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DIFFUSE BONE DISEASE AS PRIMARY CLINICAL MANIFESTATION IN PATIENTS WITH ADULT T-CELL LEUKEMIA/LYMPHOMA

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INTRODUCTION

ATLL, an aggressive mature T-cell leukemia/lymphoma caused by HTLV-1, affects an estimated 10 to 20 million globally, posing a significant public health concern, especially in endemic regions like South and Central America. Since Shimoyama's 1991 classification, efforts have focused on refining clinical subclassifications to encompass diverse presentations observed across ethnicities and endemic regions worldwide.

AIM

To describe a case series of patients from endemic areas demonstrating a novel presentation with primary bone involvement.

METHOD

We conducted a retrospective analysis of ATLL patients with bone involvement diagnosed between January 2010 and December 2023 at the University of Miami, USA, and Arzobispo Loayza Hospital, Peru.

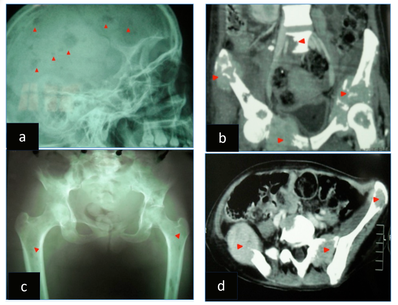
We described sociodemographic and clinical-pathologic characteristics. Treatment response adhered to Tsukasaki et al. (JCO 2009) criteria, and survival curves were estimated using the Kaplan-Meier method, with statistical significance assessed via the Log rank test.

RESULTS

A total of 12 patients with ATLL manifesting as either extranodal primary-bone disease (n=9), or bone-only disease upon relapse in patients with acute (n=2) and lymphomatous ATLL (n=1).

In regards to the extranodal primary-bone disease manifestation, 44% of patients were younger than 50-years-old (range 31-48-years-old).

Most patients (89%) did not have clinical lymphadenopathy or bone marrow involvement (67%).



56% had diffuse bone disease and 44% localized bone disease but that progressed to diffuse bone disease upon relapse.

High calcium and LDH levels were found in 25% and 38% of patients, respectively.

Three patients had HIV co-infection.

Outcomes

The median overall survival time and overall response rate to first- or second-line therapy were 16.8 months and 67% (complete response=22%), respectively.

All patients ultimately died from disease progression.

Patient	Bone disease / Marrow involvement	Presence of LAD	Histologic diagnosis / Immunophenotype*	LDH x ULN	High Ca^{+}	Treatment	Outcome / Status	PFS / OS (months)
Case 1	Diffuse bone lesions with knee tumor / No	No	PTCL, plasmocytoid variant / CD2+ CD3+ CD4+ CD5-CD25+ CD30-	1	No	AZT / IFN with PD, followed by CHOP with PR.	Progression / Deceased	14 / 16.8
Case 2	Diffuse bone lesions / Yes	No	PTCL / CD2+ CD3+ CD4+ CD5+ CD7+ CD8- CD25+ CD38+ CD30-	1.7	Yes	AZT / IFN with PD, followed by EPOCH with SD.	Progression / Deceased	3.2 / 5.3
Case 3	Chest wall and LS lesions / No	Yes	PTCL, plasmocytoid variant / CD3+ CD30+	2.8	No	EPOCH with PR followed by AZT-IFN maintenance, then PD in chest wall. Received radiation but continued progression. Received multiple lines of therapies with some achieving SD.	Progression in chest wall / Deceased	5.1 (EPOCH) / 45
Case 4	Initially localized knee tumor, then progressed to diffuse bone lesions / No	No	PTCL, plasmocytoid variant / CD2+ CD3+ CD4+ CD5+ CD25+ CD38+ CD7-CD8- CD30-	1	No	EPOCH with PR.	Progression / Deceased	14.8 / 15
Case 5	Initially localized maxillary tumor, then progressed to diffuse bone lesions / No	No	PTCL, NOS / CD2+ CD3+ CD4+ CD5- CD7- CD8- CD25+	1	No	CHOP x 4 cycles, followed by AZT / IFN maintenance with PR. Patient refused further chemotherapy. Developed diffuse bone lesions, received CHOP x 4 cycles with PR.	Progression / Deceased	13.2 (1st PR), 9.4 (2nd PR) / 31.6
Case 6	Erosive elbow lesion / No	No	PTCL, mixed cell type / CD3+ CD5+	1	No	EPOCH followed by radiation with CR.	Progression / Deceased	14 /28.3
Case 7	Diffuse bone lesions / No	No	PTCL / CD3+ CD4+	1.9	Yes	VECP followed by IFN maintenance with SD.	Progression / Deceased	8 / 10.2
Case 8	Diffuse bone lesions / Yes	No	Mature T-cell lymphoma / CD3+ CD8+	1	No	CHOEP with PD, then modified LSG-15 Japanese regimen[a] with SD.	Progression / Deceased	2.5 (LSG-15) / 28.4
Case 9	Skin and diffuse bone lesions / Yes	No	PTCL / CD3+ CD4+	Unk	Unk	EPOCH plus bortezomib and raltegravir with CR.	Progression / Deceased	6 / 9.3

Patient	Bone disease / Marrow involvement	Presence of LAD	Histologic diagnosis / Immunophenotype*	LDH x ULN	High Ca^{+}	WBC / ALC x 10^{9}/L	Treatment	Outcome / Status	PFS / OS (months)
Acute ATLL patients that relapsed with bone-only disease									
Case 10	Facial mass, lung and skin lesions then relapsed with diffuse bone lesions / Yes	Yes	ATLL / CD4+ CD25+ CD7- in peripheral blood, and CD3+ CD5+ CD4+ CD25+ CD7- in tumor	2.11	No	20 / 14.3	AZT / IFN with CR, then progression. EPOCH plus bortezomib and raltegravir with PR, then progression. Received multiple other lines of therapy with PD.	Progression / Deceased	4 (AZT / IFN), 7.4 (EPOCH) / 19.1
Case 11	Skin then relapsed with diffuse bone lesions / Yes	No	ATLL / Unknown	3.4	Yes	160.5 / 146	AZT / IFN with CR.	Sustained response / Alive	11 / 12
Lymphomatous ATLL patient that relapsed with bone-only disease									
Case 12	LAD then relapsed with diffuse bone lesions	Yes	PTCL / CD3+	1	No	2.5 / 1.4	CHOP with CR, then progression to bones only. CEOP with PR, then progression. Received other therapies with PD.	Progression / Deceased	16 (CHOP), 7 (CEOP) / 30

CONCLUSIONS

Our case series emphasizes the necessity of including ATLL in the diagnostic evaluation of patients with diffuse osteolytic lesions from HTLV-1 endemic areas.

Additionally, we propose a clinical subclassification for extranodal primary-bone lymphomatous ATLL-variant.

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