Case Report

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

Kavita Agrawala, Nirav Agrawal, Miles Levin

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-
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 resent 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 was hypertropied 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/µL with normal differential, hemoglobin 9.9 g/dL and platelets of 375 × 10³/µL. 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
| 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   | 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  | 1986             | 48/F    | Left knee                      | None                            | Fatigue, fever                                     | No                            | No                              | X-ray: non-calcified soft tissue mass in the suprapatellar bursa | Tan, firm, homogenous, friable | Malignant lymphoma of histiocytic type |
| Dorfman et al  | 1986             | 72/M    | Left knee                      | Rheumatoid arthritis, gout      | No                                                   | No                            | No                              | X-ray: marked narrowing of joint space, hypertrophic marginal lipping 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    | 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    | 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    | 1999             | 27/M    | Right knee                     | HIV                              | Weight loss                                         | No                            | No                              | X-ray: permeative pattern of femoral metaphysis, periosteal reaction and effusion. MRI: heterogenous marrow inflammation, hypertrophic synovial changes, patchy cortical destruction, distributed effusion | NR | DLBCL                          |
| Birlik et al   | 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     | 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     | 2006             | 33/M    | Right elbow                    | Hyperextension injury of right elbow | No                                                   | No                            | No                              | X-ray: no abnormality noted.       | Fleshy, tan                  | DLBCL                          |
| Chim et al     | 2006             | 66/M    | Left knee                      | Seronegative rheumatoid arthritis on methotrexate | No                                                   | No                            | No                              | US: heterogenous soft tissue mass lesion in left knee, predominantly in suprapatellar bursa and anterior joint compartment. | NR | DLBCL                          |
Loosening of Prosthetic Knee Joint

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 synovial 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.

Acknowledgments

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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