

CASE REPORT

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Treatment of Primary Cutaneous B-cell Lymphoma with Radiotherapy

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Primary cutaneous B-cell lymphomas (PCBCL) are rare and constitute 5-10% of all cutaneous lymphomas. In patients with PCBCL presenting with solitary or localized skin lesions, radiotherapy is the preferred treatment. Two patients who were treated with 4 MeV electrons, both obtained remission for 51 months. Unfortunately, at the last visit one patient relapsed on the border of the radiotherapy field and was re-treated with a generous irradiation field in 2004. Complete response was obtained again. Thus, for localized PCBCL, radiotherapy alone is an effective treatment.

Key words: cutaneous, B-cell lymphoma, radiotherapy

INTRODUCTION

APPROXIMATELY ONE-FOURTH OF NON-HODGKIN lymphomas (NHL) may arise in extranodal sites. The skin is the second most common site of extranodal involvement after the gastrointestinal tract.¹ The overall annual incidence of cutaneous lymphomas is estimated to be 0.5-1 per 100,000 people per year.² Primary cutaneous B-cell lymphomas (PCBCL) constitute approximately 5-10% of all cutaneous lymphomas in European groups vs. approximately 4.5% in U.S. groups.³

PCBCL is more common in women than in men, with a ratio 2:1; and average age is 59 years.^{1,4} The European Organization for Research and Treatment of Cancer (EORTC) divides PCBCL into three main categories (Table 1).⁵ Primary cutaneous follicular center-cell lymphomas (PCFCL) represent the most common type of PCBCL.⁶ This type generally presents with localized skin lesions, and rarely disseminates.^{6,7} For PCBCL patients presenting with solitary and localized skin lesions, radiotherapy is a preferred treatment.^{8,9} However, the optimal treatment for patients presenting with multifocal skin lesions, which is more uncommon, has not been well defined.¹⁰

For this reason, we report the treatment results of our two patients and discuss the results in light of the literature.

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PATIENTS

Patient 1

A 50-year-old man with multiple lesions of 0.3 cm in maximum thickness on the trunk was registered at our clinic in November 1999. Biopsies from these lesions were reported as PCBCL, follicular center cell (EORTC)/follicular B-cell lymphoma confined to skin (WHO) subtype. In microscopic evaluation of the lesion, a patchy infiltrate that surrounded the skin adnexa and was composed of atypical lymphoid cells was present in the dermis with focal subcutaneous involvement sparing the epidermis (Fig. 1). The infiltrate contained medium-sized atypical lymphocytes, some of which had convoluted nuclei. There were many admixed small non-neoplastic lymphocytes. Immunohistochemically, the expression of CD20 (B-cell marker) was present in the neoplastic lymphoid cells. Enzyme-linked fluorescent antibody (ELFA) test was negative for *Borrelia burgdorferi*. Systemic search for the lymphoma revealed nothing specific. A total of 36 Gy was applied with 4 MeV electrons in a 2 Gy daily fraction dose, five days a week. The radiotherapy field encompassed the lesion with 2-cm margins (Fig. 2). A bolus of 0.5 cm in thickness was used.

The patient was followed every three months with physical examination, computerized tomography (CT), and blood tests, for 51 months. A new cutaneous induration just above the lateral border of one of the previous radiotherapy fields on the back of the trunk was detected in January 2004. Biopsy of the lesion confirmed recurrence of the disease, without systemic involvement.

Table 1. EORTC classification for PCBCL

Indolent	*Follicle cell center cell lymphoma *Immunocytoma (marginal zone B-cell lymphoma)
Intermediate	*Large B-cell lymphoma of the leg
Provisional	*Intravascular large B-cell lymphoma *Plasmacytoma

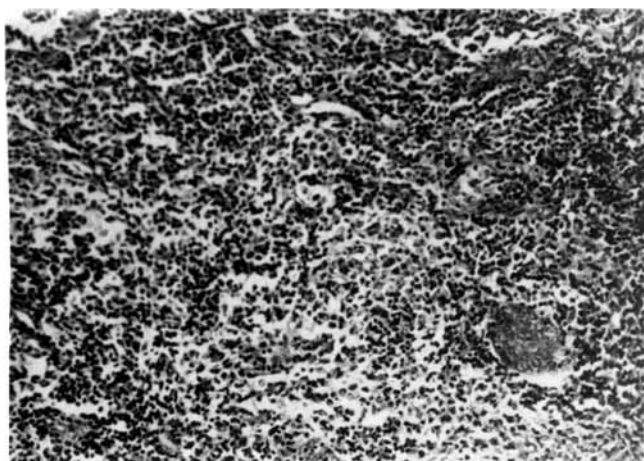


Fig. 1. Malignant lymphoma of the skin surrounded the skin adnexa (right, bottom), and was composed of medium-sized atypical lymphocytes intermingled with small non-neoplastic lymphocytes.

Radiotherapy with generous margins of approximately 3 cm as safety margins was initiated. Complete response was obtained by 40 Gy with 4 MeV electrons. He is still alive without evidence of disease.

Patient 2

A 61-year-old woman with two separate lesions (one of 0.2 cm thick on the sternum and the other of 0.1 cm thick on the post-auricular region) was registered at our clinic in March 1999. Biopsies of both lesions indicated PCBCL (Fig. 3), follicular subtype, according to the EORTC classification. Microscopically, a neoplastic infiltrate with a vague follicular pattern primarily involving the dermis was observed. Focal subcutaneous infiltration was also present. Most of the neoplastic cells consisted of small, cleaved lymphocytes. Immunohistochemically these cells showed positivity for CD20. ELFA test was also negative in this patient for *Borrelia burgdorferi*. Screening tests revealed no systemic involvement. A total of 40 Gy was applied to each involved region with 4 MeV electrons in 2 Gy daily fraction doses, to two separate fields, five days a week. As a tissue compensator, 0.3 cm-thick bolus material was

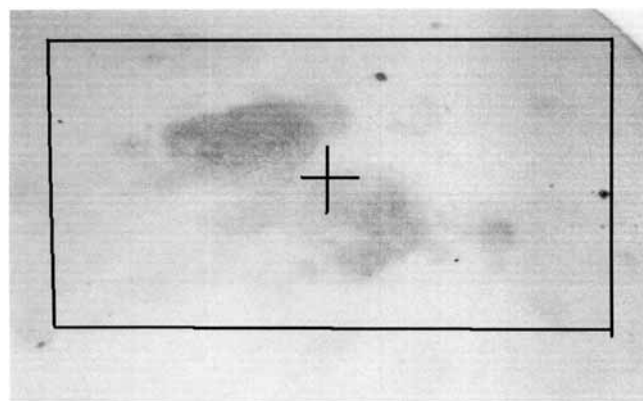


Fig. 2. Radiotherapy field of the first case.

used for both fields. The patient was followed every three months with physical examination, CT scans, and blood tests. She is still alive and without evidence of disease after 54 months.

DISCUSSION

The choice of treatment for localized forms of this disease depends on ascertainment of the local nature of the disease and on its documented favorable course.^{7,11,12} Joly *et al.*¹² studied 52 cases of cutaneous lymphomas (B- and T-cell). He reported good responses for stage I E patients. However, a 69% relapse rate made him think x-ray treatment was insufficient.¹² Esche *et al.*¹³ suggested that radiotherapy alone or after excision was sufficient treatment for small-sized I E cutaneous lymphomas (B- and T-cell) based on experience with 61 patients.

Willemze *et al.* studied 19 patients with diffuse cutaneous large cell lymphomas of the follicular center.¹⁴ Twelve of these patients were submitted to orthovoltage or megavoltage x-ray treatment. Ten showed complete remission, and two had relapse followed by death.¹⁴ In a study of 11 patients with PCBCL, orthovoltage radiotherapy led to complete response.¹⁵ Seven patients had relapse, six of whom had only skin recurrence.¹⁵ Piccinno *et al.*¹⁶ treated 31 cases of radiotherapy at a median dose of 30 Gy. The reported complete remission rate was 68%

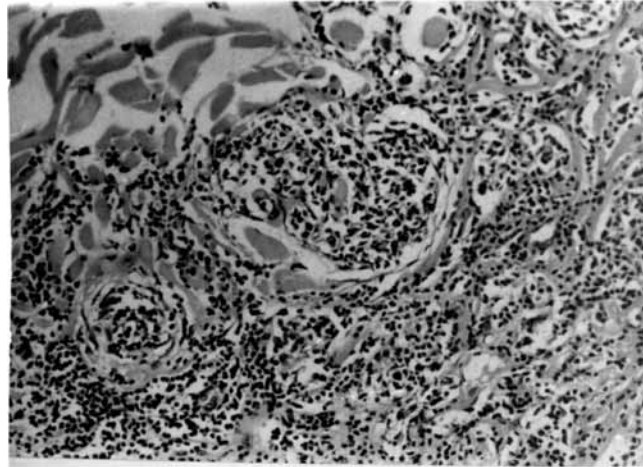


Fig. 3. Neoplastic infiltrate between the dermal collagen contained small cleaved lymphocytes with a vague follicular pattern.

Table 2. Relapse rates of several studies

Investigator	Number of patients	Cell type	Skin relapse rate (%)
Joly <i>et al.</i> ¹²	52	B- and T-cell	69
Esche <i>et al.</i> ¹³	61	B- and T-cell	20
Willemze <i>et al.</i> ¹⁴	19	B-cell	25
Pimpinelli <i>et al.</i> ¹⁵	11	B-cell	50
Piccinno <i>et al.</i> ¹⁶	31	B-cell	68
Kirova <i>et al.</i> ¹⁷	25	B-cell	16

for this study. Kirova *et al.*¹⁷ reported a 73% five-year survival rate and 92% complete response rate for 25 patients with PCBCL (of whom 19 received localized radiotherapy). Other studies also supported the role of radiotherapy for PCBCL.^{18,19} Various points of several studies are summarized in Table 2.

Smith *et al.*²⁰ treated 34 patients with radiotherapy. They reported 38% in-field or marginal recurrence with doses lower than 36 Gy.²⁰ One of the reasons for the recurrence observed in our male patient was probably the relatively low dose (36 Gy) given, like Smith *et al.* suggested.²¹ They also used 2-3 cm margin around visible disease.²¹ Eich *et al.* also expressed the importance of radiation portals with a margin of at least 2-3 cm of healthy skin and electron beams with a total dose of at least 40 Gy.²² Thus, the other reason for the recurrence of our patient might have been the tight radiation portal we used. Because of the rarity of PCBCL, no prospective randomized studies with clear-cut recommendations for treatment are available. Despite the small number of our cases, radiotherapy alone with generous margins and a total dose of 40 Gy might be safe and effective treatment for the follicular type of PCBCL.

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