Case Report | Journal of Orthopaedic Case Reports 2023 August:13(8):Page 37-41

A Rare Case of Anaplastic Large Cell Lymphoma of the Knee Joint

Bhooshan Zade[1], Vrushab Rao[1], Tushar Patil[2], Taher Chharchhodawala[3]

Learning Point of the Article:

Extranodal lymphomas are well documented and must be considered as a differential diagnosis in cases that are unresponsive to treatment and have debilitating symptoms.

Abstract

Introduction: Anaplastic large cell lymphoma (ALCL), which makes up only 2–5% of instances of NHL, is a rare and aggressive form of the disease. Anaplastic Lymphoma Kinase (ALK)-positive ALCL is a variant of the illness that is identified by the presence of an ALK gene fusion. The disease is most commonly confined to the nodes, but extranodal spread has been reported. Skin and soft tissue are the most frequently identified locations for extranodal involvement, while joints are extremely rare. We describe a rare case of ALCL affecting the knee joint that is ALK-positive.

Case Report: A 51-year-old female presented with pain in her right knee. It was diagnosed as synovitis and treated accordingly. The symptoms did not relieve and a magnetic resonance imaging (MRI) scan was performed that indicated a meniscus tear. She was treated for it; however, the symptoms worsened. She underwent two more scans (1 MRI and 1 PET) that indicated an enhancing polypoidal mass in the knee joint, and two arthroscopic procedures. The histopathology report indicated an ALK-positive ALCL. She was treated with Brentuximab vedotin + CHP followed by involved-site radiotherapy to the postoperative region with margins. The patient has had a complete clinical and pathological response which was assessed after 1 year from the start of the treatment.

Conclusion: This is the first instance of primary ALK-positive ALCL affecting the knee joint that has been documented, to the best of our knowledge. The case emphasizes the significance of taking ALCL into account when determining the differential diagnosis of knee joint tumors as well as the requirement for a thorough assessment of extranodal involvement.

Keywords: Lymphoma, knee joint, ALCL, extranodal lymphoma, ISRT, chemotherapy, arthroscopic surgery.

Introduction

Anaplastic large cell lymphoma (ALCL) is a rare subtype of mature T-cell lymphomas that are CD30 positive and may present with or without the aberrant expression of the anaplastic lymphoma kinase (ALK) protein. While, like most lymphomas, most ALCL cases are detected in lymph nodes, cases have been reported in sites outside lymph nodes, which are rare. The malignancy may present with a variety of symptoms which may lead to it being missed while diagnosing. We present a unique case of ALK-positive ALCL of the knee joint.

Case Report

A 51-year-old female presented with pain in her right knee joint in March 2022 to an outside institution. The pain was insidious

Access this article online

Website: www.jocr.co.in

DOI: https://doi.org/10.13107/jocr.2023.v13.i08.3806

Author's Photo Gallery


Dr. Bhooshan Zade


Dr. Vrushab Rao


Dr. Tushar Patil


Dr. Taher Chharchhodawala

[1]Department of Radiation Oncology, Ruby Hall Clinic, Pune, Maharashtra, India,
[2]Department of Medical Oncology, Sahyadri Hospital, Pune, Maharashtra, India,
[3]Department of Pathology, Ruby Hall Clinic, Pune, Maharashtra, India.

Address of Correspondence:
Dr. Vrushab Rao,
Department of Radiation Oncology, Ruby Hall Clinic, Pune, Maharashtra, India.
E-mail: raovrushab@gmail.com

Submitted: 08/05/2023; Review: 19/06/2023; Accepted: July 2023; Published: August 2023

DOI: https://doi.org/10.13107/jocr.2023.v13.i08.3806

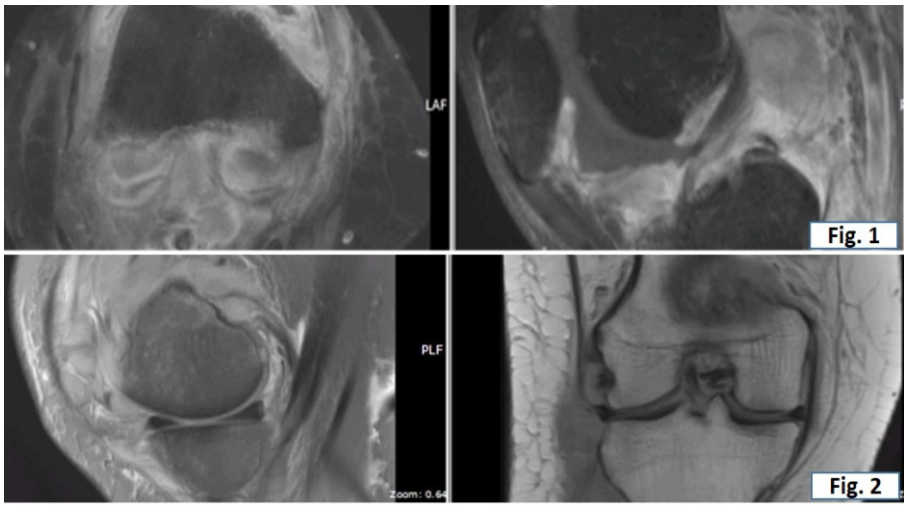

Figure 1 & 2: Magnetic resonance imaging showing polypoidal soft-tissue thickening within the entire knee joint.

in onset and gradually progressive. The pain was aggravated with motion and relieved with medications and rest. It was associated with a local rise of temperature. At that point in time, it was diagnosed to be a case of synovitis and treated with empirical antibiotics and painkillers. The pain did not reduce even after the medications.

She presented with the same symptoms again followed by fever after 1 week. The symptoms did not subside after the treatment. She underwent an MRI that showed a suspected meniscus tear with a suspected anterior cruciate ligament degeneration and synovitis. Fluid was noted in the joint capsule. No other lesions or nodes were noted. She underwent an arthroscopic procedure at an outside institution for drainage of the synovial fluid under antibiotic coverage. However, the sample was not sent for histopathology.

The symptoms were persistent and the patient complained of severe pain in the right knee, along with swelling around the knee joint and high-grade fever of around 103°F within 3 weeks. Mobility was severely restricted. The general condition of the patient started to deteriorate. There was generalized weakness, poor appetite, and unintentional weight loss. She was advised matrix therapy for the pain but it did not help. She underwent another arthroscopic procedure within 6 weeks of the first one and the tissue was sent for histopathology. The report was negative for any malignancy and Koch's disease as well. Routine treatment for infections and steroids were started.

She underwent an MRI of the right knee that revealed a polypoidal soft-tissue thickening within the entire knee joint which was mildly enhancing on the post-contrast images. Multiple linear T2 hyperintense signals were seen traversing the fibular head and styloid process which were suggestive of fracture lines with marrow edema in the adjacent bone.

2 weeks following the MRI, the symptoms aggravated. In addition, the patient had malaise and complete loss of mobility of the joint due to the pain. She had lost around 5 kgs in 1 month. An 18FDG-PET CT scan was conducted that revealed an FDG avid large peripheral enhancing soft-tissue thickening and collection noted along the right knee joint with a standardized uptake value of 52.4. Mild cortical erosion of the medial condyle of the right femur was noted. Mild juxta-articular osteopenia was observed which was indicative of the known septic arthritis or could be pigmented villonodular synovitis. FDG avid prominent right popliteal node was noted. Metabolically active enlarged right external iliac and inguinal nodal lesions were seen as likely reactive. On clinical examination, the nodes were not palpable and no other distant lymphadenopathy was noted.

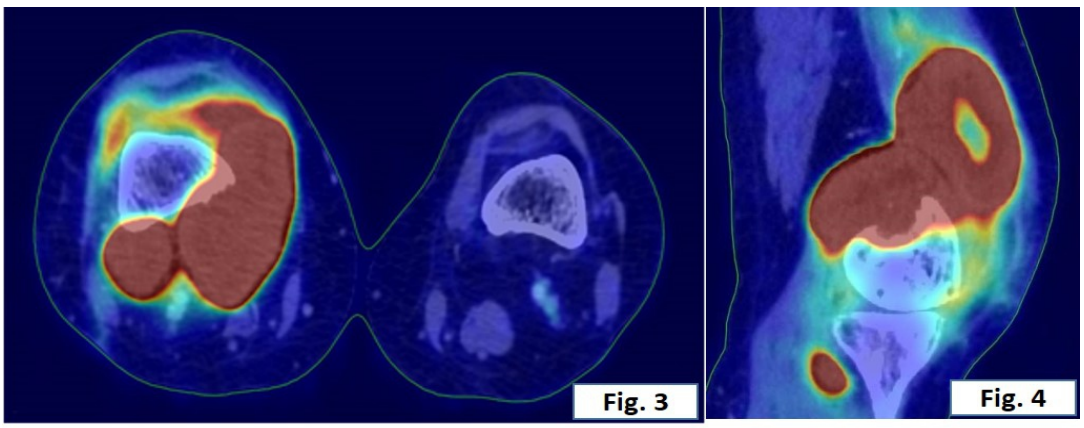

Figure 3 & 4: PET scan showing peripheral enhancing soft tissue thickening and collection noted along the right knee joint.

She underwent an open surgery of the knee joint for debulking of the lesion 1 week after the imaging and sampling of the suspicious popliteal nodes. Samples from the surgery were sent for histopathology which came positive for a CD30+ and ALK-positive

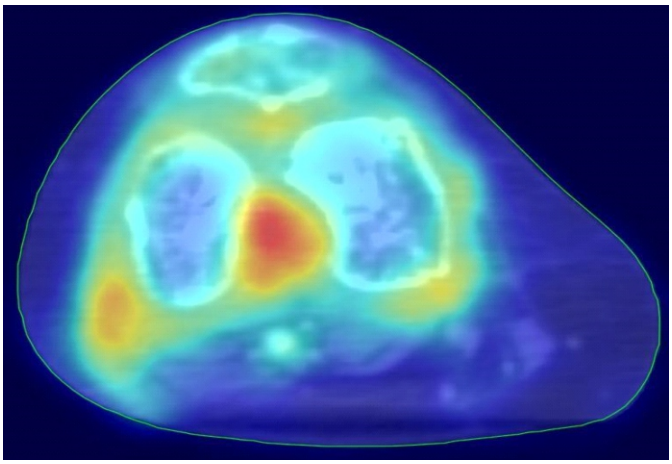

Figure 5: Restaging PET showing near complete resolution.

hematolymphoid malignancy. She was diagnosed with Stage II ALK+ ALCL of the knee joint.

She was taken up for treatment that was based on the NCCN treatment guidelines for ALK-positive ALCL. She received 6 cycles of a multiagent chemotherapy regimen consisting of brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone. A PET-CT scan was done for interim restaging after the chemotherapy that showed a near-complete resolution (with a standardized uptake value of 3.4) of the lesion in the knee joint.

This was followed by involved-site radiotherapy (ISRT) with a cumulative dose of 45 Gy in 25 fractions (36 Gy in 20 fractions to the initial volume before the chemotherapy followed by a boost of 9 Gy in 5 fractions to the residual lesion post-chemotherapy). Follow-up showed complete resolution of the symptoms. The latest PET scan 1 year since the treatment began showed resolution of the lesion.

Discussion

ALCL, like other lymphomas, is most commonly seen in the lymph nodes. It is more often seen in children as compared to adults [1, 2] Extranodal sites for its occurrence include the skin, bones, soft tissues, and lungs [3]. In the postoperative setting, ALCL is commonly found in breast implants [4]. In the knee joint ALCL is a rare entity. Among lymphomas that occur in the knee, B-cell lymphomas are more common. In patients with knee prosthesis lymphomas are rare, and among ALCL cases only ALK-negative variants have been documented [5]. Among bony ALCL cases, common sites include the iliac bones [6], the sternum [7], the proximal femur [8], vertebrae, and ribs [9, 10, 11]. Primary non-Hodgkin's lymphoma of the knee joint has also been reported, and in rare cases, it has been found to involve the synovium [12]. Cases of an ALCL primarily of the knee joint have not been observed.

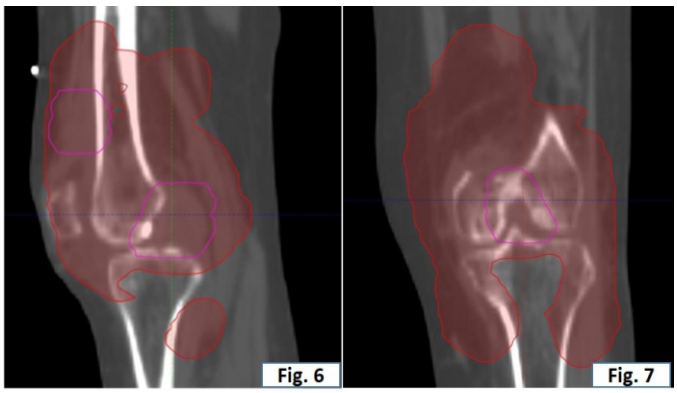

Figure 6 & 7: Radiotherapy volume.

ALCL has been documented to present with a wide variety of symptoms that makes cases with extranodal sites as the primary location hard to diagnose. There are cases reported with patients presenting with fever, malaise, weakness, loss of appetite, and weight loss [13]. Bony lesions present with pain on movement and may be picked up on the scan as a lytic lesion. Differential diagnoses, especially considering the age of the patient, generally constitute diseases of infectious etiology such as osteomyelitis, synovitis, septic arthritis, or tuberculosis. ALCL is also known to present as arthritis even when the site of the primary lesion is away from the symptomatic bones or joints [14].

ALK-positive ALCL is shown to have better prognostic outcomes as compared to ALK-negative ALCL. Aggressive treatment with brentuximab vedotin, which is a CD30-directed antibody, combined with cyclophosphamide, vincristine, and doxorubicin is chosen as the first line of treatment. Brentuximab vedotin-based chemotherapy regimens have shown to have 97% complete response rate after 6 cycles [15]. The latest NCCN guidelines suggest the use of BV-CHP as the first line of treatment in ALK-positive ALCL.

In-field radiotherapy (IFRT) and ISRT are two techniques used to deliver radiation to consolidate the action of chemotherapy in lymphomas. IFRT, which delivers radiotherapy to all the lymph nodes in a given set of anatomical boundaries, has now been replaced with ISRT which delivers radiation to the involved lymph nodes and sites only. Extranodal lymphomas are seen respecting as well as violating anatomical boundaries on imaging which poses a challenge in determining the extent of the target volume. Strict guidelines do not exist to treat these malignancies [16]. Most lymphomas are treated with a dose ranging from 30 to 36 Gy at 1.8–2 Gy per fraction. About 30–36

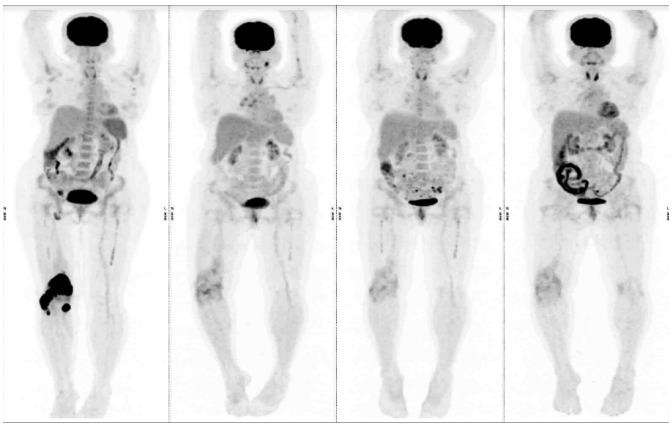

Figure 8: Complete pathological response.

Gy is also accepted for aggressive extranodal lymphomas with complete response to systemic therapy. An additional dose may be added to compound the total delivered dose to 40–45 Gy in the same fractionation schedule in cases of partial response, recurrence, or treatment failure [17]. We chose the higher total dose in our patient in view of the aggressive nature of the malignancy and the low residual uptake (SUV 3.4) seen in the restaging PET-CT scan.

Conclusion

Extranodal ALCL is an aggressive disease that is commonly misdiagnosed and may pose a challenge to treat if not detected early. Any lesions that fail to respond to initial lines of management for the probable should be promptly tested for malignancies to rule them out. As can be seen in this case, ALCL can occur in unexpected sites and timely initiation of treatment can limit the morbidity caused by it.

Clinical Message

During the course of this patient's workup, neoplastic disorders and infectious diseases, both common and rare, should be closely examined. A histological analysis is essential in these circumstances. As demonstrated in this instance, ALCL can develop in unanticipated locations, and swift intervention may mitigate the damage.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given the consent for his/ her images and other clinical information to be reported in the journal. The patient understands that his/ her names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflict of interest: Nil **Source of support:** None

References

1. Ferreri AJ, Govi S, Pileri SA, Savage KJ. Anaplastic large cell lymphoma, ALK-positive. Crit Rev Oncol Hematol 2012;83:293-302.

2. Delson G, Falini B, Muller-Hermelink HL, et al. Anaplastic large cell lymphoma, ALK-positive. In: Swerdlow SCE, Campo E, Harris NL, et al., editors. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Lyon: IARC; 2008. p. 312-6.

3. Wang S, Meng M, Wang Q, Xu K. Non-Hodgkin lymphoma of multiple extranodal involvement seen on MRI, FDG PET-CT scans: A case report. Medicine (Baltimore) 2017;96:e8456.

4. Nelson JA, Dabic S, Mehrara BJ, Cordeiro PG, Disa JJ, Pusic AL, et al Breast implant-associated anaplastic large cell lymphoma incidence: Determining an accurate risk. Ann Surg 2020;272:403-9.

5. Go JH. Metallic implant-associated lymphoma: ALK-negative anaplastic large cell lymphoma associated with total knee replacement arthroplasty. J Pathol Transl Med 2023;57:75-8.

6. Noh BJ, Han CS, Park JS, Lee J, Kim YW, Park YK, et al. ALK-positive anaplastic large-cell lymphoma with primary bone involvement: A rare case and review of the literature. Malays J Pathol 2018;40:161-7.

7. Narla SL, Kurian AJ, Subramanyan A, Parameswaran A. ALK-1 positive anaplastic large cell lymphoma presenting as extensive and exclusive osseous involvement: Report of a rare association and review of literature. J Clin Diagn Res 2018;12:ED01-3.

8. Hue SS, Iyer P, Toh LH, Jain S, Tan EE, Sittampalam K, et al. Primary bone anaplastic large cell lymphoma masquerading as Ewing sarcoma: Diagnosis by anchored multiplex PCR. J Pediatr Hematol Oncol 2017;40:e105-7.

9. Yang Y, Xie Q, Liu Y, Chen Y, Yin G. ALK-positive

anaplastic large cell lymphoma with multifocal bone involvements: A case report and review of the literature. Int J Clin Exp Med 2018;11:2745-51.

10. Mundada M, Ahmed F, Santa A. A challenging case of anaplastic large cell lymphoma with primary bony presentation. Asian J Oncol 2017;3:155-7.

11. Al-Asaadi Z, Fatin S, Patel K, Chetty N, Dubrey S. Anaplastic large cell lymphoma with axial skeletal lesions portends a poor prognosis. Br J Hosp Med (Lond) 2015;76:606-7.

12. Lee RK, Griffith JF, Ng AW, Tam HK, Chan AW. Non-Hodgkin's lymphoma of the knee: A case report. Iran J Radiol 2015;12:e7583.

13. de Campos FP, Zerbini MC, Felipe-Silva A, Simões AB, Lovisolo SM, da Fonseca LG, et al. Unusual clinical presentation of anaplastic large cell lymphoma. Autops Case Rep 2014;4:21-7.

14. Falcini F, Bardare M, Cimaz R, Lippi A, Corona F. Arthritis as a presenting feature of non-Hodgkin's lymphoma. Arch Dis Child 1998;78:367-70.

15. Lowe EJ, Reilly AF, Lim MS, Gross TG, Saguilig L, Barkauskas DA, et al. Brentuximab vedotin in combination with chemotherapy for pediatric patients with ALK+ ALCL: Results of COG trial ANHL12P1. Blood 2021;137:3595-603.

16. Wirth A, Mikhaeel NG, Aleman BM, Pinnix CC, Constine LS, Ricardi U, et al. Involved site radiation therapy in adult lymphomas: An overview of international lymphoma radiation oncology group guidelines. Int J Radiat Oncol Biol Phys 2020;107:909-33.

17. Yahalom J, Illidge T, Specht L, Hoppe RT, Li YX, Tsang R, et al. Modern radiation therapy for extranodal lymphomas: Field and dose guidelines from the International Lymphoma Radiation Oncology Group. Int J Radiat Oncol Biol Phys 2015;92:11-31.

Conflict of Interest: Nil
Source of Support: Nil

Consent: The authors confirm that informed consent was obtained from the patient for publication of this case report

How to Cite this Article

Zade B, Rao V, Patil T, Chharchhodawala T. A Rare Case of Anaplastic Large Cell Lymphoma of the Knee Joint. Journal of Orthopaedic Case Reports 2023 August;13(8):37-41.