Topical photodynamic therapy for primary cutaneous B-cell lymphoma: a pilot study.

consider mycobacterial infections and inquire about recent pedicures in patients with apparent lower-extremity furunculosis. Tissue cultures and sensitivity studies should be performed to guide treatment, given the widespread antibiotic resistance of mycobacteria species. Early recognition of the organisms and institution of appropriate therapy are critical. Physicians and the public need to be educated about the possibility of infections following pedicures, and physicians should inquire about pedicures when faced with nonhealing furunculosis of the lower legs. Public health measures should be explored to protect against such infections given the recent increase in popularity of the nail care industry.

REFERENCES

1. Wallace RJ, Brown BA, Griffith DE. Nosocomial outbreaks/pseudo outbreaks caused by nontuberculous mycobacteria. Annu Rev Microbiol 1998;52:453-90.
2. Palenque E. Skin disease and nontuberculous atypical mycobacteria. Int J Dermatol 2000;39:659-66.
3. Winthrop KL, Abrams M, Yakrus M, Schwartz I, Ely J, Gillies D, Vugia DJ. An outbreak of mycobacterial furunculosis associated with footbaths at a nail salon. N Engl J Med 2002;346:1366-71.
4. Sniezek PJ, Graham BS, Busch HB, Lederman ER, Lim ML, Poggemyer K, et al. Rapidly growing mycobacterial infections after pedicures. Arch Dermatol 2003;139:629-34.
5. Gira AK, Reisenauer AH, Hammock L, Nadaminte U, Macy JT, Reeves A, et al. Furunculosis due to Mycobacterium mageritense associated with footbaths at a nail salon. J Clin Microbiol 2004;42:1813-7.
6. Vugia DJ, Jang Y, Zizek C, Ely J, Winthrop KL, Desmond E, et al. Mycobacteria in nail salon whirlpool footbaths, California. Emerg Infect Dis 2005;11:616-8.
7. Rotman DA, Blauvelt A, Kerdel FA. Widespread primary cutaneous infections with Mycobacterium fortuitum. Int J Dermatol 1993;32:512-4.
8. Winthrop KL, Albridge K, South D, Albrecht P, Abrams M, Samuel MC, et al. The clinical management and outcome of nail salon-acquired Mycobacterium fortuitum skin infection. Clin Infect Dis 2004;38:38-44.
9. Wallace RJ Jr, Glassroth J, Griffith DE, Olivier KN, Cook JL, Gordin F. Diagnosis and treatment of disease caused by nontuberculous mycobacteria: American Thoracic Society Statement. Am J Respir Crit Care Med 1997;156(Suppl):S1-25.
10. Brown BA, Wallace RJ Jr, Onyi GO, De Rosas V, Wallace RJ 3rd, et al. Activities of four macrolides, including clarithromycin, against Mycobacterium fortuitum, Mycobacterium chelonae, and M. chelonae-like organisms. Antimicrob Agents Chemother 1992;36:180-4.

Topical photodynamic therapy for primary cutaneous B-cell lymphoma: A pilot study

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Photodynamic therapy (PDT) is a treatment based on the accumulation of a photosensitizer in the target cells and their selective destruction by irradiation with visible light. In the past 10 years, several patients with cutaneous T cell lymphoma have been successfully treated. The use of PDT in cutaneous B cell lymphoma has not been reported to date. We report the successful PDT treatment of 3 patients with early primary cutaneous B cell lymphoma. (J Am Acad Dermatol 2006;54:524-6.)

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Indolent primary cutaneous B-cell lymphomas (CBCL), that is, follicular center and marginal zone lymphoma according to the European Organization for Research and Treatment of Cancer[1] (EORTC) and the recent consensus World Health Organization–EORTC classification,[2] are characterized by mostly local or regional extension and very good prognosis (rare extracutaneous spread, despite relatively frequent cutaneous relapses, and 5-year survival rate >95%). Both types are highly responsive to local radiotherapy (RT).[2] Small, isolated

Abbreviations used:

ALA:	aminolevulinic acid
CBCL:	cutaneous B-cell lymphoma
CTCL:	cutaneous T-cell lymphoma
EORTC:	European Organization for Research and Treatment of Cancer
MF:	mycosis fungoides
PDT:	photodynamic therapy
RT:	radiotherapy

lesions can be surgically excised, with or without additional RT.[2] The treatment with multiple-agent chemotherapy should be restricted, at presentation, to the definitely occasional patients with disseminated lesions, to those refractory to or with multiple relapses after RT.[2] Other treatment modalities, such as intralesional cisplatin-epinephrine gel[3] and anti-CD20 monoclonal antibody,[2] has been reported as being of possible help in specific circumstances.

Photodynamic therapy (PDT) is a treatment modality based on the administration of a photosensitizing compound that accumulates in the target cells, followed by selective irradiation of the lesion with visible light. The combination of two individually nontoxic elements, drug and light, is responsible for PDT-mediated response (reviewed in Kalka, Merk, and Mukhtar[4]), presumably via apoptotic cell death as a major mechanism[5] with minimal or no necrotic changes. The most widely used photosensitizer is aminolevulinic acid (ALA), first proposed in 1978 by Dougherty et al[6] for the treatment of mycosis fungoides (MF). To date, other case series of MF patients (both in plaque and tumor stages) and 2 patients with $CD30^+$ cutaneous T-cell lymphoma (CTCL) successfully treated with PDT have been reported.[7-15]

To date, no reports are available concerning the use of systemic or local PDT in the treatment of CBCL. We report herein about the successful ALA-PDT treatment of 3 patients with early CBCL.

PATIENTS AND METHODS

Three patients with CBCL, whose data are summarized in Table I, were treated with PDT. The diagnosis was established by routine histopathology and immunophenotyping according to the WHO-EORTC classification.[2] In two patients (1 and 2; Table I), skin lesions (thin plaques) had never been treated. In patient 3, the treated lesion had relapsed 6 months after complete remission obtained by orthovolt RT.

ALA 20% (oil-in-water emulsion) was applied topically to the lesion and to adjacent skin under an occlusive and light-shielding dressing for 4 hours in patients 1 and 3. In patient 2, the methyl ester of

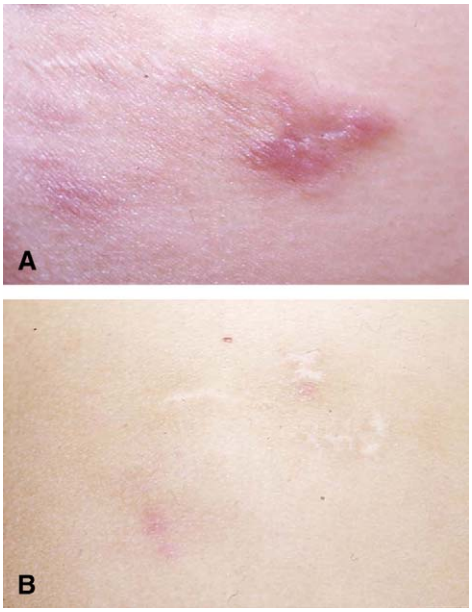

Fig 1. Patient 3. **A**, Plaque on right flank, relapsing immediately outside border of previous radiotherapy field. **B**, One week after the second (and last) PDT session.

ALA (Metvix; Photocure, Oslo, Norway and Galderma, Paris, France) was applied. The red fluorescence of porphyrins was visualized with Wood's light before treatment. Fluorescence was seen in all cases. The ALA-treated areas were then exposed to incoherent light using a light-emitting diode lamp (Aktilite PDT, model CL128; Photocure ASA, Oslo, Norway) at a wavelength of 630 nm and a light dose of 37 J/cm^2 with light intensity of 70 to 100 mW/cm^2. It illuminates areas from 80 to 180 mm at a distance from 50 to 80 mm. The patients were examined after 1 week, and, depending on the clinical results, the treatment was repeated (patient 3). Four-millimeter punch biopsy specimens were taken before treatment and after clinical remission. Clinical evaluation was performed monthly after PDT, with an 8- to 24-month follow-up.

RESULTS

The treatment was well tolerated by all patients without local anesthetics. The results are summarized in Table I. All patients underwent complete remission, defined as clinical and histologic complete remission, with a maximum of two treatment sessions at 1-week intervals. Two patients (1 and 2) were in complete remission after 1 week from the first (and only) PDT session. Patient 3 underwent complete remission after 1 week from the second PDT session (Fig 1).

DISCUSSION

PDT consists of the application of a photosensitizing agent and irradiation with noncoherent light

Table I. Summary of results in 3 patients with indolent primary cutaneous B-cell lymphoma

Patient no.	Age (y)/sex	Disease/stage	Previous tx	PDT sessions	Photosensitizer	Results	Follow-up (mo)
1	62/F	CBCL (FCL)	None	1	ALA	CR	17
2	38/F	CBCL (MZL)	None	1	Metvix	CR	8
3	56/M	CBCL (MZL)	RT	2	ALA	CR	24

ALA, Aminolevulinic acid 20%, oil-in-water emulsion; *CBCL,* cutaneous B-cell lymphoma; *CR,* complete response; *FCL,* follicle center lymphoma; *Metvix,* methyl ester of ALA; *MZL,* marginal zone lymphoma; *PDT,* photodynamic therapy; *RT,* orthovolt radiotherapy (20 Gy); *tx,* therapy.

sources. Photoactivation of photosensitizing porphyrins, which selectively accumulate in tumor cells, induces healing with minimal or no necrotic changes. PDT has been successfully used in CTCL (MF and $CD30^+$ CTCL).[7-12]

We treated 3 patients with early CBCL, with complete remission achieved in all 3 after a maximum of two PDT sessions. The successful use of ALA-PDT in indolent CBCL, to our knowledge reported herein for the first time, suggests a possible role of PDT in the treatment of localized, thin plaques as an alternative to local RT, which has to be considered the treatment of choice. Additional studies on larger series will hopefully contribute to clarify this issue.

REFERENCES

1. Willemze R, Kerl H, Sterry W, Berti E, Cerroni L, Chimenti S, et al. EORTC classification for primary cutaneous lymphomas. A proposal from the Cutaneous Lymphoma Study Group of the European Organization for Research and Treatment of Cancer (EORTC). Blood 1997;90:354-71.
2. Willemze R, Jaffe E, Burg G, Cerroni L, Berti E, Swerdlow SH, et al. WHO-EORTC classification of primary cutaneous lymphomas. Blood 2005;105:3768-85 Epub 2005 Feb 3.
3. Kempf W, Dummer R, Schmid MH, Fritz T, Wuthrich B, Burg G. Intralesional cisplatin for the treatment of cutaneous B-cell lymphoma. Arch Dermatol 1988;134:1343-5.
4. Kalka K, Merk H, Mukhtar H. Photodynamic therapy in dermatology. J Am Acad Dermatol 2000;42:389-413.
5. Agarwal ML, Clay ME, Harvey EJ, Evans HH, Antunez AR, Oleinick NL. Photodynamic therapy induces rapid cell death by apoptosis in L5178Y mouse lymphoma cells. Cancer Res 1991;51:5993-6.
6. Dougherty TJ, Kaufman JE, Goldfarb A, Weishaupt KR, Boyle D, Mittleman A. Photoradiation therapy for the treatment of malignant tumors. Cancer Res 1978;38:2628-35.
7. Forbes IJ, Cowled PA, Leong AS, Ward A, Black RB, Blade AJ, et al. Phototherapy of human tumours using haematoporphyrin derivative. Med J Aust 1980;2:489-93.
8. Wolf P, Fink-Puches R, Cerroni L, Kerl H. Photodynamic therapy for mycosis fungoides after topical photosensitization with 5-aminolevulinic acid. J Am Acad Dermatol 1994;31:678-80.
9. Boehncke W-H, Koenig K, Rueck A, Kaufmann R, Sterry W. In vitro and in vivo effects of photodynamic therapy in cutaneous T cell lymphoma. Acta Derm Venereol 1994;74:201-5.
10. Stables GI, Stringer MR, Robinson DJ. The treatment of cutaneous T cell lymphoma by topical aminolevulinic acid photodynamic therapy. Br J Dermatol 1997;137(Suppl 50):51.
11. Orenstein A, Haik J, Tamir J, Winkler E, Trau H, Malik Z, et al. Photodynamic therapy of cutaneous lymphoma using 5-aminolevulinic acid topical application. Dermatol Surg 2000;26:765-9.
12. Markham T, Sheahan K, Collins P. Topical 5-aminolevulinic acid photodynamic therapy for tumour-stage mycosis fungoides. Br J Dermatol 2001;144:1262-3.
13. Edstrom DW, Portwit A, Ros AM. Photodynamic therapy with topical 5-aminolevulinic acid for mycosis fungoides: clinical and histological response. Acta Derm Venereol 2001;81:184-8.
14. Umegaki N, Moritsugu R, Katoh S, Harada K, Nakano H, Tamai K, et al. Photodynamic therapy may be useful in debulking cutaneous lymphoma prior to radiotherapy. Clin Exp Dermatol 2004;29:42-5.
15. Coors EA, von den Driesch P. Topical photodynamic therapy for patients with therapy-resistant lesions of cutaneous T-cell lymphoma. J Am Acad Dermatol 2004;50:363-7.