Abstract. Background/Aim: Angiofibroma of soft tissue (AFST) is a rare benign soft-tissue tumor that most frequently occurs in the lower extremities. It has a characteristic genetic feature with a balanced chromosomal translocation t(5;8)(p15;q13), resulting in a fusion of aryl hydrocarbon receptor repressor (AHRR) and nuclear receptor coactivator 2 (NCOA2). Case Report: A 55-year-old woman presented with a 2-year history of left knee pain and recently noticed the development of a palpable mass. Magnetic resonance imaging exhibited a well-defined intra-articular mass with iso-signal intensity relative to skeletal muscle on T1-weighted sequences, heterogeneous high signal intensity on T2-weighted sequences and avid, diffuse enhancement on contrast-enhanced fat-suppressed T1-weighted sequences. After an ultrasound-guided core needle biopsy, the lesion was successfully treated by arthroscopically-assisted complete excision. Histologically, the tumor was composed of uniform bland spindle cells in a myxoid to collagenous stroma with a prominent vascular network. Immunohistochemically, the spindle cells were diffusely positive for CD163 and CD68 and focally positive for estrogen receptor. Moreover, AHRR-NCOA2 fusion gene was detected by reverse transcription-polymerase chain reaction. There has been no clinical evidence of local recurrence at 1-year follow-up. Conclusion: This is the first report of the detection of an AHRR-NCOA2 gene fusion associated with intra-articular AFST. AFST should be included in the extended differential diagnosis of an intra-articular soft-tissue mass, particularly if the mass is vascular. Angiofibroma of soft tissue (AFST) is a newly described soft-tissue neoplasm with characteristic histological and genetic features (1). It typically arises in the lower extremities and often affects middle-aged adults, with a slight female predominance. The most common presenting symptom is a slow-growing, painless mass within the subcutaneous soft tissue. AFST has a benign clinical course with a very low probability of recurrence after simple excision (2). There is no documented risk for metastasis. The differential diagnosis of intra-articular soft tissue tumor of the knee is broad, including both benign and malignant conditions. In 2017, we reported the first case of intra-articular AFST involving the knee joint (3). In that case, an aryl hydrocarbon receptor repressor (AHRR)-nuclear receptor coactivator 2 (NCOA2) gene fusion was not identified by reverse transcription-polymerase chain reaction (RT-PCR). Herein we describe a unique case of intra-articular AFST of the knee with the AHRR-NCOA2 chimera. The patient was informed that data concerning the case would be submitted for publication, and she provided consent.

Case Report

A 55-year-old woman presented with a 2-year history of left knee pain and recently noticed the development of a palpable mass. She had no history of knee trauma and her medical
history was non-contributory. Outside hospital imaging raised concern for the possibility of an intra-articular soft-tissue mass, and she was subsequently referred to our institution. Physical examination showed a mobile, elastic hard, non-tender mass in the anteromedial aspect of the left knee. Range of motion of the affected knee was normal. Plain radiographs revealed no evidence of osseous involvement. Magnetic resonance imaging (MRI) demonstrated a well-defined mass in the suprapatellar region, measuring 3.5 cm in maximum diameter. The mass exhibited iso-signal intensity relative to skeletal muscle on T1-weighted sequences (Figure 1A) and heterogeneous high signal intensity on T2-weighted sequences (Figure 1B). Contrast-enhanced fat-suppressed T1-weighted sequences (Figure 1C) showed avid, diffuse enhancement of the mass. Based on the MRI findings, initial differential considerations included vascular soft tissue neoplasms such as synovial hemangiom a, AFST and solitary fibrous tumor (SFT), tenosynovial giant cell tumor or synovial sarcoma.

An ultrasound-guided core needle biopsy (CNB) was performed. Microscopically, the lesion was composed of uniform bland spindle cells in a myxoid to collagenous strom a with a prominent vascular network (Figure 2A). Nuclear atypia and mitotic figures were absent. Immunohistochemically, the spindle cells were diffusely positive for CD163 (Figure 2B) and CD68 (Figure 2C) and focally positive for estrogen receptor (ER) (Figure 2D). Staining for epithelial membrane antigen (EMA), CD34, desmin, smooth muscle actin (SMA), progesterone receptor and S-100 protein was negative. The MIB-1 labelling index was 1-2%. Based on these findings, the lesion was diagnosed as an AFST. In addition, AHRK-NCOA2 fusion gene was detected by RT-PCR (Figure 3), supporting the diagnosis of AFST.

The patient subsequently underwent an arthroscopic surgery. On arthroscopic examination, the mass was found to be solid, with connections to the synovial membrane. Small blood vessels were observed on the surface of the mass (Figure 4A). The mass was completely excised under arthroscopic guidance using a bipolar radiofrequency energy system (VAPR-DePuy Mitek, Norwood, MA, USA) (Figure 4B).

The gross specimen of the excised mass was well-circumscribed, encapsulated and 3.5×2.3×1.5 cm in size. The cut surface appeared solid, yellow-tan and glistening (Figure 5). Histological and immunohistochemical findings of the excised specimen were similar to those of the CNB. The postoperative course was uneventful. There has been no clinical evidence of local recurrence at 1-year follow-up.

Discussion

AFST, first described by Mariño-Enríquez and Fletcher in 2012 (2), is characterized by the distinctive histological features along with a pathognomonic translocation, involving the NCOA2 gene (4-8). AFST behaves in a benign manner although its exact etiology is unknown (9). This case report illustrates that AFST can be included in the differential diagnosis of an intra-articular mass of the knee joint.

There are only a few case reports describing the imaging features of AFST (3, 8, 10-14). The radiologic differential diagnosis is broad and depends on location of the tumor (15). On MRI, signal characteristics are non-specific with iso- to slightly-low signal intensity relative to skeletal muscle on T1-weighted sequences and heterogeneous high signal intensity on T2-weighted sequences. Contrast enhancement is usually avid although variable enhancement patterns can be seen. The current case demonstrated T1 and T2 signal...
intensity characteristics as well as avid enhancement in keeping with the features of AFST described in previous literature (3, 8, 11).

The definitive diagnosis of AFST is made after excision and histopathological analysis. Histologically, AFST most often presents as a proliferation of uniform bland spindle cells in a variably myxoid to collagenous stroma with a prominent small thin-walled branching blood vessel, as in our case. Cytological atypia and nuclear hyperchromasia are generally absent (1). By immunohistochemistry, the neoplastic cells are variably positive for EMA, CD34, desmin and SMA (2, 8). In addition, Yamada et al. have demonstrated that CD163 and ER are supportive diagnostic markers for AFST (16). More recently, Bekers et al. examined 14 AFST cases and reported that all of them were positive for nuclear expression of NCOA2. Nevertheless, this marker lacks specificity because it is also expressed in other soft tissue neoplasms such as myxoid liposarcoma and

![Figure 2. Histological and immunohistochemical findings of angiofibroma of soft tissue. The tumor is composed of bland spindle cells in a fibromyxoid stroma with prominent branching vessels (A) (hematoxylin and eosin staining, original magnification ×100). The tumor cells are diffusely immunoreactive for CD163 (B) and CD68 (C) and focally immunoreactive for estrogen receptor (D) (original magnification ×200, respectively).](image)

![Figure 3. Detection of an aryl hydrocarbon receptor repressor (AHRR)-nuclear receptor coactivator 2 (NCOA2) fusion transcript by reverse transcription-polymerase chain reaction (PCR). A reciprocal NCOA2-AHRR fusion transcript was also detected. PCR products were analyzed by agarose gel electrophoresis. Lane 1, 100bp ladder; lane 2, AHRR exon 10-NCOA2 exon 14; lane 3, AHRR exon 9-NCOA2 exon 16; lane 4, NCOA2 exon 15-AHRR exon 10.](image)
myxofibrosarcoma (8). On the other hand, S-100 protein and cytokeratins are consistently negative (15). Our case also showed coexpression of CD163 and ER consistent with previous results (16).

In current practice, cytogenetic and molecular genetic assays can serve as a useful diagnostic adjunct for soft-tissue neoplasms (9). AFST is cytogenetically characterized by a balanced t(5;8)(p15;q13) translocation (4). A specific fusion gene, \textit{AHRR-NCOA2} is also identified by RT-PCR in a large subset of AFSTs (4, 8, 16). It has been shown that this AHRR-NCOA2 chimeric protein is able to activate the AHR signaling due to the retained transcriptional activation domain of NCOA2, leading to neoplastic transformation (4). Moreover, NCOA2 rearrangement was detected by fluorescence in situ hybridization in almost all cases examined (16, 17). In our case, positive \textit{AHRR-NCOA2} gene fusion via RT-PCR confirmed the initial histological impression.

Because of its vascularity and occasional infiltrative growth pattern, AFST may be radiologically and histologically mistaken for other vascular neoplasms or non-vascular soft tissue neoplasms such as low-grade myxofibrosarcoma, low-grade fibromyxoid sarcoma and myxoid liposarcoma (2, 15, 18). The most important differential diagnosis for the current case is SFT, which is a distinctive mesenchymal neoplasm of intermediate malignant potential (19). SFT can occur at any anatomical location, but intra-articular involvement is extremely rare (20). On MRI, SFT typically appears as a well-defined mass with isointense signal intensity on T1-weighted sequences and variable signal intensity on T2-weighted sequences (21). Focal or diffuse hypointense signal intensity corresponding to fibrous content may be seen on T2-weighted sequences (22). The presence of prominent collateral feeding vessels, although not specific, is a useful distinguishing imaging feature of SFT (23). Histologically, SFT is characterized by branching staghorn-like vessels and a patternless distribution of spindle to ovoid cells in a variably collagenous stroma (19). However, SFT lacks the innumerable small thin-walled branching vessels characteristic of AFST. By immunohistochemistry, SFT shows strong and diffuse expression of CD34 (19) and nuclear signal transducer and activator of transcription 6 (STAT6) (24, 25), unlike AFST. The discovery of a NGFI-A binding protein 2 (NAB2)-STAT6 fusion gene has recently led to more precise diagnosis of SFT (26, 27).

Figure 4. Arthroscopic view of the knee. Small vessels are observed on the surface of the mass (A). The mass was existed at the medial side of the suprapatellar pouch (B).

Figure 5. Grossly, the tumor is well-circumscribed with a yellow-tan, glistening cut surface.
AFST is adequately treated with surgical excision. It has a good prognosis, although local recurrence may occur after incomplete excision (2, 16). In the current case, we were able to achieve complete excision under arthroscopic guidance. Our case demonstrates that intra-articular AFST in the knee joint can be treated by arthroscopic excision and good results can be obtained, as reported previously (3).

In conclusion, we report the first case of intra-articular knee AFST with an AHRR-NCOA2 chimera. Successful disease control was achieved by arthroscopically-assisted complete excision. AFST should be considered in the extended differential diagnosis of intra-articular lesions.

Conflicts of Interest
The Authors declare no conflicts of interest associated with this article.

Authors’ Contributions
SN performed the operation and drafted the article. JN supervised the research and assisted with writing of the article. SN provided direct patient care. MA and KN performed the histological evaluation. TY reviewed the article. All Authors read and approved the final article.

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