CASE REPORT

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A neuroblastoma case presenting with pathologic femur fracture

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Neuroblastoma is the most common extracranial solid tumor of childhood which should be considered in the differential diagnosis of bone metastases and resultant pathological fractures, especially in children under 5 years old. We present an 11-month-old girl who presented with a pathological femur fracture and was diagnosed with metastatic neuroblastoma.

Key words: Extracranial tumor; neuroblastoma; pathological fracture.

Neuroblastoma originates from the primordial nerve cells in the adrenal medulla and sympathetic ganglions. The most common extracranial solid tumor in childhood, neuroblastoma accounts for 8 to 10% of all childhood carcinomas.[1,2] The boy to girl ratio is 1:1 and 36% of patients are under the age of 1 and 89% under the age of 5 when diagnosed.[1-3]

As the tumor shows an abdominal localization at a rate of 65 to 70%,[4] the most common presentation is abdominal distention and pain. Metastatic or late-diagnosed cases of advanced stage may be directed to orthopaedic clinics for consultation purposes due to bone involvement.

We report a patient who presented with a pathological femur fracture and was diagnosed with metastatic neuroblastoma and treated by the oncology clinic.

Case report

An 11-month-old girl was brought to the emergency orthopaedic clinic with swelling in the right leg, discomfort and high fever for two days. At physical examination, there was swelling and warmth in the right distal femur and severe pain with knee movements. There was no history of trauma. The family reported swelling and bruising around their child's eye for one week (Fig. 1). Direct radiographs showed periosteal reaction and radio-opaque lesions filling the right femur medulla up to the proximal end and destruction in the femur cortex (Figs. 2 and 3). The radiological view suggested a pathological fracture and a plaster brace was applied.

Laboratory results were as follows; white blood cells 18,300/µl, hemoglobin 6.9 g/dl, hematocrit 22.2%, platelets 264,000/µl, CRP 41 mg/l, and sedimentation rate 35 mm/hour. The patient's axillary temperature was 38.5 ºC.

The patient was admitted for further investigation. In differential diagnosis, osteomyelitis was considered due to increases in acute phase reactants and osteosar-

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coma and Ewing's sarcoma due to periosteal reaction. The peripheral smear revealed hypochromic anemia.

Under fluoroscopic control, tru-cut biopsy was performed from the pathological fracture line in the distal femur. Afterwards, an above knee plaster cast was applied. Gram staining did not reveal any microorganism and the cultures remained sterile. The patient was started on prophylactic antibiotic treatment.

Cranial magnetic resonance imaging (MRI) was performed for the mass lesion in the eye found during ophthalmology consultation. Contrast-enhanced MRI images of the bone lesions were consistent with bone metastasis (Fig. 4). Anterior displacement of the globe due to the involvement of the right orbital roof was particularly remarkable (Fig. 5).

The histopathological examination showed small blue round tumor cells suggesting childhood tumors in the differential diagnosis (Fig. 6). Abdominal MRI examination revealed a heterogeneous mass of 68×59 mm with lobulated contour in the left retroperitoneal area, enlargement in the lymph nodes, the largest of which had a 26-mm diameter in the left paraaortic interaortocaval area and bilateral iliac lymph node packages, forming a mass of 67×32 mm diameter on the right side (Fig. 7). Pathological activity was observed in the abdomen, left adrenal location, right femur diaphysis and right maxillary bone's superior in high-sensitivity metaiodobenzylguanidine (MIBG) scintigraphy (Fig. 8).[5,6]

Fig. 1. Cyanosis around the eye (raccoon eye). [Color figure can be viewed in the online issue, which is available at www.aott.org.tr]

The patient was diagnosed with Stage 4 neuroblastoma and transferred to the oncology and pediatric surgery clinics for chemotherapy and surgical treatment. The patient received 12 courses of chemothera-

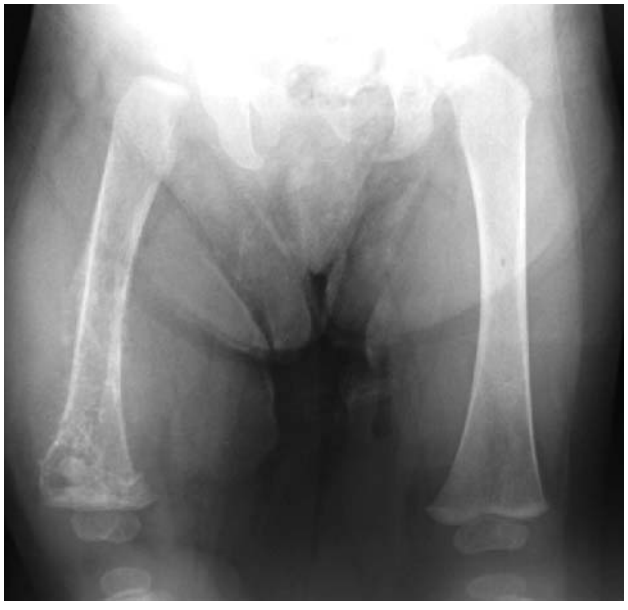

Fig. 2. Anteroposterior radiographs of both femurs.

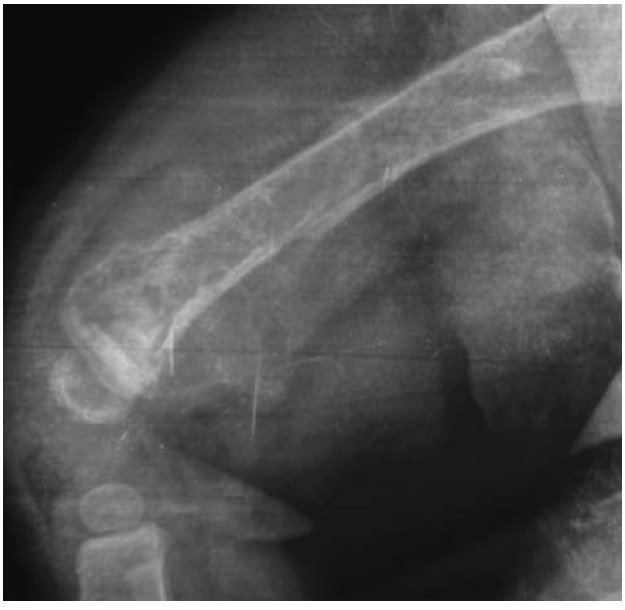

Fig. 3. Lateral radiograph of the right femur.

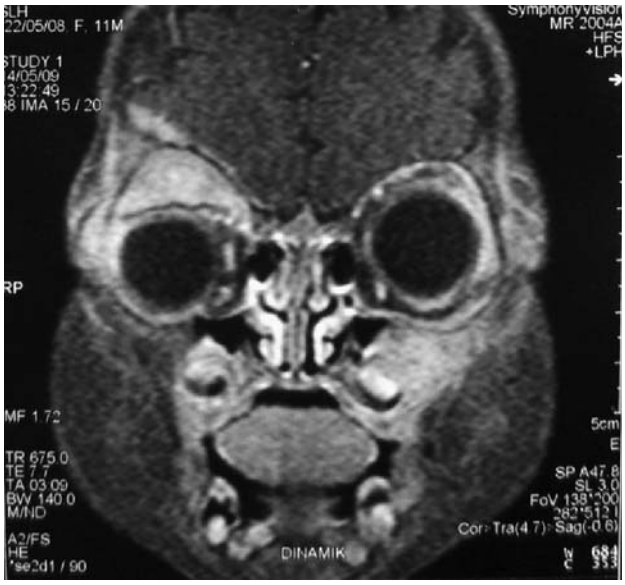

Fig. 4. Expanded mass to the superior of the right globe.

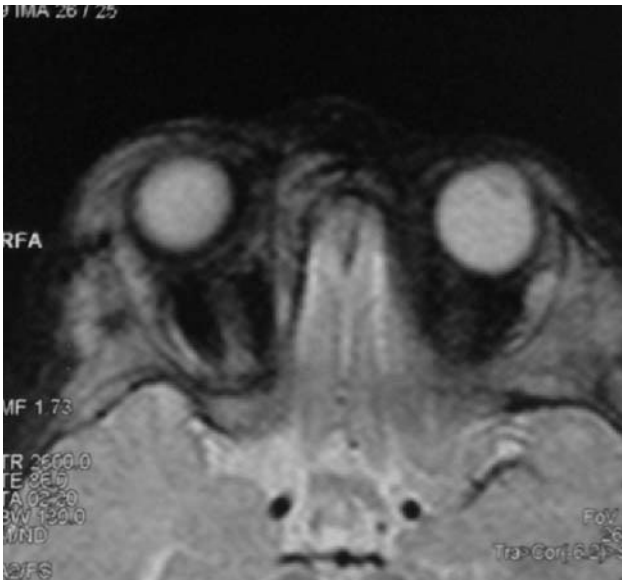

Fig. 5. Displacement toward anterior in the right globe.

py in total, 8 preoperatively and 4 postoperatively. At the 24th month follow-up, the pathological fracture was healed without deformity and the patient was free of complaint (Figs. 9-11).

Discussion

Knee pain and swelling is a common complaint in the childhood. Several intra-articular problems, such as synovitis and even neoplasia such as neuroblastoma should be considered in the differential diagnosis. Patients with neuroblastoma are usually diagnosed by pediatricians and orthopaedic consultation is sought only in cases of bone involvement. In a study by Aston, it was found that primary involvement of the musculoskeletal system occurs in only 15% of neuroblastoma cases.[7] Our case presented to our emergency orthopaedic policlinic for the first time with knee swelling, discomfort and high fever and was diagnosed with pathological femur fracture due to bone metastasis.

A moderate CRP and high sedimentation rate, moderate anemia and high LDH levels suggest malignancy rather than infection.[2] In our case, we considered infection less likely due to the level of CRP of 41 mg/l, sedimentation rate of 35 mm/hour, hemoglobin level of 6.9 g/dl and lactate dehydrogenase (LDH) level of 2230 IU/L (normal value: 4 to 12 months, 100 to 400 IU/L).

Malignancies should be considered in differential diagnosis in addition to infection in patients under the age of 5. Ewing's sarcoma and osteosarcoma are among the first malignant tumors considered in orthopaedic daily practice. With similar clinical and radiological findings to Ewing's sarcoma in patients under 5 years of age, neuroblastoma and Wilms' tumor should also be considered. As an uncommon tumor, the diagnosis of neuroblastoma may be missed. Most cases of neuroblastoma are seen when the pediatrician seek an orthopaedic evaluation. To our knowledge, there have been no previous reports on a neuroblastoma case presenting to an orthopaedic unit with a primary musculoskeletal involvement.

The "small blue round tumor cells" reported in pathological examination are seen in neuroblastoma, Ewing's sarcoma, non-Hodgkin lymphoma, rhabdomyosarcoma and neuroectodermal tumors.[8] When analyzed along with the other findings, neuroblastoma

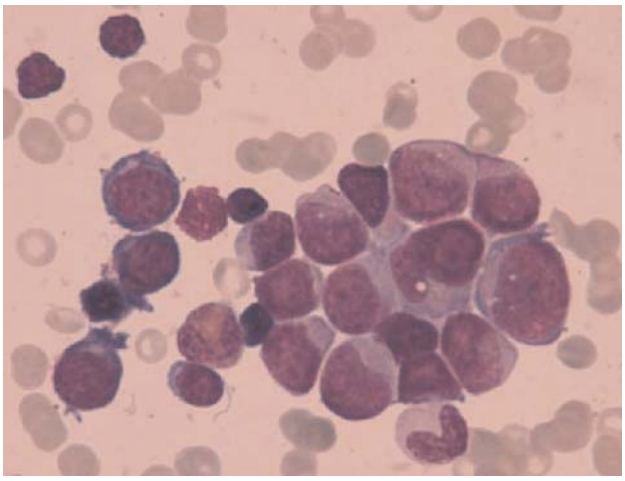

Fig. 6. Microscopic view of the tumor. [Color figure can be viewed in the online issue, which is available at www.aott.org.tr]

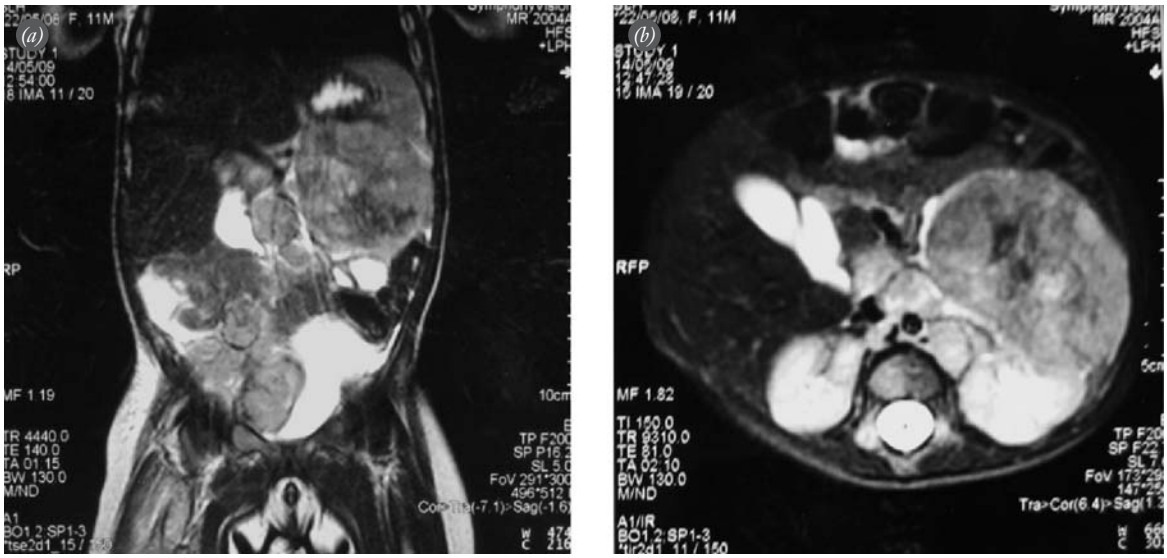

Fig. 7. **(a, b)** Images of left paraaortic mass.

was primarily considered. Although diagnosis of retinoblastoma was first considered during ophthalmologic consultation, significant involvement and expansion was observed at the bones in cranial MR examination (Figs. 4 and 5).

In neuroblastoma, the primary tumor is intra-abdominally located in 65% of cases.[3] Neuroblastoma was shown to invade the lung via lymphatic circulation and the bone narrow, bone, liver and skin via hematogenous circulation.[9] Eyelid ptosis and raccoon eye in metastatic disease are due to the infiltration of periorbital bones. Diffuse bone and bone narrow involvement cause pain, discomfort, claudication, pathologic femur, and cytopenia.[9] As a result of the USG examination performed in our case, diffuse lymphadenopathies and mass impressions inside the abdomen, pathologic fracture in the right femur and diffuse infiltration in the cranial bones were found.

Tc-99-diphosphonate scintigraphy is important in researching bone metastases.[9] MBIG scintigraphy has

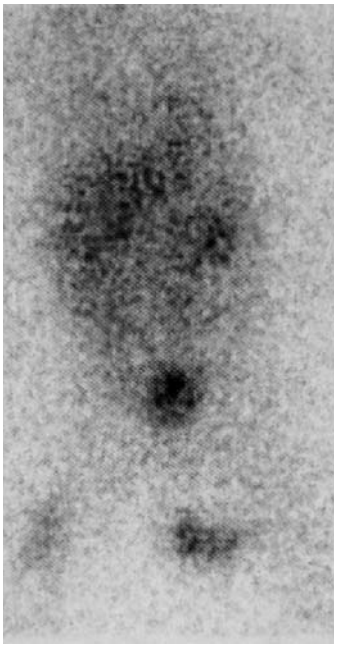

Fig. 8. Pathological involvements in MIBG scintigraphy

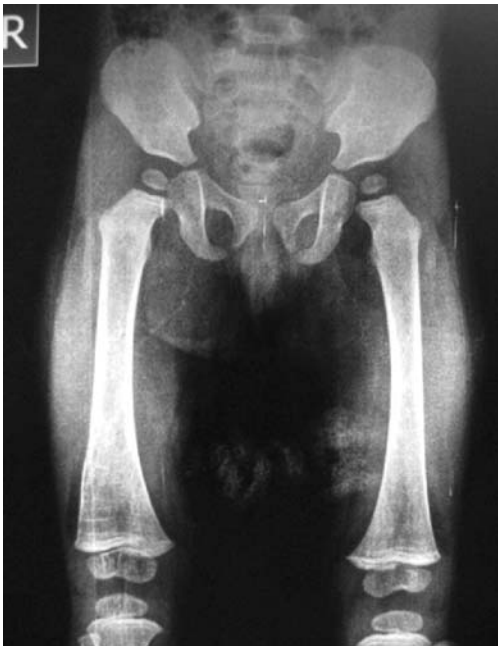

Fig. 9. Post-treatment anteroposterior radiograph of both hips and femurs.

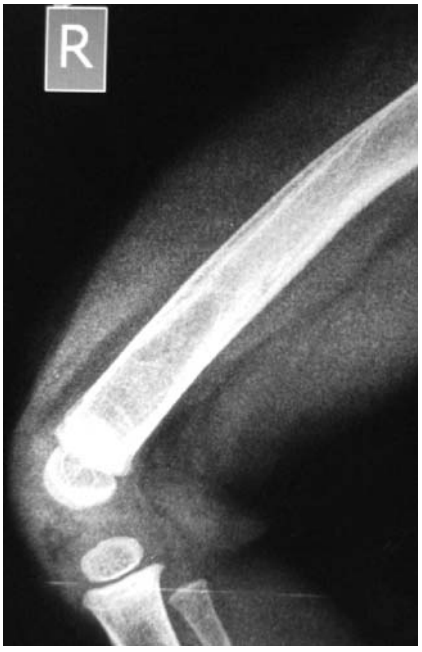

Fig. 10. Post-treatment lateral radiograph of the right femur and the knee.

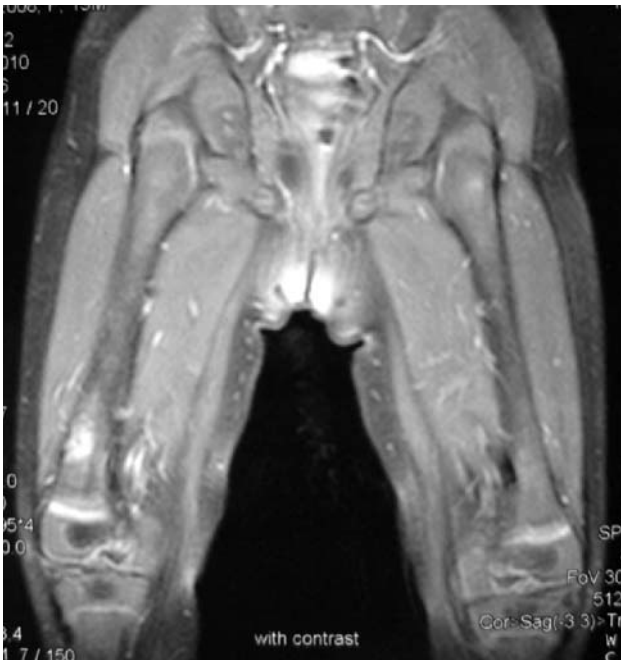

Fig. 11. Post-treatment MR image.

a high sensitivity.[10] In our case, MBIG scintigraphy revealed diffuse involvement (Fig. 8).

In all tumor patients, staging must be determined for effective treatment planning. The Evans staging system is used for neuroblastoma patients (Table 1).[11,12] While the disease makes bone and distant organ metastasis at Stage 4, Stage 4S is reported as a different group with a better prognosis.[11] For advanced stage patients, an aggressive treatment is administered with multidisciplinary joint approaches. The five-year survival rates are 80 to 90% at Stage 1, 5 to 7% at Stage 4, and 75% at Stage 4S.[13] Neuroblastoma is radiosensitive. Because of the frequency of metastatic disease in neuroblastoma, the curative effect of radiotherapy is limited. In Stage 3 and Stage 4 patients in particular, chemotherapy becomes important.[14] A total of 12 courses of chemotherapy were administered in our case, 8 prior to the excision of the intra-abdominal neuroblastoma mass performed in the Istanbul University Pediatric Surgery clinic and 4 following surgery. At the 24th month follow-up, the patient's complaints and orthopaedic pathologies were improved.

Table 1. Neuroblastoma staging.

Evans Staging System	
Stage 1	Tumor is as confined to structure of origin as can be resected.
Stage 2	Tumor is diffuse but not crossing the midline. May be ipsilateral lymph node.
Stage 3	Tumor extends beyond the midline, big as cannot be resected. Bilateral lymph nodes may be involved.
Stage 4	Distant organ metastasis (skeleton, soft tissue, other organs).
Stage 4S	Special category of distant organ metastases, especially under the age of 1 (liver, subcutaneous tissue, bone narrow). No cortical bone involvement.

In conclusion, neuroblastoma may primarily present with musculoskeletal symptoms and should be considered in the differential diagnosis of pathological fractures in children.

Conflicts of Interest: No conflicts declared.

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