BCOR-CCNB3 sarcoma arising in the proximal tibia: A case report

KAYO SUZUKI, TAKETOSHI YASUDA, YUKI HARUHARA, KENTA WATANABE, KEIKO NOMURA, MASAHIKO KANAMORI and YOSHIHARU KAWAGUCHI

1Department of Orthopedic Surgery, Faculty of Medicine; Departments of 2Pediatrics and 3Human Science 1, University of Toyama, Toyama 930-0194, Japan

Received November 4, 2021; Accepted December 31, 2021

DOI: 10.3892/mco.2022.2510

Abstract. BCOR corepressor-cyclin B3 (BCOR-CCNB3) fusion sarcoma was classified as an emerging subgroup of undifferentiated small round cell sarcoma in 2020. The incidence of BCOR-CCNB3 fusion sarcoma is reportedly 1.5-14% among undifferentiated unclassified sarcomas, representing a rare entity among primary malignant bone tumors. The present study reports a case of BCOR-CCNB3 fusion sarcoma in the proximal tibia of a boy. A 12-year-old boy presented with a 6-month history of knee pain and a slowly growing mass in the anteromedial aspect of the left proximal tibia. Plain radiography and computed tomography of the knee demonstrated a lytic lesion with cortical destruction of the proximal tibia. Magnetic resonance imaging showed the bone tumor expanding into soft tissue with almost homogeneous hypointensity on T1-weighted imaging and slightly hyperintensity on T2-weighted imaging. On histopathological evaluation, the tumor comprised a proliferation of small, round to ovoid-shaped mesenchymal cells without osteoid formation. Histopathologically, BCOR-CCNB3 sarcoma of bone was finally diagnosed based on immunohistochemical staining and additional molecular analyses. The patient underwent bone tumor resection followed by pre- and post-operative chemotherapy according to a Ewing sarcoma protocol. The patient showed no evidence of local recurrence or distant metastasis at 12 months after completion of adjuvant chemotherapy. We present herein an additional case of BCOR-CCNB3 sarcoma of the proximal tibia, and review the relevant literature on BCOR-CCNB3 sarcoma of bone.

Introduction

Undifferentiated small round cell sarcoma is a newly classified category of bone and soft tissue sarcoma according to the 2020 World Health Organization classification (1). This newly defined category includes Ewing sarcoma and small round cell sarcoma, previously known as Ewing-like sarcoma. Ewing sarcoma is the most well-known, with the characteristic chromosomal translocation abnormality t(11;22) (q24;q12) causing fusion of the EWS RNA-binding protein 1 (EWSR1) and Friend leukemia virus integration site 1 (FLI1) genes (2). So-called ‘Ewing-like sarcoma’ is also an aggressive sarcoma comprising small round tumor cells arising from bone and soft tissue. In terms of histopathological features, Ewing-like sarcoma is morphologically similar to Ewing sarcoma, but lacks the classical fusion of EWSR1 and erythroblast transformation-specific (ETS) family genes, such as FLI1 (1). According to molecular analyses over the last two decades, undifferentiated small round cell sarcoma (Ewing-like sarcoma) has been recognized to exhibit three different genetic features: capicua transcriptional repressor (CIC)-rearranged sarcoma (3); BCOR corepressor (BCOR)-rearranged sarcoma (4); and round cell sarcoma with EWSR1-non-ETS fusion (5). Of the undifferentiated small round cell sarcomas without EWSR1-ETS gene fusion, CIC-rearrangement sarcomas account for the majority, at 60-70% (6). Molecular findings support these sarcoma subtypes being biologically distinct from Ewing sarcoma.

BCOR-rearrangement sarcoma was first identified by Pierron et al in 2012 among 594 cases of undifferentiated round cell sarcoma that morphologically resembled Ewing sarcoma, but lacked the canonical EWSR1-ETS translocation (4). RNA sequencing and subsequent reverse transcription-polymerase chain reaction (RT-PCR) demonstrated a novel BCOR-cyclin B3 (CCNB3) fusion gene in 24 tumors (4%), resulting from a chromosome-X paracentric inversion (4). This inversion causes an in-frame fusion between exon 15 of BCOR and exon 5 of CCNB3. BCOR-CCNB3 fusion is the most frequent fusion
seen among BCOR-rearrangement sarcomas, accounting for ~60% (7). BCOR-rearrangement sarcoma occurs slightly more often in bone than in soft tissue, at a ratio of 1.5:1 (4). Other fusion partners of BCOR have recently been identified, namely mastermind-like transcriptional coactivator 3 (MAML3), zinc finger CCCH domain-containing protein 7B (ZC3H7B), and internal tandem duplications (ITD) (8,9). BCOR-MAML3 and ZC3H7B-BCOR fusion sarcomas have been reported in a small number of tumors arising in soft tissue (8). BCOR ITD has been reported in a subgroup of soft-tissue undifferentiated round cell sarcomas occurring in infants (9).

BCOR-rearrangement sarcoma of bone is gaining widespread recognition among pathologists, but remains less recognized by clinical orthopedic surgeons than osteosarcoma or Ewing sarcoma. We present herein an additional case of BCOR-CCNB3 sarcoma of the proximal tibia, and review the relevant literature on BCOR-CCNB3 sarcoma of bone. Our review of the literature focused on the clinical characteristics, histopathology, and prognosis of BCOR-CCNB3 sarcoma arising in bone.

Case presentation

This report was approved by the ethics committee at Toyama University Hospital (Toyama, Japan), and the patient and his parents provided written, informed consent for publication of this report. A 12-year-old boy presented with a 6-month history of knee pain on flexion of the knee joint and a slowly growing mass in the anteromedial aspect of the proximal left tibia. There was no special mention of medical history or his family history. Physical examination revealed an elastic hard mass without tenderness or redness, with mild warmth. Despite a lack of limitations to motion of the knee joint, he experienced pain on full flexion of the knee joint. Laboratory tests revealed regular leukocyte counts (6,250/µl). The C-reactive protein level was not elevated at 0.02 mg/dl. Although the normal range of alkaline phosphatase (ALP) in children is 8.6 and no distant metastases. Based on these findings from the biochemical blood test was normal. Plain radiographs of the anterior tibia. There was no special mention of medical history or his family history. Physical examination revealed an elastic hard mass without tenderness or redness, with mild warmth. Despite a lack of limitations to motion of the knee joint, he experienced pain on full flexion of the knee joint. Laboratory tests revealed regular leukocyte counts (6,250/µl). The C-reactive protein level was not elevated at 0.02 mg/dl. Although the normal range of alkaline phosphatase (ALP) in children is 1,298 U/l. Other biochemical blood test was normal. Plain radiographs of the knee demonstrated an extraskeletal mass in the soft tissue at the medial aspect of the proximal tibia. Computed tomography (CT) confirmed a lytic bone tumor with periosteal reaction in the proximal metaphysis of the tibia and a soft tissue tumor with extraosseous soft tissue extension (Fig. 2). Magnetic resonance imaging (MRI) showed the bone tumor expanding into soft tissue with almost homogeneous hypointensity on T1-weighted imaging and slight hyperintensity on T2-weighted imaging compared to muscle (Fig. 3). On 18F-fluoro-2-deoxyglucose positron emission tomography (FDG-PET)/CT, accumulation of FDG was seen only in the bone tumor of the proximal tibia, with a maximum standardized uptake value (SUV) of 8.6 and no distant metastases. Based on these findings from images, primary malignant bone tumor was highly suspected. Differential diagnoses included osteosarcoma, Ewing sarcoma, and malignant lymphoma. Open biopsy was performed to determine the histopathological diagnosis.

On histopathological evaluation, the tumor comprised proliferation of the small, round to ovoid-shaped mesenchymal cells without osteoid formation (Fig. 4A). The nuclei of some tumor cells appeared hyperchromatic with finely dispersed chromatin. Immunohistochemically, tumor cells were completely negative for AE1/AE3, S-100 protein, STAT6, CD34, c-Myc, CD117 and alpha-smooth muscle actin. CD99 (clone 12E7, DAKO, 1:100) expression revealed weak membranous immunostaining (Fig. 4B), and CCNB3 (clone HPA000496; Sigma-Aldrich, 1:100) expression revealed weak membranous immunostaining (Fig. 4B). Immunostaining for AE1/AE3, S-100 protein, STAT6, CD34, c-Myc, CD117 and alpha-smooth muscle actin. CD99 (clone 12E7, DAKO, 1:100) expression revealed weak membranous immunostaining (Fig. 4B), and CCNB3 (clone HPA000496; Sigma-Aldrich, 1:100) expression revealed weak membranous immunostaining (Fig. 4B). Immunostaining for AE1/AE3, S-100 protein, STAT6, CD34, c-Myc, CD117 and alpha-smooth muscle actin. CD99 (clone 12E7, DAKO, 1:100) expression revealed weak membranous immunostaining (Fig. 4B), and CCNB3 (clone HPA000496; Sigma-Aldrich, 1:100) expression revealed weak membranous immunostaining (Fig. 4B).

Considering the histopathological findings, the pathological diagnosis favored Ewing-like sarcoma rather than Ewing sarcoma. Additional molecular examination by RT-PCR were performed using formalin-fixed paraffin-embedded tissues. RT-PCR detected a BCOR-CCNB3 fusion transcript rather than CIC-double homeobox 4 (DUX4). Additional direct Sanger sequencing using PCR product revealed a BCOR-CCNB3 fusion (Fig. 5). The patient received 2.5 cycles of neoadjuvant chemotherapy according to a Ewing sarcoma protocol (10), using vincristine (1.5 mg/m²), doxorubicin (75 mg/m²), and cyclophosphamide (1,200 mg/m²) alternating with ifosfamide (1,800 mg/m²) and etoposide (100 mg/m²). On evaluation of the
effect of neoadjuvant chemotherapy, MRI showed a reduction in the size of the tumor, which had extraskeletal extension into soft tissue, by ~20%. FDG-PET/CT showed a decrease in maximum SUV from 8.6 to 2.5 (Fig. 6). Although there was little reduction in tumor size, the activity of tumor cells was judged to be attenuated. Following neoadjuvant chemotherapy, the patient underwent surgery. The surgery comprised wide resection of the bone tumor of the proximal tibia and endoprosthetic reconstruction with a mega-prosthesis. The remaining patellar tendon was sutured to the holes on the proximal tibia prosthesis with a multi-strand sutures made by ultra-high molecular weight polyethylene. Then, the extensor mechanism of the knee joint was reconstructed by the gastrocnemius muscle transfer using the quadriceps tendon and iliotibial band reported by Yoshida et al (11). Specimens of resected bone tumor contained less than 10% viable tumor cells and were evaluated as showing good chemosensitivity to neoadjuvant chemotherapy. Postoperatively, the patient received an additional 3.5 cycles of adjuvant chemotherapy with vincristine (1.5 mg/m^2), doxorubicin (75 mg/m^2) or actinomycin-D (0.045 mg/kg), and cyclophosphamide (1,200 mg/m^2) alternating with ifosfamide (1,800 mg/m^2) and etoposide (100 mg/m^2). Severe adverse event during chemotherapy was white blood cell decreased corresponding to Grade 4 by Common Terminology Criteria for Adverse Events (Version 5.0). The patient developed a neutropenia rated Grade 4 and received granulocyte-colony stimulating factor. Grade 3 anemia was treated with blood transfusion. The patient completed the chemotherapy regimen as planned, with no sequelae. The patient showed no evidence of local recurrence or distant metastasis at 12 months after completion of adjuvant chemotherapy. The range of motion in his knee joint was 0-125 degrees without extension lag, and he was able to walk without a
Table I. Clinical features of BCOR-CCNB3 fusion sarcoma of bone.

| Author            | Cases | Mean age, years (range) | Sex (n) | Location (n) | Treatment (n) | Outcome (n) | Medan F-U (range) | 5-year OS rate (range) | (Refs.) |
|-------------------|-------|-------------------------|---------|--------------|---------------|-------------|-------------------|-------------------------|---------|
| Cohen-Gogo et al  | 21    | 13.6 (6-22)             | Male (14) Female (5) NA (2) | Pelvis (8) Femur (6) Spine (2) Tibia (1) Toe (1) Clavicle (1) Talus (1) Rib (1) | EW (13) IA' (5) Γ' (1) AML (1) Local treatment only (1) | CR/Al (12) DOD or De (9) | 86 months (alive in sustained CR) | 76.5% | (12) |
| Pierron et al     | 4     |                         |         |              |               |             |                   |                         |         |
| Puls et al        | 7     | 13.7 (11-16)            | Male 6 Female 1 | Fibula 2 Pelvis (1) Pubic ramus (1) Femur (1) Tibia (1) Calcaneus (1) | VIDE-VAI (5) EVIAD (1) I, D, MTX (1) | NED (5) DOD (2) | 78 months (5-189) | 75% (including BCOR-CCNB3 sarcoma arising in soft tissue) | (13) |
| Peters et al      | 1     | 7                       | Male    | Calcaneus | VDC-IE | DOD | 157 months | NA | (14) |
| Shibayama et al   | 3     | 14.3 (11-17)            | Male (3) | Pubis (2) Calcaneus (1) | VDC-IE (2) Osa (1) | NED (3) | 80 months (7-102) | NA | (15) |
| Ludwig et al      | 6     | 13.1 (5-18)             | Male (6) | Sacro-iliac joint (2) Ilium (1) Tibia (1) Acetabulum (1) Fibula (1) | NA (6) | NA | NA | NA | (16) |
| Yamada et al      | 1     | 12                      | Female  | Sacrum (2) Sacrum (2) Thoracic vertebra (1) Calcaneus (1) | NA | NA | NA | NA | (17) |
| Matsuyama et al   | 4     |                         | Male (4) | Th | NA | NED (4) | 75.5 months (24-165) | NA | (18) |
| Krskova et al     | 1     | 15                      | Male    | Fibula | | DOD | 73 months | NA | (19) |
| Kao et al         | 20    | 14.3 (5-24)             | Male (19) Female (1) | Femur (5) Tibia (4) Calcaneus (3) Sacrum (3) Ilium (2) Pubic ramus (2) Elbow (1) | VDC-IE (3) VD-IE (1) EW (3) Osa then EW (1) Others (4) | NED (7) AWD (4) DOD (1) NA (8) | 45 months (10-113) | 72% (including BCOR-CCNB3 sarcoma arising in soft tissue) | (20) |
cane. Functional outcome was calculated with musculoskeletal society tumor score with the result of 90%.

**Discussion**

**BCOR-CCNB3** fusion sarcoma was first identified by Pierron et al (4) in 2012 and was classified to the emerging subgroup of undifferentiated small round cell sarcomas in 2020 (1). However, due to the newly established entity of sarcoma, a number of recent studies on **BCOR-CCNB3** have been re-diagnosed using molecular and genetic techniques from tumors previously diagnosed as undifferentiated sarcoma. This sarcoma remains a tumor that orthopedic surgeons rarely encounter. To clarify the clinical characteristics of the emerging subset of bone sarcomas with **BCOR-CCNB3** fusion, we evaluated a total of 72 cases of **BCOR-CCNB3** sarcoma of bone reported between 2012 and 2021 (including the present case), where at least the location of the affected bone or outcome at final follow-up was described (Table I) (4,12-22).

The incidence of **BCOR-CCNB3** fusion sarcoma is reportedly 1.5‑14% among undifferentiated unclassified sarcomas (4,14,16). **BCOR-CCNB3** sarcoma of bone shows a striking predilection for children, with over 90% of patients diagnosed at under 20 years old. The mean age of cases for which age was described was 13.8 years (range, 2‑25 years), similar to the cited peak incidence between 5 and 20 years old for the Ewing sarcoma family of tumors (23). Evaluating 70 cases with descriptions of sex, males are affected more frequently, with a male‑to‑female ratio of 6.7:1 (4,12‑22). The bone sites involved are most often a long bone of the limbs (n=28, 38.9%), followed by the pelvis (n=27, 37.5%), calcaneus (n=7, 9.7%), and spine (n=6, 8.3%). Among the long bone of limbs, the most common location is the femur (n=13), followed by the tibia (n=10) and fibula (n=4).

**Imaging features of **BCOR-CCNB3** sarcoma of bone** resemble those of aggressive malignant bone tumors such as Ewing sarcoma. Due to the relatively small number of cases reported and the frequency of case series lacking imaging findings, radiological imaging characteristics for **BCOR-CCNB3** sarcoma of bone are difficult to summarize. However, a recent case series and literature review by Brady et al and a review article by Sirisena et al have reported detailed features of imaging (22,25). The most common radiological features were bone lysis, seen in 60%, mixed lysis and sclerosis in 25%, and sclerotic changes in 15%. Periosteal reactions were relatively common in long bones, but to varying degrees (12,22). In the present case, radiography showed a lytic lesion with a moth-eaten appearance as a weak periosteal reaction; this may be because bone tumors tend to develop around sites of Osgood-Schlatter disease. The contralateral proximal tibia showed Osgood-Schlatter disease (data not shown). Based on the MRI findings reviewed by Sirisena et al, **BCOR-CCNB3** sarcoma of bone commonly demonstrated intermediate signal intensity on T1-weighted imaging and heterogeneous increased on T2-weighted signal intensity (25). Furthermore, a common MRI finding for some **BCOR-CCNB3** sarcomas of bone, as
well in the present case, is the presence of tumor showing extraosseous soft-tissue extension (25). On MRI, the finding of extraosseous soft tissue extension is similar to that of Ewing sarcoma (26), making that pathology difficult to distinguish from BCOR-CCNB3 sarcoma of bone. However, T2-weighted MRI of Ewing sarcoma typically shows homogeneous intensity, reflecting the proliferation of small, round, blue tumor cells (26). Another differential diagnosis from the present case on the imaging findings is primary bone lymphoma and osteosarcoma. However, primary bone lymphoma shows a predilection for the fourth to sixth decades (27). Moreover, distinguishing points between primary bone lymphoma and BCOR-CCNB3 sarcoma of bone are the level of soluble interleukin 2 receptor (sIL-2R) in serum. Akahane et al reported that sIL-2R showed 95% sensitivity and 70% specificity for primary bone lymphoma, making this marker useful for differentiating from other primary bone tumors (28). Osteosarcoma is the most common primary malignant bone tumor in the first to second decades of life. Among osteosarcomas, small cell osteosarcoma occasionally presents with radiological findings similar to those of Ewing sarcoma, showing a predominantly lytic, non-mineralized appearance on radiography (29). On MRI, small cell osteosarcoma appears as typically iso- to hypointense homogeneous lesions on T1-weighted imaging and hyperintense heterogeneous lesions on T2-weighted imaging compared to muscle (30), and these findings resembles BCOR-CCNB3 of bone.

Histopathological features of BCOR-CCNB3 sarcoma of bone typically present a tumor comprising a uniform proliferation of short, spindle-shaped to round cells with scant cytoplasm and irregular nuclei (17). Compared to typical Ewing sarcoma, tumor cells from BCOR-CCNB3 sarcoma of bone are more likely to be spindle-shaped. Some cases of BCOR-CCNB3 sarcoma reportedly show variations in cellularity and myxoid changes to the stroma (5,17). Differential diagnoses for BCOR-CCNB3 sarcoma of bone include Ewing sarcoma, CIC-rearranged sarcoma, so-called Ewing-like sarcoma, and small round cell osteosarcoma. Several reports have shown the specificity of simple CCNB3 immunohistochemical staining for BCOR-CCNB3 sarcoma, which is not found in Ewing sarcoma or CIC-rearranged sarcoma. Most BCOR-CCNB3 sarcomas exhibit strong, diffuse positivity for CCNB3 with a nuclear positivity (12,13,15). In addition, the pattern of CD99 immunohistochemical staining may also prove helpful to distinguish this tumor from Ewing sarcoma. Where typical CD99 staining in Ewing sarcoma shows a diffusely membranous positive pattern in almost all cases, patchy, weakly positive staining for CD99 is seen in ~70% of BCOR-CCNB3 sarcomas (13). Our case of BCOR-CCNB3 sarcoma of the tibia showed strong, diffuse positivity for CCNB3, including nuclear positivity, and weak positivity for CD99. A combination of morphological, immunohistochemical, and molecular findings allows accurate classification in most cases.

Although BCOR-CCNB3 sarcoma of bone is molecularly distinct from Ewing sarcoma, the clinical behaviors, radiological features, and histopathological morphology show some similarities with Ewing sarcoma. To date, multidisciplinary treatment combining chemotherapy and surgery for Ewing sarcoma has been established as standard. For the treatment of BCOR-CCNB3 sarcoma of bone, neoadjuvant chemotherapy followed by surgery and postoperative adjuvant chemotherapy, representing the same protocol applied for Ewing sarcoma, has also been proposed (12). When we reviewed the case series of BCOR-CCNB3 sarcoma of bone (Table I), 33 of the 72 cases had received chemotherapy based on the standard treatment for Ewing sarcoma. Our present case had also received neoadjuvant and adjuvant chemotherapy based on the regimen for Ewing sarcoma, and our patient showed no evidence of local recurrence or distant metastasis as of 1 year after completing adjuvant chemotherapy. In patients with localized BCOR-CCNB3 sarcoma of bone and soft tissue, the overall survival rate at 5 years is reportedly significantly better for patients who have received treatment according to the Ewing protocol than for those who have received other chemotherapeutic regimens (12). Previous reports have stated that the 5-year overall survival rate for BCOR-CCNB3 sarcoma ranges from 72 to 76.5% (12,13,20).

The patient and his parents were satisfied with the favorable oncological results of the treatment according to Ewing sarcoma. The postoperative function of the affected limb is also good, and the patient is able to walk stably without a cane.

We reported a case of BCOR-CCNB3 sarcoma arising in the proximal tibia and reviewed the literature for BCOR-CCNB3 sarcoma of bone in terms of clinical features, therapy and prognosis. BCOR-CCNB3 sarcoma requires differentiation from Ewing sarcoma and small cell osteosarcoma using diagnostic imaging, given the histopathological similarity with Ewing sarcoma. Patchy, weakly positive immunohistochemical staining for CD99 and strong, diffusely positive staining for CCNB3 are useful for diagnosing BCOR-CCNB3 sarcoma. Confirmation of the BCOR-CCNB3 fusion gene by RT-PCR is necessary for final definitive diagnosis. The prognosis of BCOR-CCNB3 sarcoma is expected to be relatively good with the introduction of multidisciplinary treatment according to the protocol for Ewing sarcoma at an early stage.

Acknowledgements

The authors are grateful to Akira Noguchi and Professor Joji Imura, Department of Pathology, University of Toyama (Toyama, Japan), for discussion of histopathological diagnosis.

Funding

This work was supported by Japan Society for the Promotion of Science (JSPS) KAKENHI (grant no. JP20K09497).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

KS and YH made substantial contributions to the conception and design. TY was responsible for the acquisition or analysis and interpretation of data. KW acquired clinical imaging data. KS, TY and KW were involved in surgical treatment. KN was mainly in charge of neoadjuvant and adjuvant chemotherapy. MK and YK critically analyzed and interpreted the data. KS

Authors' contributions

KS and YH made substantial contributions to the conception and design. TY was responsible for the acquisition or analysis and interpretation of data. KW acquired clinical imaging data. KS, TY and KW were involved in surgical treatment. KN was mainly in charge of neoadjuvant and adjuvant chemotherapy. MK and YK critically analyzed and interpreted the data. KS
made a critical revision of the article for important intellectual content. KS and TY confirm the authenticity of all the raw data. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate
This report was approved by the Ethics Committee of the Toyama University Hospital (Toyama, Japan; approval no. ‘21-22’).

Patient consent for publication
Written informed consent was obtained from the patient for publication of this report and accompanying images. A copy of the written consent is available for review upon request.

Competing interests
The authors declare that they have no competing interests.

References
1. Bridge JA: Undifferentiated small round cell sarcomas of bone and soft tissue. In: WHO classification of tumours of soft tissue and bone tumours. IARC Press, Lyon, pp326-335, 2020.
2. Turc-Carel C, Aurias A, Mugneret F, Lazard S, Sidaner I, Volk C, Thiery JP, Olswchang S, Philip I and Berger MP: Chromosomes in Ewing’s sarcoma. I. An evaluation of 85 cases of remarkable consistency of t(11;22)(q24;q12). Cancer Genet Cytogenet 32: 229-238, 1988.
3. Kawamura-Saito M, Yamazaki Y, Kaneko K, Kawaguchi N, Kanda H, Mikai H, Gotoh T, Motoi T, Fukayama M, Aburatani H, et al: Fusion between CIC and DUX4 up-regulates PEA3 family genes in Ewing-like sarcomas with t(4;19)(q35;q13) translocation. Hum Mol Genet 15: 2125-2137, 2006.
4. Pierron G, Tirode F, Lucchesi C, Reynaud S, Ballet S, Antonescu CR: Novel BCOR-CCNB3 fusion: A new subtype of bone sarcoma defined by BCOR-CCNB3 gene fusion. Nat Genet 44: 461-466, 2012.
5. Sharaglia M, Righi A, Gambarotti M and Dei Tos AP: Ewing sarcoma and Ewing-like tumors. Virchows Arch 476: 109-119, 2020.
6. Antonescu C: Round cell sarcomas beyond Ewing: Emerging entities. Histopathology 64: 26-37, 2014.
7. Le Loarer F, Pissaloux D, Coindre JM, Tirode F and Vince DR: Update on families of round cell sarcomas other than classical Ewing sarcoma. Surg Pathol Clin 10: 587-620, 2017.
8. Specht K, Zhang L, Sung YS, Nucci M, Dry S, Vaiyapuri S, Richter GH, Fletcher CD and Antonescu CR: Novel BCOR-MAML3 and ZC3H7B-BCOR gene fusions in undifferentiated small blue round cell sarcoma. Am J Surg Pathol 40: 433-442, 2016.
9. Kao YC, Sung YS, Zhang L, Huang SC, Argani P, Chung CT, Graf NS, Wright DC, Kelle SJ, Agaram NP, et al: Recurrent BCOR internal tandem duplication and YWHAE-NUTM2B fusions in soft tissue undifferentiated round cell sarcoma of infancy: Overlapping genetic features with clear cell sarcoma of kidney. Am J Surg Pathol 40: 1003-1010, 2016.
10. Grzer HE, Kraito MD, Tarbell NJ, Link MP, Fryer CJ, Pritchard DJ, Gebhardt MC, Dickman PS, Perlman EJ, Meyers PA, et al: Addition of isofsamide and etoposide to standard chemotherapy for Ewing’s sarcoma and primitive neuroectodermal tumor of bone. N Engl J Med 349: 694-701, 2003.
11. Yoshida Y, Osaka S and Ryu J: Reconstruction of the knee extensor mechanism in patients with a malignant bone tumor of the proximal tibia. Surg Today 40: 646-649, 2010.
12. Cohen-Gogo S, Cellier C, Coindre JM, Mosseri V, Pierron G, Guillemet C, Italiano A, Brugieres L, Orbach D, Laurence V, et al: Ewing-like sarcomas with BCOR-CCNB3 fusion transcript: A clinical, radiological and pathological retrospective study from the Société Française des Cancers de L’Enfant. Pediatr Blood Cancer 61: 2191-2198, 2014.
13. Puls F, Niblett A, Marland G, Gaston D, Douis H, Mangham DC, Sumathi VP and Kindblom LG: BCOR-CCNB3 (Ewing-like) sarcoma: A clinicopathologic analysis of 10 cases, in comparison with conventional Ewing sarcoma. Am J Surg Pathol 38: 1307-1318, 2014.
14. Peters TL, Kumar V, Polikepahad S, Lin FY, Sarabia SF, Liang Y, Wang WL, Lazar AJ, Doddapaneni H, Chao H, et al: BCOR-CCNB3 fusions are frequent in undifferentiated sarcomas of male children. Mod Pathol 28: 575-586, 2015.
15. Shibayama T, Okamoto T, Nakashima Y, Kato T, Sakurui T, Minamiguchi S, Kataoka TR, Shibuya S, Yoshizawa A, Toguchida J and Haga: Screening of BCOR-CCNB3 sarcoma using immunohistochemistry for CCNB3: A clinicopathological report of three pediatric cases. Pathol Int 65: 410-414, 2015.
16. Miyagi K, Alaggio R, Long A, Peron M, Guzzardo V, Benini S, Righi A and Gambarotti M: BCOR-CCNB3 undifferentiated sarcoma-does immunohistochemistry help in the identification? Pediatr Dev Pathol 30: 321-329, 2017.
17. Yamada Y, Kuda M, Kohashi K, Yamamoto H, Takemoto J, Ishii T, Iura K, Maekawa A, Bekki H, Ito T, et al: Histological and immunohistochemical characteristics of undifferentiated small round cell sarcomas associated with CIC-DUX4 and BCOR-CCNB3 fusion genes. Virchows Arch 470: 373-380, 2017.
18. Matsuyma A, Shiba E, Umekita Y, Nosaka K, Kato M, Yanai H, Miyasaka C, Watanabe R, Ito I, Tamaki T, et al: Clinicopathologic diversity of undifferentiated sarcoma with BCOR-CCNB3 fusion: Analysis of 11 cases with a reappraisal of the utility of immunohistochemistry for BCOR and CCNB3. Am J Surg Pathol 41: 1713-1721, 2017.
19. Krskova L, Kabickova E, Drakoumpilova E, Kopeckova K, Plank L, Vlkova P, Mihalova M, Zamecnik J and Kodej R: An undifferentiated sarcoma with BCOR-CCNB3 fusion transcript-pathological and clinical retrospective study. Neoplasma 65: 630-636, 2018.
20. Kao YC, Owosho AA, Sung YS, Zhang L, Fujisawa Y, Lee JC, Wexler L, Argani P, Swanson D, Dickson BC, et al: BCOR-CCNB3 fusion positive sarcomas: A clinicopathologic and molecular analysis of 36 cases with comparison to morphologic spectrum and clinical behavior of other round cell sarcomas. Am J Surg Pathol 42: 604-615, 2018.
21. Rekhi B, Kembhavi P, Mishra SN, Shetty O, Bajpai J and Puri A: Clinicopathologic features of undifferentiated round cell sarcomas of bone & soft tissues: An attempt to unravel the BCOR-CCNB3- & CIC-DUX4-positive sarcomas. Indian J Med Res 150: 557-574, 2019.
22. Brady EJ, Hameed M, Tap WD and Hwang S: Imaging features and clinical course of undifferentiated round cell sarcomas with CIC-DUX4 and BCOR-CCNB3 translocations. Skeletal Radiol 50: 521-529, 2021.
23. Khoury JD: Ewing sarcoma family of tumors. Adv Anat Pathol 12: 212-220, 2005.
24. Mar WA, Taljanovic MS, Bagatell R, Graham AR, Speer DP, Hunter TB and Rogers LF: Update on imaging and treatment of Ewing sarcoma family tumors: What the radiologist needs to know. J Comput Assist Tomogr 32: 108-118, 2008.
25. Sirisena UDN, Rajakulasingam R and Saifuddin A: Imaging of bone and soft tissue BCOR-rearranged sarcoma. Skeletal Radiol 50: 1291-1301, 2021.
26. Morphey MD, Senchak LT, Mambalam PK, Logie CI, Klassen-Fischer MK and Krandsdorf MJ: From the radiologic pathology archives: Ewing sarcoma family tumors: Radiologic-pathologic correlation. Radiographics 33: 803-831, 2013.
27. Lim D, Dregennick C, Yoon JE, Yang JS and Mannik K: Primary lymphoma of bone. Int Orthop 18: 180-183, 1994.
28. Akahane T, Shimizu T, Iseke B, Yoshimura Y and Kato H: Serum soluble interleukin-2 receptor levels in patients with malignant lymphoma of bone. J Orthop Sci 14: 248-252, 2009.
29. Warmish G, Klein MJ, Landau J, Leekritz RA and Hwang S: Imaging characteristics of primary osteosarcoma: Nonconventional subtypes. Radiographics 30: 1653-1672, 2010.
30. Zhong J, Hu Y, Si L, Geng J, Xing Y, Jiao Q, Zhang H and Yao W: Clarifying prognostic factors of small cell osteosarcoma: A pooled analysis of 20 cases and the literature. J Bone Oncol 24: 100305, 2020.

This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0) License.