Original paper

Angiomyofibroblastoma mimicking an inguinal hernia: a challenging diagnosis in a male patient

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Abstract

Introduction: Angiomyofibroblastoma is a rare benign myofibroblastic neoplasm which mainly occurs in the soft tissues of the pelvi-perineal region of females.
Aim: To present an unusual case of angiomyofibroblastoma mimicking an inguinal hernia in a 62-year-old male.
Material and methods: The patient was hospitalized with an irreducible, painless inguinal mass and surgical intervention for inguinal hernia was decided. The well-defined nodular mass was sent for histological examination.
Results: Under microscope, proliferation of spindle and oval cells around thin-walled vessels was observed, being intermingled with mature adipocytes. We did not identify necrosis, haemorrhage, cytologic atypia or mitotic figures. The tumour cells displayed positivity for desmin, vimentin, CD34, oestrogen and progesterone receptors, a low Ki67 index and unusual nuclear positivity for c-theta (PKCθ). They were negative for smooth muscle actin (SMA), S100, CD44, maspin, synaptophysin, DOG1 and CD117. The case was diagnosed as angiomyofibroblastoma, the main challenge being the differential diagnosis with aggressive angiomyxoma, which can present a similar histologic aspect and immunophenotype and recurs more frequently. No recurrences were observed 8 months after the surgery.
Conclusions: Angiomyofibroblastoma should be included in the differential diagnosis of inguinal hernia. This is the fourteenth case of angiomyofibroblastoma diagnosed in males.

Key words: angiomyofibroblastoma, inguinal mass, c-theta, CD44, maspin.

Introduction

Angiomyofibroblastoma (AMF) is a rare benign myofibroblastic neoplasm which mainly occurs in the soft tissues of the pelvi-perineal region of females. Fletcher *et al.* described this lesion for the first time in 1992 [1, 2].

In this paper we present the 14th case of AMF reported in the Medline database until the beginning of 2017, as arising in the inguinal region of a male patient [3, 4]. The particularity of the case consists in its incidental finding in the inguinal region's soft tissue, this mass being preoperatively diagnosed as a hernial sac. The unusual nuclear expression of c-theta (PKCθ) protein, a marker considered to be relatively specific for c-KIT negative gastrointestinal tumours (GIST) was described for the first time in the literature [5]. The criteria of differential diagnosis were also determined.

Case report

A 62-year-old male, previously diagnosed with high blood pressure, gout, haemoptysis and tuberculosis was admitted to the Surgical Department with an irreducible and painless slow growing inguinal mass.

After physical examination and ultrasonography, the case was interpreted as an inguinal hernia with indication for surgery. Laboratory tests presented parameter values within normal ranges, with slightly elevated blood uric acid: 9.52 mg/dl (normal values = 3.6–7 mg/dl).

The patient signed consent to surgical intervention and publication of the case was obtained before surgery. During surgery, a nodular, encapsulated mass was discovered and excised along with lymph nodes from the femoral region.

The macroscopic aspect of the gross specimen revealed an encapsulated nodule measuring 55 × 35 ×

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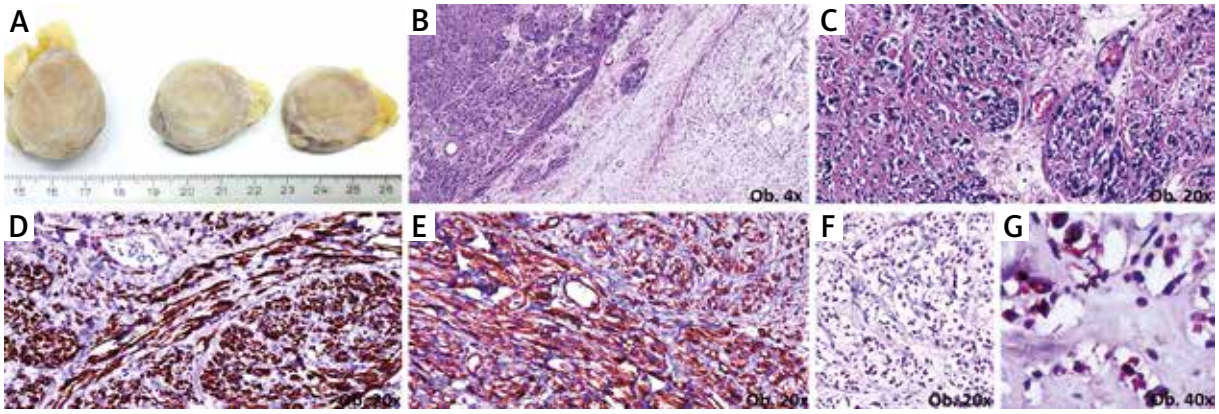

Figure 1. The angiomyofibroblastoma presented in the inguinal region of a male patient is displayed as an encapsulated solid mass with a tan colour cut surface (**A**). Microscopically, the well-circumscribed tumour (**B**) consists on small groups of round, oval-shaped and elongated cells with clear, vacuolated or eosinophilic cytoplasm and pleomorphic hyperchromatic nuclei with no nucleoli (**C**). The tumour cells are positive for desmin (**D**), CD34 (**E**) and oestrogen-receptor (**F**) and display unusual PKCθ nuclear positivity (**G**)

25 mm, with a grey, thin, smooth exterior surface and a tan colour cut surface, without haemorrhages or necroses, without infiltrating features (Figure 1).

Microscopical examination revealed a cellular proliferation with varying density, well-circumscribed by a peripheral loose connective tissue. At high-power view, the tumour was composed from round, oval-shaped and elongated cells of varying dimensions, with clear, vacuolated or eosinophilic cytoplasm, pleomorphic hyperchromatic nuclei with no nucleoli. Cells were arranged in small groups, sometimes cords, bundles and fascicles disposed around small blood vessels and were separated by connective tissue fibers. A few mature adipocytes were present, with no atypia. No necrosis, areas of haemorrhage or atypical mitotic figures were observed. The stroma was well-vascularized by small and medium-size thin-walled blood vessels and presented focal myxoid features (Figure 1).

The tumour cells displayed positivity for desmin, vimentin, CD34, oestrogen (ER) and progesterone receptors (PR), nuclear positivity for PKCθ and a Ki67 proliferation index of about 20%. They were negative for smooth

Table 1. Differential diagnosis between angiomyofibroblastoma, cellular angiofibroma and aggressive angiomyxoma [1–4, 6, 9–13]

Parameter	Angiomyofibroblastoma	Cellular angiofibroma	Aggressive angiomyxoma
Gross aspects	Well-demarcated by a thin fibrous pseudocapsule	Well-circumscribed by a thin fibrous pseudocapsule	Ill-defined, usually infiltrates the surrounding tissues (may present entrapped nerves, muscle fibers)
Cellularity	Alternating hypocellular and hypercellular areas; round and spindled cells (plasmacytoid, epithelioid) disposed in cords and nests around blood vessels; few mature adipocytes may be present (in 10% of cases); often contains mast cells	Higher cellular density, round and spindle-shaped cells distributed haphazardly or in short fascicles; may contain mature adipocytes (in 50% of cases); focal lymphocytic aggregates and few mast cells	Hypocellular proliferation of short spindle and stellate cells, radiating from vessel walls; multinucleated cells may be observed
Stroma	Oedematous, myxoid degeneration, collagen fibers which separate tumour cells	Collagenous, with thicker collagen bundles, may be hyalinized	Abundant myxoid stroma; may present hematic extravasate
Vascularisation	Abundant thin-walled, small to medium-sized vessels (capillary-type), irregularly distributed	Prominent large, larger thick-walled vessels, mostly with hyalinized walls and absence of perivascular adipocytes	Thin and thick-walled vessels, hyalinized or hypertrophic, of variable size
Immunoprofile	Desm+ (in all cases), ER+, PgR+, Vim+, CD34 (rarely), SMA (rarely), S100–	Vim+, Desm+/– (almost always negative), CD34+, Vim+, SMA+, ER–/+, PgR–/+, S100–	Desm+, CD34+, CD44+, ER+, PgR+, Vim+, S100–

Desm – desmin, ER – oestrogen receptor, PgR – progesterone receptor, Vim – vimentin, SMA – smooth muscle actin.

muscle actin (SMA), S100, CD44, maspin, synaptophysin, DOG1 and CD117 (Figure 1). The femoral lymph nodes presented normal histological architecture.

Based on the clinical picture, macroscopic features, microscopic aspects and immunophenotype of tumour cells, the final diagnosis was "Angiomyofibroblastoma". The patient was discharged without any complications 10 months after surgery.

The AMF is a rare tumour and mostly occurs in females, with a female-to-male ratio of 10 : 1. In men, the tumour can occur in the pelvi-perineal region (spermatic cord, scrotum, perineum, inguinal region) but can also involve the nasal cavity and mediastinum [3, 4].

Discussion

The AMF shares many of its aspects with cellular angiofibroma (CA) and aggressive angiomyxoma (AA). Mitotic activity is absent or low in all of these lesions and due to the overlapping histological and immunohistochemical features, the differential diagnosis becomes problematic. The AMF and CA present a benign behaviour and surgical removal is mostly curative, with exceptional recurrences in cases of incomplete excision. However, as they are well-circumscribed, complete removal is not difficult to be done. In contrast, AA is ill-defined, infiltrates the surrounding tissues and presents a higher risk of recurrence (30–40%) [6–10]. We have enumerated in Table 1 the criteria of differential diagnosis between AMF, CA and AA [1–4, 6, 9–13].

Although a benign tumour, AA may aggressively infiltrate adjacent structures [7]. In AA without nuclear atypia and/or mitotic figures and low Ki67 index, the AA is diagnosed based on the infiltrative growth features that are absent in AMF. However, the cellular AMF is difficult to be differentiated from AA [8]. In the present case, stroma presented myxoid foci but well-defined margins and absence of recurrences allowed the diagnosis of AMF. As AMF may co-exist with AA, the correct diagnosis is sometimes established after recurrences only [8].

Differential diagnosis of AMF also includes superficial angiomyxoma, spindle cell lipoma and solitary fibrous tumour. In superficial angiomyxoma, the inflammatory cells represented mostly by neutrophils and infrequent embedded epithelial components are indicators of the diagnosis. In spindle cell lipoma, the adipose tissue is the main component and the lesion is mostly identified in the head and neck regions. In solitary fibrous tumour, the blood vessels are elongated or ramified and display a staghorn architecture [11]. A lipomatous variant of AMF with presence of adipocytes ≥ 30% and possible sarcomatous transformation was also described. The pleomorphic lipoblasts present S100 positivity and do not display positivity for ER [12, 13].

The immunoprofile of tumour cells may also be helpful to differentiate AMF from CA and AA (Table 1). In patients with AMF, positivity of tumour cells for ER and PR may suggest a hormone-dependent tumour growth. McCluggage *et al*. presented the case of a 35-year-old female patient diagnosed with an ER-positive AA. The large ill-defined tumour mass infiltrating the pelvic area was incompletely excised due to the fact that the patient was not amenable to undergo further surgical interventions. This patient received gonadotropin-releasing hormone injections, a hormone that has hypoestrogenic effects and as a result, repeated magnetic resonance imaging (MRI) scans showed a continuous decrease in size of the tumour, until complete resolution [14]. Hormone therapy was not taken into consideration in our case because complete surgical excision was possible.

A question that remains unanswered in this case is the positive nuclear reaction to PKC . It usually marks the cytoplasm of c-KIT negative GISTs and is considered as a diagnostic tool for these tumours. Infrequent cytoplasmic positivity was reported for leiomyomas, schwannomas, leiomyosarcomas, and desmoid tumours [15]. This is the first report revealing PKC nuclear expression in AMF. Further studies are necessary to elucidate the significance of this positivity.

Conflict of interest

The authors declare no conflict of interest.

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