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Intraarticular Nodular Fasciitis in the Knee Joint with *USP*6-Gene Rearrangement

—A Case Report with Special Attention to Diagnostics of Intraarticular Lesions

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Abstract

Background: Nodular fasciitis (NF) is currently considered a self-limited clonal neoplastic process. It shares the rearrangement of *USP*6-gene with aneurysmal bone cysts and myositis ossificans. The presented case is of interest as this is a rare site of presentation of NF; so far only few single cases of intraarticular NF have been reported with documented *USP*6-gene rearrangement. Intraarticular neoplasias of the knee joint are rare; the most frequent being tenosynovial giant cell tumor (TSGCT). Given a nationwide annual incidence rate of 14 for the lower extremity and about 75% affecting the knee joint about 10 new cases involving the knee joint can be expected per 1 million persons/year. All other types of benign neoplasms are comparably rare while malignant intraarticular processes are extremely rare with most of them reported as single case studies. **Aim:** We report our case to emphasize the importance of preoperative diagnostics including the option of biopsy. Intraarticular malignant processes are extremely rare and frequently are operated on accidently with negative consequences for the patient. Tactics and techniques to treat benign processes depend on the correct pathologic diagnosis. **Case presentation:** The 38 year old man noticed slowly increasing swelling of his left knee joint after wakeboarding. Because of continuing discomfort 2 months later MRI diagnostic revealed, apart from retropatellar cartilage lesions, a popliteal mass compatible with a Baker cyst. The lesion of interest (later diagnosed as NF) was neither recognized by the radiologist nor the treating clinician. During the following 8 months the patient felt increasing swelling of the knee joint. The repeat MRI documented the crescent intraarticular solid synovial mass in the medial patellofemoral recess without signs

of hemosiderin impregnation. A percutaneous sonographically guided 16G needle biopsy was performed. Histologically, bland myofibroblastic proliferation suggestive of nodular fasciitis (NF) was found. The next generation sequencing (NGS) demonstrated the presence of *MYH*9-*USP*6 gene fusion, confirming the diagnosis of NF. The lesion was excised under arthroscopic control. At 1 year follow-up the patient is asymptomatic. **Conclusion:** The case is of interest because of its rare pathology. The decision how to treat was based on pathologic biopsy diagnostics including the *USP*6-gene rearrangement. In view of similar presentation of the rare malignancies we also want to stress the importance of definitive diagnostics which generally are possible only through biopsy.

Keywords

Nodular Fasciitis, Knee, Arthroscopy, Intra-Articular Lesions

1. Introduction

Nodular fasciitis (NF) is currently considered a self-limited clonal neoplastic process. It shares the rearrangement of *USP*6-gene with aneurysmal bone cysts and myositis ossificans. The presented case is of interest as this is a rare site of presentation of NF; so far only few single cases of intraarticular NF have been reported.

Intraarticular neoplasias of the knee joint are rare; the most frequent being tenosynovial giant cell tumor (TSGCT). Given a nationwide annual incidence rate of 14 for the lower extremity [1] and about 75% affecting the knee joint [2] about 10 new cases involving the knee joint can be expected per 1 million person/year. All other types of benign neoplasias are comparably rare while malignant intraarticular processes are extremely rare and mostly are reported as single case studies. An overview of intraarticular tumors of synovial joints recently was given by Jang *et al.* [3]; a list of diagnoses to be considered with reference to most recent reports is given in **Tables 1-3** to assist in the differential diagnostic evaluation of images.

We report our case to emphasize the impact of preoperative biopsy in spite of the fact that intraarticular malignant processes are extremely rare as the treatment approach for benign processes also depends on the pathologic diagnosis. Frequently malignant tumors are operated accidently [4] [5].

2. Case Presentation

The 38 year old man noticed slowly increasing swelling of his left knee joint while wakeboarding. Because of continuing discomfort 2 months later MRI (08/2018) diagnostic revealed, apart from retropatellar cartilage lesions, a popliteal mass compatible with a Baker cyst. The lesion of interest (later diagnosed as NF) was neither recognized by the radiologist nor the treating clinician (**Figure 1**).

Table 1. Intra-articular benign lesions.

Diagnosis	References	MRI Pattern according to Adams [13]	X-Ray [13]
Nodular Fasciitis	[10] [11]	SFM homogenous low signal intensity T1, heterogenous high signal intensity T2 STIR weighted	
Tenosynovial Giant Cell Tumor (formerly Pigmented Villonodular Synovitis PVNS) *Localized Type*	[3] [18]	SFM low signal intensity combined with blooming artifact due to hemosiderin	E
Tenosynovial Giant Cell Tumor *Diffuse Type*	[3] [18]	MSM DSM low signal intensity with blooming artifact as above bone invasion typical	E
Synovial Chondromatosis	[3]	MSM, DSM synovial proliferation with septation, rings and stipples, bone erosions; calcification (X-Ray, not mandatory) may develop at long-term	C E
Solitary Synovial Chondroma	[19]	SFM X-Ray usually pathognomonic solid mass with calcifications	C
Epidermal Cyst	[21]	SFM solid homogenous, sharp margins	
Angiomyolipoma	[22]	SFM diffuse process mimicking tenosynovial giant cell tumor	
Angioleiomyoma	[23]	SFM well demarkated mass, hyperintense T2, suggesting hemangioma	
Lipoma	[24]	SFM isointense to subcutaneous fatty tissue T1 and T2	
Lipoma arborescens	[3] [20]	DS "pathognomonic" synovial mass with villous frond-like projections; complete suppression T2 fat saturated images	E
Schwannoma	[18] [25]	SFM well circumscribed solid lesion hyperintense T2	

SFM = Single Solid Focal Mass within the joint. MSM = Multifocal Solid Mass defined as more than one intra-articular mass. DSM = Diffuse Solid Mass defined as a solid lesion filling the whole of the joint space. DS = Diffuse Synovitis defined as uniform or irregular generalised synovial thickening. E = Erosion present, C = Calcification present [13].

Table 2. Intra-articular malignant lesions. Presentation is very variable; therefore no pattern can be specifically defined. References refer to case studies.

Primary Sarcoma	Reference
Synovial Sarcoma-monophasic-biphysic	[15] [18]
Myxoinflammatory Fibroblastic Sarcoma	[15] [26]
Epitheloid Sarcoma	[27]
Undifferentiated Pleomorphic Sarcoma	[13] [15]
Myofibroblastic Sarcoma	[15]
Myxofibrosarcoma	[15]
Extraskeletal Myxoid Chondrosarcoma	[15]
Malignant Giant Cell Tumor of the Tendon Sheath (formerly malignant PVNS)	[14]
Synovial Chondrosarcoma	[14]
Lymphoma	[3]
Liposarcoma	[28]
Metastasis	
Lung Cancer	[29]
Renal Cell Carcinoma	[30]

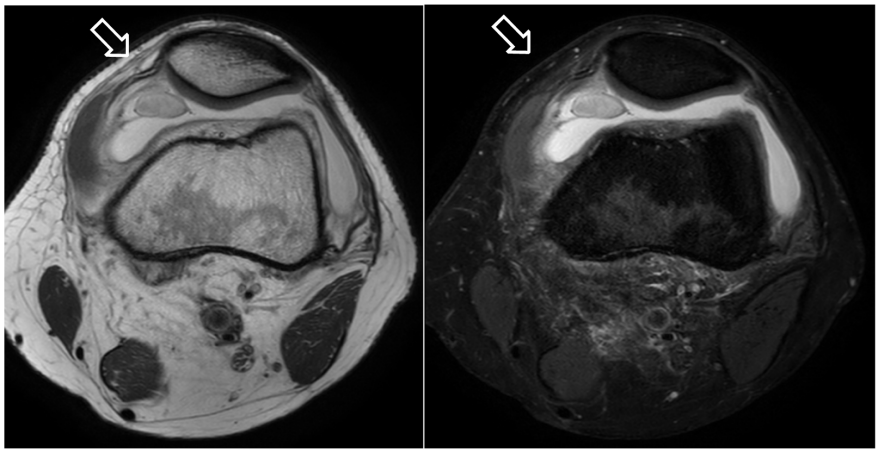


Figure 1. Transverse MRI at first presentation showing the well circumscribed lesion in the medial patellofemoral recess, in the first radiology report interpreted as edematous fat lobules (in spite different signal behaviour to subcutaneous fat).

Table 3. Intra-articular non-neoplastic lesions. References refer to case studies.

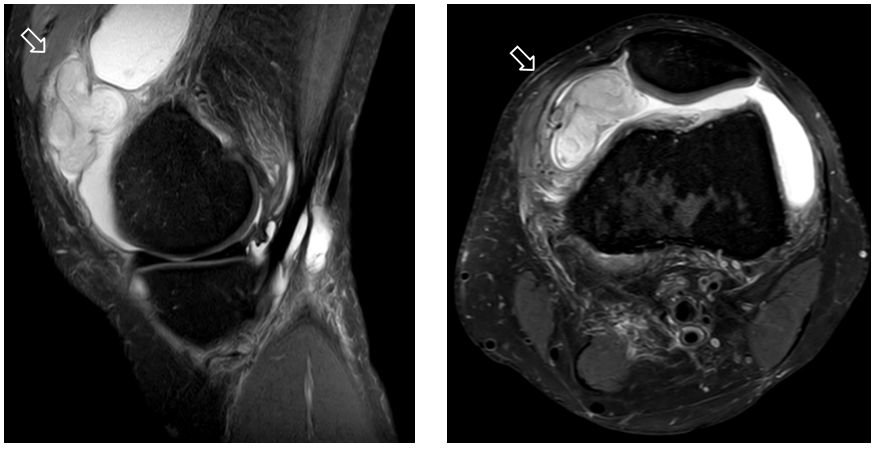
Diagnosis	Reference
Cysts	[31]
Inflammatory Arthritis/Rheumatoid/Psoriatic affections	[32]
(Pseudo-)Gout, Chondrocalcinosis	[33]
Hoffa's Fat Pad Inflammation	[13]
Tuberculous Arthritis	[12]
Non-tuberculous Infection	[12]
Coccidioidomycosis	[12]
Synovial Hemangioma	[16] [17]

During the following 8 months the patient felt increasing swelling of the knee joint. The repeat MRI (04/2019) documented the growing intraarticular solid synovial mass in the medial patellofemoral recess without signs of hemosiderin impregnation (**Figure 2**). A percutaneous sonographically guided 16G needle biopsy was performed.

Histologically (**Figure 3**) both the core biopsy sample (a and b) and the resected specimen (c) consisted of bland myofibroblastic proliferation, microscopically consistent with NF. No atypical mitotic activity, no necrosis and no pleomorphy were found. Immunohistochemically expression of SMA was observed (d), while desmin, ALK1, S100, CD34 and cytokeratins remained negative. The NGS performed on the preoperative core biopsy demonstrated the presence of *MYH9-USP6* gene fusion, confirming the diagnosis of NF.

Based on accessible location and histological typing, arthroscopically assisted resection was considered suitable for complete tumor removal. Arthroscopic tumor resection was performed, with uneventful functional recovery (**Figure 4**). The resected specimen showed macroscopically typical features of NF (**Figure 5**). Control-MRI 7 months later (12/2019) showed, apart from postoperative variations, no signs of tumor recurrence (**Figure 6**).

At 1 year follow-up the patient is asymptomatic.



(a) (b)

Figure 2. (a) Sagittal T2-weighted image of repeat MRI (8 months after imaging in **Figure 1**) revealing a distinctively enlarged patellofemoral recess containing a polycyclic partially septated tumor mass of 5.7 × 4 × 2.5 cm size; (b) Axial T2-weighted image of repeat MRI (8 months after imaging in **Figure 1**) depicting the voluminous tumor mass medially to the patella, with increased contrast medium enhancement, without hemosiderin deposits.

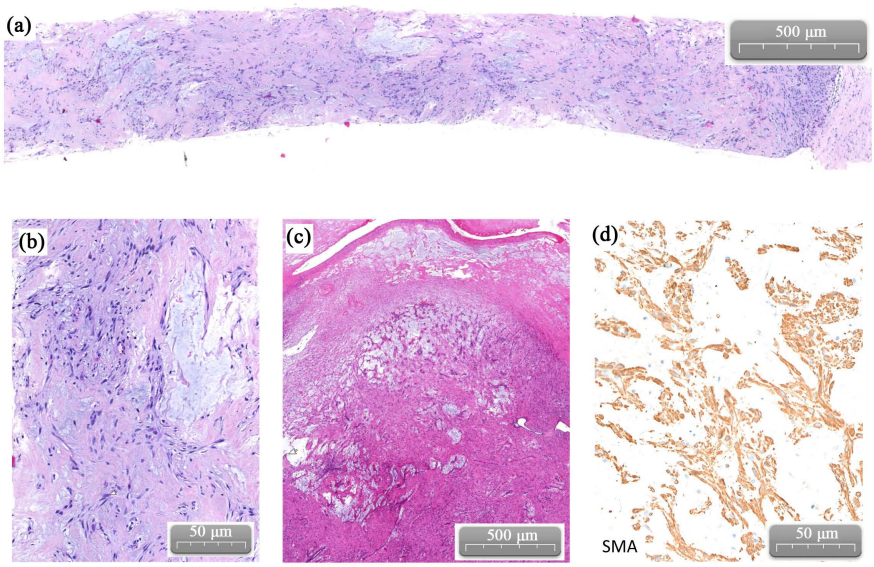
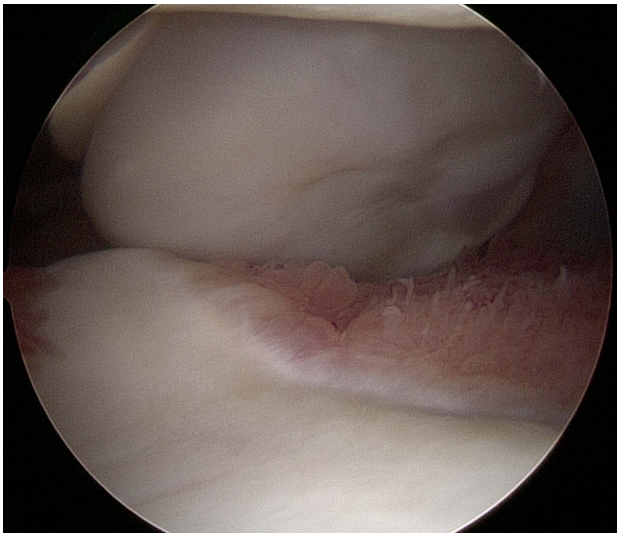


Figure 3. (a) (b) (c) (d) Histologically, both the core biopsy sample ((a) overview in original magnification 25× and (b) original magnification 200×; both in HE staining) and the resected specimen ((c), original magnification 25×, HE staining) consisted of bland myofibroblastic proliferation microscopically consistent with NF. No atypical mitotic activity, no necrosis and no pleomorphy was found. Immunohistochemically expression of SMA was observed ((d); original magnification 200×), while desmin, ALK1, S100, CD34 and cytokeratins remained negative (not shown). The NGS demonstrated the presence of *MYH9-USP6* gene fusion, confirming the diagnosis of NF. The resected specimen (c) consisted of bland myofibroblastic proliferation microscopically consistent with NF. No atypical mitotic activity, no necrosis and no pleomorphy was found. Immunohistochemically expression of SMA was observed (d), while desmin, ALK1, S100, CD34 and cytokeratins remained negative. The NGS demonstrated the presence of *MYH9-USP6* gene fusion, confirming the diagnosis of NF.



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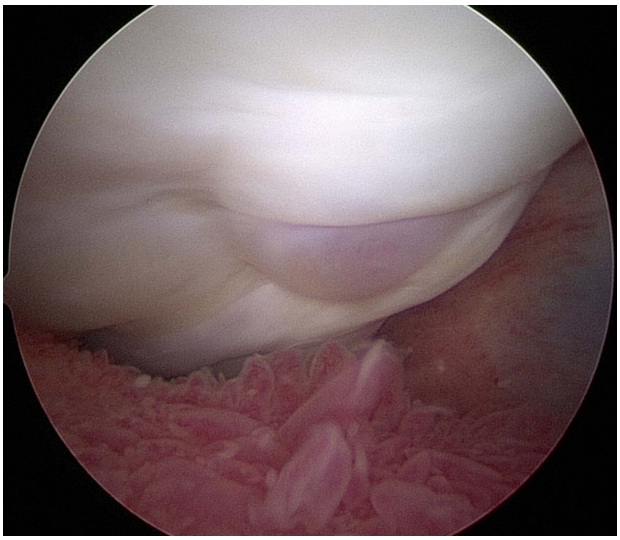
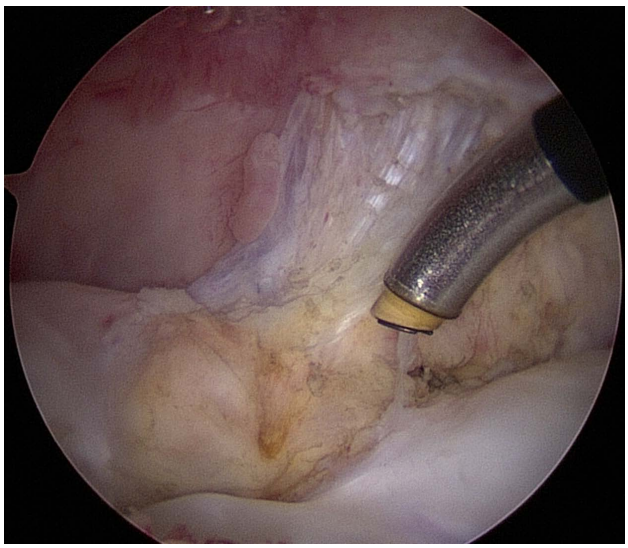
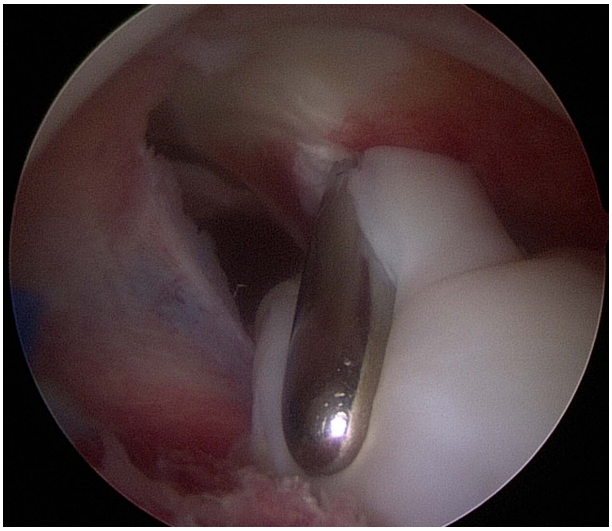


(b)

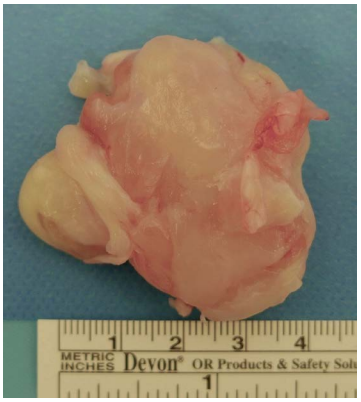


(c)



(d)

Figure 4. (a) Arthroscopic view from anterolateral portal towards medial suprapatellar recess, where the large intraarticular soft-tissue tumor is located; (b) The close-up view shows the pale white smooth surface of the polycyclic tumor mass, surrounded by reactive synovitis; (c) Arthroscopic resection of NF-tumor by coblation technique via lateral-suprapatellar portal, cutting through the broad tumor base by means of vaporizer (ArthroCare, Sunnyvale, CA), preserving the fibrous capsular layer; (d) Ablation of the entire tumor mass with grasping forceps through enlarged lateral-suprapatellar portal.



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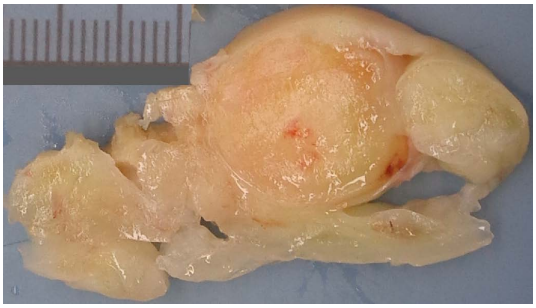
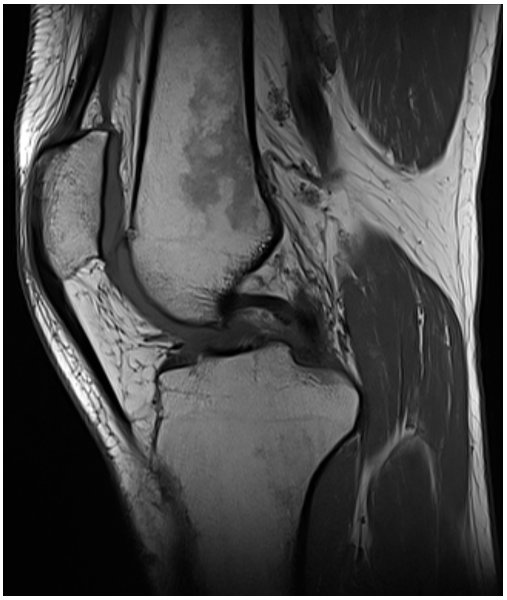


(b)

Figure 5. (a) The fresh excised specimen; (b) Cross section of the formalin fixed specimen shows nodular pale-white surface with cystic formation peripherally and smooth pseudo capsule.



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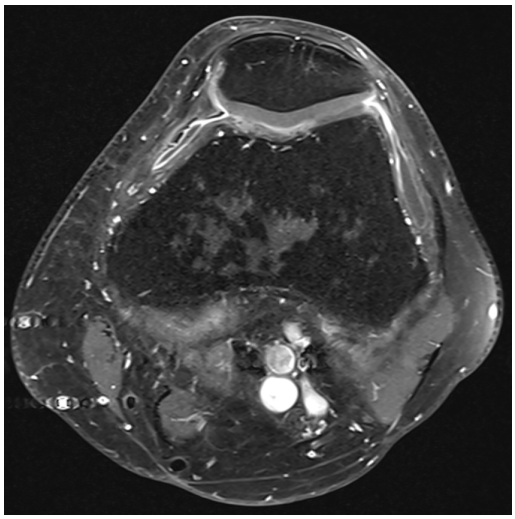

(b)

Figure 6. (a) Sagittal T1-weighted control MRI after tumor resection without evident remnants or recurrence of former NF entity in the patellofemoral compartment; (b) Axial T2-weighed control MRI depicting postoperative synovial changes with minimally increased contrast-medium enhancement medial to the patella, pre-existing degenerative chondral changes and minimal residual effusion.

3. Discussion

The intra-articular mass in the presented case was not appreciated/recognised as pathologic formation in the first MRI performed elsewhere. The enlarging mass documented in the repeat MRI 8 months later did not exhibit a pattern clearly attributable to a specific diagnosis. Considering the possibility of a malignant process (e.g. synovial sarcoma) it was decided to perform a sonographically guided core biopsy leading to the diagnosis of NF confirmed by the presence of the *MYH9-USP*6 rearrangement in the NGS study.

The presence of the *USP*6 gene rearrangement appears to be a factor involved in the development of neoplastic processes with the tendency to spontaneous regression, such as NF [6] [7] [8]. Both myositis ossificans and aneurysmal bone cyst belong to the spectrum of lesions with *MYH*9-*USP*6 gene fusion and are considered as a model of "don't touch lesions" [9]. Further observation to expect possible spontaneous regression was discussed with the patient; however with documented enlargement and increasing discomfort he opted for active treatment. Arthroscopically a marginal en-bloc resection could be performed. The MRI 7 months postoperative showed no evidence of tumor persistence and the patient is asymptomatic at 1 year follow-up.

NF commonly occurs in sucutaneous tissue, skeletal muscle, vessels [2], but is rarely seen intraarticular [10]. *MYH*9-*USP*6 gene fusion identified in intraarticular NF of the knee was first described by Miyama *et al.* [10] in two cases; a third case of intraarticular NF of the knee with *MYH9-USP*6 gene fusion was reported by Igrec *et al.* [11].

Even though intraarticular NF diagnosed without proven *USP*6-gene-rearrangement may behave and be treated similar as NF in other locations we would caution to pool and mix data as this may prevent to estimate possible differences according to the site of affection.

In the reported cases of intraarticular NF the lesions were usually operated without prior biopsy, often assumed to be TSGCT.

Fortunately intraarticular malignant processes are rare and reported as case studies or small series [12] [13] [14] [15].

However, given the impact of inappropriate initial treatment of sarcomas of any site cautious diagnostic assessment of any articular process is mandatory.

Imaging of TSGCT, the most frequent intra-articular neoplasia, is fairly typical and when hemosiderin deposits are present almost pathognomonic. However most other benign processes exhibit features also observed in TSGCT.

Synovial processes can be considered as already having contaminated the entire joint as is the case of extraarticular neoplasm having invaded the joint. Treatment modalities for benign processes may differ according to the definitive pathologic diagnosis ranging from observation (sometimes indicated in TSGCT, maybe also for NF) over arthroscopic procedures (indicated for most benign neoplasms) to open resection as favored e.g. for synovial hemangioma [16] [17].

An overview regarding diagnosis and management of neoplasms involving synovial joints recently was given by Jang *et al.* [3] including osseous processes. Chebib *et al.* [15] report on 15 cases of intraarticular sarcoma; synovial sarcoma (n = 6) and extraskeletal myxoid chondrosarcoma (n = 3) being the most frequent.

Imaging of intraarticular masses are classified by Adams *et al.* [13] according to absence or presence of calcification and bone erosions in radiography, and MRI features subdivided in four categories as solitary focal mass, multifocal solid masses, diffuse solid mass and diffuse synovitis (**Table 1**).

Sheldon *et al.* [12] classify synovial processes according to their nature as non-

infectious synovial proliferative processes, infectious granulomatous diseases, vascular malformations, malignancies, and miscellaneous.

When assessing intra-articular processes we follow a checklist according to the pathologies given in Tables 1-3. If there is doubt about diagnosis and the best treatment modality percutaneous ultrasound or CT-guided biopsy is favored whenever feasible. Primary arthroscopic or open approach should be reserved for unequivocally clear indications.

This case confirms the experience of the three reported cases of NF with *USP*6-gene rearrangement and adds informations referring to diagnosis and management of rare intraarticular neoplasm.

4. Conclusions

The diagnosis of intra-articular NF can be confirmed by the presence of *MYH*9-*USP*6 gene fusion and should be considered in the evaluation of intra-articular lesion.

Though the most frequent synovial process is TSGCT treatment strategies should be developed upon all possible other diagnoses including sarcoma, metastases, tumor-like lesions as well as infection or malformation.

Using a check-list may assist in the evaluation.

In the work-up of intra-articular synovial processes of the knee we follow a check-list as given in Tables 1-3 with reference to respective reports and the WHO classification of tumours of soft tissue and bone [2].

Patient Consent

The patient was informed that data from his case would be submitted for publication, and an informed consent was obtained.

Conflicts of Interest

The authors declare no conflict of interest regarding the publication of this paper. No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this article.

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