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A Case of Precursor B-cell Acute Lymphoblastic Leukemia Occurred with Rapid Hip Bone Destruction and Femoral Neck Fracture

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Abstract

Background: Precursor B-cell lymphoblastic lymphoma is a rare subtype of acute lymphoblastic lymphoma and sometimes presents as lytic bone lesions. Diagnosis and treatment of lytic bone lesions are always challenging. This is a rare case of delayed leukemic change of precursor B-cell acute lymphoblastic lymphoma presented with a rapid hip bone destruction.

Case presentation: A 12-year-old Japanese girl presented with progressive left hip pain, and bone destruction of her left hip two months after the onset of symptoms. She had no past medical or family history of malignancy and had no genetic abnormality. Radiograph and MRI examination showed bone destruction and osteolytic lesions in her left femoral neck and pelvis. Blast cells were not found in our initial examination of the peripheral blood and aspirated bone marrow cells. The case was finally diagnosed as Precursor B-cell lymphoblastic lymphoma as the results of bone biopsy, and blast cells were then detected after preforming multiple bone marrow aspirations. She also had pathological femoral neck fracture, but after treatment regimen by chemotherapy, her osteolytic lesions cured with obtainment of femoral neck fusion. She could walk at the final period.

Conclusion: This case highlights the importance of early diagnosis of this disease for greater curing rates. Diagnosis of Precursor B-cell lymphoblastic lymphoma was finally made based on the results of biopsy of tissues because of the delayed appearance of leukemic changes. Orthopaedic surgeons should be aware of Precursor B-cell lymphoblastic lymphoma, when making diagnosis of patients exhibiting a rapid hip bone destruction.

Keywords: Femoral neck fracture; Lymphoma/leukemia; Osteoblastic bone lesion; Pathological fracture; Precursor B-cell lymphoblastic lymphoma (PBLBL); Primary bone lymphoma

Abbreviations: ALP: Alkaline Phosphatase; CRP: C-Reactive Protein; CT: Computed Tomography; ESR: Erythrocyte Sedimentation Rate; LDH: Lactate Dehydrogenase; MRI: Magnetic Resonance Imaging; N/C: Nucleus/Cytoplasm; NSAIDs: Nonsteroidal Anti-Inflammatory Drugs; PBLBL: Precursor B Cell Lymphoblastic Leukemia; SIL2R: Soluble Interleukin-2 Receptor; WBC: White Blood Cells.

Introduction

Precursor B-cell lymphoblastic lymphoma (PBLBL) is a subtype of acute lymphoblastic lymphoma that occurs more commonly in children than in adults. PBLBL constitutes less than ten percent of cases of lymphoblastic lymphoma, and often manifests in the skin and lymph nodes and soft tissue [1]. Common clinical symptoms include fatigue, spontaneous bleeding, frequent infections, fever, night sweats and body-weight loss [2]. Thrombocytopenia, neutropenia and other signs of bone marrow failure may present in patient due to the replacement of bone marrow by intensive lymphoblasts. This type of lymphoma rarely presents as a primary solitary lytic bone lesion, which accounts for seven percent of all malignant bone tumors [3]. Patients often exhibit non-specific symptoms including bone pain, arthritis, and limping, without lymph nodal mass or bone marrow disorders, which lead to a delay of diagnosis [4,5]. In this report, we describe a case of a precursor B-cell acute lymphoblastic lymphoma present in a rapid hip bone destruction. Following the treatment regimen by chemotherapy, the patient cured and was able to walk at the final follow up period.

Case Presentation

A 12-year-old Japanese girl presented to the proximity orthopaedic hospital with a two-week history of left hip pain after marathon practice in August of 2013. She had no past medical or family history of malignancy and had no genetic abnormality. In her first visit to hospital, plain radiograph and plain magnetic resonance imaging (MRI) examinations showed no abnormalities and consequently she was diagnosed with irritable hip. Oral treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) was prescribed for pain relief. In beginning of October, her left hip pain relapsed and gradually increased despite NSAIDs treatment. She had showed mild fever in October and November. Thereafter, she revisited the hospital, and radiography examination showed bone destruction with apparent osteolytic lesion in her left acetabulum and femur head. On Plain MRI, inhomogeneous signal change (T1-weighted imaging: low-signal, T2-weighted imaging: low- or iso-signal) with mild hip effusion was found. Immediately, she was introduced to our institution as suspected case of arthritis purulenta of the hip.

In our physical examination, there was no swelling or local heat of the left hip, but tenderness was noted in the left Scarpa triangle and greater trochanter. Her left hip revealed a limited range of motion (Rt. / Lt.), with flexion of 120°/100°, extension of 0°/0°, abduction of 40°/40°, adduction of 30°/30°, external rotation of 60°/40°, internal rotation of 30°/20°. Patrick test was positive only in the left side with no leg discrepancy. Blood test showed elevations of erythrocyte sedimentation rate (ESR: 69 mm/2 h), lactate dehydrogenase (LDH: 381 Unit/L), alkaline phosphatase (ALP: 461 Unit/L), C-reactive protein (CRP:

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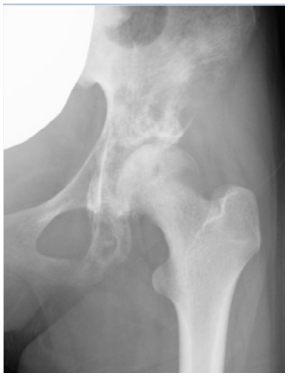

Figure 1: Plain radiograph performed in her first visit to our hospital, Left hip radiograph with bone destruction and osteolytic lesion (A-P view).

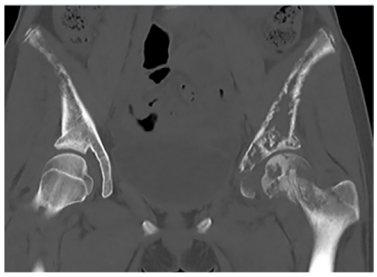

Figure 2: Plain pelvic CT scan performed in her first visit to our hospital, Plain pelvic CT showed bone destruction in left hip and both ilium (coronal view).

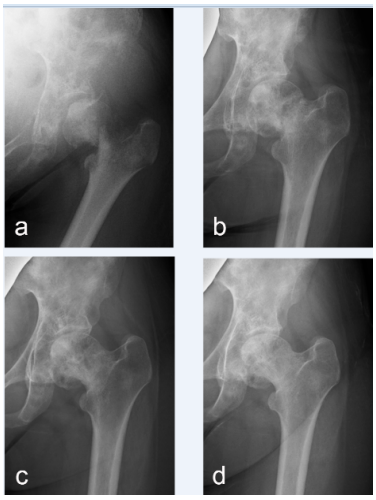

Figure 3: Dramatic changes in her left hip bone and femoral neck fusion after treatment. (a-d) Radiographic images. a: after a week of chemotherapy (On the 25th day from first visit). b: On the 160th day. c: On the 260th day. d: On the 342nd day (in out-patient clinic).

12.6 mg/L) and soluble interleukin-2 receptor (sIL2R: 875 U/ml). White blood cells (WBC: 7,900 cells/mm^2) and serum QuantiFERON test was negative. Radiograph and computed tomography (CT) scan showed bone destruction in left hip bone and bilateral ilium (Figures 1 and 2), and these lesions showed low signal in T1-weighted imaging and inhomogeneous enhancement on T2-weighted imaging in enhanced MRI. Abnormal accumulations of radiotracer at the same lesions were seen by bone scintigraphy. Contrast enhanced whole body CT scan showed no other enhanced lesions. Electrophoresis of protein was normal, and a chromosome composition was 46XX. Bone marrow aspiration was performed first from right posterior iliac crest and showed no blast proliferation. Bone biopsy from left sacrum showed atypical round circle cells proliferations which had high nucleus/cytoplasm (N/C) ratio with nucleolus. These cells were positive to PAX5, TdT, and CD79a; markers for precursor B cells and negative to CD99; a marker for T cells or primary bone tumor such as Ewing sarcoma. Finally, she was diagnosed as PBLBL. After bone biopsy, leukemic change of PBLBL was suspected because of signs of anemia and thrombocytopenia. Repeating bone marrow aspirations were performed from multiple sites and blast cells were detected from right tibia. Consequently, she was diagnosed as PBLBL with a delayed appearance of leukemic changes and she was admitted to systemic chemotherapy regimen.

After a week of chemotherapy (day 25th of her first visit to our hospital), left thigh swelling occurred with progressive osteolytic lesion and left femoral fracture as seen by radiograph (Figure 3a). Surgical intervention was impossible at this stage due to chemotherapy treatment and severe destruction in her hip bone. Therefore, we decided to continue chemotherapy and started conservative treatments including non-weight bearing and indirect traction. The osteolytic lesions and the fractures gradually became osteosclerotic, and on the day 260th of chemotherapy, the osteolytic hip lesions were dramatically improved, and the femoral neck was fused (Figures 3b-3d). Next, we started one thirds of partial weight bearing with use of 2.5 cm shoe lift. On the day 342nd, she was able to walk on full weight bearing with no pain and with no avascular necrosis.

Discussion

The occurrence of PBLBL as a primary bone tumor is rare and presents in less than five percent of all malignant bone tumors, mainly in femur and most frequently found in childhood. Prognosis is dependent on stage of disease and early treatment by an intensive lymphoma chemotherapy regimen is usually associated with high complete remission rate (95%-99%) and promising outcome (survival 60%-70%) [4]. However, diagnosis is usually difficult because of non-specific clinical symptoms, radiologic and pathologic features [5]. Clinical symptoms include bone pain, arthritis, and limping, with or without lymph nodal mass [6]. Radiography examination shows lytic (72%), mixed (25%) and blastic (3%) bone lesion [7]. Examining peripheral blood smears reveals the presence of both small and large lymphoblasts. Histopathological features include small to medium size tumor cells with scant cytoplasm, round, oval, or irregular nucleoli. Differential diagnosis based on the clinical signs may include hip arthritis, purulent hip arthritis, osteonecrosis of the femoral head, Legg-Calve-Perthes disease or slipped capital femoral epiphysis. Moreover, lymphoma/leukemia, osteosarcoma, Ewing's sarcoma, Langerhans cell histiocytosis or blastic metastasis should be also counted in differential diagnosis because patients may present similar radiographic features of PBLBL.

Our case presented with osteolytic lesions found in her left femoral neck of hip due to PBLBL. The patient firstly showed general signs of inflammation including persistent fever associated with an increase in the CRP. Bone marrow aspiration from right posterior iliac crest was performed and no blast cells were found at first. It is noteworthy to mention that our diagnosis of PBLBL was finally made based on the results of biopsy of tissues. Multiple bone marrow aspiration was required to confirm the diagnosis because of the delayed appearance of leukemic changes. Pathological examination of lesions revealed proliferation of atypical round circle cells with high N/C ratio, and the blast cells were derived from precursor B cells as evidenced by immunostaining.

Prompt initiation of chemotherapy is the first step for treatment of bone lesions in leukemia and most often leads to an improvement in pathological fractures of the femoral head and neck and neoplastic process [8]. However, failure of fracture fixation after initial treatment has been also reported. For instance, Isobe *et al.* reported a case of femoral neck fracture in a 5-year-old girl during chemotherapy for malignant lymphoma [9]. In that report, authors used conservative treatment of a months of hip casting followed by hip brace. Murakami et al. reported a case of 66-year-old woman with proximal femur fracture during chemotherapy of diffuse large B-cell lymphoma. Furthermore, she was conservatively treated by internal fixation after chemotherapy [10]. In these cases, patients were able to walk bearing full weight, and had favorable clinical results. Likewise, conservative treatment by chemotherapy was selected for our case, and finally bone fusion was obtained.

Conclusion

We reported the rare case presented with a rapid hip bone destruction associated with progression of PBLBL. Our case highlights the importance of considering malignancy in a rapid hip bone destruction for early diagnosis and treatment.

Declarations

Ethics Approval and Consent to Participate

This case report was produced in accordance with our institutional ethics policy.

Consent for Publication

Written informed consent was obtained from patient for publication of this case report and any accompanying images.

Availability of Data and Materials

This is a case report of a single patient, to protect privacy and respect confidentiality; none of the raw data has been made available in any public repository. The imaging studies and outpatient clinic records are retained as per normal procedure within the medical records of our institution.

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