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SHORT COMMUNICATION

Successful Treatment of Primary Cutaneous Anaplastic Large Cell Lymphoma with Intralesional Methotrexate Therapy

Ikumi Yokoi, Emiko Ishikawa, Ayako Koura, Yoichiro Hosokawa, Asuka Tamai, Kozo Nakai, Junko Moriue, Tetsuya Moriue, Kozo Yoneda and Yasuo Kubota

Department of Dermatology, Faculty of Medicine, Kagawa University, 1750-1 Ikenobe, Kita-gun Miki-cho, 761-0793 Kagawa, Japan. E-mail: youtoo@med.kagawa-u.ac.jp

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Primary cutaneous CD30$^+$ anaplastic large cell lymphoma (PCALCL) is the second most common type of cutaneous T-cell lymphoma. No specific chemotherapy regimen has been reported. We report a case of PCALCL that was successfully treated with intralesional methotrexate (MTX) solution.

CASE REPORT

A 74-year-old Japanese woman with a 6-month history of intractable ulcer on her left lower leg with acquired ichthyosis consulted our institution in April 2010. The lesions of the ulcer were gradually enlarging and a topical antibiotic ointment had no effect. In March 2010, several asymptomatic discrete, reddish-coloured nodules, ranging from 1 cm to 5 cm in diameter, appeared around the ulcer (Fig. 1a). Although the patient did not exhibit hepatosplenomegaly, general fatigue, fever, or body weight loss, lymphadenopathy in the left groin was noted. A biopsy specimen was obtained from one of these nodules. Histopathological findings revealed a diffuse, non-epidermotropic infiltrate with massive sheets of large tumour cells. The tumour cells had the characteristic morphology of anaplastic cells showing round, oval, or irregularly shaped nuclei, prominent eosinophilic nucleoli, and abundant cytoplasm (Fig. 1b). Immunohistochemically, the tumour cells were positive for CD3, CD5, CD30 (Fig. 1c), and TIA-1, but were negative for CD20, CD45RO, CD56, CD79α, granzyme B, and ALK. PCR analysis revealed a clonal rearrangement of the T-cell receptor Cβ gene. Peripheral blood parameters were all within normal limits, except for lactate dehydrogenase (LDH), 271 U/l (normal 110–220 U/l); alkaline phosphatase (ALP), 482 U/l (normal 100–340 U/l), soluble interleukin-2 receptor (sIL-2R), 2,365 U/ml (normal 135–483 U/ml), and thymidine kinase (TK), 17 U/l (normal 0–5 U/l). PET-CT examinations showed no abnormal findings in the internal organs. However, although clinical lymphadenopathy was noted in the left inguinal lesion, PET-CT did not reveal any uptake of F-fluorodeoxyglucose. She was treated with 2 cycles of oral low-dose etoposide phosphate (50 mg daily for 14 days), radiation therapy (X-irradiation 40 Gy plus electron beam radiation 10 Gy), and 3 cycles of cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP). Two weeks after the final cycle of CHOP, a few nodules still persisted on her left leg. These residual nodules began growing again within a few weeks. After a complete explanation of the risks and possible benefits, the patient agreed to be treated with intralesional MTX to treat the remaining nodules. We injected 2 ml of MTX solution (2.5 mg/ml) into the remaining nodules using a 27 gauge needle after local anesthesia with 1% lidocaine hydrochloride (Fig. 1d). The cumulative total dose of intralesional MTX was 70 mg. These residual tumours disappeared completely in several weeks and only some skin ulcers were remained. These ulcers subsequently healed with povidone-iodine sugar ointment (Fig. 1e). The patient exhibited no adverse effects. No local recurrence of PCALCL was observed at the site of the injections within 20 months of the follow-up.

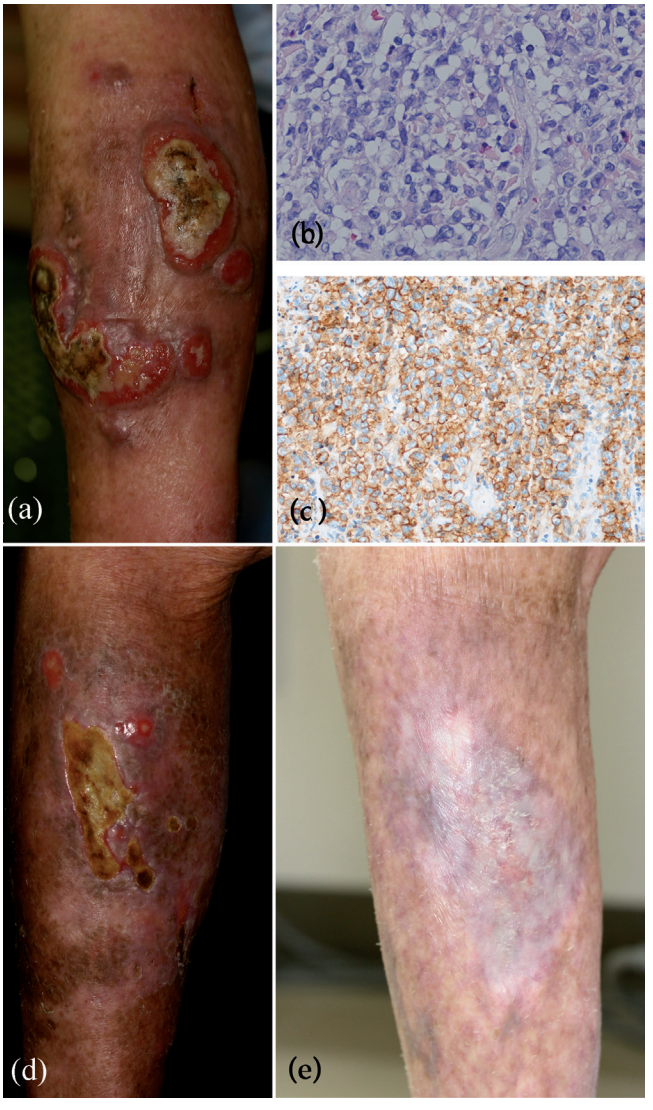

Fig. 1. Multiple tumours surrounding the ulcer on the left lower leg at the time of the patient's first presentation (a). Dense infiltration of anaplastic large cells and lymphocytes in the dermis (H&E stain ×400) (b). Neoplastic cells were strongly positive for CD30. Immunohistochemical staining ×400 (c). Multiple tumours mostly disappeared 4 weeks after starting intralesional methotrexate (MTX) (d). The injection site 6 months after intralesional MTX therapy (e).

DISCUSSION

Several therapeutic modalities exist for the treatment of PCALCL. Surgical excision and radiotherapy ap-

pear to be safe and effective treatments. However, surgical intervention may lead to marked defects with significant functional or cosmetic morbidity, depending on the size and location. In addition, old patients with comorbid conditions may be poor surgical candidates.

MTX is one of the effective treatments for $CD30^+$ lymphoproliferative disorders (LPD). The mechanism presumably relates to its inhibitory effect on DNA synthesis, anti-inflammatory effects, or both. Bekkenk et al. (1) recommended low-dose oral MTX for patients without spontaneous regression or multiple lesions. Vonderheid et al. (2) reported that compared with other treatments, MTX provided the highest response rate, exceeding 90% of all reported cases of $CD30^+$ LPD. Blume et al. (3) reported that intralesional MTX therapy injected twice to the skin lesions of PCALCL at an interval of one week was successful. Intralesional MTX has also been used in the treatment of keratoacanthoma and the specific cutaneous involvement of B-cell chronic lymphocytic leukaemia (4–6). In these circumstances, intralesional MTX may offer the advantage of being relatively noninvasive, less expensive, quickly administered, and requires fewer visits by the patient than radiotherapy or systemic chemotherapy. Although local pain at the injection site was observed as a side effect, premedication with local anesthesia was helpful in alleviating this pain. Intralesional MTX is particularly useful as a treatment in patients with PCALCL who are elderly and debilitated.

The authors declare no conflict of interest.

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