The 2008 WHO–EORTC classification for cutaneous lymphomas identifies 3 main subtypes of primary cutaneous B-cell lymphoma, including primary cutaneous diffuse large B-cell lymphoma, leg-type (PCLBCL, LT) (1), which is predominantly found in elderly people and has clinical features of erythematous or violaceous multiple tumours, frequent relapses, and a poor prognosis (1–3). Currently, CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or rituximab plus CHOP (R-CHOP) chemotherapy is considered as a standard first-line therapy for PCLBCL, LT (1, 2, 4). Radiation therapy is less effective than in other subtypes of PCLBCLs.

In case the condition of the patient does not allow application of chemotherapy, local irradiation of all visible skin lesions can be adopted. There is, however, no report or criteria for the selection of radiation treatment fields: involved field irradiation or extended field irradiation. This case report provides important insights for discussing frequent relapse and irradiation strategy in PCLBCL, LT.

CASE REPORT

A 90-year-old Japanese man presented with a 2-month history of multiple tumours on the legs. Physical examination disclosed violaceous, firm, tumours on the interior aspect of his right lower leg (Fig. 1a) and left thigh. Biopsy specimens, obtained from his left thigh, showed a dense diffuse infiltrate of large atypical lymphoid cells with cellular heteromorphism and numerous mitoses, involving the entire dermis (Fig. 1b). Tumour cells were positive for CD20 (Fig. 1c), CD79a, B-cell lymphoma 2 (Bcl-2) (Fig. 1d) and multiple myeloma oncogene 1 (MUM-1) (Fig. 1e). Clonal rearrangement of immunoglobulin heavy chain genes was detected in skin biopsy samples by Southern blot analysis. Laboratory findings on admission showed the following values: leukocytes, 4.1 \times 10^9/l; lactate dehydrogenase (LDH), 400 IU/l (normal 114–220); and soluble interleukin-2 receptor (sIL-2R), 2,638 U/ml (normal 124–466). Bone marrow biopsy showed no evidence of malignancy.

The first F-18 fluorodeoxyglucose positron emission tomography (FDG-PET) scan showed multiple regions of abnormally increased FDG uptake in his left thigh and bilateral lower legs (Fig. S1a; available from: http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1424). Based on these clinical and pathological findings, the diagnosis of PCLBCL, LT was.

Fig. 1. (a) Violaceous, firm, infiltrated tumours on the interior aspect of the patient’s right lower leg. (b) Haematoxylin and eosin staining showing lymphoid cells with irregular nuclei, prominent nucleoli, and numerous mitoses (\times 400). (c) Immunohistochemical staining for CD20 (\times 400). (d) Immunohistochemical staining for Bcl-2 (\times 400). (e) Immunohistochemical staining for multiple myeloma oncogene 1 (MUM-1) (\times 400).
confirmed. Considering his old age, complications such as cardiac disease with left ventricular asynergy and dysfunction, and multifocal involvement confined to the legs, radiation therapy without chemotherapy was selected. The patient was treated with 2 Gy X-ray irradiations within 1 radiation field at a cumulative dose of 40 Gy (the first course of irradiation). The second PET scan showed disappearance of the lesions in the lower legs. On the other hand, the left thigh lesion including the biopsy scar and left foot lesion still had high FDG uptake. Moreover, new multiple increased FDG-uptakes were detected in the right thigh (Fig. S1b). The patient was then treated with irradiation within his left foot and right thigh area (the second course of irradiation). The third PET scan revealed disappearance of uptakes in the irradiated area. In the non-irradiated area, however, the new lesions were suspected in the outside of the left thigh and left knee (Fig. S1c). We decided to irradiate the previously non-irradiated area in the lower body including new lesions as the third course. Moreover, the residual lesion after the incisional biopsy in the left thigh was treated with surgical excision. The fourth PET scan revealed the achievement of radiographic complete remission (Fig. S1d). Serum levels of sIL-2R and LDH increased to 3,400 U/ml and 786 IU/l, respectively, as disease progressed until just before the first course of irradiation (Fig. S2; available from http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1424). During radiation treatment, the levels of sIL-2R and LDH decreased to the normal range. Approximately 6 months after the radiographic complete remission, several recurrent lesions were noted on the bilateral lower legs and retroperitoneal lymph nodes with abrupt increase of sIL-2R and LDH to 9,615 U/ml and 1,846 IU/l, respectively (Fig. S2). The patient died within 2 months after the recurrence.

DISCUSSION

Systemic therapy with combination R-CHOP with or without irradiation remains the recommended treatment strategy for PCLBCL, LT. Radiation therapy alone is much less effective in PCLBCL, LT than in other types of primary cutaneous B-cell lymphomas, with higher rates of relapse (5, 6). Indeed, relapse lesions were detected in our patient approximately 6 months later from the radiological complete remission. On the other hand, Grange et al. (3) reported that 12 patients treated with R-CHOP demonstrated a complete response in 92% of cases. These previous data and our case strongly indicate that chemotherapy is more appropriate than irradiation for PCLBCL, LT regarding relapse. In other words, patients after radiation therapy need to be followed carefully because of a high risk of relapse, especially in PCLBCL, LT.

PET scan is useful in detecting suspicious lesions with a high sensitivity, monitoring disease progression, and evaluation of therapy effects (7, 8). Our patient received 3 periods of irradiation to the involved area without any adverse events and had achieved radiographic complete remission. New lesions in non-irradiated sites were detected by PET scan after the first 2 periods of involved field and additional irradiation was needed, leading to prolonged hospitalization and decreased quality of life. Our case clearly shows how serious and disturbing PCLBCL, LT is. Moreover, these therapeutic processes indicated that more extensive irradiation therapy, such as extended field irradiation or lower body irradiation, but not involved field irradiation, might have been a better choice as the initial therapy for this patient. In addition, our time-series analysis of serum sIL-2R level demonstrated the clinical utility as a marker for disease progression in PCLBCL, LT. It was previously reported that both tumour B cells and bystander cells including activated T cells have potential to produce serum sIL-2R (9).

In conclusion, this case report suggests that the combination of radiation-alone therapy and evaluation by 18-F FDG-PET is clinically useful against PCLBCL, LT aimed at achieving complete remission, especially in patients who are unsuitable for chemotherapy. More importantly, our report clearly highlights the problems related to radiation therapy, with the high frequency of relapse and the method for determination of the irradiation area.

REFERENCES