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Primary Lymphoma of Bone Diagnosed Following Total Hip Replacement Arthroplasty for Suspected Osteoarthritis

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= 국문초록 =

골관절염을 의심하여 완전 고관절 치환술 후 진단된 원발성 골 림프종 1예

울산대학교 의과대학 서울아산병원 병리과학교실, 이화여자대학교 의학전문대학원 병리과학교실*
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원발성 골 림프종은 주변의 림프절의 침윤과 관계없이 한 개의 골격을 침범하거나 혹은 내부 장기나 림프절의 침윤없이 여러 개의 골격들을 침범한다. 원발성 골 림프종의 방사선 소견은 매우 다양하고 비 특이적이며, 대개 병리학적 검사 이전에는 진단되지 않는다. 관절을 침범하는 경우에는 골관절염과 유사하게 표현될 수 있다. 원발성 골 림프종은 뼈를 침범하는 다른 악성 종양에 비해 양호한 생존율을 보이므로, 적합한 치료를 위해 정확하고 빠른 진단이 매우 시급하다. 여기서 우리는 일년 동안 지속된 고관절 통증을 주소로 내원하여 방사선적으로 골관절염 의심 하에 전 고관절 치환 관절성형술 후에 진단된 원발성 골 림프종 1예를 문헌고찰과 함께 보고한다. 병리학적 검사결과 미만성 대세포성 B-세포 림프종으로 진단되었다. 본 증례는 비 특이적인 방사선 소견과 임상 특성 때문에 원발성 골 림프종을 먼저 의심하기가 어렵다는 점과 진단에 있어 수술 중 자문의 중요성을 강조하는 증례이다.

중심 단어 : 비-호지킨 림프종 · 뼈 · 전 고관절 치환 관절성형술.

Introduction

Localized involvement of bone accompanying malignant lymphoma is unusual, constituting 7% of all bone malignancies and 5% of all extranodal lymphomas[1]. Primary bone lymphoma (PBL) is defined as a localized single bone tumor regardless of regional lymph node involvement or multiple bone tumors without visceral or lymph node involvement[1]. Although most PBLs are non-Hodgkin's lymphomas (NHLs), fewer than 1% of NHLs are PBLs[2]. Diffuse large B-cell lymphoma (DLBCL) accounts for 92% of primary NHL of bone, followed by diffuse follicle center cell lymphoma (3%), anaplastic large cell lymphoma (3%), and immunocytomas (2%)[3]. PBL has an excellent prognosis, with significantly better survival than most other primary bone malignancies[1].

PBL tends to affect adults, with a mean age of 46.1 years, and there is male predominance[4][5]. Patients most often present with bone pain, sometimes with accompa-

nying soft tissue mass[4]. Systemic symptoms are rare[4], and long bones are more often affected than flat bones, especially the diametaphysis of the distal femur[5]. Radiographic appearances are variable and non-specific[4-6]. Plain radiographs may show extensive, poorly delineated lesions, with variable sclerosis, moth-eaten, or lytic features accompanied by cortical destruction and soft tissue extension. However, radiographs may also show features that are subtle or entirely normal, with the disease revealed only by magnetic resonance imaging (MRI), computed tomography (CT), or bone scans[4][5].

Here we describe a case of unsuspected PBL in a 49-year-old woman who underwent an elective total hip replacement arthroplasty (THRA) for osteoarthritis. The case demonstrates the non-specific radiographic and clinical features of PBL, which may lead to incorrect diagnosis and management, and stresses the importance of intraoperative consultation in cases of PBL.

Case

A 49-year-old woman was referred for left hip pain with leg edema of one year's duration. She denied having any constitutional symptoms, including night sweats, unexplained fevers, or significant weight loss. Past medical and family histories were unremarkable. Laboratory data were within normal limits, except for increased C-reactive protein (CRP), 9.4mg/dL, and increased ESR, 99mm/hr. Conventional radiograph (Fig. 1A) of the left hip joint showed changes suggestive of secondary osteoarthritis with severely decreased joint space, osteolysis, collapse of the femur head, and joint effusion. Septic hip was suspected, with a possibility of developmental hip dysplasia as the underlying cause of osteoarthritis. She also showed flexion deformity of both knee joints and degenerative changes on lumbar spine with scoliosis. CT of her lower extremities (Fig. 1B) showed a destructive left hip joint and soft tissue swelling along the proximal left superficial femoral artery. MRI of her left hip (Fig. 1C) also showed similar changes resulting from secondary osteoarthritis in her hip joint and left acetabulum, accompanied by changes suggestive of inflammation in the adjacent pelvic soft tissue, left inguinal area, and left proximal femur. Suspected sequestra were also seen in the left proximal femur. Non-enhancing area in the left ischium was suggestive of bone infarction or intraosseous abscess. She was diagnosed with secondary osteoarthritis and underwent THRA for the left hip joint. During surgery, her acetabulum showed degenerative changes in articular cartilage with a deformed and collapsed femoral head. There was no pus, and no definite evidence of chronic osteomyelitis inside the acetabulum. An intraoperative frozen specimen from the medulla of the femoral neck was suggestive of a malignant neoplasm with extensive necrosis and crushing artifact.

Grossly, the femoral neck was markedly deformed and showed an ill-defined irregular firm mass almost entirely replacing the medulla of the femoral head (Fig. 2). The cut surface of the mass was whitish yellow, fibrotic, and of the consistency of fish flesh, but without hemorrhage or necrosis. The cartilaginous portion of the femoral head was eburnated. Microscopically, there was diffuse infil-

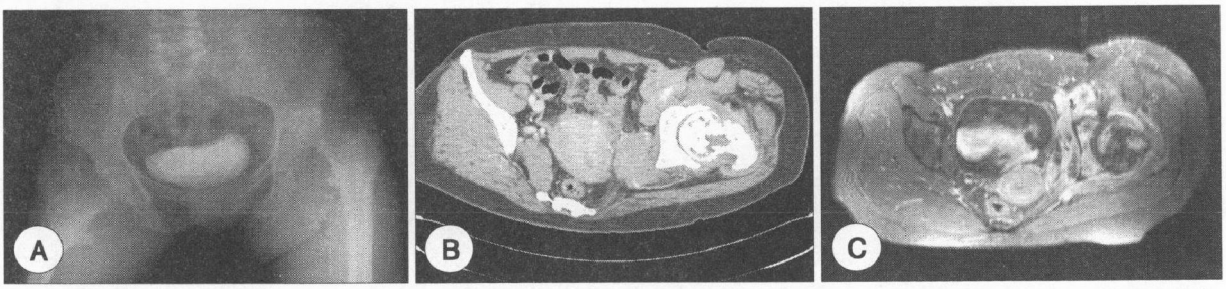

Fig. 1. Radiologic findings. A : Conventional radiograph of the left hip joint showed features of secondary osteoarthritis, including severely decreased joint space, osteolysis, collapse of the femur head, and joint effusion. B : Computed tomography of the lower extremities showed a destructive left hip joint and soft tissue swelling. C : Magnetic resonance imaging of the left hip revealed similar changes resulting from secondary osteoarthritis in the hip joint and left acetabulum accompanied by changes suggestive of inflammation in the adjacent pelvic soft tissue.

tration of atypical large lymphocytes through the medullary bone, marrow fat, and soft tissue into the highly sclerotic stroma (Fig. 3A). Fibrous stroma forced tumor cells to assume the histologic features of spindle cell sarcoma in some areas (Fig. 3B) or metastatic carcinoma in other areas (Fig. 3C). Most tumor cells showed oval to round, vesicular nuclei, fine chromatin, and 2−4 nucleoli and were sometimes of multilobated shape, suggestive of a centroblastic variant (Fig. 3D). These cells were mixed with CD3-positive non-neoplastic small lymphocytes. The tumor cell cytoplasm was mostly scanty and amphophilic. The tumor cells were immunopositive for CD20 (Fig. 4A), CD10 (Fig. 4B) and bcl6 (Fig. 4C), but negative for cytokeratin, indicative of a germinal center stage of B-cell differentiation. This lesion was diagnosed as DLBCL of centroblastic type. The bony trabeculae in the medulla were irregularly thickened or thinned with fractures.

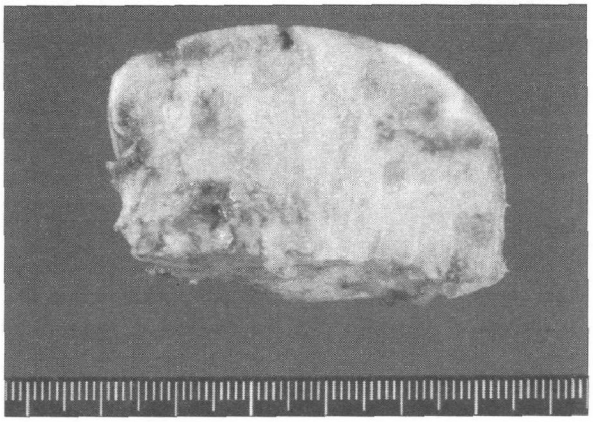

Fig. 2. Macroscopic findings. Total hip replacement arthroplasty specimen showed an ill-defined irregular firm mass almost entirely replacing the medulla of the femoral head.

The staging work-up included a bone series, abdominal ultrasound, bone scan, and post operative CT of the abdomen and pelvis, all of which showed no evidence of other lesions. The level of bone alkaline phosphatase was 26.1U/L, which was normal for a woman older than 45 years. Whole body positron emission tomography (PET) using 18-F FDG showed an irregular hypermeta-

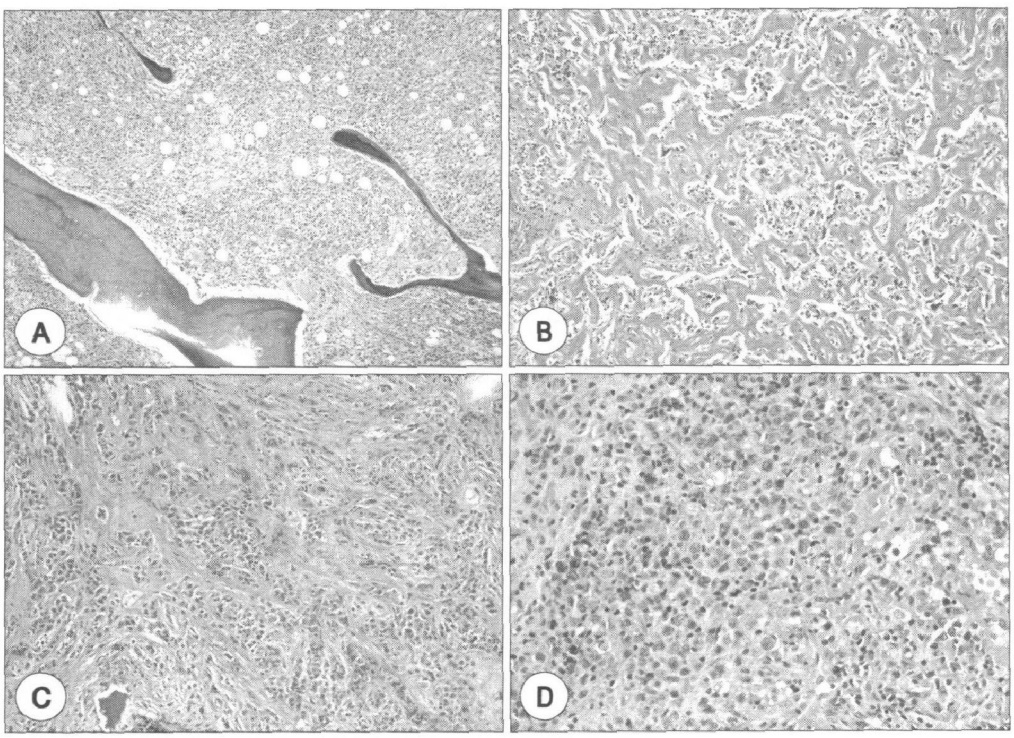

Fig. 3. Microscopic findings. A : Diffuse infiltration of atypical large lymphocytes was observed through the medullary bone and marrow fat. B, C : Fibrous stroma forced the tumor cells to assume histologic features of spindle cell sarcoma in some areas (B) or metastatic carcinoma in other areas (C). D : Most tumor cells showed oval to round, vesicular nuclei, fine chromatin, 2−4 nucleoli and sometimes multilobated shape, suggesting a centroblastic variant.

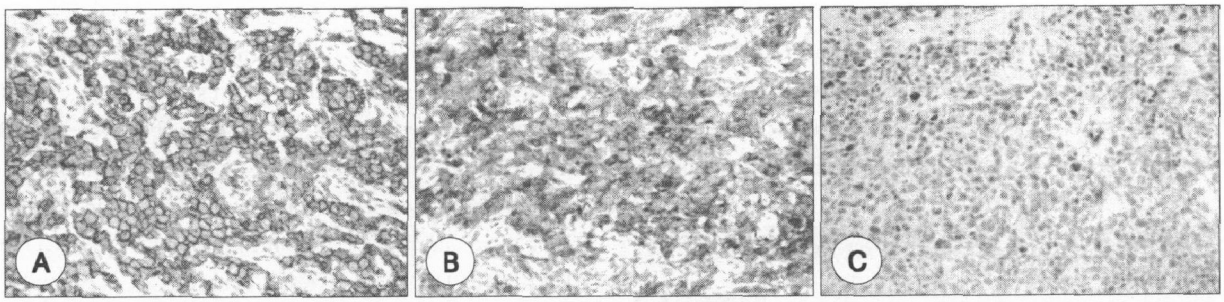

Fig. 4. Immunophenotype of the tumor cells. A-C : Tumor cells showed positivity for CD20(A), CD10(B) and bcl-6 (C) (immunoperoxidase, ×400).

bolic lesion around the femoral and acetabular components extending into the left inguinal area and left pelvic wall. The left externaliliac lymph node was enlarged with hypermetabolic activity. Bone marrow aspiration and biopsy showed no evidence of lymphoma involvement. The patient received the first of six chemotherapy cycles, consisting of cyclophosphamide, hydroxydaunomycin, vincristine, and prednisone (CHOP), followed by consolidation radiotherapy with involved field irradiation (50.4Gy). She is doing well 8 months after THRA.

Discussion

The patient described here is the eighth reported case of NHL discovered during routine pathological examination of elective THRA specimens performed for suspected osteoarthritis[7-10]. Previous cases included a low-grade follicular lymphoma[7], a large cell lymphoma[8], two cases of well-differentiated lymphocytic lymphoma[9], and three cases of low-grade B-cell NHL[10]. The rates of discrepancy between clinical diagnoses and diagnoses based on routine pathologic examinations after elective THRA are usually low, and the cessation of the latter may be cost effective[7]. However, the present case and previous unexpected cases of NHL in elective THRA specimens[7-10] suggest the importance of thorough pathologic examination of all specimens obtained during routine elective orthopedic surgery because they can lead to different postoperative treatments.

The present case demonstrates the difficulties involved in diagnosing PBL. First, there was no indication of malignancy during clinical, laboratory, and radiographic evaluations. Second, extensive necrosis and crushing artifact in the frozen specimen hindered the specific diagnosis of PBL at the time of intraoperative consultation. Crushing artifacts during fine needle aspiration and core biopsies may also cause lymphoma cells to appear as basophilic DNA smears, making open biopsies preferable, if technically possible. Spindle shaped tumor cells in thick sclerotic stroma may be confused with a sarcoma. In older patients, large-cell lymphomas can be confused with metastatic carcinomas.

Radiographic findings of PBL are nonspecific and variable[2)5)6)]. On CT, they can appear as soft tissue masses, with cortical destruction, marrow involvement, and even sequestration, but these findings are also nonspecific and poorly reflect the metabolic or functional aspects of the disease[2]. PBL may show an almost normal appearance on plain radiographs[2)5)]. MRI may be a more sensitive tool for assessing the extent of PBL, with superior illustration of the bone texture, bone marrow, and soft tissue[2)5)]. T1-weighted images show a low signal intensity, which better defines the extent of PBL[2)5)]. PBL should be suspected when a pattern of extensive marrow involvement and soft tissue mass is present on CT or MRI with minimal plain radiographic findings[2)5)]. MRI, which has high sensitivity (90%) and 67Ga scintigraphy, which has a high specificity (93%) can be used together to monitor the response to therapy[11]. PET may be helpful in disease assessment, both at staging and at follow up for detecting residual disease after treatment[12].

Prognosis is excellent for localized PBL[1)13)]. Recent studies indicate that advanced age (greater than 60 years)[13], immunoblastic histology[3], and the absence of CD10 expression on the tumor cells[13] are associated with less favorable prognosis. In contrast, centroblastic histology, the germinal center stage of B-cell differentiation, with positive immunoreactivity for bcl-6 and CD10, and the

limited extent of the tumor, as in our case, suggest a more favorable course. Therapy for localized PBL involves combined chemotherapy (e.g. the CHOP regimen), with or without involved-field radiotherapy of 45−50Gy[14)15)], or primary radiotherapy alone[14)]. Because of a high rate of distant relapse, combined-modality therapy, including anthracycline-based chemotherapy and radiation, was shown to be superior to chemotherapy or radiation alone[14)15)]. In poor responders and early relapsers, high dose chemotherapy with autologous stem cell transplantation may be an option.

Summary

we have presented a case of unsuspected PBL in a patient who underwent THRA for suspected osteoarthritis. Our findings emphasize the importance of pre- or intraoperative consultation in cases of PBL and thorough pathologic examination of all specimens obtained during routine, elective orthopedic surgeries.

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