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Photodynamic therapy can prevent recurrence of lymphomatoid papulosis

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1. Introduction

Lymphomatoid papulosis (LyP) is a benign lymphoproliferative disorder, which often takes indolent course. Topical application of corticosteroid and/or photochemotherapy are usually employed for the treatment. Herein we report a case of LyP whose recurrence was successfully prevented by topical photodynamic therapy (PDT).

2. Case report

A 55-year-old woman, who suffered from erythematous macules, papules, and erosions scattered on her trunk and extremities for five years, visited our hospital; papules were concentrated especially on her left thigh. She had been treated with topical potent corticosteroid. Although most of the skin lesions resolved within a few weeks, new papules appeared continuously.

The biopsy from the left thigh revealed perivascular dense infiltration of small lymphocytes admixed with large lymphocytes (Fig. 1a). The large lymphocytes were positive for CD3, CD4, and CD30. Whole body CT scan did not disclose visceral or lymph node involvement. The blood examination data were unremarkable. The diagnosis of LyP was established.

Photochemotherapy with psoralen and UVA on her whole body, once a week for three months, could not prevent the recurrence of LyP. On her left thigh new papules appeared almost every one or two weeks (Fig. 2a). Based on the successful treatment of mycosis fungoides with PDT [1], we applied one session of topical PDT on her left thigh. 20% aminolevulinic acid (ALA) was applied on her left thigh, occluded and light-protected for three hours. The ALA-treated area was exposed to visible light (wavelength: 380–810 nm) with a slide projector for 30 min at a distance of 15 cm. The PDT-treated area developed hematoma within a day, as we observed in mycosis fungoides on PDT [1]; the hematoma gradually resolved in several weeks. One year after PDT, LyP lesion did not recur in the PDT-treated area (Fig. 2b), although a few papules appeared on her extremities every month.

In our previous report of mycosis fungoides treated with PDT [1], the PDT-treated area formed hematoma. The biopsy taken five days after PDT revealed totally degenerated blood vessels with massive hemorrhage in the dermis. In order to investigate the mechanism of PDT on LyP, we took a biopsy 15 min after PDT, before developing hematoma. The biopsy taken from pigmented lesion revealed scattered perivascular infiltration of small lymphocytes. The reticular dermis and capillary endothelium were edematous (Fig. 1b). Apoptotic cells were not found with hematoxylin and eosin stain or with TUNEL technique (data not shown). Immunostain for high mobility group box 1 (HMGB1)

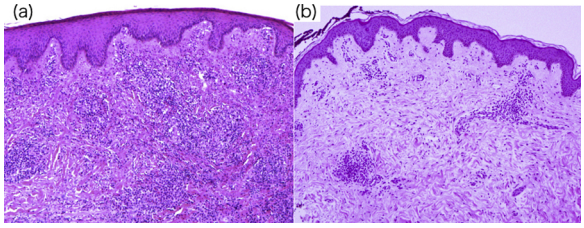

Fig. 1. Pathology at the initial diagnosis (a), and after PDT (b). (a), Dense perivascular infiltration of small and large lymphocytes. (b), Scattered perivascular infiltration of small lymphocytes. The reticular dermis and vascular endothelium were edematous. (Hematoxylin and eosin, original magnification ×4).

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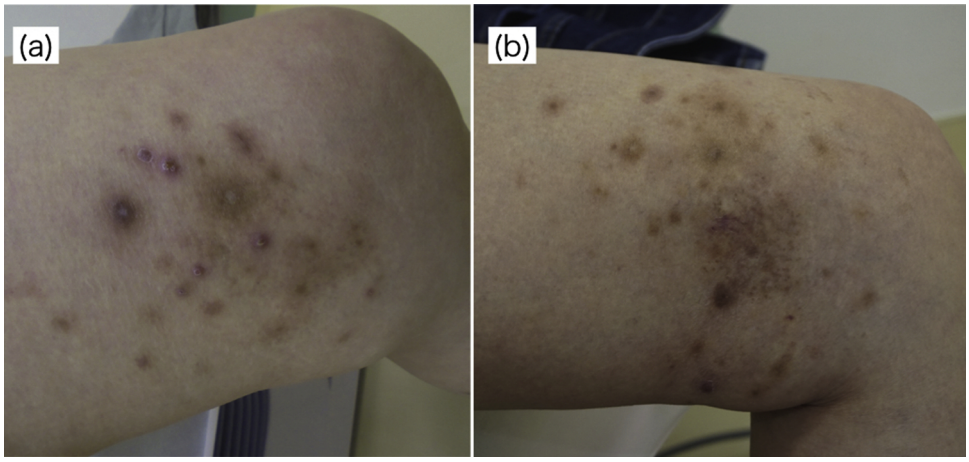

Fig. 2. Clinical pictures before (a), and one year after PDT (b). Although new LyP papules appeared continuously on her left thigh before PDT, LyP did not recur for more than one year after PDT.

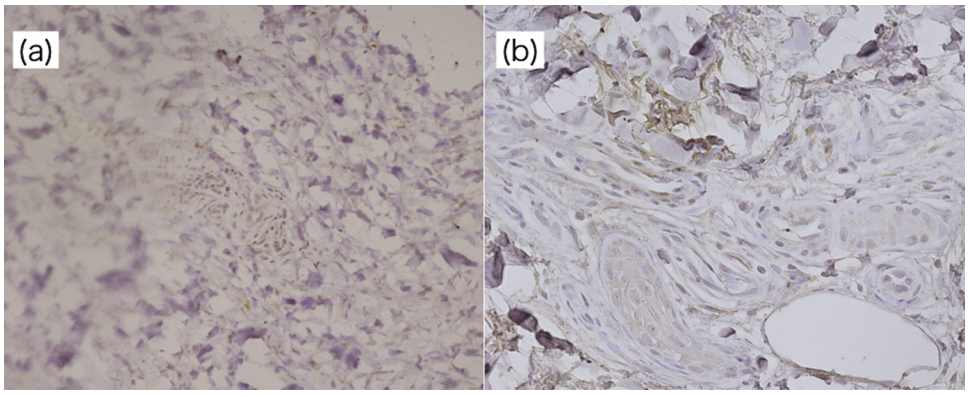

Fig. 3. HMGB1 and calreticulin immunostain after PDT.
(a), HMGB1 was positive in the cytoplasm of lymphocytes and vascular endothelium (original magnification ×20). (b), Calreticulin was positive on the surface of vascular endothelium and sweat gland apparatus (original magnification ×40). Anti-HMGB1 and anti-calreticulin mouse monoclonal antibodies were purchased from Novus Biologicals, Littleton USA.

was positive in the cytoplasm of lymphocytes and vascular endothelium (Fig. 3a). Calreticulin immunostain was positive on the surface of vascular endothelium and sweat gland apparatus (Fig. 3b).

3. Discussion

The direct effect of PDT on actinic keratosis occasionally appears immediately after the procedure, but we could not find an apparent change in LyP immediately after PDT, although the treated area formed hematoma within a day. Thus, we sought an indirect mechanism to induce cell death and vascular change, which might take several hours or days. Along with the result of immunostain for HMGB1 and calreticulin, we assumed that immunogenic cell death (ICD) might occur in the PDT-treated lesion.

HMGB1 secretion from nuclei and calreticulin binding to cell membrane are among the danger-associated molecular patterns (DAMPs), which are the features most commonly associated with ICD [2]. ICD is a self-defense mechanism against malignant neoplasms. Once neoplastic cells are damaged by chemotherapeutic agents or PDT [2], DAMPs are relocated to the surface of the cells, and released from the damaged cells. Then the DAMPs stimulate surrounding dendritic cells and Natural Killer cells, and induce apoptosis in the neoplastic cells. Thus, this process is not tumor-specific, but can induce broad degeneration in the surrounding tissue. Among the chemicals utilized in PDT, only hypericin [3] and glycoconjugated chlorin [4] were proved to induce ICD, so far. Herein we demonstrated that ALA could induce DAMPs, and speculated that ALA-PDT might work via ICD mechanism.

LyP lesions can appear in a concentrated manner, occasionally. In the previous report of LyP treated with ALA-PDT [5], the authors observed not only its efficacy on the treatment-resistant lesion, but a preventive effect, as we experienced. PDT can be a good candidate for a field therapy of LyP, as suggested in the treatment of actinic keratosis [6].

Declarations of interest

None.

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