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Intra-articular Knee Neurofibroma in a Patient with Neurofibromatosis: A Case Report and Review of Literature

Thomas Falconiero[1], Mark LaGreca[1], Arash Badragheh[2], Nathan Jones[1], Christopher Kester[3]

Learning Point of the Article:

There are few case reports written on intra-articular knee neurofibromas. This case report discusses an intra-articular knee neurofibroma found incidentally operating on a distal femur fracture. There is a paucity of literature on intra-articular knee neurofibromas; this manuscript reviews the few previous case reports and relevant literature.

Abstract

Introduction: Neurofibromatosis type I (NF1) is an autosomal dominant disorder that typically results in Café-au-lait macules and peripheral nerve sheath tumors (i. e, neurofibromas). While peripheral neurofibromas are common, intra-articular knee neurofibromas are rarely described in the literature. To date, there only have been two other case reports noting intra-articular knee neurofibromas. The authors present the case of a patient with NF1 who was found to have an intra-articular knee neurofibroma incidentally discovered during the surgical approach to a retrograde femoral nail.

Case Report: The patient is a 65-year-old female who presented to the emergency room after a fall from standing height with left distal thigh pain. X-rays were obtained and demonstrated a left supracondylar, extra-articular distal femur fracture. The patient had known NF1 with widespread cutaneous neurofibromas and was noted to have a large palpable soft-tissue mass over the anterior aspect of the knee on pre-operative examination. After an incision was made for a retrograde femoral intramedullary nail, the large soft-tissue mass prevented adequate surgical visualization. The mass was noted to track laterally around the patellar tendon, into the knee joint, communicating with Hoffa's fat pad. The mass was resected and sent for pathology. The case proceeded uneventfully. The mass sent for pathology was positive for a neurofibroma. Clinical features alongside radiographic, computed tomography, and histopathological findings are presented.

Conclusion: Intra-articular knee neurofibromas are rare and there is a paucity of literature on the topic. While found incidentally in our patient, the discovery of an intra-articular neurofibroma underscores the need for further investigation into its potential association with neuropathic arthropathy and other associated joint disorders.

Keywords: Neurofibromatosis, intra-articular lesion, distal femur fracture.

Introduction

Neurofibromatosis (NF) is an autosomal dominant genetic disorder characterized by dysregulated cellular growth of neural tissues due to mutations affecting the NF-1 gene, which inhibits the activity of RAS proto-oncogenes [1]. Diagnosis of NF type-I (NF1) includes the presence of >10 café-au-lait macules, axillary freckling as well as neoplastic abnormalities such as neurofibromas and optic gliomas. Neurofibromas usually develop from the protective coverings of peripheral nerves. Complex presentations sometimes include skeletal conditions such as scoliosis, both dystrophic and non-dystrophic, congenital pseudarthrosis of the tibia, and soft-tissue malignancies [1,2].

Intra-articular knee NF, characterized by peripheral nerve sheath

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Author's Photo Gallery


Dr. Thomas Falconiero


Dr. Mark LaGreca


Dr. Arash Badragheh


Dr. Nathan Jones


Dr. Christopher Kester

[1]Department of Orthopedic Surgery, Philadelphia College of Osteopathic Medicine, Philadelphia, Pennsylvania,
[2]Department of Medicine, Philadelphia College of Osteopathic Medicine, Philadelphia, Pennsylvania,
[3]Main Line Orthopaedics and Spine, Lankenau Medical Center, Wynnewood, Pennsylvania.

Address of Correspondence:
Dr. Thomas Falconiero,
Department of Orthopaedic Surgery, Philadelphia College of Osteopathic Medicine, Philadelphia, Pennsylvania.
E-mail: tf249555@pcom.edu

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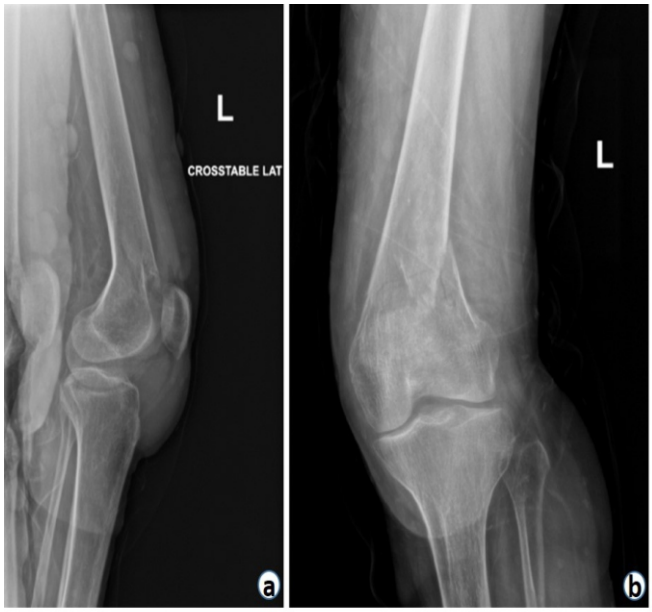

Figure 1: (a and b) Two views of anteroposterior and lateral radiographs of the left knee demonstrating an extra-articular supracondylar distal femur fracture.

tumors within the knee joint, is exceptionally rare. Specifically, there have been two case reports written on intra-articular hip neurofibromas and two intra-articular knee neurofibromas [3-6]. The two case reports written on intra-articular knee neurofibromas both describe the patients' having anterior knee pain likely due to the mass effect of the neurofibroma within Hoffa's fat pad. Other reports on intra- or extra-articular neurofibromas discuss the significant dysfunction neurofibromas can have on the affected extremity. Interestingly, the intra-articular knee neurofibroma was an incidental finding in our patient. This manuscript reviews a few case reports in the available literature and discusses the clinical relevance of knee intra-articular neurofibromas. This is the first case report to the author's knowledge that presents an intra-articular knee neurofibroma that was found incidentally during the surgical exposure for a retrograde femoral intramedullary nail (IMN).

Case Report

The patient is a 65-year-old female who presented to the emergency room after a fall from a standing height with left distal thigh pain. The patient's history included a previous cerebrovascular accident resulting in persistent left-sided weakness 4 years prior, along with a confirmed diagnosis of NF1. She ambulates with a walker at baseline due to her residual left-sided weakness. There were no reports of left knee pain or dysfunction before the fall. On examination, she was noted to have a mildly tender, large palpable soft-tissue mass over the anterior knee, just inferior to the patella. Her examination was otherwise unremarkable. Plain radiographs of the left knee revealed an extra-articular supracondylar distal femur fracture (Fig. 1a and b). Computed tomography (CT) scan of the left knee was obtained for better characterization of fracture morphology (Fig. 2a, b, c). She was placed into a well-padded knee immobilizer for comfort in the emergency room. The patient was admitted to the hospital to the medical service for operative fixation of the distal femur fracture with retrograde femoral IMN fixation. She was medically optimized and underwent surgery the following day. Upon making the standard infra-patellar incision for a retrograde femoral IMN, a

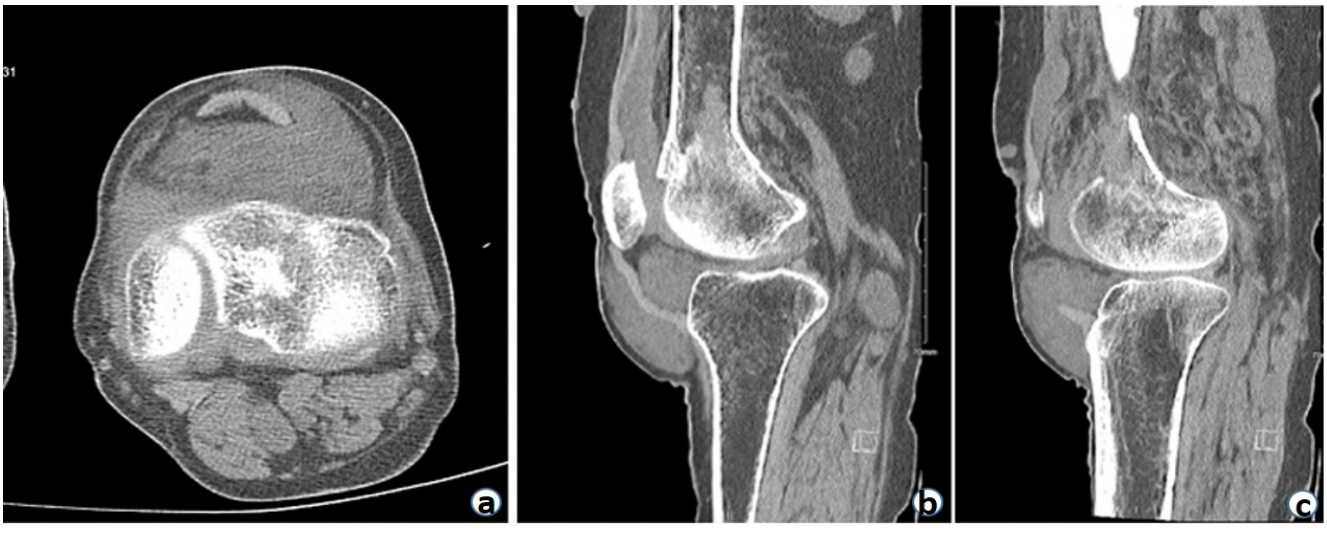

Figure 2: Multiple computed tomography cuts including axial (a) and two sagittal cuts (b and c) of the left knee demonstrating an extra-articular supracondylar distal femur fracture with a soft-tissue mass that wraps around the patellar tendon to Hoffa's fat pad.

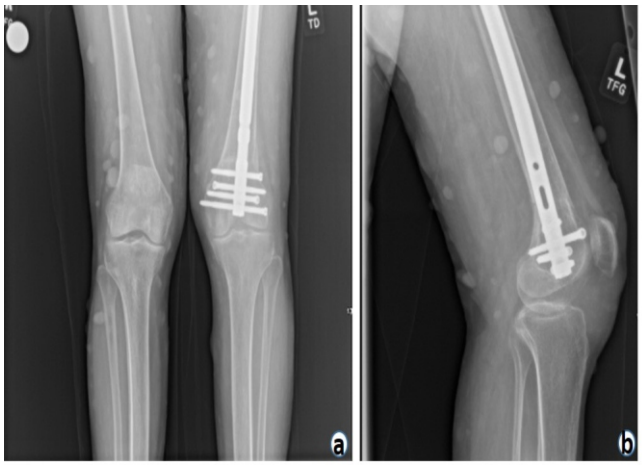

Figure 3: (a and b) Three-month post-operative X-rays of the left knee demonstrating retrograde femoral nail fixation with hardware in appropriate alignment and callus formation around the distal femur fracture site.

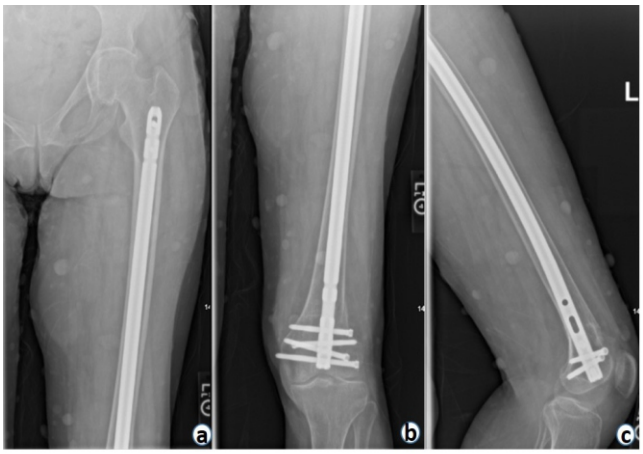

Figure 4: (a-c) Three views of the left femur status post retrograde intramedullary nail fixation with near anatomic alignment and interval callus formation, 5 months post-operative.

large soft-tissue mass was encountered anterior to the patellar tendon. This was carefully dissected out and was found to track lateral to the patellar tendon, into Hoffa's fat pad. The specimen was resected and sent for pathology. The case resumed uneventfully. The patient was recommended for toe touch weight bearing to the left lower extremity immediately postoperatively. A few days later she was discharged from the hospital to a skilled nursing facility. She was made toe touch weight bearing for about 6 weeks postoperatively and on her 6-week postoperative visit, she was allowed for weight bearing as tolerated to the left lower extremity. Pain was well controlled throughout her postoperative period and her incisions healed very well. She had painless range of motion over her hip and knee joints at her 6-week and 3-month follow-up visits. She demonstrated interval callus formation around her fracture site on her 3-month postoperative visit (Fig. 3a and b). She was seen about 1 week ago for a 5 month visit and had painless hip and knee range of motion. Her 5-month post-operative x-rays is shown in Fig. 4a, b, c.

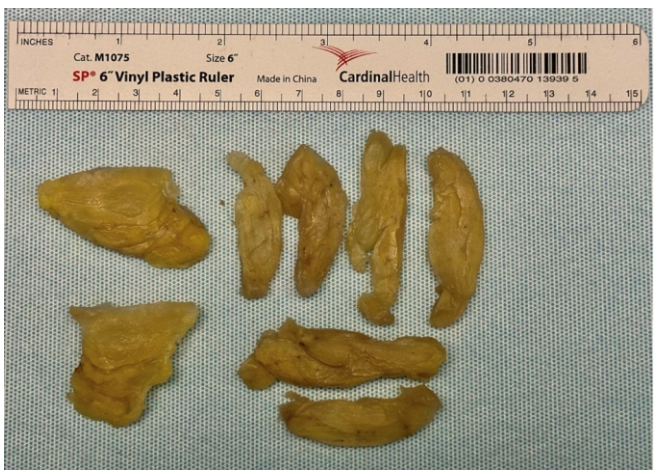

Figure 5: Gross pathology specimen taken intra-operatively.

The gross description specimen sent for histopathological examination was described as a "flat discoid segment of bright yellow lobulated fibro-adipose tissue measuring 6.9 × 5.5 × 3.0 cm in greatest dimensions" by the reading pathologist (Fig. 5). The histopathological examination confirmed the diagnosis of cutaneous diffuse neurofibroma, consistent with the patient's known diagnosis of NF1. The immunohistochemical stains, with adequate controls, were performed. The lesional cells were strongly positive for SOX10, focally positive for CD34, and negative for desmin and pancytokeratin. This is shown in Fig. 6a, b, c.

Discussion

The term "neurofibroma" was coined in 1882 by German pathologist Frederick von Recklinghausen to designate the benign tumors commonly associated with this disorder [7]. He was the first to observe that these tumors arise from the peripheral nerve sheath, which comprises a blend of Schwann cells and fibroblasts. NF1 has an estimated birth incidence of 1 in 2500 and a prevalence of 1 in 4000 worldwide, making up the majority, about 90% of all NF cases [1]. Although bone and soft-tissue involvement is widely acknowledged, intra-articular lesions appear exceptionally rare, with only a handful of cases documented in the literature. This manuscript contributes to the limited documentation of intra-articular knee neurofibromas.

Microscopically, neurofibromas have a histopathological characteristic that includes an unencapsulated heterogeneous cell population interwoven within a collagen-rich extracellular

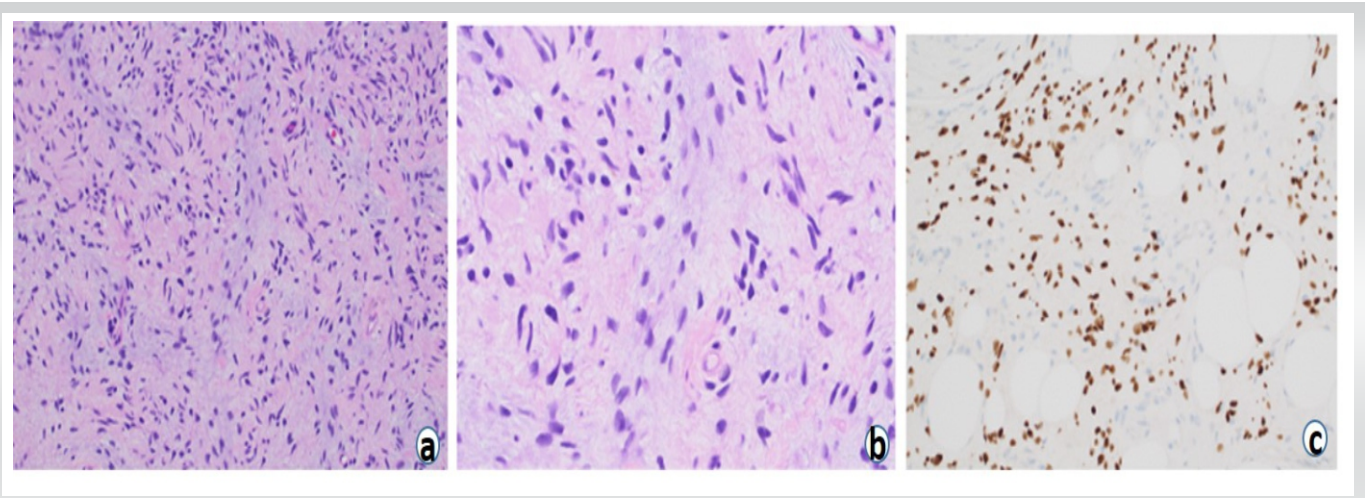

Figure 6: Histopathology slides including low power H&E [a] High power H&E [b] and Sox10 Special stain [c].

matrix [8, 9]. This matrix consists of a combination of Schwann cells, perineural cells, and fibroblasts, forming interconnected networks with nerves. The cellular morphology is often spindle-shaped cells with unclear boundaries, eosinophilic cytoplasm, and oval or twisted nuclei [8]. Plexiform neurofibromas have similar cell types but with a larger extracellular matrix and increased vascularization. Histological and immunohistochemical staining techniques, such as anti-S100 protein and anti-Vimentin antibody staining, are valuable tools for determining the Schwann cell composition of the neoplastic tissue. Schwann cells represent 60–80% of neurofibroma cells, as demonstrated by positive staining for S100 protein [9].

Despite their histopathological benignity and slow growth rate, intra-articular tumors can cause deteriorating neurological issues and loss of function over time, most commonly due to the strain exerted on peripheral nerves, nerve roots, or the spinal cord [10]. McCann et al. describe a case study of an adult male with neuropathic arthropathy who presented with a swollen right knee and valgus alignment deformity [11]. The neuropathy appeared to stem from the invasion of a neurofibroma into the spinal nerve, leading to knee instability, pain, and sensory disturbances. Other reported cases of intra-articular neurofibromas have focused on the joint degeneration and instability thought to be caused by NF1 [12, 13]. Lokiec et al. describe a case of a 5-year-old girl who had presented due to swelling of her left knee [8]. X-ray radiographs of the knee indicated severe joint degeneration and Tc-99m bone scanning showed increased uptake in the left knee. In this case, the neurofibroma had infiltrated the anterior cruciate ligament (ACL) and nerve fibers within the synovial tissue, which was thought to cause limb length discrepancies, therefore, causing considerable joint instability. Few case reports have noted the presence of neurofibromas inside the knee joint, which may contribute to leg length discrepancy and subsequent joint instability [13, 14].

The unique feature of our case is the location of the tumor inside Hoffa's pad, only noted in the literature twice to the author's knowledge. Hoffa's fat pad is crucial in providing cushioning and support to important tissues such as the ACL, patellar tendon, and inferior pole of the patella [15, 16]. Hoffa's fat pads' rich vascularization and innervation by type IVa nerve fibers increase its vulnerability to the formation of neurofibromas [16]. A neurofibroma inside this fat pad can greatly disturb knee biomechanics, resulting in aberrant joint mechanics [16]. This disruption is attributed to decreased knee extension force of the quadriceps on the tibia and a reduced sagittal angle between the quadriceps and patellar tendon, as demonstrated in cadaveric knee models [16]. Patients may experience increased pain during weight-bearing activities, reduced range of motion, and diminished overall knee stability [16]. To the authors' knowledge, the two other published case reports describing intra-articular knee neurofibromas in Hoffa's fat pad were causing anterior knee pain [3, 4]. Both patients elected to have the intra-articular knee tumor resected and went on to painless range of motion within a few months after surgery.

In our patient's case, mild-to-moderate radiographic osteoarthritic changes were noted in the left knee joint; however, she denied any pain or dysfunction related to the palpable soft-tissue mass over the anterior knee before surgery. The observed radiographic osteoarthritic changes are likely multifactorial and age-related, however, given the large intra-articular neurofibroma noted intra-operatively, the degeneration might be related to the tumor's limitation of joint motility. The restricted movement can hinder the vascular supply required for nourishing the chondrocytes leading to the

observed deterioration [17].

The primary objective in the case presented here was to address a femur fracture by employing a retrograde femoral IMN through the patellar tendon. However, during the approach, the authors discovered a neurofibroma anterior to the patellar tendon that tracked intra-articularly to Hoffa's fat pad. This incidental discovery emphasizes the need to take into account these uncommon tumors while evaluating the possible causes of discomfort over the anterior aspect of the knee.

Conclusion

Intra-articular knee neurofibromas are exceedingly rare in the available literature. In contrast, to other cases where patients complained of pain, instability, leg length discrepancy, or dysfunction, our patient did not have any symptoms related to her knee joint before her fall. This suggests that intra-articular neurofibromas can remain clinically quiescent until incidentally discovered. The presence of these tumors can limit movement, disrupt blood flow to cartilage, and cause changes linked to osteoarthritis. In addition, having a tumor in Hoffa's pad could result in restrictions on knee extension and reduced knee stability increasing the likelihood of joint deterioration and injury. It is plausible that peripheral nerve damage caused by neurofibromas contributes to the development or worsening of neuropathic arthropathy. More research should be performed on this phenomenon as a mass effect over a joint may cause pain or dysfunction.

Clinical Message

Intra-articular knee neurofibromas are rarely reported in the literature and may be associated with joint arthropathy.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given the consent for his/ her images and other clinical information to be reported in the journal. The patient understands that his/ her names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflict of interest: Nil **Source of support:** None

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