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# Possible Clinical Significance of Serum Soluble Interleukin-2 Receptor Level in Primary Bone Lymphoma: Two Case Reports

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## Key Words

Primary bone lymphoma · PBL · Soluble interleukin-2 receptor · sIL-2R · Tumor marker

## Abstract

In two patients with primary bone lymphoma (PBL) treated in our clinic, serum levels of soluble interleukin-2 receptor (sIL-2R) reflected the clinical course. In both cases, sIL-2R levels were high before treatment and normalized with the therapeutic effects of chemotherapy, coinciding with the changes in lactate dehydrogenase levels and radiographic findings. Adding to the recently reported results of the diagnostic ability of sIL-2R in PBL, our case study highlights the clinical significance of serum sIL-2R levels as a tumor marker in PBL cases.

## Introduction

Primary bone lymphoma (PBL) is an extremely rare malignant bone tumor. Patients with bone lesions usually visit rheumatology, orthopedic, or primary care clinics. Such clinicians should be reminded of the possibility of PBL when suspecting malignant bone tumors. Radiological diagnosis of PBL is often difficult because of its non-specific findings. Therefore, laboratory findings that help differentiate PBL from other primary bone tumors can play an important role. Serum soluble interleukin-2 receptor (sIL-2R) levels in patients with common primary malignant bone tumors except PBL were reported not to be significantly elevated compared to those in healthy subjects in previous reports [1, 2]. Recently, Akahane et al. [3] reported sIL-2R levels being significantly higher in PBL than in other malignant bone tumors and benign bone tumors/tumor-like lesions

and commented that the sIL-2R level is a valuable marker for diagnosing PBL. However, we were not able to find reports discussing the changes in serum sIL-2R levels during the clinical course in PBL. In this report, we present two PBL cases who had high serum levels of sIL-2R on presentation and normalized serum levels after the treatments. We show the clinical course of the two PBL patients and discuss the possible clinical significance of sIL-2R levels in PBL.

## Case Report

### Case 1

In May 2007 a 52-year-old man visited the National Hospital Organization Tokyo Medical Center (NTMC) with left buttock pain which had lasted for 6 months. X-ray and computed tomography (CT) tests were performed. The radiograph showed osteosclerotic and osteolytic changes in the wing of the ileum and the acetabulum (fig. 1a). A pathological fracture was observed in the acetabular roof. On CT imaging, we found expanded soft tissue around the ileum (fig. 1b). Bone scintigraphy showed highly increased accumulation of <sup>99m</sup>Tc-HMDP in the left acetabulum and indicated sole bone lesion. A whole-body CT scan and gallium scan revealed no evidence of visceral or lymph node involvement. From these results, a solitary primary malignant bone tumor was suspected.

### Case 2

In August 2006, a 67-year-old man with a 1-month history of right hip pain visited the NTMC due to difficulty in walking. The radiograph showed osteolytic change in the acetabulum (fig. 1c). CT imaging showed moth-eaten pattern of destruction of the anterior part of the acetabulum and expanded soft tissue (fig. 1d). A whole-body CT scan, and bone and gallium scans were carried out. The scans revealed a solitary bone lesion. Thus, primary bone tumor of the right acetabular roof was suspected.

In both cases, laboratory tests at hospitalization showed high levels of serum sIL-2R [case 1: 2,880 U/ml, case 2: 1,140 U/ml (reference value: 188–570 U/ml)] and slightly elevated levels of lactate dehydrogenase (LDH) [case 1: 263 U/l, case 2: 241 U/l (reference value: approx. 119–229 U/l)]. The open biopsies of the tumors demonstrated proliferation of abnormal lymphoid cells. Immunohistochemistry revealed positive staining for CD20 and leukocyte common antigen, and was negative for CD3. Thus, both cases were diagnosed as PBL (diffuse large B-cell lymphoma). According to the Ann Arbor staging system, both localized bone lesions were regarded as stage I. The chemotherapy [R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone); case 1: 8 courses, case 2: 6 courses] was performed under the supervision of the hematology department.

In case 1, osteosclerotic changes increased and the pathological fracture line became unclear in radiographic images after the chemotherapy (fig. 2a). New bone formation and increased osteosclerosis around the acetabulum as well as intrapelvic migration of the femur head were recognized in case 2 (fig. 2b). In both cases, soft tissue mass around the affected bone lesions was obviously decreased after treatment, as seen on CT images (fig. 2c, d). These radiological findings indicated the regression of pelvic bone lesions after treatment. Serum sIL-2R levels and LDH levels were normalized in both cases (fig. 3a, b), and linked with radiological therapeutic response of the affected bones.

## Discussion

PBL is an extremely rare bone tumor; its frequency is considered to be about 3–7% of all primary malignant bone tumors, approximately 3% of all extranodal lymphomas, and less than 1% of all malignant lymphomas [4–7]. According to WHO classification, PBL can be categorized into two groups as follows: group 1, lymphoma involving a single skeletal site, with or without regional lymph-node involvement, and group 2, lymphoma

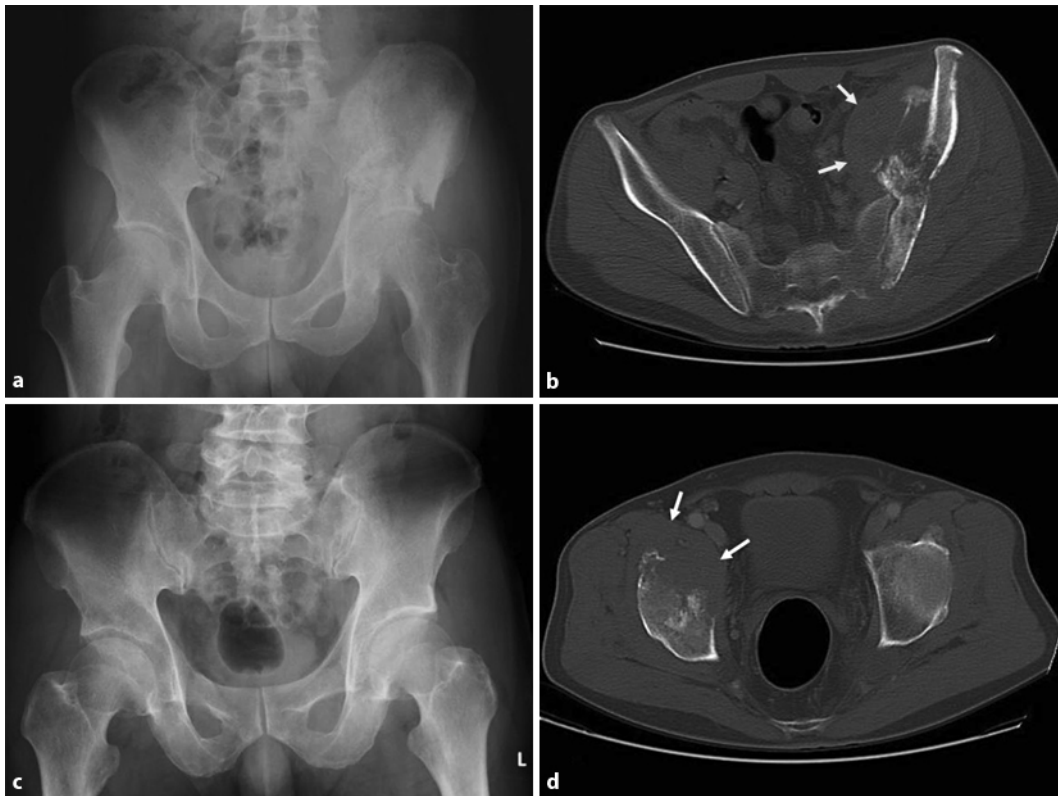
involving multiple bones, without visceral or lymph-node involvement [6]. Recently, several clinical reviews applying these criteria of PBL have been published [4, 5, 7–12]. There was a slight male predominance and a tendency for senior adults to be affected more often, although PBL can occur at any age. The pelvis or proximal part of the femur is the common site of the tumor. Most cases of PBL are reported to be non-Hodgkin's diffuse large B-cell lymphomas. Stage of disease, age, serum LDH levels, response to chemotherapy, and the use of combined modality therapy are considered to be prognostic factors in PBL. Radiographs and CT images of PBL usually present non-specific findings, mostly various patterns of osteolysis and osteosclerosis coexisting in the bone. As a result, radiological differential diagnosis of PBL from other types of primary bone tumors such as Ewing's sarcoma, osteogenic sarcoma, and chondrosarcoma is often difficult. Therefore, laboratory findings that help differentiate PBL from other common bone tumors are important.

So far, the significance of measuring sIL-2R levels has been rarely reported in clinical reviews of PBL [4, 5, 7–12]. In other primary malignant bone tumors including osteosarcoma, Ewing's sarcoma, chondrosarcoma, and malignant giant cell tumor, median serum levels of sIL-2R are reported not to be significantly elevated compared with those of healthy controls [1, 2]. Recently, Akahane et al. [3] reported that the serum sIL-2R level is valuable for differentiating PBL from other osteolytic malignancies or benign bone lesions that resemble malignant tumor radiographically.

In our two PBL cases, the reduced sIL-2R levels after R-CHOP therapy were linked with the reduction of the tumor size and the osteosclerotic changes in the bone lesions. Moreover, the changes in sIL-2R levels were similar to those in LDH levels known as a prognostic factor of PBL [8]. The fact that sIL-2R levels were associated with the clinical course of PBL means such measurements play an important role in the disease monitoring. Adding to the recently reported results of the diagnostic significance of sIL-2R in PBL, our case study tentatively indicates the clinical significance of sIL-2R levels as a tumor marker in PBL cases.

#### Disclosure Statement

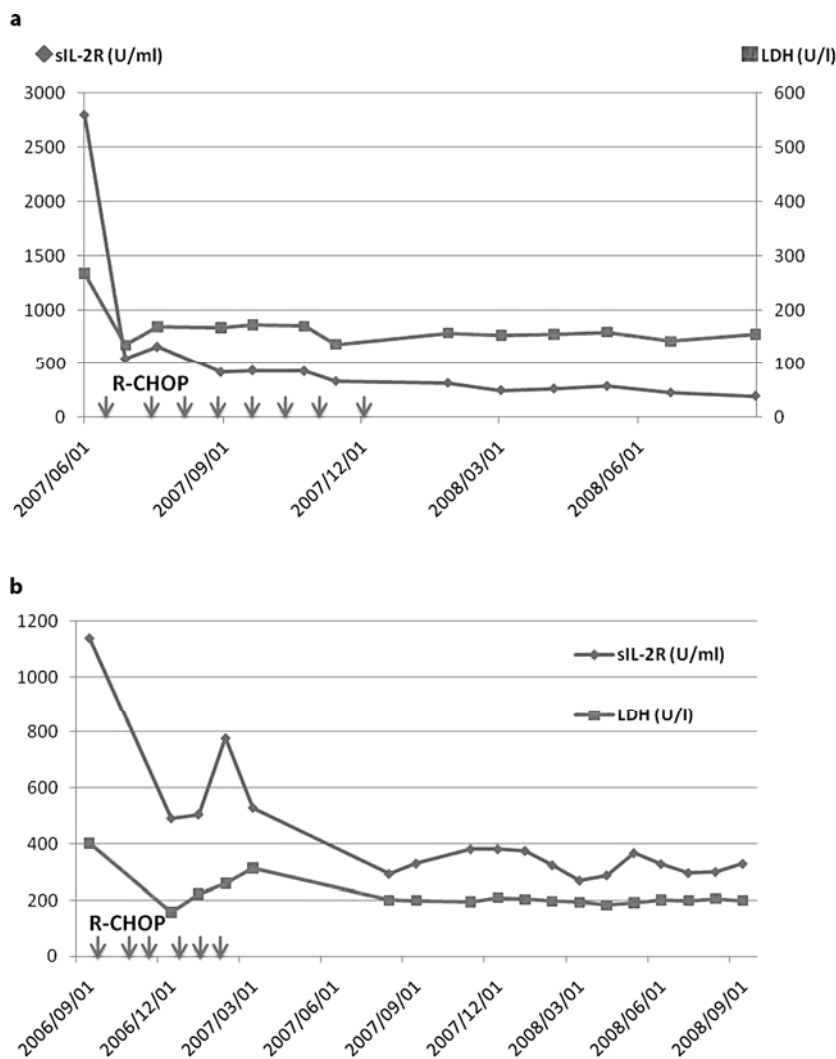
All authors have no conflict of interest to declare.



**Fig. 1.** Radiographs and CT images at hospitalization. **a** Radiograph from June 2007. Osteosclerotic and osteolytic changes in the left iliac wing and a pathological fracture of the left acetabulum were observed in case 1. **b** CT imaging from June 2007. Expanded soft tissue around the left ileum can be recognized (arrows) in case 1. **c** In September 2006, radiography showed an osteolytic change in the right acetabulum in case 2. **d** CT image from September 2006 shows a moth-eaten pattern of destruction of the anterior part of the right acetabulum and expanded soft tissue (arrows) in case 2.



**Fig. 2.** Radiographs and CT images after chemotherapy (R-CHOP). **a** In March 2008, radiography showed an increased osteosclerotic change and an obscure fracture line in case 1. **b** In February 2007, radiography showed new bone formation and increased osteosclerosis around the acetabulum as well as intrapelvic migration of the femur head in case 2. **c** In March 2008, CT imaging revealed increased osteosclerosis and the necrotic soft tissue mass around the affected bone lesion (arrows) in case 1. **d** In February 2007, CT imaging revealed the necrotic soft tissue mass around the affected bone lesion (arrows) in case 2.



**Fig. 3.** Serum sIL-2R levels of our two PBL cases normalized after R-CHOP therapy. **a** Case 1, **b** case 2.

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