DOI: https://doi.org/10.30795/scijfootankle.2019.v13.951

CASE REPORT

Scientific Journal of the Foot & Ankle

Primary non-Hodgkin's lymphoma of the talus: case report

Linfoma não-Hodgkin primário do tálus: relato de caso

Gianfrancesco Marconato[1], Joao Luiz Vieira da Silva[2], Renan Marson Costa[1], Márcio Fernando Aparecido de Moura[2]

1. Hospital de Clínicas da Universidade Federal do Paraná, Curitiba, PR, Brazil.
2. Universidade Federal do Paraná, Curitiba, PR, Brazil.

ABSTRACT

Lymphoma is a blood cancer that begins in different types of lymphoid or histiocytic cells in various states of maturity. Primary lymphoma of bone is rare, and clinical manifestations include localized pain and edema. The diagnosis takes into consideration the clinical picture, imaging tests and pathological anatomy. In this article, we present the case of a patient with restricted daily activities and loss of quality of life due to primary non-Hodgkin's lymphoma of the talus. After chemotherapy, the clinical condition of the patient improved. Level of Evidence V; Expert Opinion ***Level of Evidence V; Expert Opinion.***

Keywords: Lymphoma, Non-Hodgkin; Talus; Ankle; Bone neoplasms.

RESUMO

O linfoma é uma neoplasia de origem hematogênica formada por células linfoides ou histiocitárias de diferentes tipos e em vários estados de maturidade. O linfoma primário do osso é raro e as manifestações clínicas incluem dor e edema localizados. O diagnóstico leva em consideração o quadro clínico, exames de imagem e anatomia patológica. Neste artigo, apresentamos o caso de um paciente com restrição das atividades diárias e perda da qualidade de vida devido a um linfoma primário não-Hodgkin do tálus. Após realização de quimioterapia o paciente evoluiu com melhora do quadro clínico.

Nível de Evidência V; Estudos Terapêuticos; Opinião do Especialista.

Descritores: Linfoma não Hodgkin; Tálus; Tornozelo; Neoplasias ósseas.

How to cite this article: Marconato G, Silva JLV, Costa RM, Moura MFA. Primary non-Hodgkin's lymphoma of the talus: case report. Sci J Foot Ankle. 2019;13(2):184-8.

INTRODUCTION

Lymphoma is a blood cancer and is subdivided into Hodgkin's lymphoma and non-Hodgkin's lymphoma. Any lymphoma can affect the skeleton as the exclusive site of involvement or as one of the sites affected by the disseminated form of the disease[1-3].

According to the World Health Organization (2013), primary lymphoma of bone is a cancer involving lymphatic cells that produce one or more bone masses, without other lymphatic or extranodal involvement[1-3].

The most frequent site affected is the femur, followed by the pelvis, tibia, humerus and spine. The bones of the foot, particularly the talus, are rarely affected[3].

Chemotherapy, the current gold standard for the treatment of patients with primary lymphoma of bone, consists of cyclophosphamide, doxorubicin, vincristine and predni-

Work performed at the Universidade Federal do Paraná e Hospital de Clínicas da UFPR, Curitiba, PR, Brazil.

Correspondence: Gianfrancesco Marconato. Endereço: Rua Alcebíades Plaisant 961, Água Verde, Curitiba, PR, Brazil, CEP: 80620-270
E-mail: gianf17@gmail.com
Conflicts of interest: não há. **Source of funding:** own.
Date received: March 15, 2019. **Date accepted:** May 19, 2019. **Online:** June 30, 2019

sone (CHOP) or CHOP combined with rituximab (R-CHOP). Regarding treatment outcomes, chemotherapy was reported to be superior to radiotherapy alone[3].

In the literature, there are few reports on this condition. Therefore, the aim of this study is to describe a rare case of primary bone lymphoma of the talus in a 42-year-old patient who underwent chemotherapy.

CASE REPORT

This study was approved by the Research Ethics Committee with registration in the Brazil Platform under CAAE number: 07937119.0.0000.0096.

A.C.B.J, male, 42 years old, with no history of comorbidities. In May 2017, A.C.B.J reported a history of pain in the left ankle, progressing with an increase in local volume; imaging tests were not performed at this time, and there were no complaints regarding other body systems. He was screened for gout, which was not confirmed. In October 2017, he had difficulties putting weight on the limb and, thus, limped and had increased volume in the lateral region of the ankle, pain below the lateral malleolus and pain on passive movement. Joint range of motion was preserved, with 20º extension, 40º flexion, 20º inversion and 10º eversion. There were no signs of instability. Sensitivity was preserved when compared with the contralateral limb. He did not have a fever, complaints regarding other body systems nor palpable lymph nodes. Radiographs were performed at that time with the following report: "apparent reduction in bone density in the left talus" (Figure 1). A lytic lesion was observed in the talus, central with a permeating pattern, showing no periosteal reaction or soft tissue involvement, and nuclear magnetic resonance imaging was requested for further investigation. This exam resulted in the following report: "heterogeneous bone lesion of the talus, suggestive of an expansive lesion (...)" (Figure 2).

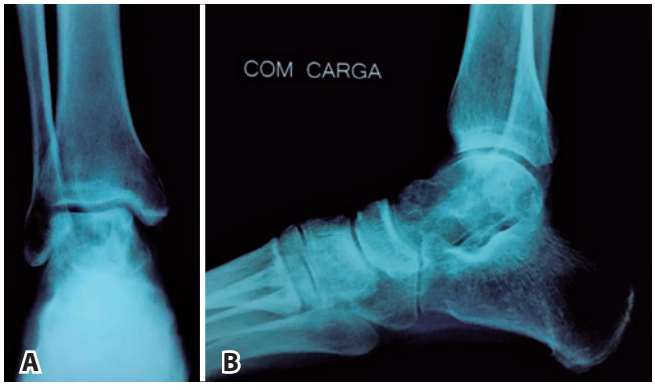

Figure 1. X-rays from the initial investigation of the left ankle. A) X-ray, anteroposterior view. B) X-ray, profile view.
Source: Author's personal archive.

Laboratory tests, such as blood count, renal function, liver function, blood clotting tests and electrolytes, were within normal limits.

In October 2017, the patient was instructed to use crutches and to bear weight as tolerated.

Open biopsy of the talus was performed on 03/21/2018. Immunohistochemistry revealed tumor cells that were positive for CD10, CD20 and B-cell lymphoma (BCL-6) but negative for CD3, CD30, and CD246, a "histological profile and immunohistochemical profile consistent with CD10 positive, diffuse B-cell lymphoma". The findings led to the diagnosis of diffuse-cell lymphoma of the talus. After the biopsy, the patient was instructed to not put any weight on the limb.

Bone scintigraphy and computed tomography of the chest and abdomen showed no evidence of disseminated disease.

Computerized tomography with positron emission tomography (PET-CT) was performed during follow-up on 05/30/2018 with the Hematology and Oncology team, with the following report: "Diffuse heterogeneity of the bones of the tarsus and metatarsus on the left foot as well as the talus and calcaneus associated with a soft tissue component with marked glycolytic activity compatible with a known neoplastic/lymphoproliferative process"(Figure 3).

The R-CHOP chemotherapy protocol was initiated on 06/12/2018. The patient underwent 6 sessions, with the last on 09/25/2018. A new PET-CT was performed on 10/25/2018, with the following report: "Reduction in the size and metabolic activity of the neoplastic process (...), with persistent significant metabolism" (Figure 4). Radiotherapy was not applied at this time due to the risk of bone necrosis and deformities.

Radiography during follow-up, in November 2018, showed bone recovery, and the patient was allowed to bear weight as tolerated with the use of an orthesis.

The patient was able to bear partial weight for a short period of time. In December 2018, he was able to walk normally without complaints. He is currently asymptomatic and performs activities without any limitations. The disease is in remission.

The treatment plan includes performing a new PET-CT in the first half of 2019 and, after this exam, if necessary, performing radiotherapy.

DISCUSSION

Primary lymphoma of bone represents 3% to 5% of all primary bone tumors, 1% to 2% of lymphomas and 5% of non-Hodgkin's lymphomas without lymph node involvement. The literature suggests a slight predominance in males (1.5:1), with a mean age ranging from 45 to 60 years[1-2].

A striking clinical feature of primary non-Hodgkin's lymphoma of bone (PLB) is the contrast between the overall well-being of the patient and a painful and destructive lesion. In fact, most patients have bone pain of varying intensity and duration, with an insidious and slow onset, and only few cases exhibit systemic symptoms such as fever, night sweats and weight loss[4-5].

The radiographic characteristics usually suggest an aggressive lesion of the affected bone. The pattern is usually osteolytic, with ill-defined margins. Cortical destruction,

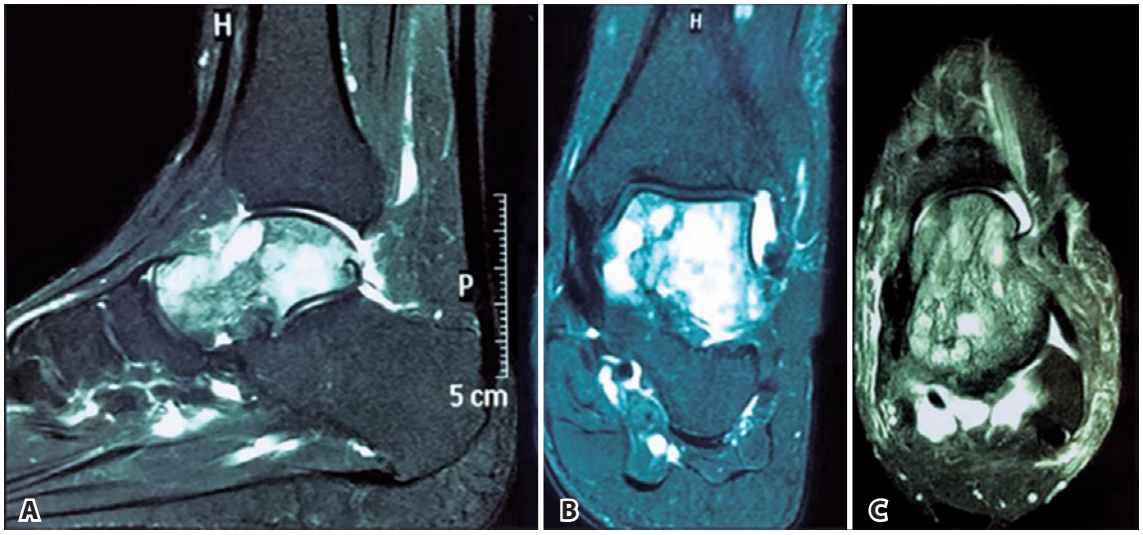

Figure 2. T2-weighted nuclear magnetic resonance images. A) sagittal. B) coronal. C) axial.
Source: Author's personal archive.

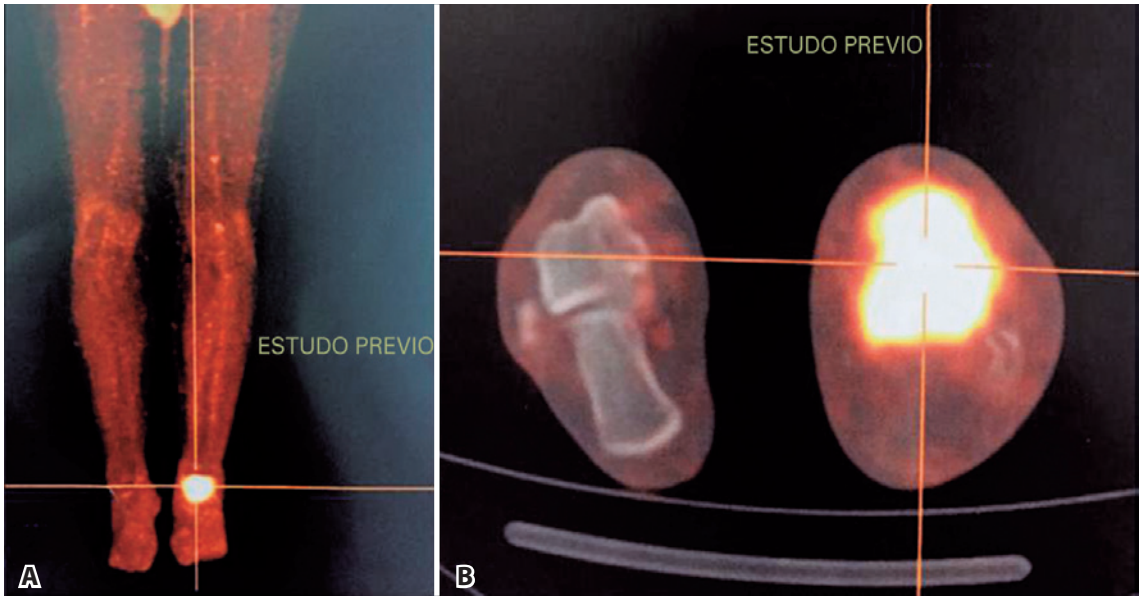

Figure 3. PET-CT images showing diffuse heterogeneity of the tarsal bones of the left foot with marked glycolytic activity, indicative of neoplastic processes. A) coronal image of the lower limbs. B) axial image of the tarsal bones.
Source: Author's personal archive.

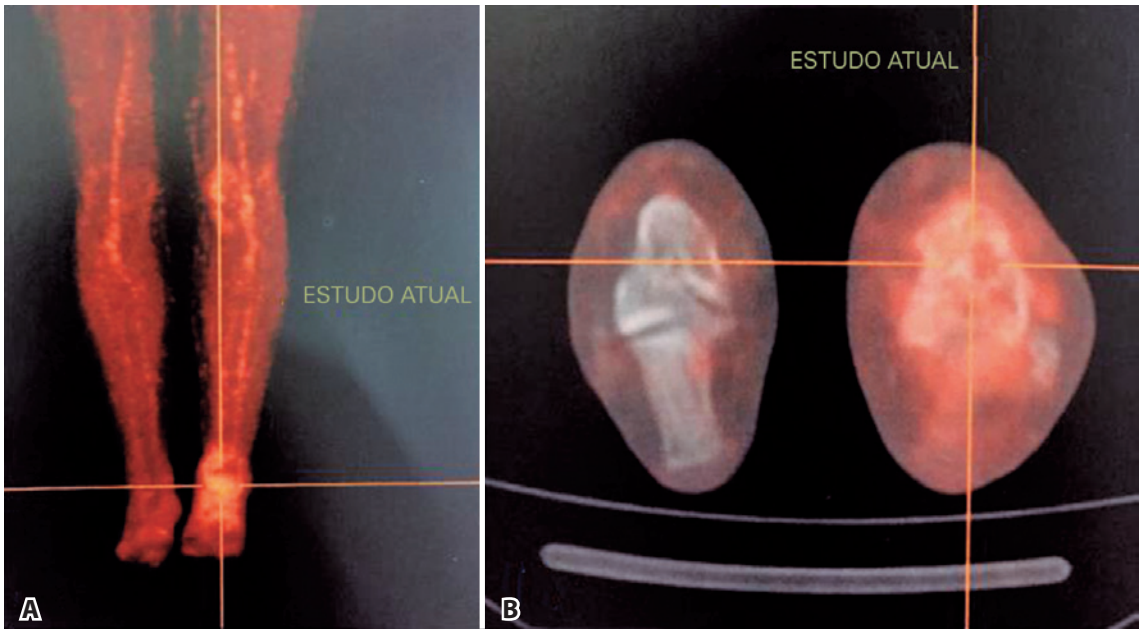

Figure 4. PET-CT images 5 months after the first exam. Note the reduction in the size and metabolic activity of the neoplastic process. A) coronal image of the lower limbs. B) axial image of the tarsal bones.
Source: Author's personal archive.

pathological fracture and soft tissue involvement are indicative of worse prognosis. When found alone, however, these characteristics are nonspecific and can be observed in other common conditions considered in the differential diagnosis, such as infection, osteonecrosis, neuropathic disease and other cancers[5].

Complementary exams, such as computed tomography or magnetic resonance imaging, are needed to assess the extent of the disease. The latter exhibits great sensitivity in the detection of bone marrow abnormalities, which is useful for planning the biopsy procedure[2].

Good general well-being with localized complaints strongly contrasts with the symptoms of secondary lymphoma or other tumors[5].

In patients with previous surgery, infection should be ruled out. The combination of a detailed medical history, laboratory tests (ESR and CRP) and tissue culture are usually used for diagnosis. Talus osteonecrosis is usually posttraumatic or is associated with conditions that affect the immune or blood clotting systems[5].

Biopsy is the basis for diagnosis and follow-up. High-grade tumors are rare; it is more common to find intermediate-grade tumors, followed by low-grade tumors. Most PLB cases present with diffuse large B-cell lymphoma (DLBCL). Immunohistochemistry shows positivity for CD20, CD79a and Bcl-2 - B-cell markers - and negativity for CD3, CD5, CD10, CD23, cyclinD1 and terminal deoxynucleotidyl transferase - T cell or follicular cell markers[5-6].

DLBCL is the most common histological subtype, corresponding to approximately 80% of cases, followed by follicular lymphoma, lymphoplasmacytic lymphoma, anaplastic lymphoma, NK/T cell lymphoma, Burkitt lymphoma, other indolent lymphomas and Hodgkin's lymphoma[7].

Primary and secondary lymphomas of bone are histologically indistinguishable. They are differentiated by the absence of general symptoms in primary lymphomas. In addition, secondary lymphomas usually affect the axial skeleton, whereas primary lymphomas affect the appendicular skeleton[7].

In this case study, there was a history of chronic pain, slow progression, and gradual difficulty with weight bearing. The imaging tests showed heterogeneous and expansive characteristics. The histopathological and immunohistochemical tests were indicative of DLBCL, with CD3-negative markers and CD20-positive markers.

Prior to the introduction of chemotherapy, the PLB is treated with local radiotherapy, with a 5-year survival rate of 55-65%. Survival rates increase with chemotherapy, reaching values between 80-90%[8].

Prior to 1990, chemotherapy consisted of cyclophosphamide, doxorubicin, vincristine, prednisolone and methotrexate (the CHOP-M regimen); after 1990, methotrexate was excluded (the CHOP regimen). Rituximab, an anti-CD20 monoclonal antibody, was later introduced to improve the efficacy of the treatment (the R-CHOP regimen)[8].

Pfreundschuh et al.[9] conducted a randomized study with young patients with non-Hodgkin's lymphoma treated with different chemotherapy regimens. The first group was treated with the CHOP regimen, and the second group was treated with the R-CHOP regimen. Patients from the R-CHOP group had 6-year survival rates of 74.3%, and those from the CHOP groups had survival rates of 55.8%; this difference was statistically significant, demonstrating the importance of rituximab[9].

Coiffier et al.[10] published a randomized study in a population between 60 and 80 years of age. All patients were in need of chemotherapy treatment. In one group, the R-CHOP regimen was used; the relapse rate was 41%, and the 2-year survival rate was 70%, indicating that the R-CHOP regimen was more effective than the CHOP regimen, with resulted in values of 61% and 63%, respectively[10].

In our case, the R-CHOP regimen was used for 6 sessions for a period of 15 weeks. The patient had a good clinical response to chemotherapy, with significant improvement in his condition and quality of life. The disease is currently in remission.

CONCLUSION

We observed in this case that the correct diagnosis, based on biopsy and immunohistochemical tests, and the appropriate treatment, with the R-CHOP regimen, provided good results to date. However, follow-up and evaluation with new tests are needed to identify signs of regression.

Authors' contributions: Each author contributed individually and significantly to the development of this article: GM *(https://orcid.org/0000-0002-2767-7797) wrote the article, interpreted the results of the study, participated in the review process, approved the final version; JLVS *(https://orcid.org/0000-0002-9038-2895) conceived and planned the activities that led to the study, participated in the review process, aprovou a versão final; RMC *(https://orcid.org/0000-0001-9978-1975) participated in the review process and approved the final version; MFAM *(https://orcid.org/0000-0002-9873-930X) participated in the review process and approved the final version. *ORCID (Open Researcher and Contributor ID).

REFERENCES

1. Messina C, Christie D, Zucca E, Gospodarowicz M, Ferrari AJM. Primary and secondary bone lymphomas. Cancer Treat Rev. 2015;41(3):235-46.
2. Munoz N, Rivero CA, González Ávila B. Primary bone lymphoma: report of 7 cases. Med Clin (Barc). 2018;151(10):421-22.
3. Sato S, Kaneuchi Y, Hakozaki M, Yamada H, Kawana S, Hasegawa O, et al. Primary malignant lymphoma of the talus - a case report and review of the literature. Mol Clin Oncol. 2017;7(4):574-8.
4. Annibali O, Fabbriciani G, Tafuri M, Massarotti M, Sedati P, Tomarchio V, et al. Primary bone lymphoma of the talus - a challenging diagnosis. Tumori. 2015;103(1):62-5.
5. Nickish F, Tashjian RZ, Ritter M, Terek RM, DiGiovanni CW. Primary malignant non-Hodgkin lymphoma of the talus - a case report. Foot Ankle Int. 2005;26(7):568-71.
6. Bansal S, Dharra N. Primary malignant non-Hodgkin lymphoma of the talus. J Cancer Res Ther. 2015;11(3):649.
7. Patel S, Sudesh P, John R, Gupta P. Primary non-Hodgkin's lymphoma of talus in a child – a rare presentation. Foot (Edinb). 2014;24(4):210-2.
8. Ford DR, Wilson D, Sothi S, Grimer R, Spooner D. Primary bone lymphoma-treatment and outcome. Clinical Oncology. 2007;19(1): 50-5.
9. Pfreundschuh M, Kuhnt E, Trumper L, Osterorg A, Trneny M, Shepherd L, et al. CHOP-like chemotherapy with or without rituximab in young patients with good-prognosis diff use large-B-cell lymphoma: 6-year results of an open-label randomised study of the MabThera International Trial (MInT) Group. Lancet Oncol. 2011;12(11):1013-22.
10. Coiffier B, Lepage E, Briere J, Herbrecht R, Tilly H, Bouabdallah R, et al. CHOP chemotherapy plus rituximab compared with CHOP alone in elderly patients with diffuse Large-B-Cell lymphoma. N Engl J Med. 2002;346(4):235-42.