Case Report

Diffuse Large B-Cell Lymphoma Discovered following Total Knee Arthroplasty: A Case Report and Literature Review

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Keywords

Osteoarthritis · Total knee arthroplasty · Diffuse large B-cell lymphoma

Abstract

Total knee arthroplasty is performed routinely for osteoarthritis of the knee joint. We report a case of high-grade diffuse large B-cell lymphoma as an unexpected diagnosis after histopathological examination of unusual-looking synovium during total knee arthroplasty in a 68-year-old patient without any systemic symptoms.

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Introduction

Non-Hodgkin's Lymphoma (NHL) is associated with uncontrolled proliferation of the lymphoid cells. The musculoskeletal system is involved in about 5–25% of the patients as metastasis or, rarely, as a primary lymphoma of the bone [1–3]. Skeletal lesions are most of the times asymptomatic and, hence, escape clinical attention. However, they present as nonspecific symptoms of pathological fracture or localized pain and tenderness [4]. Therefore, even if rare, we must not forget to count these malignancies in the differential. Here, we

present a case wherein an atypical synovium identified during a routine knee arthroplasty for osteoarthritis, after biopsy, unfolded the diagnosis of diffuse large B-cell lymphoma (DLBCL).

Case Report

A 68-year-old woman presented to our outpatient department with complaints of pain in both knee joints in the last 2 years with restricted routine activities and reduced range of movements. On examination, both knees had medial joint line tenderness with crepitus felt on palpation. There was no laxity. Varus deformity which was correctable up to 10° was noted without distal neurovascular deficits. The range of movements of both knees was 10° – 90° . There was no history of trauma in the past. Patient did not have any medical comorbidities and had not visited any hospital in past for any kind of orthopedic treatment. X-ray of both knee joints was performed, and patient was diagnosed with Kellgren-Lawrence grade IV osteoarthritis of the knees with varus deformity (shown in Fig. 1) [5]. The patient was explained regarding bilateral total knee replacement for severe osteoarthritis. The patient was deemed fit for surgical intervention after thorough examination by cardiologist, dentist, and anesthetist. Routine blood tests and urine investigations were within the normal range. The patient was admitted a day prior to surgery. Informed consent was procured. The more painful right knee was decided to be replaced first as a part of staged replacement protocol.

Using the medial parapatellar approach, the right knee joint was exposed. Synovium was found to be unexpectedly thickened, pigmented, hemorrhagic, and adherent to the underlying bone over the distal end of femur. Due to suspicion of synovial pathology in addition to the already diagnosed osteoarthritis, biopsy too was taken and sent for histopathological examination. A total knee replacement was performed without any complications (shown in Fig. 2). Patient recovered well and was discharged from the hospital after 5 days. Patient was followed up at 2 weeks for staple removal. The patient was walking with the help of walker; full weight-bearing over the knee. The range of movement in the right knee postoperatively was 0° – 90° but now painless.

It was shocking to learn that the histopathology of the synovial biopsy had revealed diffuse infiltration of synovium with medium-to-large-sized lymphoid cells along with numerous blastic variants. Ancillary immunohistochemical analysis showed the tumor cells to be CD3 negative and CD20, CD10, BCL-2, BCL-6, and C-MYC positive with a high Ki-67 proliferative index of 85–90% (shown in Fig. 3). The histological features were consistent

Fig. 1. Radiographs of both knees in AP and lateral views showing the grade IV osteoarthritis of the knee joints.

Fig. 2. Postoperative radiographs of the right knee in AP and lateral views.

Fig. 3. Histopathological pictures; H and E showing diffuse infiltration of synovium with medium-to-large-sized lymphoid cells along with numerous blastic variants (a), CD3 is negative (b), BCL-2 is positive (c), c-MYC is positive (d), CD20 is positive (e), Ki-67 is also positive with high-proliferative index (f).

with high-grade lymphoma with adult Burkitt's lymphoma, WHO 2008 classified as DLBCL-not otherwise specified.

Patient was admitted to hemato-oncology department for further evaluation. There were no systemic symptoms. Complete blood count, renal, and liver function tests were normal. Fluorodeoxyglucose-positron emission tomography scan revealed multiple enlarged lymph nodes on both sides of the diaphragm, multiple skeletal lesions involving right tibia, femur, bilateral iliac bones, and sacrum. Diffuse soft tissue lesions involving synovial space of bilateral knee joints were also found (shown in Fig. 4). The PET scan indicated stage IV B-cell lymphoma [6].

Our patient was then started with combination chemotherapy under supervision of hemato-oncologist, using rituximab, cyclophosphamide, vincristine, and prednisolone. She was found unfit for regular high-dose chemotherapy. After the initial cycle of chemotherapy, unfortunately, the disease progressed and patient succumbed to her illness.

Fig. 4. FDG-PET scan showing multiple enlarged lymph nodes on both sides of the diaphragm, multiple skeletal lesions, and diffuse soft tissue lesions involving synovial space of bilateral knee joints indicating stage IV B-cell lymphoma. FDG-PET, fluorodeoxyglucose-positron emission tomography

Discussion

DLBCL is the most common type of NHL accounting for about 25% of all NHLs [7]. It has a highly varied presentation. However, it typically involves the lymph nodes of neck or abdomen. It may also present as a mass lesion anywhere in the body and about 30% of them have systemic symptoms such as fever, night sweats, or weight loss [8]. Extra-nodal DLBCL is seen in up to 40% of the cases; the gastrointestinal tract being the most common site [9]. Primary skeletal lymphoma is rare and it accounts for about 3–5% of all extra-nodal NHLs. Synovial involvement occurs due to direct extension from the bone. Primary synovial involvement without bone involvement is very rare [10]. The main pathophysiological mechanism for NHL is B-cell hyperactivity and chronic inflammation. Probably due to its malignant character, NHL will be irresolute to anti-inflammatory drugs, also in case of musculoskeletal involvement [11].

Studies have shown that patients with rheumatoid arthritis and immunocompromised states are at high risk for DLBCL. Patients with rheumatoid arthritis have 2.7-fold increased risk in the occurrence of lymphoma than the general population [12, 13]. Arredondo et al. [14] reported NHL as an unexpected diagnosis in a patient with long-standing rheumatoid arthritis on immunosuppressive medications during shoulder arthroplasty. Visser et al. [15] reported a similar case in a patient with autoimmune rheumatoid arthritis without any systemic symptoms. In another article, Agrawal et al. [16] reported DLBCL in a patient 14 weeks post-total knee arthroplasty, when patient presented with loosening of the prosthetic joint.

On review of literature from 1980 to till date, we found 19 cases of primary synovial lymphoma (Table 1) [1, 2, 15–30]. The literature showed involvement of various joints such as knee (most common), elbow, wrist, sternoclavicular joint, and small joints of hand and feet. Most of the patients presented with joint pain, stiffness, swelling, and decreased range of

Table 1. Literature review of primary synovial lymphoma from 1980 to till date

Author	Year of publication	Age/sex	Joints involved	Past medical history	Systemic complaints	Lymphadenopathy/hepatosplenomegaly	Radiological findings	Gross appearance of tissue	Diagnosis
Adunsky et al. [17]	1980	54/F	Right sternoclavicular	None	No	No/no	X-ray: hyper-condensation of the medial edge of the right clavicle, with marginal erosions and lysis of adjacent manubrium sterni	Soft, greyish	Malignant lymphoma of lymphocytic, poorly differentiated, diffuse type
Tiwari et al. [18]	1982	76/F	Left knee	No	Night sweats, weight loss	Left inguinal/no	X-ray: no abnormality noted	Synovial thickening	Diffuse NHL
Dorfman et al. [1]	1986	48/F	Left knee	None	Fatigue, fever	No/no	X-ray: non-calcified soft tissue mass in the suprapatellar bursa	Tan, firm, homogeneous, friable	Malignant lymphoma of histiocytic type
Dorfman et al. [1]	1986	72/M	Left knee	Rheumatoid arthritis, gout	No	No/no	X-ray: marked narrowing of joint space, hypertrophic marginal lippling in the distal femur and proximal tibia	Marked erosion of articular cartilage, surrounding osteophyte formation	Malignant lymphoma of non-Hodgkin's type
Hasse et al. [19]	1990	36/F	Left knee	Right axilla immunoblastic lymphoma treated with local radiation only (11 years ago)	No	No/no	X-ray: no abnormality noted	Mass originating from synovial membrane infiltrating into periosteum of femoral condyles and gastrocnemius muscles	Malignant B-cell immunoblastic lymphoma
Bagga et al. [20]	1996	39/F	Right knee	Renal transplant secondary to glomerulonephritis; right knee replacement for avascular necrosis 4 years ago	NR	NR/NR	X-ray: a lesion at the posterior aspect of right proximal tibia with small effusion. Three-phase bone scan: increased uptake at periprosthetic region	NR	DLBCL
Jamieson et al. [21]	1998	61/M	Knee	None	No	No/no	None on radiograph; effusion, synovial thickening on MRI	NR	NHL
Peeva et al. [22]	1999	27/M	Right knee	HIV	Weight loss	No/no	X-ray: permeative pattern of femoral metaphysis, periosteal reaction and effusion MRI: heterogeneous marrow inflammation, hypertrophic synovial changes, patchy cortical destruction, distributed effusion	NR	DLBCL
Daneshpouy et al. [23]	2002	29/M	Wrist	Sjogren syndrome	No	No/no	X-ray was normal	NR	T-cell lymphoma with eosinophilia
Birlik et al. [24]	2003	69/F	Right fourth finger	No	No	No/no	X-ray: destruction of proximal phalanx of fourth finger, soft tissue swelling	NR	Articular B-cell lymphoma

Author	Year of publication	Age/sex	Joints involved	Past medical history	Systemic complaints	Lymphadenopathy/hepatosplenomegaly	Radiological findings	Gross appearance of tissue	Diagnosis
Khan and Hutchinson [25]	2004	65/M	Left knee	Ankylosing spondylitis	No	No/no	X-ray: bony destruction with large effusion. MRI: bony erosion, gross synovial hypertrophy, 3 cm mass seen posterior to the femur	NR	DLBCL
Jawa et al. [26]	2006	33/M	Right elbow	Hyperextension injury of right elbow	No	No/no	X-ray: no abnormality noted	Fleshy, tan	DLBCL
Chim et al. [27]	2006	66/M	Left knee	Seronegative rheumatoid arthritis on methotrexate	No	No/no	US: heterogeneous soft tissue mass lesion in left knee, predominantly in suprapatellar bursa and anterior joint compartment	NR	DLBCL
Mileti et al. [2]	2007	31/F	Knee	None	No	No/no	X-ray was normal. MRI showed medial meniscus tear	Hypereamic, Hypertrophic synovium	DLBCL
Neri et al. [28]	2010	58/M	Left elbow	None	No	No/no	X-ray: erosion of lateral epicondyle MRI: extensive ill-defined bone marrow signal intensity affecting distal portion of humerus. A synovial effusion with a solid component was detected	Hemorrhagic synovial tissue	DLBCL
Visser et al. [15]	2012	69/F	Left knee	Seronegative rheumatoid arthritis, right knee replacement	No	No/no	X-ray: severe lateral osteoarthritis of the left knee with loss of height of the lateral tibial plateau	Pigmented vitreous tissue	DLBCL-NOS
George et al. [29]	2013	68/M	Left subtalar and talonavicular	Rheumatoid arthritis	No	No/no	X-ray: osteoarthritis of subtalar and talonavicular joint. US: marked synovitis in the subtalar joint	Hypertrophied, dark synovium	DLBCL
Lee et al. [30]	2015	28/F	Right knee	None	No	No/no	X-ray of the knee showed mild to moderate osteolysis of the medial femoral condyles and moderate resorption of the medial condylar cortex. US of the knee showed a small-to-moderate-sized joint effusion with severe synovial thickening at the anteromedial aspect of the knee	NR	DLBCL
Agrawal et al. [16]	2019	74/F	Left knee	Right knee replacement 6 months back	No	NR/NR	X-ray of left knee showed marked degenerative changes with diffuse joint space narrowing of the medial and lateral compartments with subchondral cystic changes	Hypertrophied with white fibrous scars, areas of necrosis, and dark colored masses	DLBCL

NR, not reported; US, ultrasound; DLBCL, diffuse large B-cell lymphoma; NHL, non-Hodgkin's lymphoma; DLBCL-NOS, DLBCL-not otherwise specified.

movements. Rheumatoid arthritis was the most common medical condition in the patients associated with lymphoma; immunosuppressed state was the next common association. Three patients had associated systemic complaints such as fever, night sweats, or weight loss. Only one of the patients had inguinal lymphadenopathy and none of them had hepatosplenomegaly on presentation. Our patient had history of bilateral knee osteoarthritis. The patient did not show any systemic symptoms of DLBCL such as fever, weight loss, loss of appetite, or night sweats or signs such as lymphadenopathy or hepatosplenomegaly. Even her blood investigations, liver function tests, and kidney function tests were within normal limits. Intra-operative findings of thickened, pigmented, hemorrhagic, and adherent synovium lead to suspicion of some underlying pathology. The diagnosis in this case report was based on the synovial tissue immune-histological analysis and later PET-CT scan.

Conclusion

Our report describes a case of an elderly woman diagnosed with DLBCL involving the synovium in addition to the involvement of multiple groups of lymph nodes. It was an extremely rare presentation without any systemic signs or symptoms pertaining to the malignancy. It was because of identification of abnormal synovium during the replacement surgery and a quick decision to sample the tissue for histopathology, which led to the diagnosis, and hence, a chance for the patient to be evaluated further and treated. It was unfortunate that we lost the patient but this case teaches us all that we should be well aware of such an atypical presentation of DLBCL. Also, we must learn that ignoring any pathology, small or big, during operative procedures is not advisable. A prompt decision to biopsy any suspicious tissue viz abnormal synovium, bone, or intra-articular elements could prove to be extremely valuable in making a precise important diagnosis.

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Statement of Ethics

The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The patient's son gave written informed consent to publish her case (including publication of radiological images). All information was anonymized.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

S.L.K. collected the data, analyzed the data, and compiled the manuscript. A.D.P. was the operating surgeon and supervised the manuscript, and G.B. managed the lymphoma part and coauthored the manuscript.

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