Acute Sciatica: An Unusual Presentation of Extramedullary Relapse of Acute Lymphoblastic Leukemia

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Abstract
A 10-year-old boy who had been treated for acute lymphoblastic leukemia presented with persistent numbness of the left big toe and progressive pain of the ipsilateral lower leg. He had received allogeneic bone marrow transplantation 3 months after a testicular relapse. He was in hematologic remission at admission but as progressive swelling of his left leg continued, bone marrow relapse developed. A muscle biopsy revealed leukemic infiltrates in the surrounding muscles of the left sciatic nerve, and swelling of the nerve was found on a magnetic resonance imaging scan. His symptoms/signs subsided soon after reinduction chemotherapy. Unfortunately, he didn’t survive because of a fungal sepsis that developed during the neutropenic state. This case represents a rare neurologic complication of what is currently an uncommon presentation for relapse of acute lymphoblastic leukemia, with acute sciatica and without coexisting epidural or leptomeningeal leukemia.

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Key words: Acute lymphoblastic leukemia; Acute sciatica; Extramedullary relapse; Leukemic relapse

1. Introduction
Acute lymphoblastic leukemia (ALL) is the most common malignancy in children, and accounts for 25% of all childhood malignancies and 75% of childhood leukemia [1]. Although the introduce of multi-agent chemotherapy has markedly increased the survival of these patients, 10% to 30% still experienced a relapse; of which bone marrow, central nervous system, and testes were the most common sites [2]. Once the relapsed leukemia patients received an allogeneic bone marrow transplantation (allo-BMT), the frequency of extramedullary relapse increased.

Facial nerve palsy, Bell’s palsy, and neuralgia have been reported to be initial symptoms of leukemic relapse [3]. However, acute sciatica has not been previously described with the relapse of ALL. We present a 10-year-old boy with extramedullary relapse of ALL after allo-BMT from a matched unrelated donor, who suffered from this unusual symptom that indicated leukemic relapse.
swelling developed in 3 days. He visited our emergency department and was admitted for further evaluation.

On admission, physical examination showed swelling, tenderness, and local heat of the left leg without erythematous change. Range of motion of the lower extremities showed normal motion of his left side hip, knee, and ankle. Tenderness during knee extension and passive plantar dorsi flexion were found. Left leg distal pulsation was detectable and left inguinal area showed swelling and multiple lymphadenopathy. The findings of the neurological examination were compatible with acute sciatica, but the surrounding tissue swelling of his left leg was quite unusual; tumor infiltration or infection were considered and further image studies were arranged. Musculo-skeletal ultrasound and magnetic resonance imaging showed marked swelling and edematous change at the left sciatic nerve with surrounding lobulated soft tissue mass (Figure 1). Gallium scan tumor survey revealed diffuse Ga-67 uptake in the medio-posterior aspect of the left thigh, extending upward to the left inguinal region and left iliac chain.

The initial laboratory tests, including complete blood count, biochemistry studies, and cerebrospinal fluid cytology, showed no evidence of recurrence of leukemia. Bone marrow aspiration for chimerism study showed 98% donor’s type at admission, and the bone marrow smear revealed 7% of blasts, and we suspected leukemic relapse. To confirm the pathology of the soft tissue masses surrounding the left sciatic nerve, sono-guided core biopsy was performed. The results showed small round blue cells (Figure 2) positive for CD3, LCA, and TdT antigen, consistent with T-cell lymphoblast. Bone marrow chimerism study performed 10 days after admission revealed only 28% donor’s type; secondary graft loss and leukemic relapse were impressed.

The patient suffered from severe sharp pain of the left leg that couldn’t be relieved by nonsteroidal anti-inflammatory drugs, dextromethorphan, and morphine sulfate. When chemotherapy was commenced with prednisolone and high-dose cytarabine, his left thigh swelling and tenderness improved dramatically with obvious leg circumference decrease in 3 days. The symptoms and signs gradually resolved in 1 week, but drop foot and muscular atrophy were found because of severe sciatic nerve damage.

Subsequently, pancytopenia with neutropenic fever developed and persisted for 4 weeks, and multiple antibiotics were prescribed during the period. *Candida tropicalis* was cultured from blood, urine and stool 10 days after the fever, which was treated by amphotericin B, and liposomal amphotericin B then shifted to voriconazole and itraconazole because of persistent fever. Unfortunately, his condition deteriorated and he finally died from cardiopulmonary failure.

3. Discussion

Peripheral nerve involvement is rare for pediatric ALL patients. The most commonly seen neurological involvements are cranial nerves with otolaryngologic manifestation, which may be due to the leukemia infiltration of the meninges [5]. Sudden onset of facial nerve paralysis has been described as a presentation of ALL in a pediatric patient [6]. Bell’s palsy had also been diagnosed with ALL by Ozcakar et al [7]. “Sanctuary sites” have been proposed for those protected from systemic chemotherapy by biological blood barriers (eg, central nervous system) or other distinct growth conditions (eg, lower temperature) [8].

Our patient had an extramedullary relapse with leukemic cells that infiltrated along the sciatic nerve, which has not been described in the literature. The initial symptom of the relapse was numbness of the left big toe, which was regarded as peripheral neuropathy. It was not considered a pathologic change until tenderness and progressive swelling of the leg developed. Compartment syndrome and infections were ruled out after further investigations. The possibility of leukemic relapse or posttransplantation lymphoproliferative disease required further tissue proof to make a final conclusion.

![Figure 1. Magnetic resonance image of legs; longitudinal (A) and transverse section (B). Postcontrast marginal enhancement was noted from the left of ischial tuberosity downward extension to left thigh in T2 weight image of magnetic resonance imaging. Generalized soft-tissue edema of skin, and subcutaneous layer and fascia of left thigh were found.](image1)

![Figure 2. Muscle biopsy of the patient. Under hematoxylin and eosin stain, the specimen shows massive lymphocyte infiltration within muscle tissue.](image2)