



Case Report

CD30+ primary cutaneous tumoral adult T-cell leukemia/lymphoma successfully treated with zidovudine and interferon

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ABSTRACT

Adult T-cell leukemia/lymphoma (ATL) is an aggressive neoplasia of mature peripheral T lymphocytes associated with human T-cell lymphotropic virus type 1 (HTLV-1). The primary cutaneous tumoral (PCT) type of adult T-cell leukemia/lymphoma presents as nodules and tumors without internal organ involvement, but with a bad prognosis. Here, we report a middle aged woman, who manifested a nodular lesion on the right leg. Histopathology showed moderately dense, lymphoid infiltrate of atypical, medium sized cells in the dermis and subcutaneous tissue. The cells were positive for CD3, CD4, CD30, and CD25, and negative for CD8, CD20, and anaplastic lymphoma kinase. The biopsy specimen showed a Ki-67 proliferation index of 90%. Serological testing for HTLV-1 was positive. The patient was diagnosed to have CD30+ PCT type ATL and was treated initially with localized radiation. The lesion regressed, however, there was a recurrence of the disease, which was treated with low dose interferon-alfa (IFN- α) and zidovudine, following which patient attained complete resolution and remained symptom free during the follow up period of 2 years. Our case highlights the usefulness of low dose IFN- α and zidovudine in the management of PCT type of CD30+ ATL.

Keywords: Cutaneous, Tumoral, Adult T-cell leukemia, Zidovudine, Interferon

INTRODUCTION

Adult T-cell leukemia/lymphoma (ATL) is an aggressive neoplasia of mature peripheral T-lymphocytes, associated with human T-cell lymphotropic virus type 1 (HTLV-1). Apart from the known four types (acute, chronic, smouldering, and lymphoma type), a fifth subtype - primary cutaneous tumoral (PCT) form has also been described recently. The PCT type of ATL presents with nodules and tumors without hypercalcemia, lymphadenopathy, or internal organ involvement.^[1]

The treatment of ATL still remains a therapeutic challenge. High dose zidovudine and interferon-alfa (IFN- α) therapy has shown a significant improvement in survival of patients with acute, chronic, and smoldering types of ATL, but no reports are available regarding its efficacy in PCT form.^[2] Here, we report a case of CD30 positive PCT type of ATL responding completely to low dose IFN- α and zidovudine.

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CASE REPORT

A 35-year-old woman presented with a painful lesion on the right leg of 1 month duration. Eight months ago she had noted an asymptomatic plaque at the same site. On the basis of clinical and histological findings, she was diagnosed to have borderline tuberculoid leprosy and was treated with dapson 100 mg once a day per orally and rifampicin 600 mg once a month per orally for 6 months. On examination, there was a tender, erythematous nodule of 8 × 3 cm on the medial aspect of the right leg [Figure 1]. Biopsy showed normal epidermis with moderately dense, atypical lymphoid infiltrate of medium sized cells in the dermis extending to subcutaneous tissue, but without epidermotropism [Figures 2a and b]. The cells were CD3 and CD4 positive and CD8 and CD20 negative. The cells showed an intense positivity for CD30 [Figure 2c]. They were anaplastic lymphoma kinase (ALK) negative. Ki-67 proliferation index was 90%. A diagnosis of anaplastic large cell lymphoma was made. However, the presence of



Figure 1: Erythematous nodule on the right leg in a patient with CD30+ primary cutaneous tumoral adult T-cell leukemia/lymphoma.

medium sized cells and high proliferative index prompted us to investigate further and the serological testing was positive for HTLV-1. Repeat immunohistochemical analysis revealed an intense CD25 positivity [Figure 2d]. Peripheral smear and serum levels of calcium, urea, creatinine, albumin and lactate dehydrogenase were within normal limits. Bone marrow trephine biopsy showed no infiltration by malignant cells. Computed tomography of thorax, abdomen and pelvis was normal. X-ray skull did not reveal any lytic lesions. On the basis of above findings, we made a diagnosis of CD30+ PCT type ATL. The nodule regressed completely following 8 Gy single fraction radiotherapy [Figure 3]. Four months later, the patient noted a painful nodule of size 3 x 3 cm on the posterior aspect of right thigh on an erythematous background [Figure 4a]. The skin biopsy and immunohistochemistry again revealed features suggestive of CD30+ PCT type ATL. Bone marrow trephine biopsy was normal. The patient was started on methotrexate 30 mg per orally once a week for 4 months. Since the nodule did not show any tendency for resolution, methotrexate was stopped. The patient was started on zidovudine 100 mg three time a day per orally and IFN- α -2b subcutaneously at a dose of 3 million units/day. Since she developed fever and myalgia after 7 days of treatment, IFN- α was reduced to once a week dose and zidovudine was continued at the same dose for 4 months. The nodule subsided completely after 1 month of treatment and showed no recurrence during the 2 year follow-up [Figure 4b].

DISCUSSION

ATL is a distinct neoplasia of peripheral T-lymphocytes caused by HTLV-1. ATL is classified into five types: Smoldering, chronic, PCT, lymphoma, and acute depending on the natural history, clinical characteristics, and prognosis. PCT type ATL differs from the non-leukemic smoldering type (<5% atypical cells) by the presence of nodules or tumors on the skin with a worse prognosis. The non-leukemic

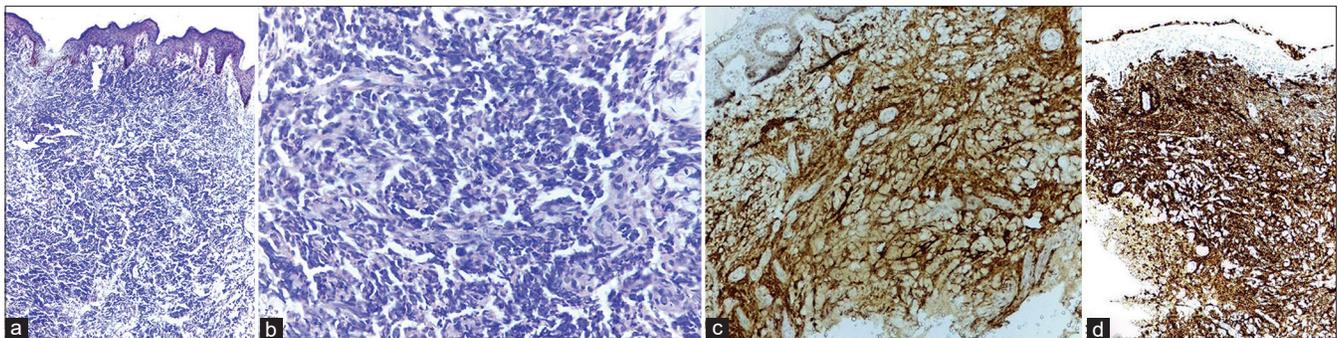


Figure 2 (a): Moderately dense infiltrate of medium sized atypical lymphoid cells in the dermis extending to the subcutaneous tissue (H and E, $\times 40$); (b): diffuse infiltrate of medium sized atypical lymphoid cells with scant cytoplasm and irregular nuclear borders (H and E, $\times 100$); (c): cells strongly positive for CD30 (Diaminobenzidine, $\times 400$); (d): cells strongly positive for CD25 (Diaminobenzidine, $\times 400$).



Figure 3: Regression of nodule after localized radiotherapy.



Figure 4 (a): Nodule on the posterior aspect of right thigh in a patient with CD30+ primary cutaneous tumoral adult T-cell leukemia/lymphoma; (b): Nodule subsided completely after 1 month of treatment with zidovudine and IFN- α .

smoldering form without pulmonary involvement and PCT are considered as primary cutaneous ATL.^[3]

ATL cases that express CD30 positivity in more than 30% of cells are classified as CD30 positive ATL. CD30 expression has been predominantly reported in the acute type representing advanced stage of ATL.^[4] Kaku *et al.* had reported CD30+ ATL manifesting as cutaneous nodules with spontaneous regression and recurrence.^[5] However, our patient showed no tendency for spontaneous regression.

Radiotherapy is a skin-directed treatment, best utilized for patients with mainly cutaneous lesions in ATL.^[6]

A worldwide meta-analysis has shown that treatment of ATL with zidovudine and IFN- α recorded a 100% overall survival at a median follow-up time of 5 years in chronic and smoldering types ATL. In these studies, high doses of IFN- α

(6–9 million units) and zidovudine (800–1000 mg in daily divided doses) have been recommended.^[7]

Even though, the acute, chronic, smoldering, and lymphoma types of ATL have been reported from India, there is a rarity of reports on PCT from the country.^[8]

Our patient received a diagnosis of borderline tuberculoid leprosy before the detection of PCT type of ATL. Cutaneous T-cell lymphoma may clinically present with features highly suggestive of leprosy including peripheral nerve thickening.^[9] The tuberculoid spectrum of leprosy might share some common histopathological features with T-cell lymphoma.^[10] However, we could not procure and reassess the initial histopathology slide of our patient on which a diagnosis of leprosy was made, since the initial evaluation was carried out in another center. Hence we are unable to comment on whether ATL was misdiagnosed as leprosy or ATL developed subsequent to leprosy in our case.

The complete response of PCT ATL to low dose IFN- α and zidovudine, to the best of our knowledge, has not been reported in the literature.

CONCLUSION

Low dose IFN- α and zidovudine may be an effective therapeutic option in the management of PCT form of ATL.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

Dr. Anza Khader and Dr. Kidangazhiathmana Ajithkumar are on the editorial board of the Journal.

REFERENCES

1. Oliveira PD, Farre L, Bittencourt AL. Adult T-cell leukemia/lymphoma. *Rev Assoc Med Bras* (1992) 2016;62:691-700.
2. Bazarbachi A, Plumelle Y, Ramos CJ, Tortevoe P, Otrrock Z, Taylor G, *et al.* Meta-analysis on the use of zidovudine and interferon-alfa in adult T-cell leukemia/lymphoma showing improved survival in the leukemic subtypes. *J Clin Oncol* 2010;28:4177-83.
3. Bittencourt AL, Barbosa HS, Vieira MD, Farré L. Adult T-cell leukemia/lymphoma (ATL) presenting in the skin: Clinical, histological and immunohistochemical features of 52 cases. *Acta Oncol* 2009;48:598-604.

4. Higuchi M, Matsuda T, Mori N, Yamada Y, Horie R, Watanabe T, *et al.* Elevated expression of CD30 in adult T-cell leukemia cell lines: Possible role in constitutive NF-kappaB activation. *Retrovirology* 2005;2:29.
5. Kaku Y, Koga M, Imafuku S, Nakayama J, Koga K, Sakata N, *et al.* A case of CD30-positive adult T-cell leukemia/lymphoma presenting spontaneous regression and recurrence of skin lesions. *Nishi Nihon Hifuka* 2014;76:210-3.
6. Maemoto H, Ariga T, Nakachi S, Toita T, Hashimoto S, Heianna J, *et al.* Appropriate radiation dose for symptomatic relief and local control in patients with adult T cell leukemia/lymphoma. *J Radiat Res* 2019;60:98-108.
7. Bazarbachi A, Panelatti G, Ramos JC, Tortevoeye P, Otrrock Z, Taylor G, *et al.* A worldwide meta-analysis on the use of zidovudine and interferon-alpha for the treatment of adult t-cell leukemia/lymphoma. *Blood* 2007;110:2049.
8. Khader A, Shaan M, Balakrishnan S, Ambooken B, Muhammed K, Rajan U. Multifaceted adult T-cell leukemia/lymphoma in India: A case series. *Indian J Dermatol* 2015;60:103.
9. Khader A, Vineetha M, George M, Manakkad SP, Balakrishnan S, Rajan U. Neurolymphomatosis in primary cutaneous CD4+ pleomorphic small/medium-sized T-cell lymphoma mimicking Hansen's disease. *Indian J Dermatol* 2017;62:315-7.
10. Shukla A, Dabadghao SS, Gupta S, Jain P. Skin manifestation of angioimmunoblastic T-cell lymphoma mimicking Hansen's disease on histology. *Int J Res Dermatol* 2020;6:570-2.

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