photodynamic therapy (PDT) has several cutaneous complications: photosensitivity is well known, but the other complications are rarely reported. Since late 1997, we have studied the dermatologic complications of using porfimer sodium PDT to treat either Barrett esophagus with high-grade dysplasia or gastroesophageal cancer in 72 consecutive patients. Cutaneous complications of PDT included serious phototoxicity requiring oral corticosteroid treatment (22 patients; 31%), herpes zoster (HZ) requiring hospitalization and intravenous antiviral treatment (1 patient; 1%), and erythema multiforme drug reaction related to porfimer sodium (1 patient; 1%). PDT-associated dermatologic complications were common and were not related to cutaneous photosensitivity.

Photodynamic therapy (PDT) with porfimer sodium (Axcan Scandipharma, Birmingham, Alabama) has been approved for use in the United States since 1995.[1] One of the most challenging aspects of such treatment is the complication of prolonged photosensitivity.[2] Although phototoxic reactions are a known complication of PDT, few data regarding the incidence and severity of such reactions are available. Similarly, nonphototoxic cutaneous reactions are seldom reported for patients undergoing PDT.[3]

Materials and Methods

Since late 1997, at the first PDT center established in Florida, we have used PDT (with 2 mg/kg intravenous porfimer sodium) to treat 72 consecutive patients with Barrett esophagus or suspected early neoplasm. These patients underwent complete evaluation including standard- and high-frequency catheter endoscopic ultrasound (Olympus EU-M3, Olympus America, Melville, New York) and contrast-enhanced computed tomography of the chest and abdomen. Of the 16 patients referred for treatment of Barrett esophagus with high-grade dysplasia, 2 were diagnosed with T1N0M0 adenocarcinoma after endosonography. Thus, 7 patients with superficial adenocarcinoma and 14 patients with high-grade dysplastic Barrett esophagus received PDT intended to be curative. The other 51 patients, who had advanced gastroesophageal cancer, received palliative PDT.

Wolfsen[4] described the PDT administration method used. Forty-eight hours after porfimer sodium infusion, patients underwent endoscopy (Olympus GIF-100) with conscious sedation through use of meperidine and midazolam. Red light (630 nm) from a KTP laser pumped-dye module (Laserscope, San Jose, California) was delivered endoscopically using a 2.5-cm cylindrical diffuser (no balloon centering device was used). Power density was 400 mW/cm of diffuser; 150 to 300 J/cm was delivered from diffuser to target area.

Results

Porfimer sodium PDT was used to treat 21 patients with either Barrett esophagus with high-grade dysplasia or T1N0M0 adenocarcinoma and to provide palliative care for 51 patients with advanced gastroesophageal cancer. Cutaneous complications occurred in 22 patients (31%); the mean age of these patients was 72 years (range, 50–86 years); 3 of these patients were women. Most complications were phototoxic reactions involving erythema, blistering, swelling, and pain on sun-exposed skin areas (Figure). These reactions, which occurred in 7 patients with Barrett esophagus with high-grade dysplasia and in 15 cancer patients, responded to medical treatment with oral corticosteroids and more vigilant photoprotection.

Two patients had unusual reactions not previously reported.[3,5] A 74-year-old white woman with persistent mucosal adenocarcinoma developed severe herpes zoster (HZ) on the thoracic wall (T8 distribution) after chemoradiation treatment.

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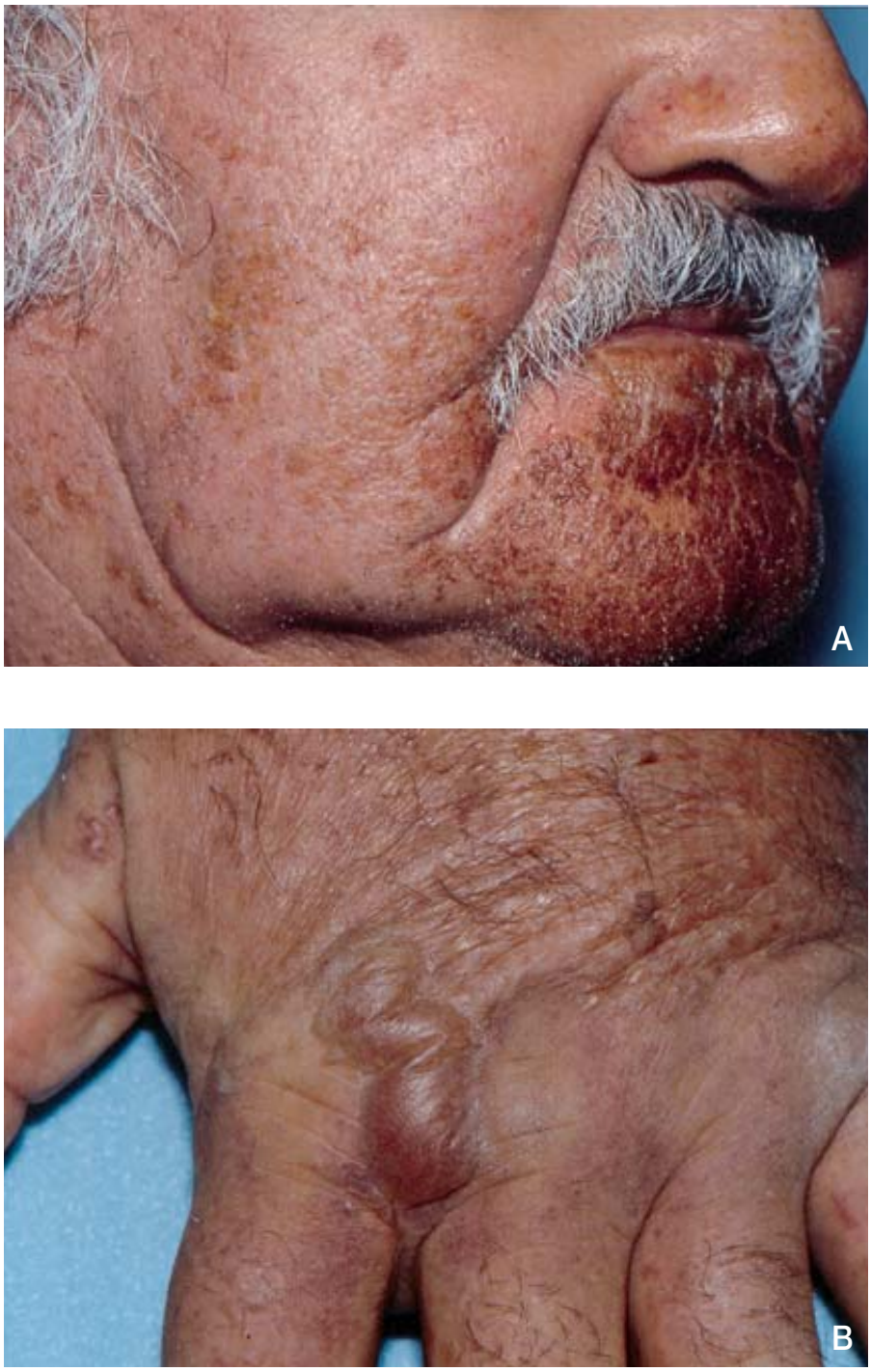

Five days after porfimer sodium photodynamic therapy, a 74-year-old white man with advanced esophageal adenocarcinoma developed cutaneous phototoxic reaction (erythema, blistering, edema) over his sun-exposed face (A) and left hand (B).

Pain control and intravenous antiviral therapy required that this patient be hospitalized. Advanced age may be associated with development of HZ; in previous patients, we did not note this association. Similarly, systemic adenocarcinoma is associated with development of HZ, but this patient's disease was limited to the esophagus, and prior radiation treatment did not involve distribution of the HZ infection. The second patient was an 85-year-old man who developed a protracted case of erythema multiforme–type drug reaction to porfimer sodium. This patient was on no other medication and had no other medical condition that could explain his reaction.

Comment

Porfimer sodium PDT is increasingly used for treatment of dysplastic Barrett esophagus and early esophageal cancer, as well as for palliative care of patients with late gastroesophageal cancer.[6,7] Although most case reports include descriptions of phototoxic reactions, few studies have specifically addressed the dermatologic consequences of PDT.[3,5] Our study was designed to determine the type, incidence, and severity of such complications among the 72 patients treated to date.

This article documents cutaneous complications occurring in one third of patients undergoing PDT with porfimer sodium. Studies in Minnesota and Florida have found similar rates of photosensitivity in patients undergoing PDT.[8] In addition, the timing of phototoxic reactions was found not to vary seasonally. Almost all our patients experienced cutaneous phototoxicity reactions such as erythema, blistering, and swelling over the face, neck, upper chest, and hands. Often, these symptoms were severe and protracted and required medical attention. Although some authors favor using acetaminophen and diphenhydramine to treat these symptoms,[3,9] we prefer oral corticosteroids.

Two other patients experienced complications previously not associated with PDT. One patient developed a severe case of thoracic wall HZ infection (shingles) producing pain, nausea, and vomiting. Pain control and intravenous antiviral therapy required hospitalization. The other patient experienced a severe prolonged case of erythema multiforme, a diffuse skin reaction characterized by erythema, swelling, pain, and pruritus. Cutaneous biopsies confirmed the diagnosis and suggested a drug reaction as the cause. After careful review and elimination of other possible offending medications, we could attribute this reaction only to porfimer sodium. This patient's condition responded to the use of topical and systemic corticosteroids.

Our study found that cutaneous complications of PDT are common and are usually related to phototoxicity. Careful patient education in photoprotection techniques, close patient follow-up, and early dermatologic referral and intervention are recommended. As PDT use proliferates in treating esophageal cancer, lung cancer, and macular degeneration, treating physicians must remain aware of the severity and spectrum of dermatologic complications.

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