Case Report

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Clear Cell Sarcoma of the Soft Tissue in the Distal Phalanx of the Great Toe: A Case Report

제 1족지 원위부에 발생한 투명세포육종: 증례 보고

Heejun Park, MD[1], Woo Young Kang, MD[1]*, Ok Hee Woo, MD[1], Aeree Kim, MD[2]

Departments of [1]Radiology and [2]Pathology, Korea University Guro Hospital, Korea University College of Medicine, Seoul, Korea

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***Corresponding author**
Woo Young Kang, MD
Department of Radiology,
Korea University Guro Hospital,
Korea University College of Medicine,
148 Gurodong-ro, Guro-gu,
Seoul 08308, Korea.

Tel 82-2-2626-1338
Fax 82-2-863-9282
E-mail quartet0@hanmail.net

Clear cell sarcoma (CCS) is a rare malignant soft tissue tumor originating from neural crest cells. Histologically resembling malignant melanoma but lacking cutaneous precursor lesions, CCS is characterized by a specific chromosomal translocation (t[12;22][q13;q12]). Primarily affecting young adults, this tumor typically arises in the extremities, especially the knee, foot, and ankle. To our knowledge, distal toe involvement is uncommon. Herein, we present a case initially diagnosed on magnetic resonance imaging as a superficial soft tissue tumor resembling malignant melanoma but subsequently confirmed as CCS of the great toe.

Index terms Sarcoma, Clear Cell; Soft Tissue Neoplasm; Toes; Magnetic Resonance Imaging

INTRODUCTION

Clear cell sarcoma (CCS) is an uncommon soft tissue tumor primarily affecting tendons or aponeurosis, accounting for approximately 1% of all sarcomas (1). Predominantly affecting young adults with a slightly female predominance, CCS typically presents as a slow-growing, painless mass, most commonly in the lower limbs, particularly around the ankle and foot (2). Histologically similar to malignant melanoma (MM), CCS can be challenging to differentiate. Microscopic examination reveals uniform, clear to eosinophilic cells with central round nuclei and prominent nucleoli. Molecular testing such as reverse transcription-polymerase chain reaction and fluorescence in situ hybridization (FISH) which can distinguish CCS from MM by detecting the characteristic t(12;22)(q13;q12) chromosomal translocation be helpful (3). While CCS commonly occurs in deep foot and ankle structures associated

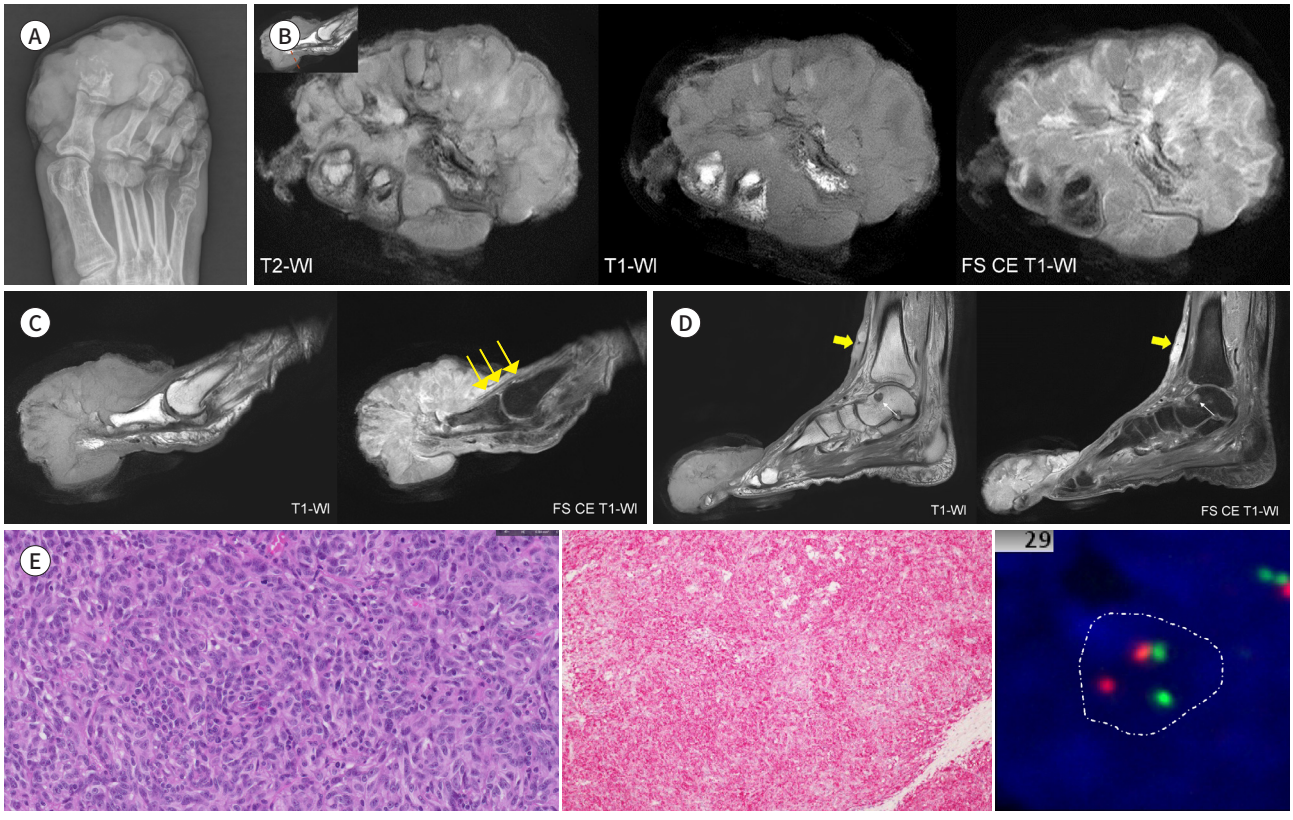
with tendons or aponeurosis, cases involving the toes are rare. This report presents a pathologically confirmed case of CCS in the great toe, including its MRI findings.

CASE REPORT

An 84-year-old male presented with a large, pinkish, ulcerated mass on his right great toe that had been growing for two years. He recalled injuring his toenail two years prior, followed by gradual swelling and subsequent ulceration. Physical examination revealed a tender mass with a foul odor. A plain radiograph showed a soft tissue mass in the right great toe that had destroyed the distal phalanx (Fig. 1A).

MRI of the right foot revealed a large, multilobulated, exophytic soft tissue mass measur-

Fig. 1. An 84-year-old male with clear cell sarcoma of the soft tissue in the distal phalanx of the great toe.
A. Anteroposterior radiograph of the right foot demonstrates severe bone destruction of the distal phalanx by a soft tissue mass.
B. Coronal T1- and T2-weighted MRI reveal a multilobulated, exophytic soft tissue mass with surface ulceration and heterogeneous high signal intensity. FS T1-CE imaging demonstrates diffuse heterogeneous enhancement.
C. Sagittal T1-weighted and FS T1-CE images show the mass extending proximally to the base of the proximal phalanx, encasing the extensor hallucis longus tendon (arrows).
D. Sagittal T1-weighted and FS T1-CE images demonstrate a superficially enhancing lesion around the tibialis anterior tendon (yellow arrows) and an intraosseous enhancing lesion in the talus (white arrows), suggestive of metastasis. The mass exhibits higher signal intensity compared to the skeletal muscle on T1-weighted imaging.
E. Histopathologic findings: tumor cells display epithelioid to spindle-shaped morphology with eosinophilic to amphophilic cytoplasm and prominent nucleoli (hematoxylin and eosin stain, ×400) (left). Immunohistochemical staining demonstrates cytoplasmic HMB-45 immunoreactivity, indicative of a melanin component (immunoperoxidase, ×100) (middle). Dual-color interphase FISH reveals split signals for the EWSR1 gene within a single cell, indicative of EWSR1 (22q12) gene rearrangement (FISH analysis, ×400) (right).
CE = contrast-enhanced, FISH = fluorescence in situ hybridization, FS = fat-saturated, WI = weighted image



ing approximately 7.4 cm in the great toe. This mass exhibited irregular surface ulceration and extensive bone destruction of the distal phalanx. On T1- and T2-weighted images, the mass appeared heterogeneously hyperintense, with diffuse heterogeneous enhancement on fat-saturated T1-contrast-enhanced imaging (Fig. 1B). The mass extended proximally to the base of the proximal phalanx, encasing the extensor hallucis longus tendon (Fig. 1C). Additionally, multiple intraosseous enhancing lesions, suggestive of bone metastases, were identified in the fourth metatarsal neck, cuboid, and talus. A superficially enhancing nodular lesion was also noted around the ipsilateral tibialis anterior tendon (Fig. 1D). Given the diffuse skin ulceration, T1-weighted hyperintensity, and evidence of soft tissue and bone metastases, an initial radiological diagnosis of MM was made.

Positron emission tomography-computed tomography confirmed hypermetabolic activity in the aforementioned bones and superficial lymph nodes of the right lower extremity and inguinal region, supporting the diagnosis of metastasis. Subsequently, a transmetatarsal amputation was performed. Due to extensive bone destruction, the relationship between the tumor and surrounding tendons and aponeurosis could not be determined surgically. Histopathological examination revealed a nodular mass composed of spindle cells arranged in fascicles and nests separated by fibrous bands. Tumor cells exhibited pleomorphism, bizarre nuclei with prominent nucleoli, and mitotic figures. Immunohistochemistry demonstrated strong reactivity for HBM 45, S-100, SOX10, vimentin, and BCL2. FISH analysis revealed a typical break-apart pattern with separated red and green signals within a single cell, confirming the presence of EWSR1 rearrangement (Fig. 1E) and establishing a diagnosis of CCS.

This study was approved by the Institutional Review Board of our institution, which waived the requirement for informed consent (IRB No. 2024GR0266).

DISCUSSION

In 1965, Enzinger introduced the term “clear cell sarcoma of tendons and aponeuroses” to describe a rare malignant tumor originating from these tissues. Characterized by a clear cell appearance due to glycogen accumulation, the tumor was later confirmed to exhibit melanocytic differentiation with cytoplasmic melanosomes in 1973. Due to its histological resemblance to MM, it was once termed “malignant melanoma of soft parts” in 1983 (1) but is now classified as a “tumor of uncertain differentiation” in the 2020 World Health Organization classification of soft tissue tumors (4).

Typically presenting as a small mass in the foot and ankle (43% of cases), CCS frequently affects the lower extremity (60%–75% of cases). Although it can occur in other locations, such as the head and neck, kidneys, gastrointestinal tract, and torso, distal toe involvement is extremely rare (1, 3). The present case represents an unusual occurrence due to its rarity and severe associated bone destruction.

Radiologic findings of CCS demonstrate significant variability on T1- and T2-weighted images, ranging from low to high intensity (5). The presence of melanin can shorten T1 relaxation times, resulting in increased signal intensity on T1-weighted images but lower intensity on T2-weighted images (6). However, some cases exhibit hypointensity on both sequences despite undetectable intracellular melanin (7), limiting the diagnostic accuracy of MRI. In this case,

the large size of the mass, extensive bone destruction, diffuse skin involvement, and metastatic behavior on MRI initially suggested a primary malignant skin tumor or MM.

CCS typically presents as a lobular, encapsulated lesion on gross examination. Microscopically, the tumor comprises well-defined nests separated by collagenous fibers (8). Tumor cells exhibit polygonal or fusiform shapes with clear or pale eosinophilic cytoplasm and centrally located round nuclei containing prominent basophilic nucleoli, reflecting intracellular glycogen accumulation as demonstrated by periodic acid-Schiff staining (9). Neoplastic cells show minimal pleomorphism and typically express HMB-45, S-100, melan-A, microphthalmia transcription factor (MITF), and vimentin immunohistochemically. Cytogenetically, CCS is associated with the t(12;22)(q13;q12) translocation, resulting in the EWSR1-ATF1 fusion protein that upregulates MITF and stimulates melanin synthesis (10). In the present case, the t(12;22)(q13;q12) translocation confirmed the CCS diagnosis.

We report a rare case of CCS with unusual T1-weighted hyperintensity challenging its differentiation from MM. Radiologists should consider CCS in the differential diagnosis of soft tissue tumors with high T1 signal intensity. Given the distinct pathophysiology and therapeutic implications of CCS and MM, molecular genetic confirmation is essential.

Author Contributions

Conceptualization, P.H., K.W.Y.; data curation, P.H., K.W.Y.; investigation, P.H., K.W.Y.; writing—original draft, P.H.; and writing—review & editing, all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

ORCID iDs

Heejun Park https://orcid.org/0009-0003-4458-1409
Woo Young Kang https://orcid.org/0000-0002-8507-1363
Ok Hee Woo https://orcid.org/0000-0003-3953-933X
Aeree Kim https://orcid.org/0000-0001-9645-2156

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제 1족지 원위부에 발생한 투명세포육종: 증례 보고

박희준[1] · 강우영[1*] · 우옥희[1] · 김애리[2]

투명세포육종은 신경능선세포에서 기원하는 드문 악성 연부조직종양의 한 종류로서 조직학적으로는 악성 흑색종과 유사하나 피부 전조 병변이 없고 특징적인 염색체 전위 t(12;22)(q13;q12)를 가지는 병이다. 주로 젊은 연령대의 환자에서 사지, 그중에서도 무릎이나 발, 발목 부위의 건이나 건막 등에서 발생하는 것으로 알려져 있으나 원위부 발가락에 생긴 사례는 매우 드물다. 저자들은 자기공명영상에서 엄지 발가락에 생긴 악성흑색종과 같은 표재성 악성 연부조직종양으로 진단하였으나 병리학적으로 투명세포육종으로 확진한 증례를 보고하고자 한다.

고려대학교 의과대학 구로병원 [1]영상의학과, [2]병리과