A case report of aggressive course of CD30+ primary cutaneous anaplastic large cell lymphoma

Wen-Tian Lyu, MD*, Qi-Bin Song, MD, Wang Qiong, MD, Jing Liu, MD, Ren Yong, MD, Feng-Tao Yi, MD, Dong-liang Han, MD

Abstract
Introduction: CD30+ primary cutaneous anaplastic large cell lymphoma (PC-ALCL) is a rare T-cell neoplasm, and has been reported to present with an indolent behavior. The PC-ALCL with aggressive behavior has not been reported in the literature.

Patient concerns: We treated a patient with PC-ALCL that exhibited indolent behavior in the past 2 years and aggressive behavior within the last 3 months before presentation.

Diagnosis: Aggressive CD30+ primary cutaneous anaplastic large cell lymphoma.

Interventions: The radiotherapy regimen was individualized in terms of the target volume delineation and dose prescription, and the dose–response relationship was evaluated.

Outcomes: The mean distance of microscopic infiltration was 14.1 mm in depth and 14.3 mm circumferentially. The lesion completely regressed after the delivery of 40 Gy in 20 fractions over 4 weeks. The tumor did not recur over the next year.

Conclusion: An aggressive disease course is rare for indolent CD30+ PC-ALCL, which has similar histopathological characteristics as indolent PC-ALCL. The radiotherapy strategy should be individualized with curative intent.

Abbreviations: CTV = the clinical target volume, HE staining = hematoxylin–eosin staining, ISRT = involved site radiotherapy, LyP = lymphomatoid papulosis, MF = mycosis fungoides, PC-ALCL = primary CD30+ cutaneous anaplastic large cell lymphoma, PTV = planning target volume.

Keywords: aggressive behavior, CD30+ primary cutaneous anaplastic large cell lymphoma, clinical manifestation, pathology, radiotherapy

1. Introduction

CD30+ primary cutaneous anaplastic large cell lymphoma (PC-ALCL) is a rare ALK-negative T-cell neoplasm with an annual incidence of 10 per million persons.[1] Patients with this malignancy usually present with indolent solitary or localized nodules with or without ulcerative lesions. PC-ALCL with indolent behavior is radiosensitive, as indicated by its 95% complete clinical response rate and 90% 5-year disease-specific survival rate.[2,3] Most studies about radiotherapy for PC-ALCL were retrospective analyses, and these studies examined PC-ALCL with indolent behavior and assessed the relationship between clinical response and the radiation dose. Involved-site radiotherapy has been recommended as the appropriate modality for treating primary cutaneous lymphoma.[4–7] It is necessary to consider individualized radiotherapy regimens for rare tumor types. We recently received a patient who developed an ulcerative lesion on the neck skin 3 months before presentation, and this lesion arose from an indolent node over the preceding 2 years. The pathological result was consistent with normal PC-ALCL, which usually exhibits indolent behavior. However, both the lesion and the magnetic resonance imaging (MRI) revealed an aggressive nature that had not been described in the literature. The radiotherapy strategy was individualized with curative intent.

1.1. Patient information/clinical findings

A 91-year-old paralyzed male with a 20-year history of hypertension presented with a rapidly growing ulcerated lesion on the skin of his neck (40 × 30 mm²). Figure 1 presents the lesion, which was treated with radiotherapy (8 Gy in 4 fractions). This lesion began as an intact nodule that had appeared >2 years before presentation, and it began to ulcerate in the last 3 months before presentation. The rupture, which was nonpainful, had...
rapidly grown. Computed tomography (CT) revealed no extranodular lesions. The Karnofsky score was 40. The patient was not admitted to the hospital, and he returned home after each radiotherapy session.

1.2. Diagnostic assessment and therapeutic interventions

This study was approved by the ethic committee of Huanggang Center Hospital. With the informed consent of the patient’s family, we conducted the treatment and study on this patient. Core needle biopsy of the lesion was performed to examine the morphology of the neoplastic cells via hematoxylin-eosin (HE) staining. The expression of CD45, CD4, CD30, CD19, CD20, Pax-5, CD3, CD5, CD8, EMA, perforin, CD56, CD34, and ALK in the neoplastic cells was analyzed. According to HE staining, the microscopic appearance of this tumor indicated the presence of anaplastic large cells in the dermis and subcutaneous tissue. Immunohistochemistry revealed that the lesion was negative for CD20, CD8, CD3, ALK, and S-100 and positive for CD4 and Ki-67 (50%). CD30 positivity was identified in all cells. The pathological findings were consistent with a diagnosis of PC-ALCL (Fig. 2).

A 1.5 Tesla MR system was used to scan the neck. The scanning section thickness was 3 mm. T1- and T2-weighted images were used to define the gross tumor volume and CTV. T2-weighted MRI demonstrated that the invisible part of this lesion resided subcutaneously, and its extent of invasion differed among the three dimensions. The visible part of the lesion measured 14.1 mm in depth on average. The invisible part that developed from microscopic infiltration and resided subcutaneously measured 14.3 mm circumferentially (Fig. 3).

The clinical manifestation of this tumor was extremely different from the typical manifestation of PC-ALCL, which usually has indolent characteristics. The ulcerative lesion in this case was characterized as a continuous expansion of skin lesions that began as an indolent nodule appearing 2 years before presentation and progressing to an ulcerative lesion of 40 × 30 mm² during the previous 3 months. The histopathology of the lesion was completely consistent with that of CD30+ PC-ALCL. And MRI also revealed that the tumor was aggressive with subcutaneous infiltration up to 14 mm. In summary, the tumor was clinically diagnosed as aggressive CD30+ PC-ALCL, which originated from an indolent CD30+ PC-ALCL. According to the ISCL/EORTC TNM classification, the tumor was staged as T1aN0M0.[8]

Due to the early stage and high radiosensitivity of this lymphoma, a radiotherapy regimen with a radical intent was figured out. Radiation was delivered using a Varian 600CD linear accelerator. The Pinnacle treatment planning system was used in this work. The head and neck of the patient were immobilized through CT simulation. A 1-cm-thick bolus was placed between the headrest and the site at which the tumor was located. CT images (3-mm-thick sections) were sent to the treatment planning system. T2-weighted sequences plus a 2-mm margin defined the bulk of the microscopic infiltration (clinical target volume, CTV). The CTV plus a 3-mm setup error was used to determine the planning target volume (PTV). Involved-site radiotherapy was achieved using this scheme. And a 6-Mev electron ray was selected to treat the lymphoma.

The radiation dose was 40 Gy delivered in 2-Gy fractions over 4 weeks (5 fractions/week). The radiation was targeted to the PTV (Fig. 4). The lesion was nearly eradicated by the radiotherapy regimen (40 Gy in 20 fractions, Fig. 5). One week after the completion of treatment, the ulceration had healed.

![Figure 1](image1.png)

Figure 1. A progressive ulcerative lesion that was treated with radiotherapy at a dose of 8 Gy delivered in four fractions.

![Figure 2](image2.png)

Figure 2. Hematoxylin-eosin staining. (A) The dermis was densely infiltrated by atypical lymphocytes without involvement of the epidermis (original magnification, ×200). (B) The dermis was densely infiltrated by atypical lymphocytes, which mostly consisted of anaplastic large cells (original magnification, ×400). (C) CD30 staining was completely positive (original magnification, ×400).
completely. The tumor did not relapse during 1 year of follow-up before the patient’s death due to cerebral infarction.

2. Discussion

Primary cutaneous T-cell lymphoma is a type of primary cutaneous lymphoma, which includes primary cutaneous CD30+ T-cell lymphoproliferative disorders (PCTLDs), mycosis fungoides (MF), and Sézary syndrome.\[7,8\] PCTLDs have customarily been classified on the basis of their clinical presentation as lymphomatoid papulosis, PC-ALCL, and borderline cases with overlapping clinical and histopathological features.\[9\]

PC-ALCL is a rare, generally indolent cancer with a favorable prognosis including a 5-year disease-specific survival rate of 90%.\[2,3\] Spontaneous or partial tumor remission occurs in 44%
Radiotherapy image

Radiotherapy image

Radiotherapy image

Figure 5. The presentation of aggressive CD30+ primary cutaneous anaplastic large cell lymphoma and the treatment response. The tumor was treated via radiotherapy using the following protocols: 8 Gy in four fractions (A), 20 Gy in 10 fractions (B), and 34 Gy in 17 fractions (C).
the pictures taken before radiotherapy and the pictures after radiotherapy. In addition, the patient died of cerebral infarction 1 year after radiotherapy, and therefore, progression-free and overall survival could not be evaluated.

3. Conclusions
Aggressive CD30+ PC-ALCL can arise from indolent PC-ALCL. The mechanism of this transformation is unclear. The diagnosis should be based on the combination of pathology, clinical behavior and MRI. Individualized radiotherapy can be applied with curative intent.

Author contributions
Conceptualization: Wen-Tian Lyu.
Data curation: Wen-Tian Lyu, Wang Qiong, Ren Yong, Dong-liang Han.
Formal analysis: Wen-Tian Lyu, Qi-Bin Song, Ren Yong.
Methodology: Wen-Tian Lyu, Qi-Bin Song, Jing Liu.
Project administration: Wen-Tian Lyu, Qi-Bin Song, Jing Liu.
Resources: Feng-Tao Yi, Dong-liang Han.
Supervision: Wen-Tian Lyu.
Visualization: Wen-Tian Lyu.
Writing – original draft: Wen-Tian Lyu.
Writing – review & editing: Wen-Tian Lyu.

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