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CASE REPORT

Intra-articular fibroma-like perivascular epithelioid tumor (PEComa) mimicking tenosynovial giant cell tumor, diffuse type

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Abstract

Perivascular epithelioid cell tumors (PEComas) are rare mesenchymal neoplasms composed of perivascular epithelioid cells that are immunoreactive for both melanocytic and myogenic markers. Recently, a fibroma-like PEComa associated with tuberous sclerosis complex (TSC) has been identified. We describe the first intra-articular case of a fibroma-like PEComa in a 44-year-old man who presented with a hypointense intra-articular knee mass, which was mistaken for tenosynovial giant cell tumor, diffuse type. This case report demonstrates that fibroma-like PEComa should be included in the extended differential diagnosis of intra-articular soft tissue masses. In addition, given their strong association with *TSC* mutations, a diagnosis of fibroma-like PEComa should trigger an evaluation for TSC.

Keywords Perivascular epithelioid cell tumor (PEComa) · Fibroma-like PEComa · Tuberous sclerosis complex (TSC) · Magnetic resonance imaging (MRI)

Introduction

Perivascular epithelioid cell tumors (PEComas) are rare mesenchymal neoplasms composed of perivascular epithelioid cells that are immunoreactive for both melanocytic and myogenic markers [1–5]. PEComas occur most frequently in the abdominal and pelvic organs, the skin and soft tissues, and rarely in bone [4, 6–10]. Recently, Larque et al. identified a fibroma-like PEComa, which was associated with tuberous sclerosis complex (TSC) [11]. TSC is an autosomal dominant disorder resulting in proliferation of hamartomatous lesions [12]. A strong association between TSC and PEComas has been recognized and alterations in TSC genes have been identified in sporadic PEComas [13, 14]. Fibroma-like PEComas morphologically resemble collagenous fibromas and are indistinguishable from PEComas on immunohistochemistry with reactivity for both melanocytic and myogenic markers [11]. The previously described three cases of fibroma-like PEComa occurred in young and middle-aged women and involved the chest wall and the extremities (wrist and foot, extra-articular), respectively [11] and no intra-articular location has been reported. MR imaging was described in one case in the chest wall, which demonstrated markedly hypointense signal intensity on all pulse sequences and no enhancement [11]. Here we present a case of a 44-year-old man with a history of tuberous sclerosis who presented with an intra-articular fibroma-like PEComa of the knee which was initially mistaken for a tenosynovial giant cell tumor, diffuse type. This case report demonstrates that fibroma-like PEComa should be included in the extended differential diagnosis of intra-articular soft tissue masses. In addition, given their strong association with *TSC* mutations, a diagnosis of fibroma-like PEComa should trigger an evaluation for TSC.

Case report

A 44-year-old man presented with right lower extremity pain due to a growing mass in the anteromedial aspect of the right knee. Past medical history was positive for tuberous sclerosis complex (TSC) with seizure disorder, angiomyolipoma of the

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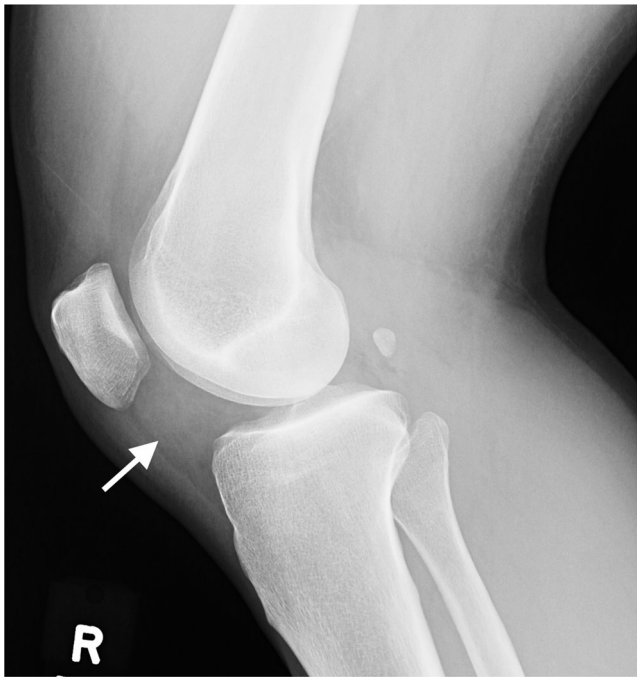

Fig. 1 Lateral radiograph of the right knee demonstrating an infrapatellar soft tissue mass (*arrow*)

kidney, and multiple angiofibromas and fibrous plaques of the face. The knee mass was identified 10 years prior to presentation on clinical examination and radiographs, which showed a mass in the infrapatellar fat pad of Hoffa without calcifications (Fig. 1). The mass was thought to be benign and related to TSC. Excision of the mass was planned, however, the patient declined surgery. Ten years later the patient noted progressive growth of the mass and pain during activity. On physical examination, the mass was firm and tender on palpation. He denied any history of trauma, fever, night sweats, or weight loss. A non-contrast MRI was performed that demonstrated an intra-articular nodular mass, measuring 6.5 × 4.2 × 2.6 cm, centered in the infra-patella fat pad of Hoffa. The mass was markedly hypointense on all pulse sequences with small foci of internal hyperintense signal on T1-weighted images (Fig. 2). No joint effusion, additional masses, or associated erosions were identified. Due to the signal characteristics and intra-articular location, the presumed diagnosis was tenosynovial giant cell tumor, diffuse type, and surgical excision was planned.

During surgery, the mass was found to be firm and fibrous, suggestive of a fibroma or desmoid tumor. Gross examination

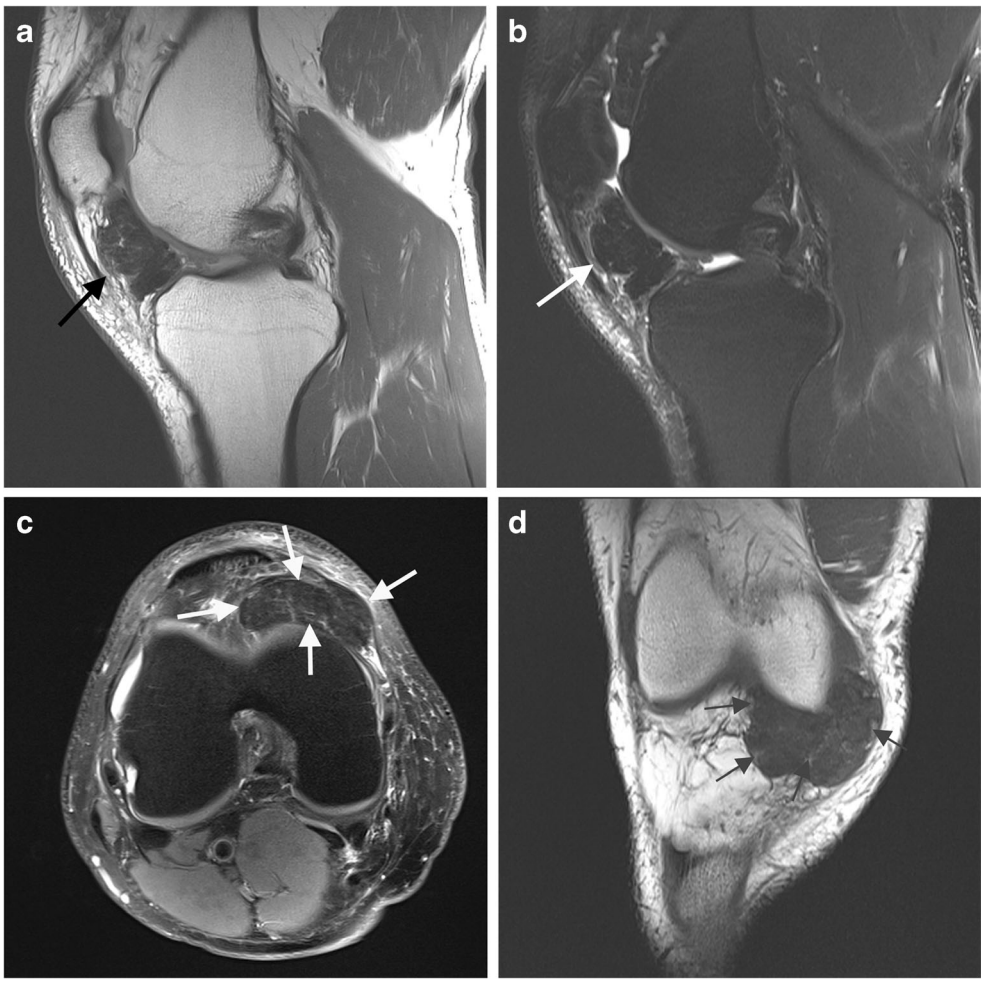

Fig. 2 MR imaging of the right knee showing markedly hypointense mass in the infrapatellar fat pad on sagittal proton density (**a**), sagittal (**b**) and axial (**c**) fat-suppressed T2-weighted images (*arrows*). Coronal T1-weighted image (**c**) shows small foci of T1 hyperintense signal (*arrows*) within the hypointense mass

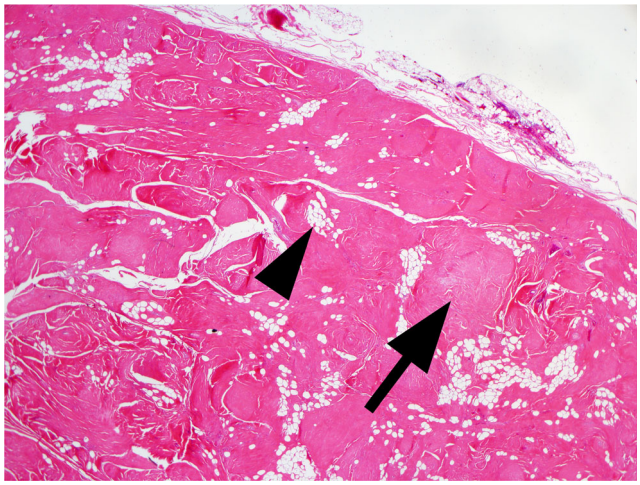

Fig. 3 Low-power magnification showing a circumscribed, lobulated, hypocellular lesion with a dense pink collagenous stroma (*long arrow*) and admixed islands of mature adipose tissue (*arrowhead*)

of the specimen revealed a yellow 6.5 cm, lobulated, circumscribed mass. On sectioning, the mass displayed firm, gritty yellow-white cut surfaces. Low-power microscopic examination of the mass revealed a lobulated, circumscribed, hypocellular lesion composed predominantly of a densely collagenous stroma with admixed islands of mature adipose tissue (Fig. 3). High-power magnification revealed admixed bland appearing ovoid to spindled and stellate-shaped cells embedded within the dense stroma with some admixed thin walled vascular channels (Fig. 4a). Focally, the spindle cells showed a vaguely circumferential or perivascular arrangement around vessels (Fig. 4b). The cells showed a moderate amount of cytoplasm with indistinct cell borders. No cellular atypia or mitotic activity was identified. The main histologic differential diagnosis for this lesion included fibroma and angiomyolipoma. Angiomyolipoma was excluded based on the lack of smooth muscle present within the lesion, while an intra-articular fibroma was excluded based on the results of immunohistochemistry [15]. The immunohistochemical analysis showed Melan-A (< 20% of tumor cells), MART1 (> 50% of tumor cells), and smooth muscle actin (30-40% of tumor cells) positivity confirming melanocytic and myogenic differentiation leading to a diagnosis of fibroma-like PEComa (Fig. 5). Additional immunohistochemical stains for desmin, S100, TFE3, HMB45, and muscle actin were negative. Appropriate positive and negative controls were included on sections for each immunostain performed.

Following surgery, the patient was able to resume his normal activities without restrictions.

Discussion

We report the first case of an intra-articular fibroma-like PEComa in a patient with tuberous sclerosis, which was mistaken for a tenosynovial giant cell tumor, diffuse type, due to its MR imaging appearance and intra-articular location.

Perivascular epithelioid cell tumors (PEComas) are rare mesenchymal tumors and include angiomyolipoma, lymphangioleiomyomatosis, clear cell sugar tumor of the lung, as well as unusual visceral and soft tissue tumors [2, 6, 16–19]. PEComas typically exhibit both epithelioid and spindle cell morphology and express melanocytic and myogenic markers, most classically Human Melanoma Black 45 (HMB-45). Other markers, such as Melan-A, smooth muscle actin, and transcription factor E3 (TFE3) have been reported [1, 3–5]. PEComas occur most frequently in the abdominal and pelvic organs, the skin and soft tissues, and rarely in bone [4, 6–10].

Recently, a new tuberous sclerosis complex (TSC)-related neoplasm has been described in three young to middle-aged women. The tumor resembled PEComa on immunochemistry, being positive for HMB-45 and smooth muscle actin and negative for TFE3, but morphologically resembled a soft tissue fibroma due to its dense collagenous stroma. All three patients had a history of TSC [11]. TSC, an autosomal dominant disorder, is associated with proliferation of hamartomatous lesions [12]. Prior studies have demonstrated a strong association between TSC and PEComas. Furthermore, alterations in TSC genes have been identified in sporadic PEComas [13,

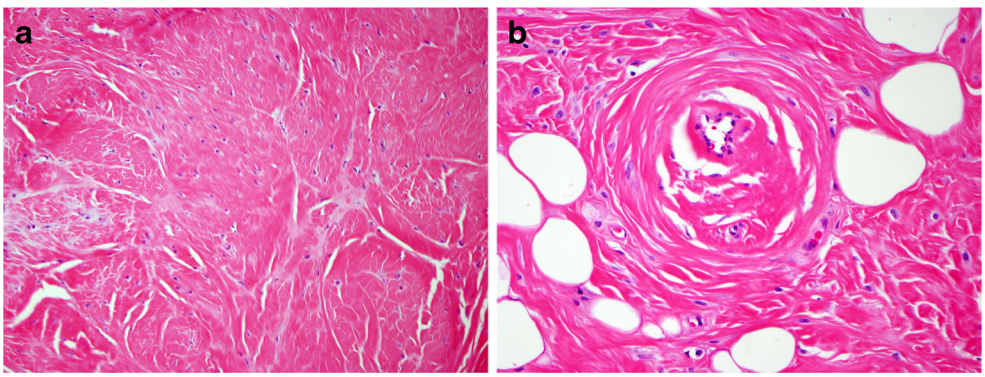

Fig. 4 **a** High-power magnification showing dense collagenous stroma with bland appearing ovoid-spindled cells. **b** High-power magnification showing a circumferential arrangement of tumor cells around a vessel which are partially distorted by the dense fibrosis

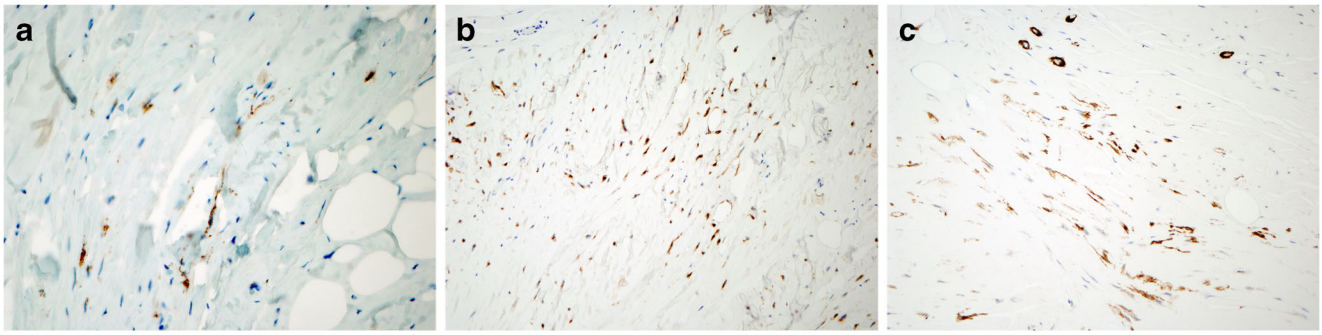

Fig. 5 High-power magnification of tumor cell positivity for Melan-A (**a**), MART1 (**b**), and smooth muscle actin (**c**)

14]. The previously identified cases involved the chest wall in one case and the extremities in two cases, respectively. The MR imaging appearance of fibroma-like PEComa has been described in one case of chest wall involvement with markedly hypointense signal on all pulse sequences and no enhancement [11].

Our patient had a history of TSC and presented with an intra-articular knee mass, which was asymptomatic for more than 10 years but was slowly growing and became symptomatic prior to presentation. On MR imaging, the mass was located in the infrapatellar fat pad of Hoffa and was hypointense on all pulse sequences with small internal foci of T1-hyperintensity which corresponded to the small islands of fat seen on histology. Because of the signal characteristics and the intra-articular location, the mass was thought to represent tenosynovial giant cell tumor, diffuse type. The infrapatellar fat pad of Hoffa is an intra-articular structure, located between the joint capsule and the synovial-lined joint cavity, and is therefore intracapsular but extrasynovial. Common differential diagnoses for soft tissue masses involving the infrapatellar fat pad of Hoffa include Hoffa disease, intracapsular chondroma, post-arthroscopy and post-surgery fibrosis, as well as extension of articular and synovial processes, such as tenosynovial giant cell tumor, chondromatosis, lipoma arborescence, synovial hemangioma, or ganglion cysts [20]. A case of an intra-articular angiomyolipoma of the knee joint extending into the infrapatellar fat pad has been described in a 12-year-old girl without a history of TSC. However, no case of intra-articular of fibroma-like PEComa has been reported. The predominately hypointense signal intensity of the tumor was due to fibrous tissue seen on histology. Differential diagnoses of predominately hypointense intra-articular lesions on MR imaging include gout, amyloid, tenosynovial giant cell tumor, diffuse type, and blood products [20–22].

In conclusion, this is the first description of an intra-articular fibroma-like PEComa in a patient with TSC. Given the MR imaging characteristics of low signal intensity on all pulse sequences, this tumor should not be mistaken for tenosynovial giant cell tumor. In addition, fibroma-like PEComa should be included in the extended differential diagnosis of intra-articular soft tissue masses. In addition, given its strong association with *TSC* mutations, a diagnosis of fibroma-like PEComa should trigger an evaluation for TSC.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval IRB approval was not required for this case report per guidelines of our institution's IRB and no informed consent was required.

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