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Review Article

Angioleiomyoma of the knee: An uncommon cause of leg pain. A systematic review of the literature

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ABSTRACT

Objective: Angioleiomyoma is a rare benign painful soft tissue tumor, whose knee location is rare. Due its rarity, and not characteristic aspect on MRI the preoperative diagnosis is difficult.
Methods: We performed a systematic review of the literature, including a case of venous type angioleiomyoma that we have recently managed.
Results: A total of 24 published papers with 30 cases (including our illustrative case) were identified and included in our review. The mean patient age was 42.3 years (range18-63). The average size of the lesion was 17.8 mm. The presenting symptom was leg pain in 90% of cases. On magnetic resonance imaging (MRI), the lesion appeared isointense in T1 in 80% of cases and hyperintense on T2 in 90% of cases. Avid homogeneous enhancement after gadolinium administration was detected in 94% of cases. All patients underwent surgery and total resection was achieved in 100% of cases. No recurrence was observed after a mean follow-up of 19.5 months.
Conclusion: Angioleiomyoma occurs rarely in the knee and generally is associated with localized or radiating pain. The preoperative diagnosis is difficult also after completion of MRI study and requires high index of suspicion. Angioleiomyoma widens the spectrum of soft tissue lesions of the extremities and should be included in the differential diagnosis of lesions in this area.

1. Introduction

Angioleiomyoma, also known as vascular leiomyoma, is a rare benign soft tissue tumor of smooth muscle origin, arising from the muscular layer of vessel wall [1]. The most common presentation is a painful solid subcutaneous swelling. The incidence of angioleiomyoma is roughly 5% among all soft tissue tumors [2]. Lower limbs location is uncommon and its subcutaneous location at the knee joint is rare [2]. The initial presenting symptom for angioleiomyoma of the knee is localized or radiated pain in case of compression of neural structures. Accordingly, when this lesion is located in the extremities a differential diagnosis is difficult and should consider other more common neurosurgical pathologies including peripheral nerve sheath tumor. We reviewed the published cases of angioleiomyoma of the knee and we reported an additional unusual case of venous type angioleiomyoma (Figs. 1 and 2). The purpose of our study was to clarify clinical, diagnostic and therapeutic aspects of this lesion.

2. Materials and methods

2.1. Literature search

A PubMed and MEDLINE search was performed for angioleiomyoma of the knee. PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-analyses) were followed [3]. The search terms “angioleiomyoma” “angiomyoma”, “leiomyoma” were used in “AND” combination with “knee”, “extremities” “leg”. The inclusion criteria were the following: (1) studies reporting case reports or case series of patients with angioleiomyoma of the knee. Exclusion criteria were the following: (1) review articles, (2) studies published in languages other than English, (3) studies reporting angioleiomyoma in other anatomical parts.

2.2. Data collection

From each study, we extracted the following information: (1)

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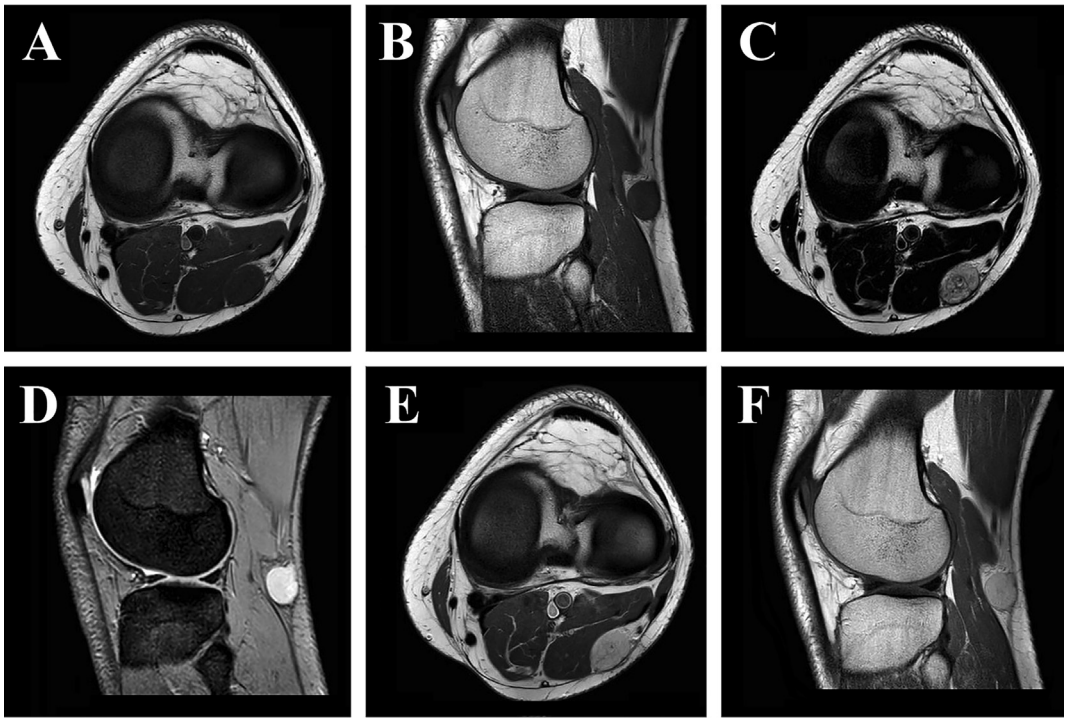

Fig. 1. Magnetic resonance imaging of the left knee in a 42-year-old man presenting with a painless swelling lesion for a year demonstrating a well-circumscribed, capsulated soft tissue mass isointense to the muscle on T1-weighted images (A, B), hyperintense on T2-weighted scan (C) and hyperintense on multiecho fast field echo T2-weighted image (D). On post-contrast sagittal and axial T1-weighted images (E, F), the tumor showed homogeneous gadolinium enhancement. The patient underwent uneventful surgical resection.

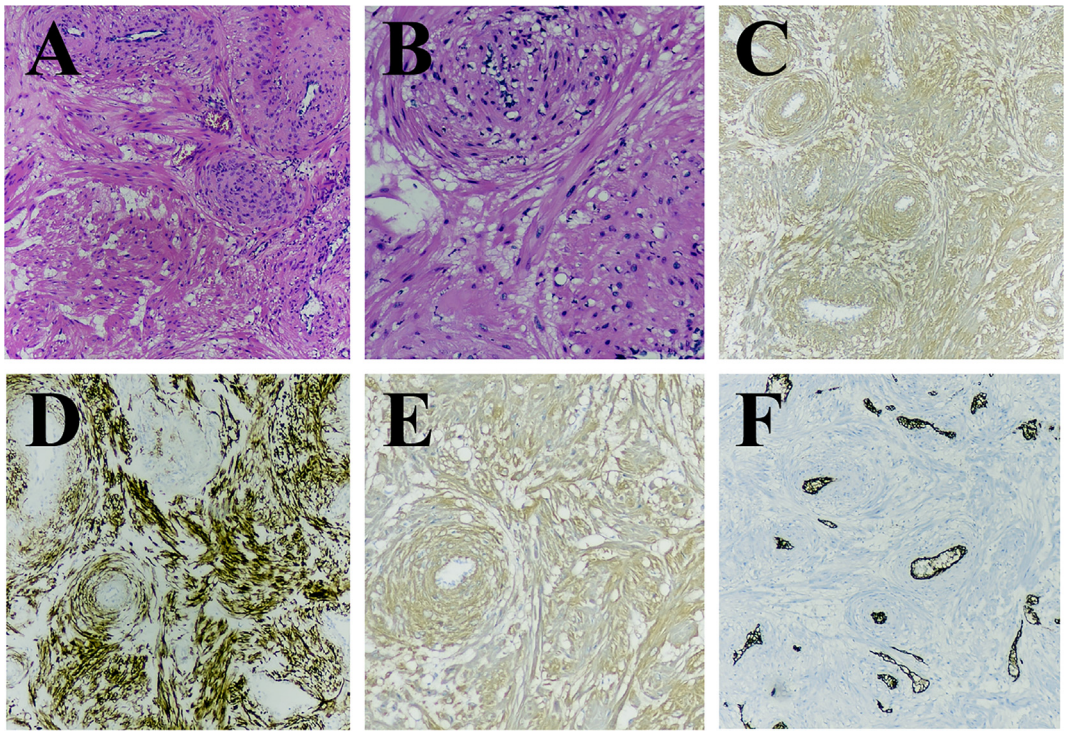

Fig. 2. Histopathological examination (H&E 10× and 20×) demonstrated a solid neoplasm composed of elongated cells organized in tight fascicles, surrounding blood vessels with thickened walls (H&E 10× and 20×, A–B respectively). Immunohistochemistry (IHC) showed strong positivity for SMA (C), desmin (D) and caldesmon (E) and negativity for CD34 (F), in absence of marked cellular atypia and/or mitoses. The morphological appearance along with the immunohistochemical profile agreed with the diagnosis of venous type angioleiomyoma.

patient's demographics; (2) number of patients with angioleiomyoma of the knee; (3) radiological features of the angioleiomyoma; (4) treatment modality; (5) histopathological results; (6) clinical outcome. When reported, pathologic type was classified according to Morimoto classification [4].

2.3. Outcomes

The primary objectives of this study were to examine the clinical presentation and the results of surgical treatment of angioleiomyoma of the knee.

3. Results

3.1. Present case report

Here we reported a 42-year-old man presenting with a painless swelling lesion at the left knee for a year, without motor deficits. He was previously treated with conservative treatment (including rest, knee brace and ice application) and corticosteroid injections in the knee, without relief. There was no history of trauma. Radiographs of the left knee showed no abnormalities. A magnetic resonance imaging (MRI) of the knee showed a capsulated 20 × 19 × 13 mm soft tissue mass isointense to the muscle on T1-weighted images (T1WI) and hyperintense on T2-weighted images (T2WI), with homogeneous gadolinium enhancement after gadolinium administration. The patient underwent surgical resection. Histopathological examination (H&E) demonstrated a solid neoplasm composed of elongated cells organized in tight fascicles, surrounding blood vessels with thickened walls. Immunohistochemistry (IHC) showed strong positivity for SMA (C), desmin (D) and caldesmon (E) and negativity for CD34 (F), in absence of marked cellular atypia and/or mitoses. The morphological appearance along with the immunohistochemical profile agreed with the diagnosis of venous type angioleiomyoma. Patient was discharged from the hospital on the next day, reporting pain relief. No recurrence was reported at last follow-up.

3.2. Literature review

Studies included in this review are summarized in Table 1 [5–27]. Twenty-four studies and 30 patients presenting with angioleiomyoma of the knee were analyzed in this review [5–27].

3.3. Demographic and radiological characteristics

Overall the median age of patients was 42.3 years (18–63) and the proportion of female patients was 66.7%. The right knee was more involved than left side (70.4% Vs 29.6%). Mean lesion size resulted 17.8 ± 7.1 mm ($\alpha = 0.05$), ranging from 0.3 cm to 10 cm. The more common presenting symptom was leg pain (90%), which was sporadically associated with loss of full extension of the knee (10%) and lumbar pain (3%). Twenty-five cases provided details about clinical characteristics of pain, which resulted paroxysmal, localized and initiated by pressure or light touching in 20 patients (80% of cases) and radiating to the inferior limb in 20% of cases. Three patients (10%) referred no history of pain and presented a painless ulcer (one case) [12] and soft tissue swelling (two cases) [27]. Preoperative ultrasound was performed just in five patients (17%). Lesion appeared well-defined, oval-shaped and hypoechoic in all cases. Preoperative MRI was performed in 20 patients (67%) and revealed a well-defined round to oval lesion. Lesion resulted isointense to the muscle on T1 images in 80% of cases and hyperintense on T2 images in 90% of cases. Post-contrast the lesion showed homogeneous enhancement in 94.1% of cases and non-homogeneous enhancement just in one patient (5.9%). Surgical resection was performed in all cases and invariably resulted in total resection. Nineteen cases (63.3%) reported clinical follow-up, which resulted 19.5 ± 12.4 months ($\alpha = 0.05$). None of the analyzed studies reported recurrence. Eighteen cases (60%) reported details of pathologic examination according to Morimoto classification [4]. Solid type angioleiomyoma was found in 16 patients (88.8%). Pleomorphic type was found in one case [24] and venous type angioleiomyoma was reported in another case (present case).

4. Discussion

4.1. Epidemiology

Vascular leiomyomas or angioleiomyomas are benign solitary tumors of smooth muscle origin that arise from the smooth muscle of blood vessels in the deep layers of the dermis or in the subcutaneous tissue [17]. According with our review, the peak incidence is in the fourth to the sixth decades of life, with a female predominance [2]. Etiology is unclear; repetitive micro trauma, hormonal changes and venous stasis have been proposed as causative factors [28].

4.2. Histopathological features and symptoms

Stout [29] published the first comprehensive review of this rare lesion in 1937. In 1973, Morimoto [4] described three subtypes of angioleiomyoma: solid, cavernous and venous. Solid subtype is composed of closely compacted smooth muscle and numerous small vascular channels, the venous subtype has vascular channels with thick muscular walls and the cavernous type consists of dilated, large vascular channels with the least amount of smooth muscle [4]. The solid type is three times as common in females and typically involves the lower extremities, whereas the cavernous type is four times as common in males and typically involves the head and upper limbs [17]. At microscopic examination, angioleiomyoma shows tortuous vascular channels surrounded by smooth muscle bundles and areas of myxoid change that explain hyperintensity of the tumor on T2WI. On immunohistochemistry, angioleiomyoma is usually positive for smooth muscle actin, desmin and caldesmon, and negative for myeloid progenitor cell antigen (CD34), with no cellular atypia and/or mitoses. Majority of these tumors in the knee are solid type (88.8%) and often painful. According to our review pain is generally paroxysmal, aggravated by physical stimulation, and is the presenting feature in 90% patients. Venous type angioleiomyoma is rare in the lower extremities and usually painless [28], as our case confirms. Paroxysmal pain, which is often burning and excruciating in intensity, is triggered by pressure or even by either light touching and is described as drilling, burning and radiating [15,21,25,27]. The pathogenesis of this pain is still unknown [30–32]. Generally, patients are evaluated by multiple physicians and tried several medications, including high doses of gabapentin and corticosteroid injections in the knee or in the spine, without relief [15]. Physical examination is required to detect the painful nodule in the knee.

4.3. Differential diagnosis and outcome

Preoperative diagnosis is difficult and requires a high index of suspicion. First of all, degenerative disc disease, hip and/or knee osteoarthritis have to be excluded [33], as also located pain due to phlebitis, vein thrombosis or an incompetent of vein located behind the knee, like the great saphenous vein or the Giacomini vein [34]. Very often telemedicine can help both doctor and patient to reach the final diagnosis faster after performing a computerized tomography (CT) scan or MRI [35,36], but a physical examination for this kind of lesion is required to detect the painful nodule in the knee. A differential diagnosis includes peripheral nerve sheath tumor, hemangioma, lipoma, giant cell tumor of the tendon sheath, osteoid osteoma and chondromyxoid fibroma [3,5,37]. On ultrasound examination, angioleiomyoma appears oval-shaped, mildly hypoechoic, with well-defined margins and with homogenous structure suggestive of the benign nature of the lesion [17,37]. On MRI, angioleiomyomas usually appears isointense or slightly hyperintense on T1WI and slightly hyperintense on T2WI compared with skeletal muscle. The lesion shows strong and homogeneous enhancement after administration of gadolinium [26]. A preoperative radiograph or CT scan of the knee can not provide additional information to reach the diagnosis of angioleiomyoma, however

Table 1
Summary of the studies included in the review.

Authors	Year	Age (years)	Sex	Tumor location (side)	Size (mm)	Clinical presentation	Radiologic Features		Pathologic type according to Morimoto classification [4]	Follow-up (months)
							MRI	Gd-Enhancement		
Hwang et al. [25]	1998	53	F	Right knee	4	Pain	T1: Iso-I, T2: Hyper-I	NA	Solid	NA
Gulati et al. [23]	1999	20	F	Left knee	10	Pain	T1: Iso-I, T2: Hyper-I	Homogeneous	NA	NA
Kawagishi et al. [24]	2000	38	F	Right knee	15 × 11	Pain	NA	NA	Pleomorphic	24
Murty & Ireland [22]	2000	37	F	Right knee	8	Pain	NA	NA	NA	6
Thienpont et al. [21]	2002	47	F	Right knee	10	Burning and excruciating pain	NA	NA	NA	NA
DiCaprio et al. [20]	2003	27	F	Right knee	3	Chronic pain	NA	Homogeneous	NA	NA
Okahashi et al. [19]	2006	43	F	Right knee	50 × 40 × 20	Recurrent pain and a loss of full extension	T1: Iso-I, T2: Hyper-I	NA	NA	NA
Yoo et al. [26]	2009	63	F	–	20	Pain	T1: Iso-I, T2: Hyper-I	Homogeneous	NA	NA
Cantisani et al. [17]	2009	60	M	Right knee	35	Chronic burning disabling pain	T1: Hypo-I, T2: Hyper-I	Homogeneous	Solid	12
Al-Jabri et al. [18]	2009	40	F	Right knee	10 × 8 × 6	Recurrent pain	NA	NA	NA	NA
Jalgaonkar et al. [16]	2011	45	M	Right knee	4–11	Painful nodule	T1: Iso-I, T2: Hyper-I	Homogeneous	Solid	16
Jalgaonkar et al. [16]	2011	42	M	Right knee	4–11	Hyperesthetic nodule	T1: Iso-I, T2: Hyper-I	Homogeneous	Solid	16
Jalgaonkar et al. [16]	2011	51	F	Right knee	4–11	Painful nodule, sleep disturbance	T1: Iso-I, T2: Hyper-I	Homogeneous	Solid	16
Jalgaonkar et al. [16]	2011	42	F	Left knee	4–11	Pain during emotional stress	T1: Iso-I, T2: Hyper-I	Homogeneous	Solid	16
Jalgaonkar et al. [16]	2011	43	F	Left knee	4–11	Hyperesthetic nodule	T1: Iso-I, T2: Hyper-I	Homogeneous	Solid	16
Kumar et al. [13]	2014	36	M	Left knee	30 × 25	Mildly painful mass	T1: Hypo-I, T2: Hyper-I	Homogeneous	Solid	NA
Fukawa et al. [14]	2014	30	M	Left knee	15	Recurrent pain	T1: Iso-I, T2: Iso-I	Non-Homogeneous	NA	12
Woo et al. [27]	2014	35	F	–	7 × 5	Soft tissue swelling	NA	NA	Solid	6
Woo et al. [27]	2014	44	M	–	15 × 12	Pain	NA	NA	Solid	10
Raval et al. [15]	2014	42	F	Right knee	5–10	Severe pain	T1: Hypo-I, T2: Hyper-I	Homogeneous	Solid	6
Gupta et al. [12]	2015	22	M	Left knee	100 × 80	Painless ulcer	NA	NA	Solid	12
Mattox et al. [10]	2016	52	F	Right knee	37 × 26	Low back pain with lower extremity radiation	NA	NA	Solid	1
Aydin et al. [11]	2016	38	F	Right knee	10	Painful and mobile swelling	T1: Hypo-I, T2: Hyper-I	Homogeneous	Solid	NA
Araki et al. [8]	2017	18	F	Left knee	6	Severe pain	T1: Iso-I, T2: Hyper-I	NA	NA	18
Klumpp et al. [9]	2017	47	F	Right knee	10	Recurrent stabbing pain	T1: Iso-I, T2: Hyper-I	NA	NA	NA
Cao et al. [7]	2018	41	M	Right knee	15	Pain	T1: Iso-I, T2: Hyper-I	Homogeneous	Solid	96
Cao et al. [7]	2018	72	F	Right knee	18 × 16	Pain	T1: Iso-I, T2: Iso-I	Homogeneous	Solid	84
Maurya et al. [5]	2019	36	M	Right knee	38 × 24 × 27	Chronic intermittent pain	T1: Iso-I, T2: Hyper-I	Homogeneous	NA	NA
Rohena et al. [6]	2019	63	F	Right knee	5	Pain and burning sensation	NA	NA	NA	1
Our case	2020	42	M	Left knee	20 × 19 × 13	Soft tissue swelling	T1: Iso-I, T2: Hyper-I	Homogeneous	Venous	3

Hyper, hyperintese; Iso, isointense; Hypo, hypointense.

Table 2
Differential diagnosis of lesions of the knee region with magnetic resonance imaging.

Lesion type	MRI				Suggestive features
	T1WI	T2WI	Gadolinium enhancement		
Angioleiomyoma	iso/hyper	hyper	+ +	homogeneous enhancement	Dural tail and hyperostosis
Lipoma	hyper	hyper	0	no	Saturates on fat-saturated sequences on T1WI
Giant cell tumors of tendon sheath	hypo	hypo	+	moderate enhancement	–
Neurofibroma	hypo	hyper	+ +	homogeneous enhancement	Hyperintense rim and central area of a low signal may be seen on T2WI
Hemangioma	hyper	hyper	+	moderate enhancement	STIR: iso or hyper
Chondromyxoid fibroma	hypo	iso/hyper	+ +	homogeneous enhancement	Peripheral nodular enhancement
Glomus tumor	iso	hyper	+ +	homogeneous enhancement	–
Osteoid osteoma	hypo	hypo	–	no	–
Pigmented villonodular synovitis	iso	iso/hyper	+	variable enhancement	Hyperintense areas may be present likely due to joint fluid or inflamed synovium
Synovial chondromatosis	iso	hyper	0	no	Areas of mineralization with focal areas of signal void

Hyper, hyperintese; Iso, isointense; Hypo, hypointense; MRI, magnetic resonance imaging; T1WI, T1-weighted images; T2WI, T2-weighted images.

it can be very useful at characterizing bone-forming tumors, like a osteoid osteoma, as it typically shows a focally lucent nidus within surrounding sclerotic reactive bone at CT scan [38]. Differential diagnosis on MRI includes lipoma, giant cell tumor of tendon sheath, neurofibroma, hemangioma, chondromyxoid fibroma, osteoid osteoma, pigmented villonodular synovitis, and synovial chondromatosis (Table 2) [5,39]. One of leading diagnoses in radicular pain in the leg are osteoid osteomas that are benign small (1.5–2 cm) bone-forming tumors that classically cause night pain that is relieved by the use of salicylate analgesia. Similarly, clinical presentation of pigmented villonodular synovitis and synovial chondromatosis is usually with joint swelling, pain and occasionally joint dysfunction. Benign peripheral nerve sheath tumors, like neurofibromas, can present with neurogenic dysfunction, pain or numbness in the leg. On the other hand, lipomas are subcutaneous soft painless mass. Surgical resection is the curative treatment for angioleiomyoma and no recurrences were reported in our analysis, although an overall recurrence of 0.4% has been reported for angioleiomyoma of the extremities [15,27,40].

5. Conclusion

Angioleiomyoma of the knee is rare and after preoperative MRI can be mistaken for other more common lesions including nerve sheath tumors. Surgical resection is the curative treatment and recurrence is exceptional. Angioleiomyoma widens the spectrum of the soft tissue lesions of the knee and should be included in the differential diagnosis of lesions in this area.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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