

Primary Synovial Diffuse Large B-Cell Lymphoma Presenting as Loosening of Prosthetic Joint: A Case Report and Review of Literature

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Abstract

Primary synovial diffuse B-cell lymphoma is a rare clinical condition. The condition presents primarily with localized joint symptoms such as swelling, pain and reduced range of motion. It may or may not be associated with lymphadenopathy, hepatosplenomegaly or B-type constitutional symptoms. We report a case of a 74-year-old woman who presented with persistent left knee pain and swelling after left knee replacement secondary to osteoarthritis. There was a concern for mechanical loosening of internal left knee prosthetic joint. On revision surgery (14 weeks after the initial surgery), hypertrophied synovium with areas of fibrotic scars, necrotic tissue and dark colored masses was resected. She was found to have diffuse large B-cell lymphoma (DLBCL) after histological analysis. In cases with persistent joint symptoms or postoperative complications, arthroscopy or arthrotomy should be considered and any atypical appearing tissue should be sent for histopathological analysis.

Keywords: Diffuse large B-cell lymphoma; Synovial; Osteoarthritis

Introduction

Non-Hodgkin's lymphoma (NHL) consists of different subtypes of neoplasms derived from B-cell or T-cell or natural killer cell lineage. B-cell lymphoma accounts for 85% of all cases of NHL. Musculoskeletal involvement can be seen in 5-25% cases of NHL either as metastasis or rarely as a primary lymphoma of bone or soft tissue [1]. The primary lymphoma of synovium is extremely rare. As a result, the diagnosis can be missed.

We report a very rare case of primary synovial diffuse

large B-cell lymphoma (DLBCL) presenting as a postoperative complication of mechanical loosening of internal left knee prosthetic joint. This was seen 14 weeks after a left total knee replacement was performed in a patient with long standing osteoarthritis.

Case Report

A 74-year-old woman was admitted to our hospital for elective left knee replacement for osteoarthritis. Patient had chronic left knee pain for the prior 10 years. She had been diagnosed with osteoarthritis based on the X-ray of the knee. Initially, the pain was managed with non-steroidal anti-inflammatory medications. However, over the course of past 1 year, the pain had worsened and was interfering with her daily activities. She denied any fever, chills, numbness, tingling or pain in other joints. She denied weight loss, night sweats or new lumps.

She had past medical history of hypertension and bilateral knee osteoarthritis. She had past surgical history of right knee replacement with no complications 6 months prior to this admission. She was a former smoker with history of 3 - 4 cigarettes for 20 years. She denied any alcohol or recreational drug use. Her family history included gastric cancer in the mother who died at unknown age.

Vitals were within normal range. Physical examination was normal except of left knee which revealed moderate effusion and tenderness to palpation of medial and lateral joint space. There was no erythema or warmth noted. Range of motion was mildly restricted.

X-ray of left knee showed marked degenerative changes with diffuse joint space narrowing of the medial and lateral compartments with subchondral cystic changes and degenerative spurring suggestive of moderate osteoarthritis.

Treatment course

With informed consent from the patient, the orthopedic surgeon proceeded with left total knee replacement. Intraoperatively, markedly hypertrophic synovium and areas of fibrotic tissue was noted. A large effusion was present which was clear. The fluid was sent for culture. Also, synovium and intra-articular tissue biopsies were taken and sent for culture. Aerobic, an-

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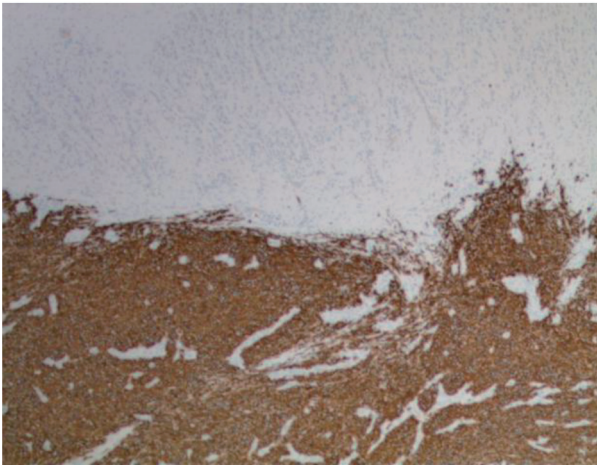


Figure 1. Low power ($\times 20$) image showing the reactive thick fibrosynovial tissue within the knee joint, with associated giant cell reaction to cement (top of picture) with the atypical subjacent diffuse mononuclear cell infiltrate. The differential includes both reactive/infectious conditions and malignancy.

aerobic, acid fast bacilli stain and fungal culture was negative. The patient tolerated the procedure well. She was discharged on day 3 postoperatively.

Ten weeks after the first procedure, the patient followed up with orthopedics for persistent left knee pain, swelling and reduced mobility. She was recommended to undergo manipulation of left knee under anesthesia due to concern for postoperative adhesions formation. Patient agreed for the procedure. Intraoperatively, a scant amount of bloody fluid was aspirated and sent for cultures. The cultures were negative. The patient tolerated the procedure well and was discharged in 2 days postoperatively. Post-procedure, she continued to have severe left knee pain, swelling and reduced mobility. Orthopedics was concerned about mechanical loosening of internal left knee prosthetic joint. Fourteen weeks after the first procedure, she underwent revision left knee replacement surgery. Intraoperatively, she had marked arthrofibrosis of left knee. The tissue

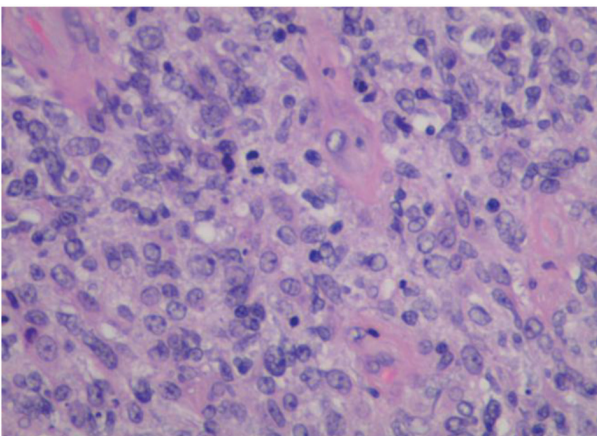


Figure 2. High power ($\times 400$) image showing the diffuse infiltrate of large lymphoma cells with admixed histiocytes, mitosis and karyorrhexis debris.

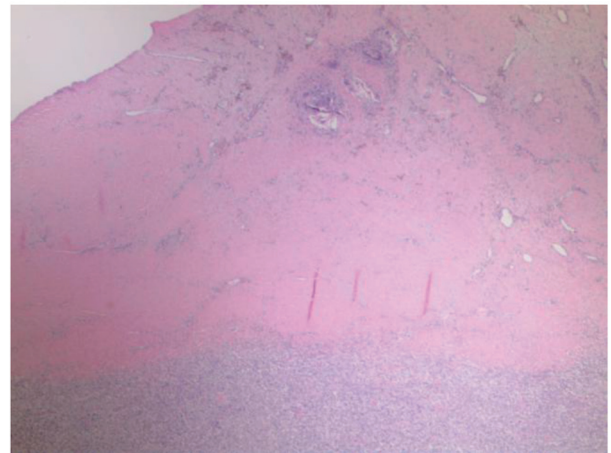


Figure 3. Low power ($\times 40$) image of CD20 immunohistochemical stain confirming the morphologic suspicion of diffuse large B-cell lymphoma.

was hypertrophied with white fibrous scars, areas of necrosis and dark colored masses. During this revision surgery, synovium and intra-articular tissue was sent for pathological analysis.

Pathological analysis of the resected tissue showed diffuse lymphoid infiltrate within fibrous tissue of medium to large atypical cells. The cells had irregular nuclei, moderate cytoplasm and conspicuous nucleoli (Figs. 1 and 2). Immunohistochemistry was positive for CD20, CD10, BCL-2 and BCL-6 (Fig. 3). The findings were consistent with germinal center DLBCL. Epstein-Barr virus testing was negative. The Ki-67 proliferation index averaged 60%, but was up to 80% focally. Fluorescence *in situ* hybridization (FISH) was negative for BCL2/BCL-6/MYC rearrangements.

The patient was referred to the oncologist. Complete blood count showed white cell count of $7,350/\mu\text{L}$ with normal differential, hemoglobin 9.9 g/dL and platelets of $375 \times 10^3/\mu\text{L}$. Lactate dehydrogenase (LDH) was elevated to 359 U/L. Antinuclear antibody (ANA) test was negative. Rheumatoid factor (RF) was negative. Positron emission tomography/computed tomography (PET/CT) from skull base to the upper thigh showed hypermetabolic activity in the region of left knee prosthesis with maximum standardized uptake value (SUV) of 25.9 consistent with lymphoma. It also showed hypermetabolic left inguinal lymphadenopathy with SUV of 12.7 and pelvic sidewall lymphadenopathy with SUV of 14.1. DLBCL was staged as II-E. She was treated with rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP) chemotherapy.

Discussion

DLBCL is the most common type of NHL. It accounts for approximately 25% of all NHLs [2]. It can manifest clinically with variable symptoms. The typical presentation includes nodal enlargement most commonly in neck or abdomen. But it can present as a mass lesion anywhere in the body. About 30% of the patients may have systemic B symptoms such as fever, night sweats or weight loss [3]. Extranodal DLBCL can be present in up to 40% of the cases [4]. The most common site

Table 1. Literature Review of Cases of Primary Synovial NHL (1980 to Present)

Author	Publication year	Age/sex	Joints involved at presentation	Significant past medical history	Systemic complaints (fever, night sweats, weight loss)	Lymphadenopathy at presentation	Hepatosplenomegaly at presentation	Imaging findings	Gross appearance of biopsy tissue	Diagnosis
Tiwari et al [13]	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 [16]	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 [15]	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
Peeva et al [14]	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
Birlik et al [18]	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
Khan et al [12]	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 [7]	2006	33/M	Right elbow	Hyperextension injury of right elbow	No	No	No	X-ray: no abnormality noted.	Fleshy, tan	DLBCL
Chim et al [11]	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

Table 1. Literature Review of Cases of Primary Synovial NHL (1980 to Present) - (continued)

Author	Publication year	Age/sex	Joints involved at presentation	Significant past medical history	Systemic complaints (fever, night sweats, weight loss)	Lymphadenopathy at presentation	Hepatosplenomegaly at presentation	Imaging findings	Gross appearance of biopsy tissue	Diagnosis
Neri et al [6]	2010	58/M	Left elbow	None	No	No	No	X-ray/US: 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 [8]	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 [9]	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

NR: not reported; MRI: magnetic resonance imaging; US: ultrasound.

of extranodal involvement is the gastrointestinal tract.

Primary bone lymphoma is a rare disease and it accounts for 3-5% of all extranodal NHLs [5]. Synovial involvement can occur due to direct extension from bone. Primary synovium lymphoma without bone involvement is extremely rare. On the review of the English-language literature from 1980 to present, we found 14 cases of primary synovial B-cell NHL [1, 6-18] (Table 1). The reported literature showed various joint involvement such as knee (most common), elbow and small joints of hand and feet. The presenting symptoms primarily included joint pain, stiffness, swelling, or reduced mobility. Three patients had associated systemic complaints such as fever, night sweats or weight loss. Only one patient had lymphadenopathy (left inguinal). No patient had hepatosplenomegaly on presentation. Studies have shown increased risk of NHL specifically DLBCL in patients with rheumatoid arthritis and immunocompromised states [19, 20].

Our patient had a history of bilateral knee osteoarthritis. Our patient presented as a clinically challenging diagnostic problem due to several reasons. 1) Due to rarity of primary synovial DLBCL and a recent uneventful right total knee replacement, the clinical suspicion for the disease was very low. 2) The patient did not show any systemic symptoms of DLBCL such as fever, weight loss or night sweats or signs such as lymphadenopathy or hepatosplenomegaly. 3) The patient's worsening symptoms of left knee pain, swelling and reduced mobility were attributed to progressing osteoarthritis. 4) Intraoperative findings of marked synovial hypertrophy and areas of fibrotic tissue were likely attributed to osteoarthritis versus infection. Therefore, the tissue samples were sent for cultures and not for histology. These factors may have caused delay in the diagnosis by as much as 14 weeks. On subsequent revision procedure, the surgeon noticed areas of necrosis and dark colored masses and samples were sent for histological analysis.

It is prudent to consider B-cell NHL as a differential diagnosis in a patient with unremitting joint pain, swelling and reduced mobility after a joint replacement for osteoarthritis. In our clinical practice, we do not routinely send tissue samples for histological analysis during elective joint arthroplasties. However, intraoperatively any abnormal appearing synovium (such as marked hypertrophy in our case), bone or intra-articular tissue must be sent for histological analysis for timely diagnosis. Tissue biopsy can lead to definitive diagnosis.

Conclusion

Our report illustrates a very rare case of a 74-year-old woman diagnosed with primary synovial DLBCL presenting as mechanical loosening of internal knee prosthetic joint. It is crucial to be aware of atypical presentation of DLBCL because it can lead to timely diagnosis and prompt treatment of this life-threatening yet a curable condition.

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None to declare.

Financial Disclosure

None to declare.

Conflict of Interest

Each author declares that there is no conflict of interest regarding the publication of this paper.

Informed Consent

Informed consent was given by the patient.

Author Contributions

KA and NA drafted the manuscript and did literature review. ML contributed to the pathological section of the manuscript.

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