Desmoid-type Fibromatosis of the Lower Extremity: A Unique Case of Complete Lesion Resolution Following Core Needle Biopsy

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Highlights:

- Desmoid-type fibromatosis are locally aggressive fibroblastic/myofibroblastic neoplasms often exhibiting infiltrative growth and local recurrence.
- Radiologists should be aware that a subset of desmoid-type fibromatosis lesions will regress without treatment and may rarely completely resolve as in the presented case.
- Biopsy induced regression has been described in other neoplasms and the exact cause of phenomenon is unclear

ABSTRACT

Desmoid-type fibromatosis (DF) is a rare neoplasm characterized by fibroblastic and myofibroblastic proliferation. While characterized as a benign lesion that does not metastasize, desmoid-type fibromatosis exhibits a wide range of behavior from aggressive local tissue invasion and post-surgical recurrence to spontaneous regression. Tumor regression can occur following systemic medical therapy or rarely may occur in the absence of therapy. We present a case of a 50-year-old female with a left thigh vastus medialis intramuscular mass which underwent imaging work-up and subsequent core needle ultrasound-guided biopsy showing results of desmoid-type fibromatosis. Following biopsy, the tumor showed prompt, complete regression with complete MRI resolution 2 months following biopsy. The patient showed no evidence of disease recurrence out to one year on MRI surveillance. This case report will discuss desmoid-type fibromatosis imaging features, treatment strategies, spectrum of disease behavior, and atypical behavior such as the spontaneous tumor regression as seen in this case report. To our knowledge there have been no reported cases of DF spontaneous regression 2 months following a core needle biopsy. Understanding the variable behavior of desmoid-type fibromatosis can assist the radiologist in guiding management of these lesions with the goal of optimizing clinical outcomes and preventing unnecessary aggressive treatments for stable or regressing disease.

Keywords: Extra-abdominal Desmoid, Fibromatosis, Desmoid Regression, Desmoid Biopy

1. INTRODUCTION

Desmoid-type fibromatosis (DF) is defined by the World Health Organization Classification of Soft Tissue Tumors as a locally aggressive fibroblastic/myofibroblastic neoplasm with infiltrative growth and a tendency for local recurrence [1]. These neoplasms can be classified based on their location as extra-abdominal, intra-abdominal, or abdominal wall. DF can result in significant morbidity and in some cases mortality owing to disease progression near vital structures or presentation in head, neck, and mesentery. Aggressive local recurrence can occur after resection [2-3]. Overall, DF is rare with an annual incidence of 2-4 cases per million accounting for less than 3% of all soft-tissue tumors [4-5]. Most cases present at 15 to 60 years of age with a peak incidence between the ages of 25 and 35 [6]. The majority of DF cases occur sporadically, however there is an association with hereditary syndrome familial adenomatous polyposis (FAP). Together, DF and FAP are known as Gardner syndrome. Non-syndromic extra-abdominal lesions most frequently involve the extremities, head, neck, and chest wall [2].

Recent studies have demonstrated a wide range of DF behavior from progressive infiltrative disease to disease recession. This variable disease behavior has shifted treatment strategy from early surgical resection and radiation therapy to disease surveillance with graduated treatment beginning with systemic therapy [7-16]. Surgery and radiation therapy still have a role in recalcitrant or aggressive cases or those lesions that start in the abdominal wall with high likelihood of favorable margins [3, 17]. Although spontaneous regression is a described outcome in a minority of cases, a DF case with complete regression in the post-biopsy period has not been described in the literature.

We present the imaging and histology of an interesting case of an extra-abdominal DF tumor arising within the left vastus medialis muscle. Immediately after the ultrasound-guided core biopsy, the tumor showed regression on imaging and completely resolved within 2 months of biopsy. Given the rising role of disease surveillance in the treatment of DF, the radiologist should be aware of features that favor aggressive progression (lesions with high percent volume of T2 intensity) as well as the possibility of marked spontaneous DF regression [18]. Careful assessment of DF tumor size, MRI signal, and behavior on imaging is important in the post-biopsy period as this case demonstrates that regression and even complete tumor resolution is possible. Failure to appreciate disease stability or appropriately report DF tumor regression may subject the patient to unnecessary systemic therapies, radiation, or surgical therapies.

2. CASE REPORT

A 50-year-old female presented to the emergency department in 2016 with a complaint of left thigh pain for one week related to a palpable mass noted two weeks prior to presentation. Medications and past medical history included azathioprine and mesalamine for ulcerative colitis, lisdexamfetamine for attention deficit hyperactive disorder, and alprazolam for reflex sympathetic dystrophy. The patient had no history of prior DF or clinical findings of familial adenomatous polyposis (FAP). Laboratory analysis at the time of presentation showed normal white blood cell count, erythrocyte sedimentation rate, and creatine kinase levels. A CT scan with iodinated contrast demonstrated a 2.5 x 1.5 x 5.9 cm (anteroposterior x transverse x craniocaudal) enhancing mass within the left vastus medialis muscle (Fig. 1). An MRI performed the next day demonstrated a similar size mass with T1 intermediate signal and T2 hyperintense signal which ranged from slightly hyperintense to extremely hyperintense (as compared to skeletal muscle). T2 hyperintense signal comprised nearly 100% of the mass volume. The mass had avid, homogenous gadolinium contrast enhancement (Fig. 2).

Following orthopedic oncology clinical assessment, ultrasound-guided biopsy of the lesion was performed one week after presentation. Ultrasound showed a circumscribed, mildly hypoechoic soft tissue mass without posterior acoustic features, and without significant internal vascularity (Fig. 3). Six core needle biopsies were obtained using a 14-gauge spring loaded biopsy device.

Histopathological analysis of the biopsy specimen showed a dense, fibrous spindle cell proliferation with a highly infiltrative pattern involving skeletal muscle. Immunohistochemical stain for beta-catenin demonstrated diffuse cytoplasmic and occasional nuclear positivity consistent with desmoid fibromatosis (Fig. 4).

After receiving the biopsy results, the orthopedic oncology team referred the patient to radiation oncology. The patient agreed to proceed with a simulation treatment CT scan. Prior to that study, a whole body MRI was performed 3 weeks following biopsy and showed no additional suspicious lesions. Curiously, on this wide field of view MR study, there was decreased T2 signal in the left thigh mass. A small field of view MRI of the thigh was immediately performed (3 weeks after biopsy) and showed a significant decrease in size of the vastus medialis mass which now measured 1.9 x 0.3 x 3.1 cm (anteroposterior x transverse x craniocaudal). The mass signal had undergone marked conversion to T2 intermediate and dark elements. The mass no longer had internal T2 hyperintense signal or internal gadolinium enhancement (Fig. 5). The radiation therapy plan was abandoned and the patient agreed to have close imaging surveillance of the mass.

Another MRI of the left thigh was obtained 2 months following biopsy. There was no imaging evidence of a mass on T1, T2, or T1 fat saturation post contrast imaging indicating macroscopic mass resolution (Fig. 6). The patient denied any symptoms. The patient underwent surveillance MR imaging out to 1 year following biopsy with no evidence of mass recurrence. It has been 4 years since biopsy and the patient denies subjective mass recurrence.

3. DISCUSSION

DF is a non-metastatic neoplasm that exhibits a wide range of behavior from relentless local invasion to regression. One recent study involving 168 DF patients managed with active surveillance demonstrated disease progression in 36%, stable disease in 36%, disease regression in 27%, and complete regression in 12% of the cases although regression time course was not specifically discussed [19]. DF is not malignant, however, there are 4 case reports of a sarcoma co-developing with DF tumors [16, 20-22]. It is not known if the origin of these sarcomas were truly associated with DF, were an incidental association, or were related to DF treatment effects.

DF disease features which determine this variability in tumor behavior have not been completely elucidated, although there are imaging characteristics to which the radiologist should pay special attention [18]. Factors implicated in disease progression include large tumor size, trauma, surgical intervention, and alterations in systemic hormones such as in pregnancy [4, 23]. Recent literature suggests the percentage of the lesion containing MRI T2 hyperintesity may also predict prognosis [18].

DF histologic features include low to moderately cellular, long and broad fascicles containing spindled cells that are uniform in appearance. The cells lack cytologic atypia and are arranged in long, sweeping bundles. The stroma is collagenous with variably prominent blood vessels, some with perivascular edema [24]. Keloidal-like collagen, hyalinization, and myxoid change have been described [1] but these changes were not present in our case. Immunohistochemistry features include aberrant B-catenin nuclear staining which is helpful in confirming the diagnosis, especially in small biopsy samples [25]. Specimens from our case showed characteristic nuclear B-catenin positivity.

MRI is the best imaging modality for extra-abdominal DF evaluation as MRI provides the highest tissue contrast to muscle and is superior for showing the true macroscopic extent of disease in relation to neurovascular and osseous structures. DF lesions feature a variable mixture of fibroblasts, cellular matrix, collagen fibers, and myxoid stroma. MRI signal and enhancement characteristics correspond to a lesion's histopathological composition. DFs demonstrate T2 hyperintensity to skeletal muscle when there is a high proportion of cellular matrix and intermediate to low T2 signal when collagen is a more predominant component of the lesions. All DFs are typically isointense to muscle on T1-weighted imaging [2, 6, 26]. Lesion components with high cellularity or myxoid components demonstrate avid contrast enhancement. Lesions with higher collagen fiber content demonstrate mild to absent enhancement [2]. A non-specific finding of non-enhancing bands has been described and corresponds to collagenous stroma [26].

Interestingly, the pre-biopsy MRI evaluation of the DF lesion in this case report showed the lesion to have nearly 100% T2 hyperintense signal by volume. The study by Cassidy, et al would characterize this as a lesion at high risk for progression requiring treatment [18]. The opposite was true in this case with lesion T2 hyperintensity completely resolving on the post-biopsy MRI. DF lesion surveillance findings of decreasing lesion size, decreasing T2 signal and decreasing enhancement are established MRI features of regression [2, 6, 18, 26-27], all features demonstrated in this case report in the immediate weeks following biopsy.

MR imaging is most commonly used for disease surveillance, but ultrasonography (US) may serve as a surveillance adjunct for superficial tumors in the torso, abdomen, or extremities. US appearance is variable with lesions frequently appearing oval, poorly marginated, and with variable echogenicity and vascularity [2, 28]. A layered echotecture appearance is often present and corresponds with heterogeneous tissue composition of cell, matrix, and collagen [2]. Tissue contrast in US is lower than in MRI, so US surveillance is more effective in mass-like disease. US may underestimate worsening infiltrative disease which may be better depicted on contrast enhanced MRI.

CT is not a primary modality to evaluate extra-abdominal DF as tissue contrast between the lesion and adjacent muscle is often poor. CT is used for intra-abdominal lesions in initial and surveillance imaging as the mesenteric fat provides better lesion contrast. CT may be superior to MRI in demonstrating disease involvement of the enteric tract and can evaluate for complications like bowel obstruction [2]. CT characteristics of attenuation and enhancement will vary based on the lesions cellular content [6, 29]. Lesions with high collagen can be hyperdense to surrounding muscle or hypodense if there are significant myxoid elements [6]. CT imaging of extremity lesions may be performed in the emergency department setting as in this case secondary to imaging resource availability.

Given the wide range of DF behavior from advancing local invasion to regressing disease and the possibility that some clinical outcomes are actually worsened by surgical resection, management and therapeutic approaches to DF have changed in the last decade [7-16] . Recent consensus guidelines favor initial surveillance of at least 12 months or up to 24 for tumors that do not pose risk to function loss or intolerable symptoms [17, 30-31]. The 2018 National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology reflect this shift away from surgical management and recommend observation for DF tumors less than 7 cm in size. For tumors greater than 7 cm in size, a trial of systemic therapy is recommended prior to surgery [30]. Disease cure is not possible in the majority of DF cases, therefore alternative treatment goals including local tumor control with an emphasis on improving patient function and providing pain-relief are secondarily sought. A multidisciplinary team is needed for surveillance and treatment of these neoplasms. Surgical oncologists, radiation oncologists, pathologists, and radiologists play an important role in management [2]. For DF disease that has failed conservative therapies, has intolerable symptoms, or threatens critical physiologic functions, surgical resection is appropriate with local control achieved in 75-80% of cases [30, 32-33]. In cases where surgical resection may place functional outcome at risk (disease encasing neurovascular structures or vital organs), systemic strategies such as anti-inflammatory medications, hormonal therapy, cytotoxic therapy, and molecular targeted therapies are employed [34-37]. Percutaneous cryotherapy has shown early promise as a viable treatment for extraabdominal DF in a small study, especially for disease that has failed other management strategies [38]. Radiation therapy is a viable option for DF of the extremities, but generally is avoided for intra-abdominal or retroperitoneal disease [30]. Radiation therapy was considered in our case, but not employed after post-biopsy imaging demonstrated lesion regression.

DF regression in response to therapy or in the absence of therapy occurs in a subset of cases. A summary of the desmoid regression literature is summarized in Table 1 showing rates of regression ranging from 0-27%. Van Houdt, el al had the largest series of 168 cases, all of which were initially managed with active surveillance. Complete regression was noted in 12 cases (7%). The most frequent site of complete regression was the abdominal wall (7 cases) with 2 cases of complete regression in the extremities [19]. The current case report demonstrates unique DF behavior with partial tumor regression occurring at 3 weeks, and complete tumor regression on MRI occurring at 2 months following core needle biopsy. The authors could not find any reports of a desmoid tumor showing complete MR imaging resolution following needle core biopsy. Hypotheses to explain the DF behavior in this case report could include local anesthesia/biopsy mediated immunologic response or tumor vessel disruption.

Resolution after biopsy has been reported for other neoplasms ranging from eosinophilic granuloma to primary and metastatic carcinoma [39-45]. Spontaneous regression was defined by Everson as the complete or partial regression of a neoplasm without treatment or with treatment considered inadequate to produce tumor regression [45]. The overall frequency of spontaneous regression is estimated at 1 in 60,000 to 100,000 cancer cases [46]. While spontaneous regression of a tumor without treatment is a well-known phenomenon, regression post-biopsy remains an underreported phenomenon. Best known cases of post-biopsy regression occur in neuroblastomas and lymphomas [47-48]. Other case reports of post-biopsy tumor resolution include merkel cell carcinomas, renal malignancies, squamous cell carcinomas (skin and lung), primary breast lymphoma, and pulmonary adenocarcinoma [40-45, 49-50]. The exact mechanism of biopsy induced regression remains unclear with immunologic and tumor necrosis among many mechanisms suggested [45, 51-53].

4. CONCLUSION

In summary, DF exhibits a range of variable behavior and a flexible clinical approach is needed to maximize clinical outcomes. As demonstrated in this case report, one extreme of the DF behavior spectrum includes complete resolution following core needle biopsy. Gaining an appreciation of DF’s variable behavior is important for radiologists and clinicians alike, particularly when applying lesion treatment and surveillance strategies. Radiologists should understand that a subset of DF lesions will regress without treatment and should recognize imaging signs of regression to avert overly aggressive treatment.

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Tables:

	Cohort number (n)	Number of cases undergoing surveillance only	Cases of partial or complete regression (% of cases demonstrating regression)
Shen C et al. [9] (retroperitoneal)	29	3	0 (0%)
Van Houdt WJ et al. [19] (all sites)	168	168	45 (27%)
Krieg AH [19] (extra-abdominal)	96	15	3 (3%)
Duazo-Cassin L et al. [11] (breast)	63	17	6 (10%)
Park JS et al. [12] (all sites)	47	20	1 (2%)
Colombo C et al. [13] (abdominal wall)	216	122	27 (13%)
Fiore M et al. [14] (all sites)	92	40	13 (14%)
Barbier O et al. [15] (extra-abdominal)	26	26	1 (4%)

Bonvalot S et al. [8] (abdominal wall)	147	102	29 (20%)

Table 1. Studies undertaken between 2008-2020 demonstrating varying degrees of desmoid regression.

Figures and Legends:

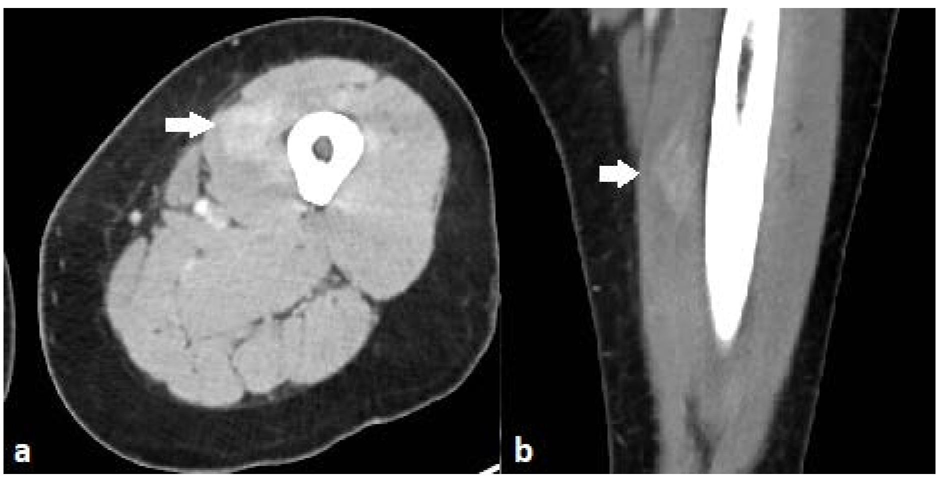

Fig. 1 Contrast enhanced CT images of a left vastus medialis desmoid tumor prior to biopsy . **a** Axial CT image and **b** sagittal CT image with iodine contrast shows an enhancing, ovoid, intramuscular mass (arrows) measuring 2.5 x 1.5 x 5.9 cm (anteroposterior x transverse x craniocaudal dimension). [Contrast: 95 mLs of iopamidol 370, intravenously administered]

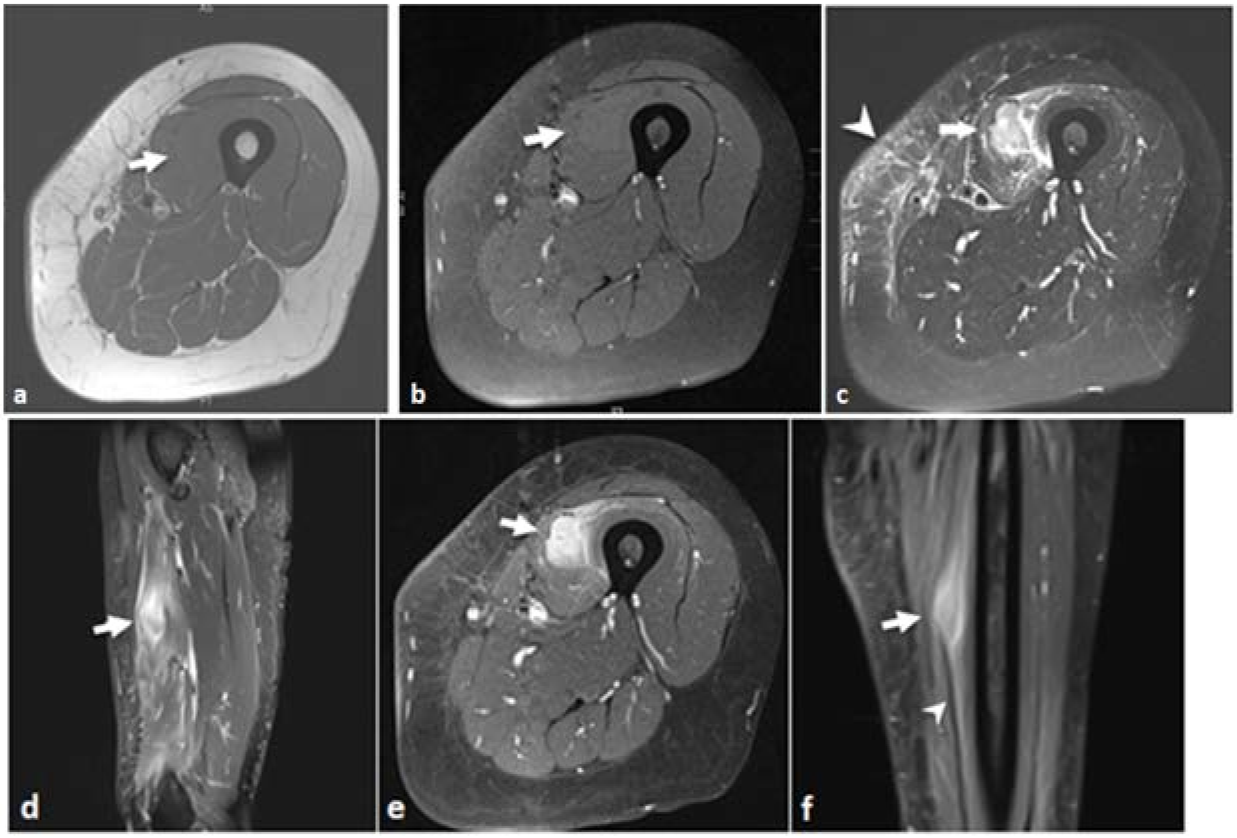

Fig. 2 MR images of a left vastus medialis desmoid tumor prior to biopsy. **a** Axial T1 and **b** axial T1 fat suppressed MR images show the mass (arrows) has isointense signal to surrounding muscle. **c** Axial T2 fat suppressed MR image shows a heterogeneous hyperintense mass (arrow) denoting high cellular content. There is surrounding muscle edema signal extending to the femur periosteum and also medial superficial fat edema (arrowhead). d Sagittal STIR MR image shows the hyperintense mass (arrow) and surrounding muscle edema signal. e Axial and f coronal T1 fat suppressed post gadolinium contrast MR images shows uniform mass enhancement (arrows) with linear enhancement extending along the adjacent myotendinous junction (arrowhead). [1.5T Magnet strength **a** 651/13 [TR/TE]; **b** 626/13 [TR/TE]; **c** 5440/91 [TR/TE]; **d** 3500/30 [TR/TE]; **e** 626/13 [TR/TE]; **f** 675/13 [TR/TE]; Contrast: 12 mLs of gadoterate meglumine, administered intravenously].

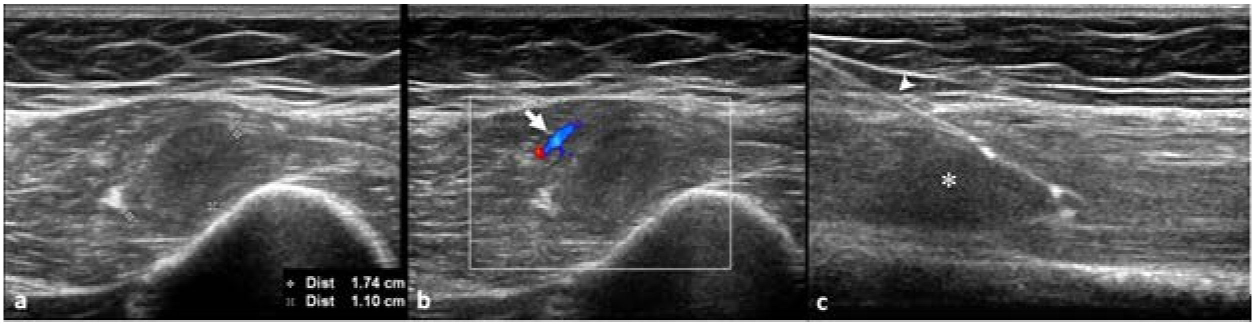

Fig. 3 Ultrasound-guided core needle biopsy of a left vastus medialis desmoid tumor. **a** Transverse US image shows a mass (measurement calipers) which is slightly hypoechoic to adjacent muscle. There is no posterior acoustic shadowing or increased transmission. **b** Transverse US image with color Doppler shows no mass internal vascularity. There is an adjacent blood vessel (arrow). **c** Longitudinal US image shows the mass (asterisk) and the 14-gauge core biopsy needle (arrowhead).

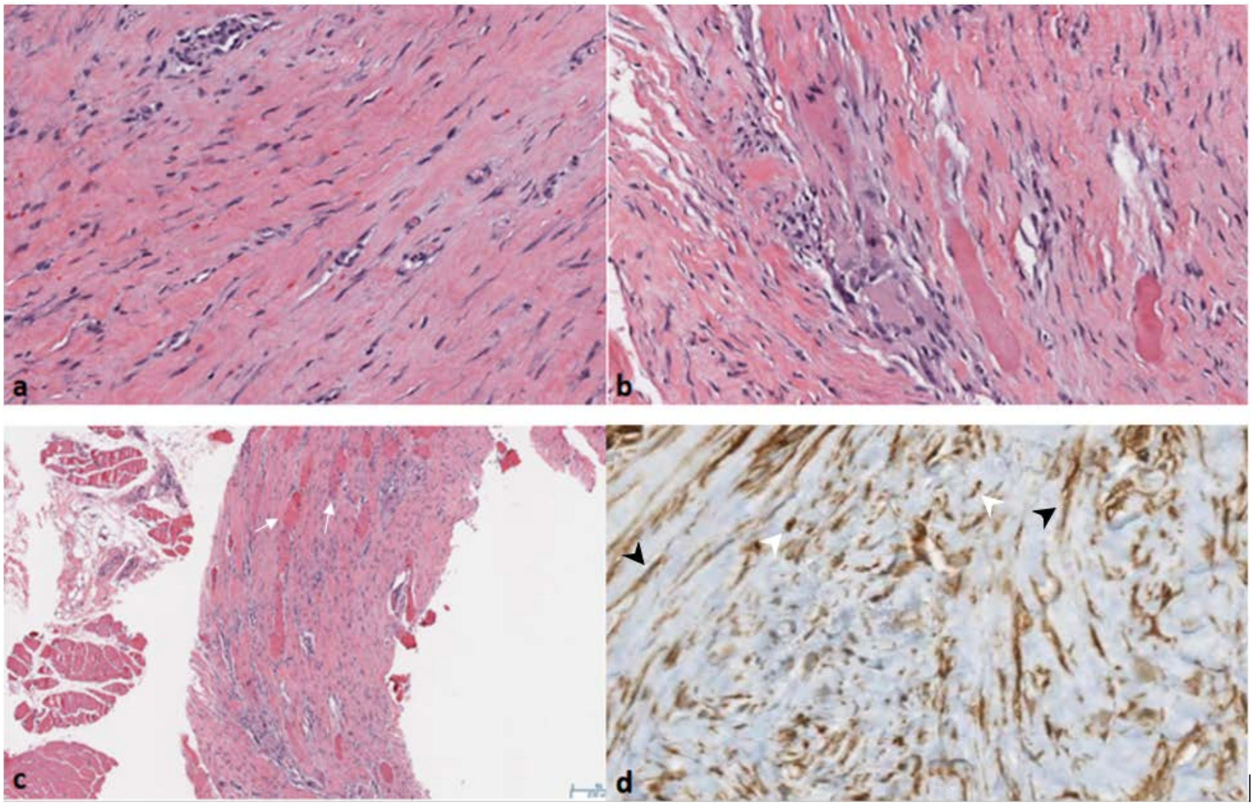

Fig. 4 Histology images of a left vastus medialis desmoid tumor. **a, b** (hematoxylin and eosin; 100 x magnification) and **c** (hematoxylin and eosin; 40 x magnification) showing long, sweeping fascicles with thin walled vessels infiltrating skeletal muscle (arrows). **d** Low power image with b-catenin stain shows nuclear (white arrowhead) and cytoplasmic (black arrowhead) b-catenin positivity (brown color).

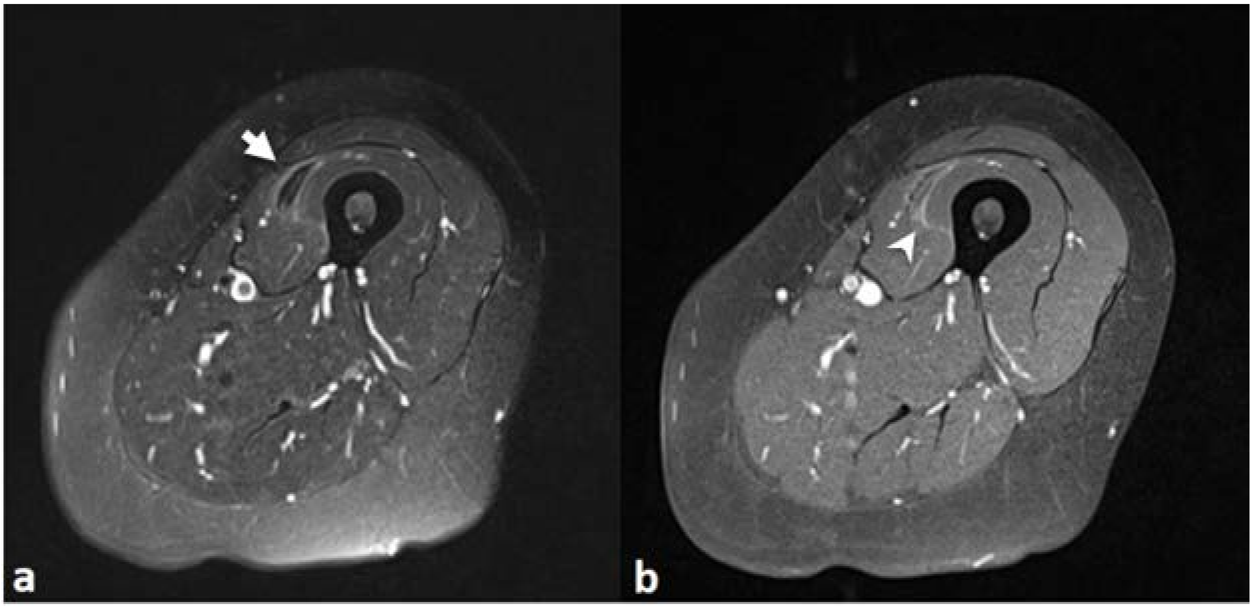

Fig. 5 MRI images 3 weeks after biopsy of a left vastus medialis desmoid tumor. **a** Axial T2 fat suppressed MR image shows a small remnant of the mass (arrow) measuring 1.9 x 0.3 x 3.1 cm (anteroposterior x transverse x craniocaudal). There is now a complete absence of T2 hyperintense signal. There is central intermediate signal with peripheral dark signal consistent with macroscopic collagen. **b** Axial T1 fat suppressed post gadolinium MR image shows no internal mass enhancement. There is subtle thin linear enhancement at the margin of the mass (arrowhead). [1.5T Magnet strength **a** 3240/88 [TR/TE]; **b** 672/11 [TR/TE] Contrast: 12 mLs of gadoterate meglumine, administered intravenously]

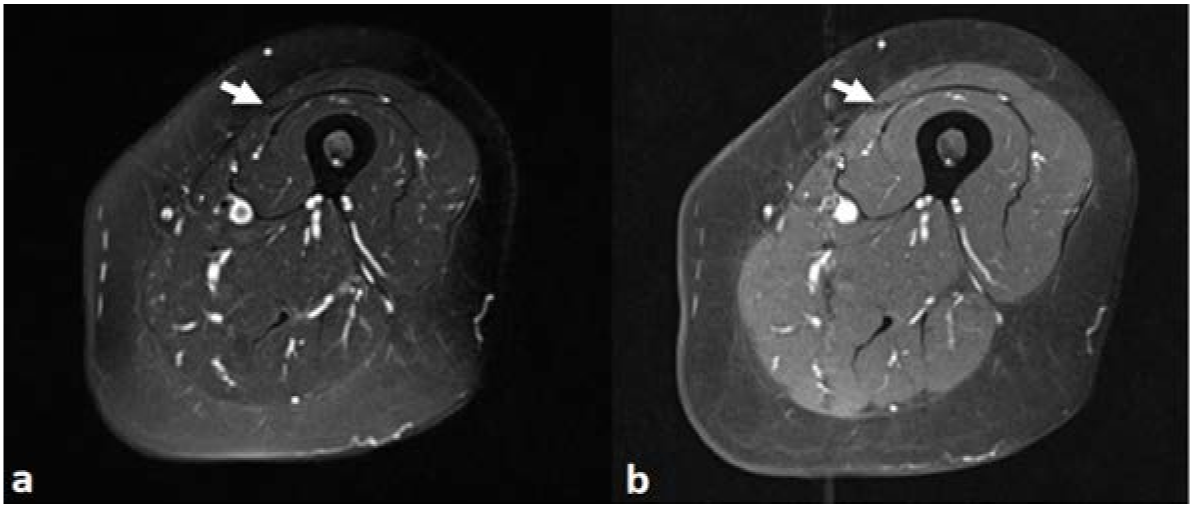

Fig. 6 MRI images 2 months after biopsy of a left vastus medialis desmoid tumor. **a** Axial T2 fat suppressed and **b** axial T1 fat suppressed post gadolinium MR images show no evidence of mass or abnormal signal in the previous region of biopsy (arrows). [1.5T Magnet strength **a** 3500/84 [TR/TE]; **b** 606/13 [TR/TE]; Contrast: 13 mLs of gadoterate meglumine, administered intravenously]