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Radiographic aspects in individuals infected by human T-lymphotropic virus type 1 (HTLV-1) with joint pain

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Abstract

Background: Joint pain in the absence or with little synovitis is observed in a large percentage of HTLV-1 infected subjects. As the virus infect CD4 + and CD8 + positive, macrophages and B cells an exaggerated production of pro-inflammatory cytokines is detected in these patients. However, the possible association of HTLV-1 infection with autoimmune diseases has not been documented definitively and the clinical characteristics of HTLV-1 associated arthropathy has not been defined. The objective this study is to describe clinic and radiographic features in HTLV-1-infected individuals with complaints of joint pain.

Methods: Cross-sectional study enrolling HTLV-1-infected individuals with chronic joint pain, aged up to 75 years, both genders and seronegative controls with osteoarthritis. All participants underwent conventional radiography of the hips, knees and ankles.

Results: Eighty-one HTLV-1 infected patients and 30 subjects with osteoarthritis participated in the study. Polyarticular and symmetrical arthritis prevailed in the HTLV-1 positive group (54%), while oligoarticular and asymmetrical (44%) were more common in controls ($p < 0.05$). The frequency of enthesophytes (90%) in HTLV-1-infected patients was greater than in the control group (73%) ($p < 0.05$). Radiographic features were similar in HTLV-1 carriers and in patients with probable or definite HTLV-1 associated myelopathy. The presence of enthesophytes in the absence of joint space reduction or osteophytes was only observed in HTLV-1-infected individuals ($p < 0.001$). Magnetic resonance imaging of the ankles of five HTLV-1-infected patients and five controls demonstrated a higher frequency of enthesitis, bursitis and osteitis in the HTLV-1 infected group.

Conclusion: HTLV-1-associated arthropathy is clinically characterized by symmetrical polyarthralgia and the main radiological finding is the presence of enthesophytes in the absence of osteophytes and joint space narrowing.

Keywords: HTLV-1, HTLV-1-associated arthropathy, Arthralgia, Radiographic aspects

Background

Human T-lymphotropic virus type 1 (HTLV-1) was the first identified human retrovirus [1]. Four decades later, the natural course of HTLV-1 infection and the clinic manifestations of this viral infection are not fully known. An estimated 10–20 million individuals are currently infected with HTLV-1, with higher concentrations found

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in endemic regions of developing countries, such as Brazil [2, 3]. The two main diseases associated with HTLV-1 infection are adult T-cell leukemia/lymphoma (ATLL) and HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP), which occur in less than 5% of infected individuals [4, 5]. Nonetheless, evidence has been accumulated that HTLV-1 infection is associated with other diseases and may present a variety of clinical manifestations, including overactive bladder, dry syndrome, infective dermatitis, polymyositis, periodontal disease, arthropathy and erectile dysfunction [5–7].

HTLV-1-associated arthropathy was initially attributed to the occurrence of autoimmunity in infected individuals [8, 9], but other studies did not confirm the existence of association between this viral infection with rheumatoid arthritis, *Sjögren* syndrome or other systemic rheumatic disease [10, 11]. In a few HTLV-1 infected patients with arthritis, atypical lymphocytes were found in the synovial fluid [12], proviral DNA was identified in synovial cells [13] and the presence of Tax protein messenger RNA was documented in the synovial stromal cells [14]. Moreover, transgenic mice expressing the Tax protein develop inflammatory arthropathy [15]. These observations influenced the concept that joint disease in HTLV-1 was associated with a chronic synovitis as observed in rheumatoid arthritis [12]. However, from a clinical perspective, polyarthralgia, not arthritis, is the more relevant finding in HTLV-1-infected patients with joint manifestations [7, 16]. Actually, edema/warm was only observed in 23% of HTLV-1 infected subjects who had chronic joint pain [16]. Moreover, to date, no diagnostic criteria for HTLV-1 associated arthropathy (HAAP) has been established and the radiographic features of the joints in such patients have not been described. The aim of this study was to describe clinic and radiographic features of HTLV-1 infected subjects with joint pain, to better define HTLV-1 associated arthropathy.

Methods

This study was performed in the HTLV-1 outpatient clinic of the Federal University of Bahia Hospital, Salvador, Brazil, from 2016 to 2018. This is a cross sectional study comparing clinic and radiographic features of HTLV-1 infected patients of both gender with age between 18 and 75 years who had joint pain for at least 01 year. Of the 104 HTLV-1 infected subjects who complained of joint pain, 23 were excluded, 15 due to incomplete radiographic data, and 8 who had diagnosis of systemic rheumatic disease under the American College of Rheumatology (ACR) criteria [17]. Additional exclusion criteria were previous history of joint surgery and contraindication to perform conventional radiographic. Participants were 81 HTLV-1-infected individuals and a control group consisted of 30 HTLV-1 seronegative individuals with hip, knee or ankle osteoarthritis followed in the Rheumatology clinic and evaluated by EMC in a period of 2 months. The diagnosis of osteoarthritis was performed according to the ACR criteria [17]. HTLV-1 infection was diagnosed by ELISA (Cambridge Biotech Corp, Worcester, MA) and confirmed by Western blot (HTLV blot 2.4; Genelab, Singapore). The cases were classified as HTLV-1 carriers and those who had probable or definite myelopathy [18]. HTLV-1 carriers were HTLV-1 infected without evidence of neurologic diseases, probable HAM/TSP were patients who didn't have motor disability but have sensory signals as urinary dysfunction mainly characterized by overactive bladder [18]. Definite HAM/TSP had spastic paraparesis and Osame motor disability score greater than 1 [18]. All included individuals answered a questionnaire, were independently evaluated by two rheumatologists and had conventional radiographs of the hips in anteroposterior (AP) incidence and of the knees and ankles in AP and lateral incidences. These images were independently analyzed by two blind radiologists regarding the diagnosis of the arthropathy. In the case of discrepancies between radiological evaluations, a third radiologist was consulted. The joints of the hips, knees and ankles were selected to be evaluated due to great frequency of involvement in accordance with complaints of HTLV-1 infected individuals, and due to the common involvement of these joints in patients with osteoarthritis [19]. The assessment of joints using conventional radiography was performed due to low cost, abundant availability and the possibility of detecting a range of joint alterations. Additionally, magnetic resonance imaging (MRI) of both ankles was performed in 5 HTLV-1 infected patients and in 5 with osteoarthritis who presented enthesophytes on conventional radiography, in a device with a magnetic field of 1.5 T, weighted FSE sequences were performed in T1 and T2, in multiple planes.

This study was approved by the Institutional Review Board of The Federal University of Bahia, resolution number 7/2016, and all participants provided a written informed consent.

The Fisher's exact and chi-square tests were used to compare among categorical variables, while the Student's t test was used to compare age between groups. Statistical analysis was performed using SPSS® software version 21 (IBM, USA). Results with $p < 0.05$ were considered statistically significant.

Results

The demographic characteristics, clinical forms of HTLV-1 infection and patterns of joint pain complaints in the cases and controls are shown on Table 1. No

Table 1 Demographic and clinical characteristics of 81 HTLV-1-infected patients and 30 controls with osteoarthritis

Demographic and clinical features	HTLV-1 + (n = 81)	Control (n = 30)	*p*
Age (years)	60 (± 9) [a]	59 (± 9) [a]	0.78[b]
Gender			
Female	59 (73%)	25 (83%)	0.32[c]
Male	22 (27%)	5 (17%)	
Clinical/neurological status			
Carrier	48 (59%)	–	
Probable HAM/TSP	22 (27.1%)	–	
Definite HAM/TSP	11 (13.5%)	–	
Pattern of joint pain			0.0001[d]
Polyarticular and symmetric	44 (54%)	3 (10%)	
Polyarticular and asymmetric	4 (5%)	4 (13%)	
Oligoarticular and symmetric	16 (20%)	4 (13%)	
Oligoarticular and asymmetric	13 (16%)	13 (44%)	
Monoarticular	4 (5%)	6 (20%)	
Main joints with pain complaint			
Knees	72 (89%)	27 (90%)	1.00 [d]
Hips	31 (38%)	3 (10%)	0.005 [d]
Ankles	54 (67%)	12 (40%)	0.004 [d]

[a] Mean (Standard Deviation); [b] Student's t test; [c] Fisher's exact test; [d] Chi-square test

Table 2 Frequencies of main radiographic findings in 81 HTLV-1-infected patients and 30 controls with osteoarthritis

Radiographic findings	HTLV-1 + N = 81	Control N = 30	*p*[a]
Joint Space Narrowing in at least one joint	34 (42%)	29 (97%)	0.0001
Osteophytes in at least one joint	46 (57%)	28 (93%)	0.0001
Enthesophytes in at least one joint	73 (90%)	22 (73%)	0.035
Enthesophytes with joint space narrowing or Osteophytes	49/73 (67%)	22/22 (100%)	0.001
Enthesophytes without joint space narrowing and without osteophytes	24/73 (33%)	0	

[a] Fisher's exact test

differences were seen between the groups with respect to age and gender. The prevailing pattern of joint pain in the HTLV-1-infected subjects was polyarticular and symmetrical (54%), while the control group predominantly exhibited oligoarticular and asymmetrical pattern (44%) ($p < 0.0001$). The knee was the joint with more frequent reports of pain in both groups, followed by the ankles and hips.

The frequency of radiographic changes in the cases and controls is shown on Tables 2 and 3. While the presence of osteophytes and joint space narrowing were the main radiological findings in the control group with osteoarthritis, the frequency of enthesophytes was higher (p˂0.001) in HTLV-1-infected patients than in controls. While joint space reduction and osteophytes were more prevalent in patients with osteoarthritis, the presence of enthesophytes in the absence of joint space

Table 3 Radiographic findings by joint in 81 patients infected with HTLV-1 and 30 controls with osteoarthritis

Radiographic Findings	HTLV-1 + N = 81	Control N = 30	*p*[a]
Knees			
Joint space narrowing	30 (37%)	29 (97%)	0.0001
Osteophyte	46 (57%)	27 (90%)	0,001
Enthesophyte	29 (36%)	9 (30%)	0.6
Hips			
Joint space narrowing	8 (10%)	3 (10%)	1.000
Osteophyte	4 (5%)	6 (20%)	0.02
Enthesophyte	46 (57%)	11 (37%)	0.08
Ankles			
Joint space narrowing	1 (1%)	5 (17%)	0.005
Osteophyte	9 (11%)	13 (43%)	0.0001
Enthesophyte	69 (85%)	19 (63%)	0.01

[a] Fisher's exact test

reduction or osteophytes was only observed in HTLV-1 infected patients (p 0.001).

Further analysis of the three main radiographic findings in each joint indicated higher frequencies of osteophytes in the knees, ankles and hips, as well as joint space narrowing in the knees and ankles in the group with osteoarthritis compared to HTLV-1-infected patients (p 0.02). While no difference was found between the groups regarding the presence of enthesophytes in the knees and hips, this finding was more frequent in the ankles ($p = 0.01$) of HTLV-1-infected patients than in controls (Table 3). Among the cases, 48 (59%) were carriers, 22 (27.1%) had probable HAM/TSP and 11 (13,5%) had definite HAM/TSP. The polyarticular pattern of joint pain was observed in carriers, probable and definite HAM/TSP. The knee was the main joint involved in all the 3 subgroups of HTLV-1 infected subjects (85%; 88% and 94% respectively; $p > 0.05$), and frequency of osteophytes in at least one joint was 60%, 54% and 48% in carriers, probable and definite HAM/TSP respectively ($p > 0.05$). The frequency of enthesophytes without joint space narrowing and without osteophytes was higher in patients with definite HAM/TSP (46%) than in carriers (33%) and in probable HAM/TSP (24%), but these differences did not achieved significance. No difference was observed regarding the radiographic findings between the HTLV-1 carriers and patients with probable or definite HAM. Other less frequent findings included subchondral sclerosis, identified in four HTLV-1-infected individuals and two controls and diffuse osteopenia in three HTLV-1 carriers. Representative radiographic findings in the hip, knee and ankle of one HTLV-1-infected patient are shown in Fig. 1. Enthesophytes in the

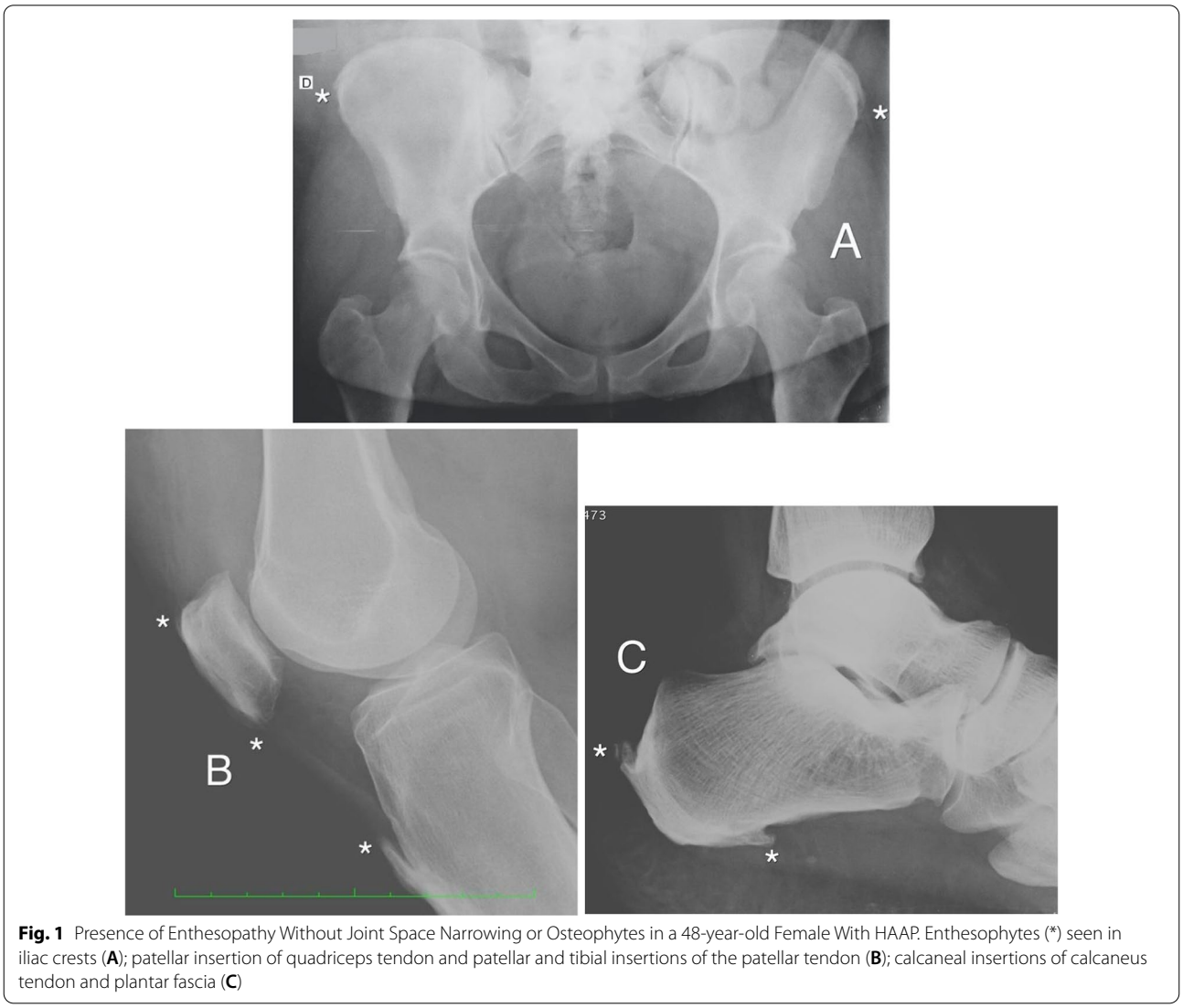

Fig. 1 Presence of Enthesopathy Without Joint Space Narrowing or Osteophytes in a 48-year-old Female With HAAP. Enthesophytes (*) seen in iliac crests (**A**); patellar insertion of quadriceps tendon and patellar and tibial insertions of the patellar tendon (**B**); calcaneal insertions of calcaneus tendon and plantar fascia (**C**)

absence of joint space narrowing and osteophytes are evident in all three joints.

MRI of ankles was performed in 5 patients of each group who presented enthesophytes on conventional radiography (Fig. 2). The comparative frequencies of findings in the HTLV-1-positive and osteoarthritis groups were: enthesitis 90% versus 40% (p 0.01), bursitis 70% versus 10% (p 0.006) and osteitis 50% versus 0% (p 0.01), respectively. No difference was observed regarding the frequency of tendinitis between the groups.

Discussion

The arthropathies are a group of musculoskeletal diseases affecting the joints, including osteoarthritis and inflammatory disorders as rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and reactive arthritis, among others [19–22]. While neurological impairment associated with HTLV-1 infection, characterized as HAM/TSP, is well-known [4, 5], joint pain despite very frequent is not well studied in HTLV-1-infected patients. While polyarthralgia was observed in 56% of HTLV-1 infected subjects only 27% of age- and gender-matched seronegative individuals complained of these manifestations [16]. Despite cases of HTLV-1-infected patients with severe joint involvement characterized by synovitis have been reported [23], the predominant joint complaint in infected individuals is polyarthralgia, with scant evidence of arthritis [16]. Here HTLV-1 associated arthropathy was clinically characterized by symmetrical polyarthralgia and the main radiographic finding was the occurrence of enthesophytes in the absence of osteophytes and joint space narrowing.

As HTLV-1-associated diseases are more frequently observed after the fifth decade of life, osteoarthritis is expected to occur in infected individuals, which can represent a confounding factor in the establishment of criteria for HTLV-1 associated arthropathy. Here we compared clinical manifestations and radiographic findings between HTLV-1-infected individuals with a history of joint pain for at least one year and patients with osteoarthritis. As inflamed joint is not a common manifestation in HTLV-1 infected subjects, we did not considerer to include as control patients with systemic rheumatic disease. Our findings indicate that while a polyarticular and symmetrical pattern of joint involvement was observed in HTLV-1-infected patients, individuals with osteoarthritis presented predominantly an oligoarticular and asymmetrical involvement. While osteophytes and joint space narrowing was more frequent in patients with osteoarthritis, enthesophytes were the main radiographic finding in individuals with HTLV-1.

The incidence of osteoarthritis and most systemic rheumatic diseases is greater in females [24] and in our series joint pain was more frequent in females of both groups. Accordingly, we cannot exclude that the greater number of women studied herein may be related to women's greater interest in seeking medical care [25]. HTLV-1-associated diseases, including arthropathy, are more frequently observed in patients with HAM/TSP than in carriers [26]. However, in our study, the observed rates of chronic joint pain were similar in HTLV-1 carriers and in patients with HAM.

Radiographic findings in osteoarthritis are mainly characterized by the presence of osteophytes, joint space narrowing, bone cysts and subchondral bone sclerosis [19]. Accordingly, we found a higher frequency of osteophytes and joint space narrowing in controls with osteoarthritis compared to HTLV-1 infected patients. Alternatively, enthesophytes were more common in the HTLV-1 group. Enthesophytes are calcification that result from an

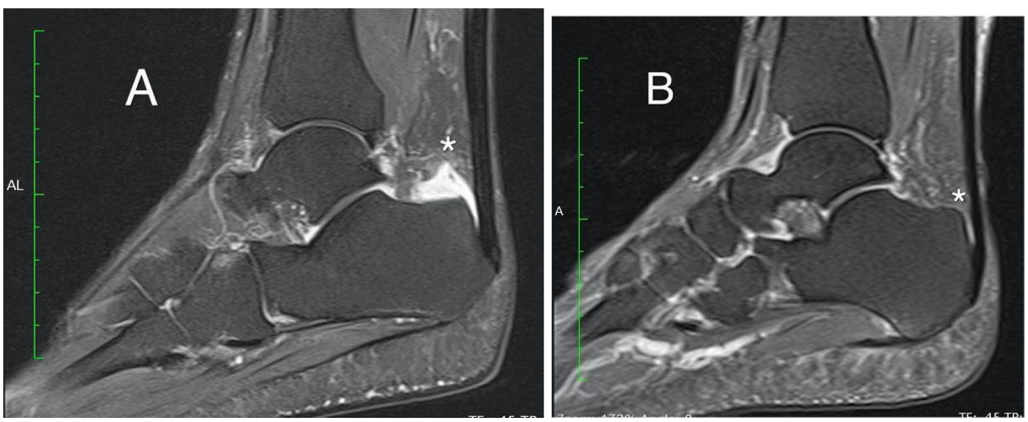

Fig. 2 MRI of the Ankle of a Patient With HAAP and in a Patient with Osteoarthritis. Liquid distension of the deep retrocalcaneal bursa in a HTLV-1 + patient (**A**), and in a patient with osteoarthritis (**B**). Deep retrocalcaneal bursa (*)

inflammatory process where a tendon, ligament, aponeurosis or joint capsule is inserted into bone structure. This is a very common finding in inflammatory seronegative arthropathies, which include ankylosing spondylitis and psoriatic arthritis [27]. Here in addition to the enthesophytes bursitis and osteitis were found in the MRI of ankles in HTLV-1 infected subjects. The most relevant finding in the HTLV-1 infected group was the high frequency of enthesophytes. They were documented in the hips, knees and ankles, but were more frequent in the ankles of HTLV-1 infected individuals than in the control group. Enthesophytes are also common in patients with osteoarthritis and they were observed in the control group. However, the occurrence of enthesopathy in the absence of osteophytes and joint space narrowing was only observed in HTLV-1-infected subjects.

The majority of the diseases associated to HTLV-1 are mainly observed in patients with definite HAM/TSP [5–7]. However, we have previously shown that HTLV-1 carriers present higher frequency of HTLV-1 associated diseases than seronegative controls. Here the pattern of joint pain, the main joint involved and the radiographic features were similar in HTLV-1 carriers and in patients with probable and definite HAM/TSP indicating that the pathogenesis of the HTLV-1 associated arthropathy may be different from the one related to neurologic diseases, but future studies are necessary to determine how the virus and or the abnormalities in the immune response observed in HTLV-1 infection may cause arthropathy.

One of the limitations of our study was the fact that more specific and more sensitive imaging techniques for the detection of joint involvement were not used. However, conventional radiography, besides being a cheap, rapid and easily accessible method, does contribute to characterization of joint pathologies in the patients studied. Importantly, alterations detected on conventional radiography continue to be part of the diagnostic criteria for osteoarthritis [17]. In rheumatoid arthritis, joint features detected in conventional radiography were part of the diagnostic criteria of the disease up to 2010 when due to the limitation to detect of early changes in the count it was list out [28]. In patients with rheumatoid arthritis a characteristic finding of the disease is joint destruction [29] and it is important to highlight that in the present study, joint destruction was not observed in any HTLV-1 infected patient with joint pain.

Understanding the existence and importance of structures adjacent and related to the enthesis that contribute to dissipate the forces of stress helps to better understand the processes that affect the entheses. The study of enthesis of the calcaneus tendon should be extended to adjacent fibrocartilage, bursa, fat and fascia [30]. While the calcaneus enthesis is avascular in its fibrocartilaginous region, vessel growth may occur in association with the tissue repair response. The synovium, present in the retrocalcaneal bursa, is vascularized and vulnerable to inflammation and the high levels of pro-inflammatory cytokines observed in HTLV-1 infection may explain a higher frequency of retrocalcaneal bursitis and osteitis in the HTLV- 1 infected subjects compared to patients with osteoarthritis.

Conclusion

Based on our study HTLV-1 associated arthropathy is characterized mainly by symmetric polyarticular pain and enthesophytes in the absence of joint space narrowing and osteophytes in the ankles.

Abbreviations

HTLV-1: Human T-lymphotropic virus type 1; ATLL: Adult T-cell leukemia/lymphoma; HAM/TSP: HTLV-1 associated myelopathy/tropical spastic paraparesis; HAAP: HTLV-1 associated arthropathy; EMC: Eugênia Maria Campos, Rheumatologist; ACR: American College of Rheumatology; MRI: Magnetic resonance imaging.

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Author contributions

JMSC: Design and conception of the study. Interpretation and analysis of data. Draft and design of the work. Revision of the work. EMTAC: Interpretation and analysis of data. Draft and design of the work. Revision of the work. JLNF: Analysis and interpretation of data. Draft and design of the work. Revision of the work. HMC: Interpretation and analysis of data. Draft and design of the work. Revision of the work. JACN: Analysis and interpretation of data. Draft and design of the work. Revision of the work. TOC: Analysis and interpretation of data. Draft and design of the work. Revision of the work. EMC: Design and conception of the study. Interpretation and analysis of data. Draft and design of the work. Revision of the work. All authors have read and approved the manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of The Federal University of Bahia, resolution number 7/2016.

Consent for publication

All participants provided a written informed consent.

Competing interests

The authors declare that they have no competing interests.

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References

1. Poiesz BJ, Ruscetti FW, Gazdar AF, et al. Detection and isolation of type C retrovirus particles from fresh and cultured lymphocytes of a patient with cutaneous T-cell lymphoma. Proc Natl Acad Sci USA. 1980;77:7415–9.
2. Gessain A, Cassar O. Epidemiological aspects and world distribution of HTLV-1 infection. Front Microbiol. 2012;3:388.
3. Grassi MFR, dos Santos NP, Lírio M, et al. Tuberculosis incidence in a cohort of individuals infected with human T-lymphotropic virus type 1 (HTLV-1) in Salvador. Brazil BMC Infect Dis. 2016;16:491.
4. Osame M, Usuku K, Izumo S, et al. HTLV-I associated myelopathy, a new clinical entity. Lancet. 1986;1:1031–2.
5. Souza A, Tanajura D, Toledo-Cornell C, et al. Immunopathogenesis and neurological manifestation associated to HTLV-1 infection. Rev Soc Med Trop. 2012;45:545–52.
6. Murphy EL, Wang B, Sacher RA, et al. Respiratory and urinary tract infections, arthritis and asthma associated with HTLV-I and HTLV-II infection. Emerg Infect Dis. 2004;10:109–16.
7. Poetker SKW, Porto AF, Giozza SP, et al. Clinical manifestation in individuals with recent diagnosis of HTLV Type I infection. J Clin Virol. 2011;51:54–8.
8. Motokawa S, Hasunuma T, Tajima K, et al. High prevalence of arthopathy in HTLV-I carries on Japanese island. Ann Rheum Dis. 1996;55:193–5.
9. Eguchi K, Matsuoka N, Ida H, et al. Primary Sjögren's syndrome with antibodies to HTLV-I: clinical and laboratory features. Ann Rheum Dis. 1992;51:769–76.
10. Lee S-J, Lee JS, Shin M-G, et al. Detection of HTLV-1 in the labial salivary glands of patients with Sjögren's syndrome: A distinct clinical subgroup? J Rheumatol. 2012;39:809–15.
11. Sebastian D, Nayiager S, York DY, et al. Lack of association of Human T-cell lymphotrophic virus type 1 (HTLV-1) infection and rheumatoid arthritis in an endemic area. Clin Rheumatol. 2003;22:30–2.
12. Nishioka K, Maruyama I, Sato K, et al. Chronic inflammatory arthropathy associated with HTLV-I. Lancet. 1989;1:441.
13. Yamamoto K, Aono H, Nakajima T, et al. Oligoclonal proliferation of human T-cell leukemia virus type I infected lymphocytes in lesions of virus-induced arthropathy. Biochem Biophys Res Commun. 1995;208:1040–5.
14. Kato T, Asahara H, Kurokawa MS, et al. HTLV-I env protein acts as a maior antigen in patients with HTLV-I associated athropath. Clin Rheumatol. 2004;23:400–9.
15. Iwakura Y, Tosu M, Yoshida E, et al. Induction of inflammatory artropathy resembling rheumatoid arthritis in mice transgenic for HTLV-I. Science. 1991;253:1026–8.
16. Caskey MF, Morgan DJ, Porto AF, et al. Clinical manifestations associated with HTLV Type I infection: a cross-sectional study. AIDS Res Hum Retrovir. 2007;23:365–71.
17. Altman RD. Criteria for classification of clinical osteoarthritis. J Rheumatol Suppl. 1991;27:10–2.
18. De Castro-Costa CM, Araújo AQ, Barreto MM, et al. Proposal for diagnostic criteria of tropical spastic paraparesis/HTLV-I-associated myelopathy (TSP/HAM). AIDS Res Hum Retrovir. 2006;22:931–5.
19. Parker JH, Hong JY, Han K, et al. Prevalence of symptomatic hip, knee, and spine osteoarthritis nationwide health survey analysis of an elderly Korean population. Medicine. 2017;96: e6372.
20. Scott DL, Wolfe F, Huizinga TW. Rheumatoid arthritis. Lancet. 2010;376:1094–108.
21. Ogdie A, Weiss P. The epidemiology of psoriatic arthritis. Rheum Dis Clin N Am. 2015;41:545–68.
22. Amrami KK. Imaging of the seronegative spondyloarthopathies. Radiol Clin N Am. 2012;50:841–54.
23. Koster MJ, McPhail ED, Chowdhary VR. Synovial infiltration in human T lymphotropic virus type I-associated adult T cell leukemia/lymphoma. Arthritis Rheumatol. 2015;67:945.
24. Magnusson K, Turkiewicz A, Englund M. Nature vs. nurture in knee osteoarthritis – the importance of age, sex and body mass index. Osteoarthritis Cartilage. 2019 Jan 8 (E-pub ahead of print).
25. Vaidya V, Partha G, Karmakar M. Gender differences in utilization of preventive care services in the United States. J Womens Health. 2012;21:140–5.
26. Carvalho MM, Giozza SP, Santos AL, et al. Frequency of rheumatic disease in individuals infected with HTLV-1. Rev Bras Reumatol. 2006;46:315–22.
27. Balint PV, Terslev L, Aegerter P, et al. Reliability of a consensus-based ultrasound definition and scoring for enthesitis in spondyloarthritis and psoriatic arthritis: an OMERACT US initiative. Ann Rheum Dis. 2018;77:1730–5.
28. Chang EY, Chen KC, Huang BK, et al. Adult Inflammatory Arthritides: What the Radiologist Should Know. Radiographics. 2016;36:1849–70.
29. Harshan S, Dey P, Ragunathan S. Effects of rheumatoid arthritis associated transcriptional changes on osteoclast differentiation network in the synovium. PeerJ. 2018;6: e5743.
30. McGonagle D, Lories RJU, Benjamin M. The concept of a "synovio-entheseal complex" and its implications for understanding joint inflammation and damage in psoriatic arthritis and beyond. Arthritis Rheum. 2007;56:2482–91.

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