

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

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Received November 4, 2021; Accepted December 31, 2021

DOI: 10.3892/mco.2022.2510

Abstract. BCL6 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); BCL6 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

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Abbreviations: EWSR1, EWS RNA-binding protein 1; FLI1, Friend leukemia virus integration site 1; ETS, erythroblast transformation-specific; CIC, capicua transcriptional repressor; BCOR, BCL6 corepressor; RT-PCR, reverse transcription polymerase chain reaction; CCNB3, cyclin B3; MAML3, mastermind-like transcriptional coactivator 3; ZC3H7B, zinc finger CCCH domain-containing protein 7B; ITD, internal tandem duplications; ALP, alkaline phosphatase; CT, computed tomography; MRI, magnetic resonance imaging; FDG-PET, ¹⁸F-fluoro-2-deoxyglucose positron emission tomography; SUV, standardized uptake value; sIL-2R, soluble interleukin 2 receptor; DUX4, double homeobox 4

Key words: *BCOR-CCNB3*, BCOR-rearrangement sarcoma, RT-PCR, clinical characteristic

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/ μ l). The C-reactive protein level was not elevated at 0.02 mg/dl. Although the normal range of alkaline phosphatase (ALP) in children is wide, the value of ALP was slightly high at 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 on anteroposterior view and a lytic lesion with cortical destruction of the proximal tibia on lateral view (Fig. 1). 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 18 F-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

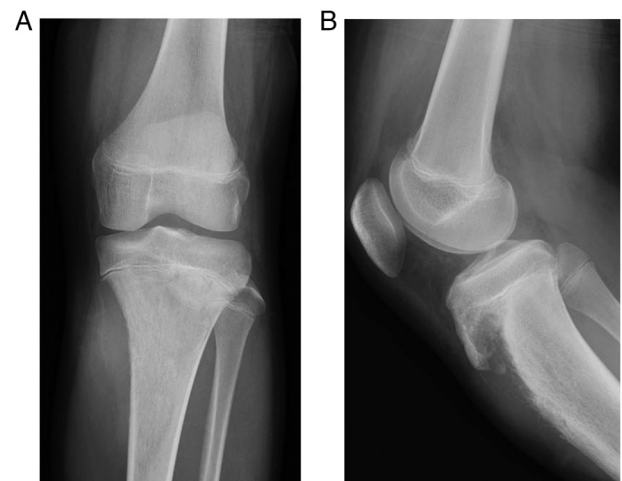


Figure 1. Plain radiographs of the knee. (A) Anteroposterior view shows an extraskeletal mass in the soft tissue at the medial aspect of the proximal tibia and saucerization of the tibial metaphysis. (B) Lateral view reveals cortical destruction as a moth-eaten appearance of the anterior proximal tibia.



Figure 2. Computed tomography of the proximal tibia. (A) Sagittal plane shows lytic lesions from the proximal epiphyseal line to the tibial metaphysis. (B) Axial plane shows the formation of an extraskeletal mass and erosion of the anterior tibia.

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, 1:200) expressed strong and diffuse nuclear positivity (Fig. 4C). 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

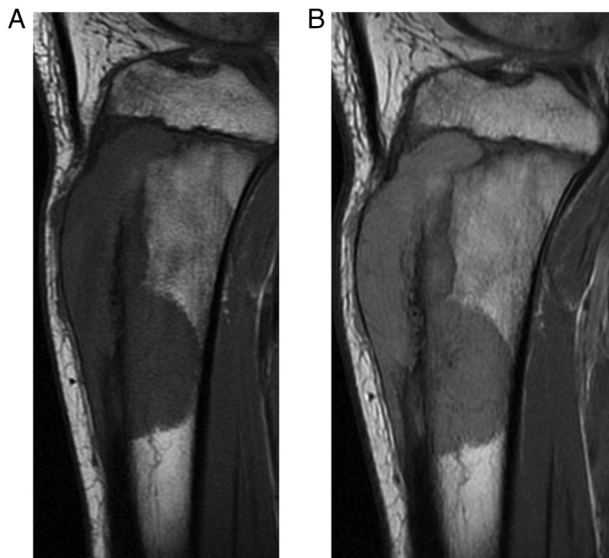


Figure 3. T1- and T2-weighted MRI. (A) On T1-weighted imaging, the bone tumor extending into extraosseous soft tissue appears homogeneously hypointense compared with bone. (B) On T2-weighted imaging, the bone tumor extending into extraosseous soft tissue exhibits signal hypointensity.

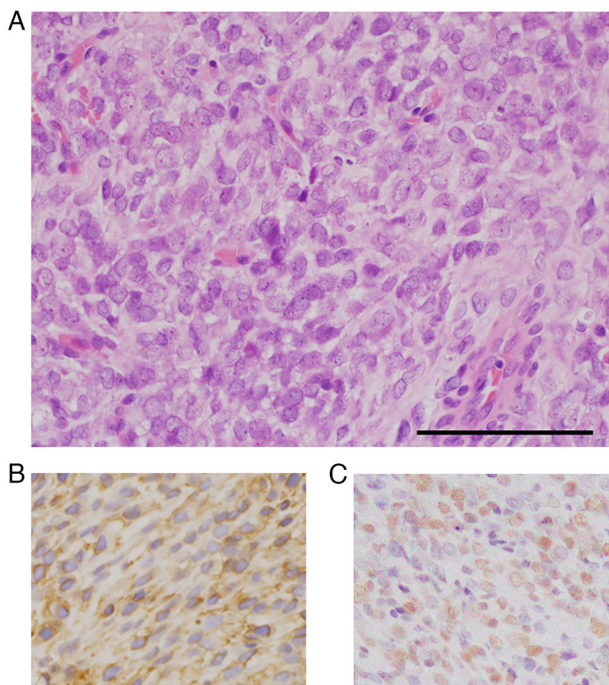


Figure 4. Histopathological findings of a specimen obtained by open biopsy. (A) Hematoxylin and eosin staining demonstrated proliferation of small, round to ovoid-shaped mesenchymal cells without osteoid formation (scale bar, 100 mm). (B) CD99 immunohistochemistry reveals patchy, weakly positive staining in membranes of tumor cells (magnification, x200). (C) Cyclin B3 immunohistochemistry shows strong, diffuse nuclear positivity (magnification, x200).

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

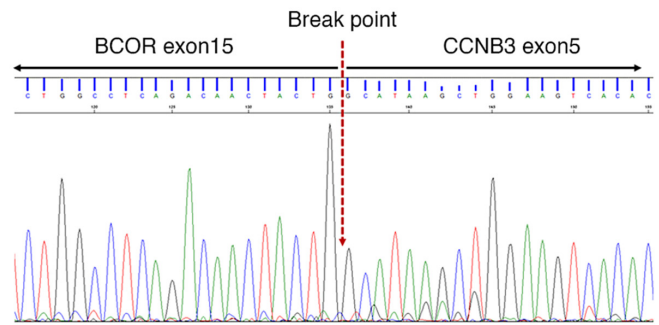


Figure 5. Sanger sequencing of reverse transcription polymerase chain reaction product. Sequencing confirmed identical fusion points of *BCOR* exon 15 with *CCNB3* exon 5. *CCNB3*, cyclin B3; *BCOR*, BCL6 corepressor.

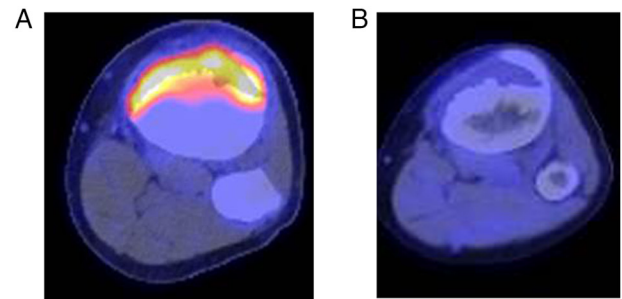


Figure 6. FDG-PET/CT before treatment initiation and after neoadjuvant chemotherapy. (A) Increased FDG accumulation was observed in the tibial bone tumor before initiation of treatment, with a maximum SUV of 8.6. (B) FDG accumulation in tibial bone tumor after neoadjuvant chemotherapy was reduced, with a maximum SUV of 2.5. FDG, ^{18}F -fluoro-2-deoxyglucose; PET, positron emission tomography; CT, computed tomography; SUV, standardized uptake value.

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 ($1,200 \text{ mg/m}^2$) alternating with ifosfamide ($1,800 \text{ mg/m}^2$) 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)	Median F-U (range)	5-year OS rate	(Refs.)
Cohen-Gogo <i>et al</i> [These 21 bone tumor cases included all cases in the article reported by Pierron <i>et al</i> (4)]	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) I* (1) AML (1) Local treatment only (1)	CR/AI (12) DOD or De (9)	86 months (alive in sustained CR)	76.5%	(12)
Puls <i>et al</i>	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 <i>BCOR-CCNB3</i> sarcoma arising in soft tissue)	(13)
Peters <i>et al</i>	1	7	Male	Calcaneus	VDC-IE	DOD	157 months	NA	(14)
Shibayama <i>et al</i>	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 <i>et al</i>	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 <i>et al</i>	1	12	Female	Sacrum	NA	NA	NA	NA	(17)
Matsuyama <i>et al</i>	4		Male (4)	Sacrum (2) Thoracic vertebra (1) Calcaneus (1)	NA 4	NED (4)	75.5 months (24-165)	NA	(18)
Krskova <i>et al</i>	1	15	Male	Fibula	NA	DOD	73 months	NA	(19)
Kao <i>et al</i>	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) NA (8)	NED (7) AWD (4) DOD (1) NA (8)	45 months (10-113)	72% (including <i>BCOR-CCNB3</i> sarcoma arising in soft tissue)	(20)

Table I. Continued.

Author	Cases	Mean age, years (range)	Sex (n)	Location (n)	Treatment (n)	Outcome (n)	Median F-U (range)	5-year OS rate	(Refs.)
Rekhi <i>et al</i>	2	6 25	Male Male	Tibia Vertebra	Regimen unclear	AWD DOD	4 months 8 months	NA	(21)
Brady <i>et al</i>	5	14 (2-17)	Male (4) Female (1)	Spine (2) Femur (1) Tibia (1)	VDC-IE (4) Other (1)	NED (4) DOD (1)	22.4 months (2-41)	NA	(22)
Present case	1	12	Male	Pelvis (1) Tibia	VDC-IE	NED	18 months	NA	

Ref., reference number; F-U, follow-up; NA, not available; EW, chemotherapy for Ewing sarcoma, but details unknown; IA*, ifosfamide-adriamycin based chemotherapy; I*, ifosfamide-based chemotherapy; AML, chemotherapy according to current acute myeloid leukemia protocol; V, vincristine; D, doxorubicin; C, cyclophosphamide; I, ifosfamide; E, etoposide; A, actinomycin D; MTX, methotrexate; Osa, chemotherapy according to osteosarcoma protocol; CR, complete remission; AI, alive; DOD, dead of disease; De, dead; NED, no evidence of disease; AWD, alive with disease; OS, overall survival.

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). *BCOR-CCNB3* sarcoma of bone often arises in the metaphyseal-diaphyseal portion of the femur or tibia (12). These more common locations of *BCOR-CCNB3* sarcoma of bone are similar to those reported for skeletal Ewing sarcoma (24).

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*-rearrangement 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

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.

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