EWING SARCOMA OF THE DISTAL PHALANX OF THE GREAT TOE IN A 10-YEAR-OLD BOY: CASE REPORT AND LITERATURE REVIEW

Peeters S.[1], Van Laethem A.[1], Sciot R.[2], Renard M.[3], Labarque V.[3], Vanden Bempt I.[4], Verhamme B.[1]
[1]Department of Dermatology, [2]Department of Pathology
[3]Department of Pediatric Hematology and Oncology, [4]Department of Human Genetics
University Hospital Leuven, Belgium

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Abbreviation **ES** = Ewing sarcoma.

Case report. A 10-year-old boy presented with a mildly painful swelling of the right great toe. The swelling had been progressively enlarging for about three months and had not responded to antibiotic therapy. The patient had a past history of unilateral cleft lip.

Clinical examination revealed a diffuse reddish-violet swelling of the right great toe. The lesion was firm but compressible, associated with hypertrophy of the toe (Fig. 1).

The differential diagnosis included osteomyelitis, subungual vascular tumor, subungual osteochondroma, and subungual fibroma. Radiologic investigations were therefore performed for further evaluation.

Plain radiographs of the right great toe showed an irregular radiolucent and sclerotic area on the dorsal aspect of the distal phalanx, along with a soft-tissue subungual mass (Fig. 2).

Ultrasound examination revealed an additional soft-tissue structure in the dorsal subungual region, with irregular cortical margins of the distal phalanx.

MRI (Fig. 3) demonstrated an expansile osseous lesion with hypertrophy of the distal phalanx and a homogeneous, contrast-enhancing solid subungual component.

Based on these findings, a malignant process was suspected, and biopsy/excision was performed.

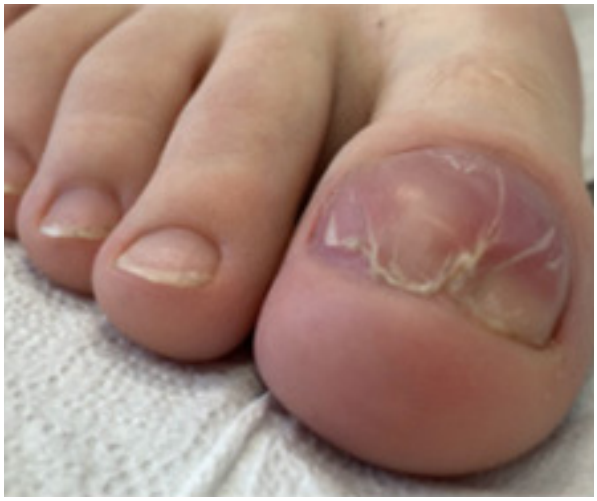

Fig. 1

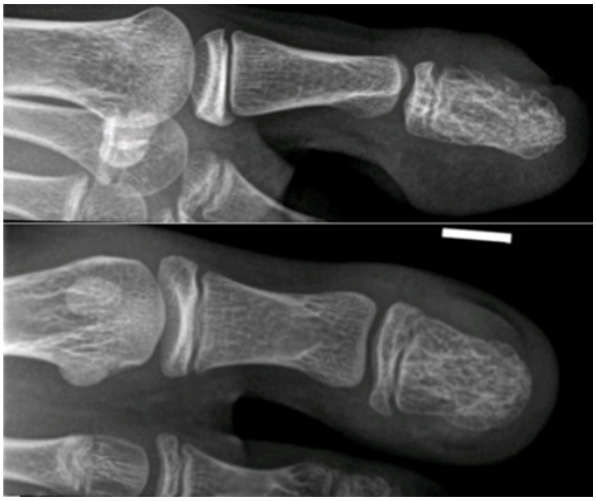

Fig. 2

Fig. 1, 2: Ewing sarcoma of the great toe in a 10-year-old boy (Fig. 1). The X-ray shows an expansile lesion of the distal phalanx with destruction of the dorsal cortical bone (Fig. 2).

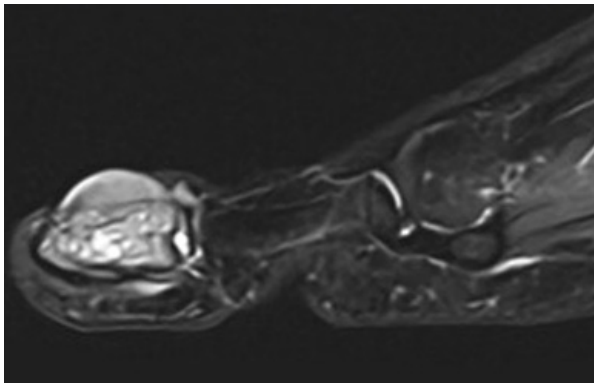

Fig. 3

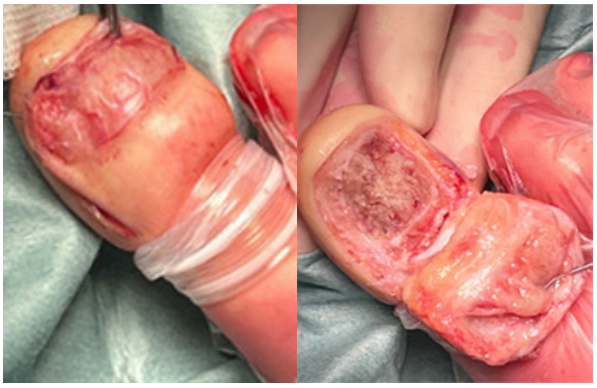

Fig. 4

Fig. 3, 4: MRI (Fig. 3) demonstrates an expansile bone lesion and a solid subungual mass. A "U"-shaped incision was performed, followed by lifting of the entire nail apparatus and the proximal nail fold to expose the tumor (Fig. 4).

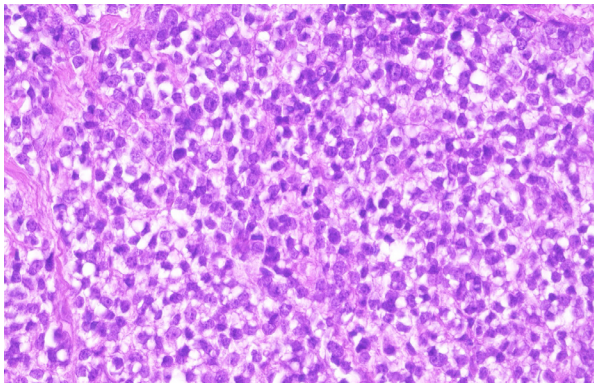

Fig. 5

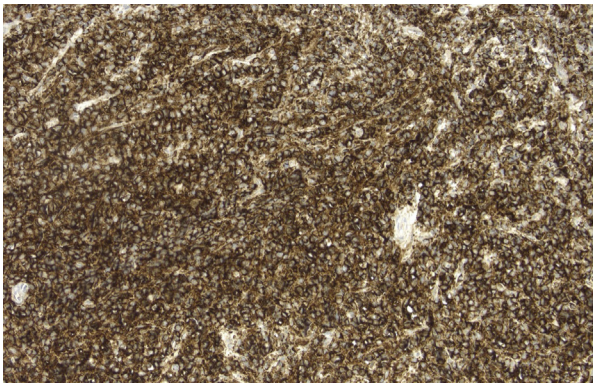

Fig. 6

Fig. 5, 6: Malignant mesenchymal small round cell tumor (Fig. 5, H&E, x40), CD99 positive (Fig. 6, x40).

A "U"-shaped incision was made, followed by elevation of the entire nail apparatus and proximal nail fold to expose the tumor (Fig. 4). The mass was excised from the underlying phalanx, and the bone surface was curetted. The nail apparatus was repositioned, and the wound was closed with reconstructive plastic repair.

Histologic examination of the biopsy specimen revealed a diffusely infiltrating malignant mesenchymal tumor composed of small undifferentiated round cells (Fig. 5).

Immunohistochemistry showed strong membranous positivity for CD99, a characteristic feature of ES (Fig. 6). The tumor cells were negative for desmin, myogenin, cytokeratin, TdT, CD45, ERG, and S100. Unfortunately, FISH and molecular studies could not be performed due to decalcification of the specimen.

Staging studies included PET-CT, chest X-ray, lymph node and abdominal ultrasound, bone marrow aspiration, and bone biopsy. PET-CT revealed mild heterogeneous hyperemia of the skin over the right great toe, compatible with postoperative changes, with no other suspicious lesions detected.

Treatment followed the Euro Ewing 2012 protocol, consisting of induction chemotherapy with vincristine, doxorubicin, and cyclophosphamide, alternating with ifosfamide and etoposide. After nine cycles, MRI showed a modest reduction in the extent of the tumor within the distal phalanx epiphysis and adjacent subcutaneous soft tissues.

Amputation was then performed at the mid-proximal phalanx level. Histologic examination of the resected specimen confirmed the presence of a small residual focus of known ES. Adjuvant chemotherapy with five additional cycles was subsequently administered.

The patient remains under follow-up and, two years after diagnosis, shows no evidence of recurrence.

Discussion. Ewing sarcoma (ES) is the second most common primary malignant bone tumor after osteosarcoma. The disease predominantly affects patients between 10 and 20 years of age, accounting for approximately 80% of all cases. ES may arise from either bone or soft tissues, with about 80% of cases being osseous in origin. It can involve any part of the body, but the axial skeleton is affected in about 45% of cases (pelvis 20%, ribs 10%, other axial bones 15%). The distal skeleton accounts for approximately 35% (femur 12%, humerus 4%, and other distal bones 19%). When extra-skeletal soft tissues are involved, the most common sites include the thigh, gluteal region, back, leg, and retroperitoneal space (1, 2, 3).

The foot represents an exceptionally rare site for ES. Although any bone of the foot may be affected, the calcaneus and metatarsals are the most frequent locations (4-7). Involvement of the toes is uncommon, with only 12 cases reported in the literature. Five cases involved one of the phalanges, whereas six were classified as extraosseous Ewing sarcomas. In one case, the initially affected structure was not clearly specified. The distal phalanx of the great toe is an exceedingly rare location, with only four previously reported cases. Only one of these involved the distal phalanx of the hallux (8-19).

ES is an aggressive tumor, and the presence of metastases at diagnosis represents the most unfavorable prognostic factor. Approximately 20-25% of patients present with metastases at the time of diagnosis. In patients with localized disease who respond well to multimodal therapy, the 5-year survival rate ranges from 70% to 80%, whereas it drops below 30% in metastatic cases. The most common metastatic sites are the lungs, bone, and bone marrow (1, 3, 20, 21).

In our literature review, four patients died. In one of these, metastatic disease was already present at diagnosis, while in the other three, distant metastases developed after initial treatment.

Clinical manifestations vary depending on the tumor's location and size, as they are related to the mass effect or invasion of adjacent structures. Local pain and a palpable mass are the most frequent symptoms, as observed in our case. Because of their nonspecific nature, early symptoms are often misinterpreted as post-traumatic, inflammatory, or growth-related conditions. Diagnostic delay is common, with a median interval between symptom onset and correct diagnosis ranging from 3 to 9 months (6, 20, 22). Systemic symptoms such as fever, anorexia, and weight loss may occur but were absent in our patient.

Laboratory findings (1, 2) may include elevated inflammatory markers, anemia, leukocytosis, increased erythrocyte sedimentation rate, elevated serum lactate dehydrogenase (LDH), alkaline phosphatase, and C-reactive protein levels. However, our patient's laboratory values were within the normal range.

The differential diagnosis includes benign lesions such as subungual vascular tumors and enchondromas, as well as infectious conditions such as osteomyelitis (18). Definitive diagnosis of ES relies on histopathologic examination. Histology typically shows small, round, blue cells with a high nuclear-to-cytoplasmic ratio. Tumor cells usually exhibit strong membranous positivity for CD99, although this marker is not specific for ES. In our case, diagnosis was confirmed by CD99 positivity.

The most specific diagnostic feature is the *EWSR1* gene fusion with transcription factors, most commonly FLI1 (85%). A less common translocation (approximately 10%) involves *EWSR1*::*ERG* fusion (3).

Tumor imaging and metastatic assessment are essential for determining the tumor size and detecting metastases. Radiographic findings in ES include osteolytic lesions, periosteal reaction, cortical destruction, and the presence of a soft-tissue mass. MRI is crucial for evaluating local tumor extent in both osseous and extraosseous ES. Bone scintigraphy and PET, often combined with CT, are used to detect metastases, whereas chest CT remains the preferred modality for identifying small pulmonary lesions (3, 21, 23, 24).

Bone scintigraphy is unnecessary when FDG-PET/CT shows no evidence of distant metastasis. Bone marrow aspiration and biopsy are traditionally performed to assess bone marrow involvement. In our case, chest radiography, PET-CT, lymph node and abdominal ultrasound, bone marrow examination, and bone biopsy were all negative.

Treatment generally consists of a combination of chemotherapy, surgery, and/or radiotherapy, requiring a multidisciplinary approach. Initial therapy usually involves induction chemotherapy to reduce the size of the primary tumor and treat micrometastatic disease. Standard regimens are polychemotherapeutic, typically including vincristine, doxorubicin, and cyclophosphamide, alternating with ifosfamide and etoposide. This is followed by local control – via surgery and/or radiotherapy – and subsequent consolidation chemotherapy.

Complete surgical excision is the preferred method for local control whenever feasible. When complete excision is not achievable or would entail unacceptable morbidity (such as in spinal or axial tumors), radiotherapy represents the indicated alternative (20, 21, 24).

Adjuvant radiotherapy significantly reduces the risk of local recurrence in patients with poor histologic response, large tumor volume (>200 mL), or inadequate surgical margins. In cases of extraosseous ES, the therapeutic regimen is similar to that used for osseous ES (21).

In our case, the patient received induction chemotherapy, followed by amputation of the great toe and subsequent consolidation chemotherapy.

Conclusion. The present case describes an extremely rare manifestation of ES and provides a valuable contribution to the limited literature on this unusual presentation. Only one other case of ES involving the distal phalanx of the great toe has been reported.

We also emphasize the importance of considering Ewing sarcoma in the differential diagnosis of acral lesions. Early diagnosis and prompt treatment—combining chemotherapy and surgical resection—are essential to achieving optimal outcomes in patients with Ewing sarcoma.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Address to:
Dr. Sara Peeters
Department of Dermatology, University Hospitals Leuven
Herestraat 49, Leuven, 3000, Belgium
e-mail: sara.1.peeters@uzleuven.be

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