

Oncology

Renal Angiomyxolipoma: Its First Appearance! ☆



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ABSTRACT

Angiomyxolipoma is considered a very rare subtype of lipoma, with the latter being the most common type of mesenchymal neoplasm. Only 17 cases have been described in English medical literature. Angiomyxolipomas have been described in many locations, mostly in the subcutaneous tissue. In this report, we present the first case of renal angiomyxolipoma ever encountered. Diagnosis was made after many differential diagnoses had been ruled out. Subsequent management and follow-up are illustrated along with a discussion and review of literature.

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Introduction

A rare variant of lipoma, angiomyxolipoma (vascular myxolipoma) was first reported by Mai et al¹ in 1996. The tumor was composed of an admixture of myxoid stroma, mature adipose tissue, and vascular channels. Since then, an additional 17 cases have been reported across a broad age range and in different locations. We report the first case in English medical literature of renal angiomyxolipoma in an adult male. Among adult soft-tissue tumors, adipose tissue tumors are by far the most common. Although ordinary subcutaneous lipomas do not represent a major diagnostic problem, the remaining benign tumors and tumor-like lesions of adipose tissue can be more challenging, especially if occurring at unusual locations and/or containing other tissue elements.^{2,3} Our case will be the 18th reported case of angiomyxolipoma and the first of renal origin. A review of the literature along with a discussion of diagnosis and follow-up are illustrated in the report.

Case presentation

Clinical history

We report a 43-year-old man who presented to our urology clinic with left flank pain of 1-year duration. On investigation, he was discovered to have bilateral kidney masses and splenomegaly

after a computed tomography (CT) scan (Fig. 1). Radiologic findings were highly suspicious for lymphoma in the presence of splenomegaly and distal ileal wall thickening. CT-guided needle core biopsy of the left kidney tumor was done.

Diagnosis

The microscopic examination demonstrated a proliferation of benign spindle cells showing bland, elongated, occasionally wavy nuclei. Few cells had a more plump nucleus with open chromatin and small nucleolus. There were scattered chronic inflammatory cells consisting of lymphocytes and plasma cells. The entire cellular population was bathed in a vascularized myxoid background. No epithelial proliferation or malignancies were noted in the biopsied material. Immunohistochemistry showed spindle cells positive for vimentin and CD34, focally positive for smooth muscle actin (SMA) and negative for Human Melanoma Black (HMB) 45. The findings were in favor of inflammatory myofibroblastic tumor showing benign fibromyxoid proliferation with scattered inflammatory infiltrate. There was no evidence of lymphoma, carcinoma, or other malignancy in the submitted material.

Clinical follow-up

The patient was advised surgical resection because of obstructive symptoms and mass effect of the tumor: abdominal pain, pseudo-obstruction, early satiety, and cachexia. The resected surgical specimen (Fig. 2) consisted of 2 tan-white, well-circumscribed, rubbery masses measuring 12 × 12 × 10 cm and 10 × 7 × 6 cm with a glistening external surface. On the cut surface, the specimens had a light yellow color, a solid composition, and myxoid texture.

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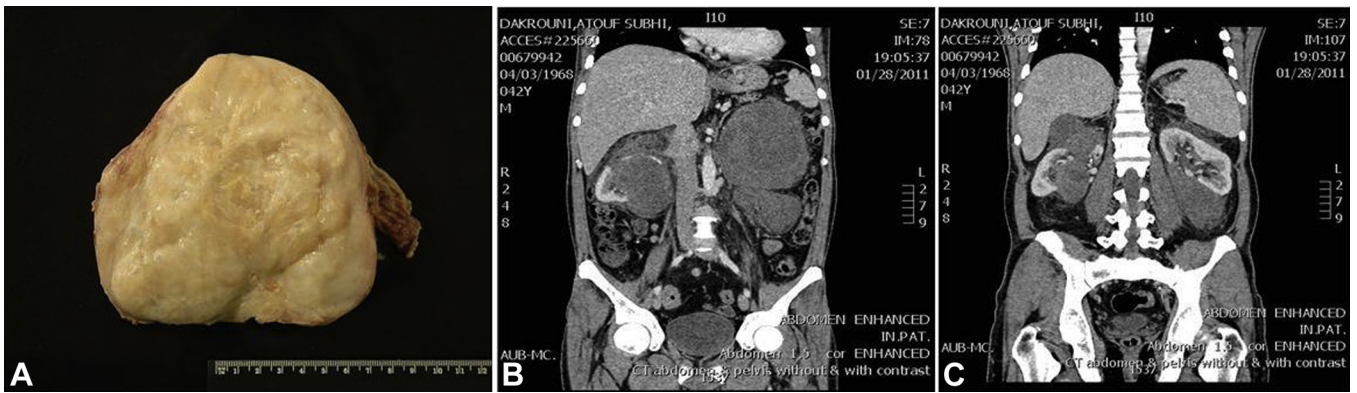


Figure 1. (A, right) Gross full-thickness section of one of the masses. Note the well-circumscribed nature of the lesion and the vaguely nodular architecture. (B and C, left) CT scan showing bilateral kidney masses and splenomegaly and distal ileal wall thickening.

Representative formalin-fixed paraffin-embedded sections were stained with hematoxylin and eosin. Immunohistochemical studies were performed using CD34 (monoclonal, 1/10; Becton-Dickinson), vimentin, S-100, SMA, desmin, HMB-45 (monoclonal, 1/100; Biogenics), Ki-67, anaplastic lymphoma kinase (ALK), cytokeratin AE1/3, estrogen, progesterone, CD117, and synaptophysin.

Microscopically, the tumor was predominantly composed of a random mixture of myxoid areas, denser more fibrotic areas, mature adipose tissue, blood vessels, and chronic inflammatory cells. The myxoid areas ranged from being hypocellular to moderately cellular and contained many small blood vessels. The cells comprising these areas ranged from spindle with tapered ends, hyperchromatic nuclei, and inconspicuous nucleoli to ones that were round to oval with even, finely granular chromatic, and small nucleoli. Mitoses were not identified. The sparsely cellular densely fibrous areas contained mature adipose tissue (comprised approximately 15% of the submitted material), both thin- and thick-walled vessels with occasional thrombosed lumens, and perivascular lymphocytic aggregates.

The immunohistochemical panel revealed diffuse and strong staining of the spindle cells with CD34 and vimentin and focal positivity with SMA and estrogen receptor. Ki-67 stained approximately 5% of the spindle cell nuclei. The mature adipose tissue stained for S-100 protein. CD34, SMA, and vimentin also highlighted the vascular component. The remaining markers (S-100, desmin, HMB-45, ALK, cytokeratin AE1/3, progesterone, CD117, and synaptophysin) were negative.

Discussion

The first case of angiomyxolipoma (vascular myxolipoma) was reported by Mai et al¹ in 1996. Since then, 17 additional cases of this rare neoplasm have been reported.⁴ The patient age ranged from 9 to 69 years, with a male-to-female ratio of 5:1. Lesion duration ranged from 3 months to 7 years. Although this neoplasm occurred in different locations (scalp, thigh, wrist, knee, forearm, etc), 9 were localized to subcutaneous tissues, 1 occurred in the spermatic cord, 1 in a subungual location, 1 in the buccal mucosa, 2 intra-articular, 1 in the oral cavity, 1 in the colon, and 1 in the posterior mediastinum.³ Our patient is the first to present with renal angiomyxolipoma (Table 1).

The combination of adipose tissue, spindle cells, vascular channels, and myxoid stroma may overlap with several other neoplasms that share similar morphologic features. Distinguishing clinical, morphologic, and immunohistochemical features of each entity, which may enter the differential diagnosis, are summarized in Table 2.^{4,5}

To date, only 1 case of angiomyxolipoma has been studied cytogenetically. In 1 case report by Sciote et al,² analysis revealed translocations $t(7;13)(p15;q14)$ and $t(8;12)(q12;p13)$, genetic aberrations similar to ordinary lipoma, spindle cell and/or pleomorphic lipoma, and myxoma. In instances where the clinical, morphologic, and immunohistochemical findings overlap with other neoplasms, cytogenetic analysis may be of utility in resolving difficult cases (Table 2).^{4,5}

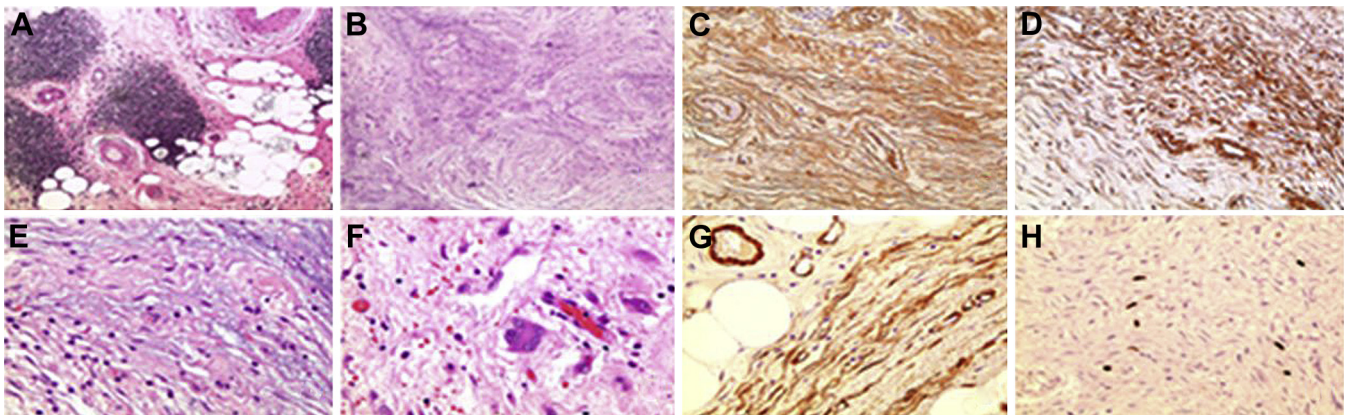


Figure 2. Hematoxylin and eosin stain. (A) Fibrous area showing bland spindle cells intermixed with mature adipocytes, small- and medium-sized blood vessels, and aggregates of lymphocytes. (B) Scattered spindle cells and thin-walled blood vessels in an abundant myxoid stroma. (C) Spindle cells contain wavy, tapered, hyperchromatic nuclei and inconspicuous nucleoli. Scattered mononuclear cells are present. (D) Scattered epithelioid cells with moderate eosinophilic cytoplasm, oval-shaped nuclei with granular chromatin, and conspicuous nucleoli. Immunohistochemistry: (E) the spindle cells are strongly positive for CD34, (F) vimentin, and (G) SMA. (H) Ki-67 stains around 5% of the spindle cells.

Table 1
Clinical and immunohistochemical features of angiomyxolipomas reported in the literature^{1–3}

| Case | Reference | Immunohistochemistry | | | | | | | | | Gender / Age (y) | Number of Lesions | Symptoms | Location | Greatest Dimension (cm) | Duration | Duration of FU Without Recurrence |
|------|----------------------|----------------------|----------|-------|-----|--------|--------|-------|-----|----------|------------------|-------------------|---------------------|------------------------------|-------------------------|-----------|-----------------------------------|
| | | CD34 | Vimentin | S-100 | SMA | Desmin | HMB-45 | Ki-67 | ALK | CK AE1/3 | | | | | | | |
| 1 | Mai et al | NP | + | + | + | NP | – | NP | NP | NP | M/32 | Single | Pain | Spermatic cord | 2.5 | 3 mo | 18 mo |
| 2 | Zamecnik | + | NP | NP | – | NP | – | NP | NP | NP | M/57 | Single | – | Scalp | 1.5 | NS | 8 y |
| 3 | Okafor et al | + | + | + | NP | NP | – | NP | NP | NP | M/50 | Single | – | Back | 3.5 | 3 y | NS |
| 4 | Sciot et al | + | + | + | + | NP | – | NP | NP | NP | F/60 | Single | – | Thigh | 6.2 | 4 mo | 6 mo |
| 5 | Tardío et al | + | + | + | + | – | – | <5% | NP | NP | M/66 | Single | – | Scalp | 2.5 | NS | 13 mo |
| 6 | Lee et al | + | + | + | + | – | NP | <3% | NP | NP | M/44 | Single | – | Forearm | 6 | 7 y | 6 mo |
| 7 | Lee et al | + | + | + | + | – | – | NP | NP | NP | M/57 | Single | – | Wrist | 5 | 2 y | 10 mo (no enlargement) |
| 8 | Sanchez et al | NP | NP | NP | NP | NP | NP | NP | NP | NP | M/43 | Single | Pain | Subungual area | 0.6 | 1 y | NS |
| 9 | Kang et al | + | + | – | – | – | – | <5% | NP | NP | M/38 | Multiple | – | Gluteal area and extremities | 2-5 | 3 y | Lost to FU |
| 10 | Song et al | + | + | + | + | – | – | NP | NP | NP | M/69 | Single | – | Iliac crest | 2 | 3 y | 2 mo |
| 11 | Kim et al | NP | NP | NP | NP | NP | NP | NP | NP | NP | M/9 | Single | Pain | Suprapatellar | 8.5 | 5 y | NS |
| 12 | Martínez-Mata et al | + | + | + | + | NP | – | 0% | NP | NP | M/12 | Single | – | Buccal mucosa | 6 | NS | 4 y |
| 13 | Pukar et al | + | + | + | + | – | – | NP | NP | NP | F/15 | Single | Pain and distention | Colon | 4 | 6 mo | NS |
| 14 | Bergin et al | + | + | NP | NP | NP | NP | NP | NP | NP | F/51 | Single | Pain | Knee | NS | 8 mo | NS |
| 15 | Al Shraim et al | NP | NP | NP | NP | NP | NP | NP | NP | NP | M/4 | Single | Pain | Plantar | 2.5 | 1 y | NS |
| 16 | Hantous-Zannad et al | NP | NP | NP | NP | NP | NP | NP | NP | NP | F/49 | Single | Pain | Posterior mediastinum | 6.5 | Few weeks | NS |
| 17 | Hammedi et al | + | + | + | + | – | – | <1% | | | M/50 | Single | Painless swelling | Thigh | 10 | 2 y | NS |
| | Present case | + | + | – | + | – | – | 5% | – | – | M/ (43) | Multiple | Pain | Bilateral kidneys | 12 | 1 y | 3 y |

CK, cytokeratin; F, female; FU, follow-up; M, male; NP, not provided; NS, not specified.

Table 2
Comparing clinical, morphologic, and the immunohistochemical features between angiomyxolipoma and its differential diagnoses^{4,5}

| Entity | Clinical Features | | Histopathologic Features | | Cytogenetics |
|-------------------------|---|------------------------------------|--|---|--|
| | Most Common Location | Gender Predilection /Age Range (y) | Morphology | IHC | |
| Angiomyxolipoma | Subcutaneous in variable locations | M/9-69 | Alternating myxoid areas and fibrovascular areas with adipose tissue | Spindle cells are CD34, vimentin (+), SMA (-/+), and S-100, desmin, HMB-45, and ALK (-) | t(7;13)(p15;q14) |
| Spindle cell lipoma | Subcutaneous nodule in posterior neck, shoulder, or back | M/45-60 | Less conspicuous vascular pattern and myxoid stroma. Ropy collagen bundles. Scattered bizarre giant cells. | Spindle cells are CD34 (+) | t(8;12)(q12;p13) (Sciot et al) |
| Superficial angiomyxoma | Superficial tissues of trunk and head and neck | M/20-40 (18-19) | Stromal neutrophils. Epithelial structures. | Spindle cells are vimentin and CD34 (+), variably (+) for SMA, MSA, and desmin | Loss of 16q, 13q (p471 ref35 + p472 ref115,126,127) |
| Angiomyolipoma | Kidney | F/50-60 | Bundles of smooth muscle with a perivascular arrangement | Smooth muscle is SMA, desmin, HMB-45, Melan-A, and CD117 (+) | Not mentioned |
| Angiolipoma | Forearm. Multiple lesions, tender to palpation, size <2 cm. | M/young adults | Lacks a prominent myxoid stroma. Vascular channels with fibrin thrombi. | Virtually all the spindle cells are endothelial cells with CD31 (+) | Trisomy 7 or 8 (p1159 ref 193,194) |
| Angiomyofibroblastoma | Vulva | Not specified in book | Clusters of eosinophilic epithelioid cells surround prominent vessels. May contain mature adipose tissue. | Cells express vimentin, desmin. Usually negative for actin and CD34 | LOH of TSC genes on 9q and 16p (189,195) |
| Aggressive angiomyxoma | Genital, perineal, and pelvic regions | F/30-40 | Lacks a lipomatous component | Spindle cells are vimentin, desmin, MSA, SMA (+), variably (+) for CD34 | Normal cytogenetics in majority (15,16,17) |
| Lipoblastoma | Upper and lower extremities | M/birth-3 | Multilobular architecture containing lipoblasts in different stages of differentiation. | — | Single case with t (X;2) (p471 ref 35) |
| Myxoid liposarcoma | Lower extremities | 50-60 | Contains lipoblasts and plexiform capillaries. | — | Not mentioned |
| Myxofibrosarcoma | Upper and lower extremities | 50-70 | Spindle cells with hyperchromatic, mildly pleomorphic nuclei. Elongated curvilinear capillaries. | Spindle cells are vimentin (+) and focally SMA and MSA (+) | Clonal aberration involving 12q13-15 (p1091 ref 125-126) |

F, female; IHC, immunohistochemistry; LOH, loss of heterozygosity; M, male; MSA, Mouse Serum Albumin; TSC, thymic stromal cells.

Since his last operation, the patient has been clinically asymptomatic. Follow-up consisted of imaging by CT scan every 6 months for the first year and then yearly for the last 2 years. The last CT scan done 3 months ago showed no tumor recurrence. Laboratory studies have been consistent with normal renal function and reserve.

Conclusion

Angiomyxolipomas have thus far been regarded as benign neoplasms. This may be attributed to their circumscribed nature, bland morphologic features, absence of necrosis and mitotic activity, a low proliferation index (Ki-67), and nonrecurrent nature on follow-up. Angiomyxolipoma is a rare benign neoplasm with characteristic histopathologic and immunohistochemical features, usually located in the subcutaneous tissue, with a characteristic morphology and a consistent immunoprofile, whose line of differentiation is not completely clarified.^{2,4} Its location, as demonstrated

in this case report, can be variable. The pathologic behavior, prognosis, and follow-up have only been extrapolated from existing reported cases. Strong evidence will not be possible, except after a significant number of reported cases and analysis of their natural course of disease.

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