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Case Series

Pathology Section

Diverse Presentations of Angiomyxomas: A Series of Three Cases

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ABSTRACT

Angiomyxomas are uncommon mesenchymal tumours that typically arise in the vulvovaginal and pelvic regions of women and only rarely in men. Their indolent growth and resemblance to other soft-tissue lesions often complicate clinical diagnosis. We describe three cases that demonstrate both classical and unusual patterns of presentation. Two young women, aged 22 and 35 years, presented with slowly enlarging vulvar masses. Both lesions were ill-defined, gelatinous, and composed microscopically of stellate and spindle cells within a loose myxoid stroma containing numerous thick-walled vessels. Immunohistochemistry revealed desmin and Oestrogen Receptor (ER) positivity with a low proliferative index, supporting the diagnosis of angiomyxoma. The third case involved a 49-year-old man who presented with acute intestinal obstruction due to ileal intussusception. The resected lesion showed similar morphologic features with desmin, Smooth Muscle Antigen (SMA), and Cluster of Differentiation 34 (CD34) positivity, and was distinguished from inflammatory fibroid polyp by the absence of onion-skin perivascular arrangement. All patients underwent complete excision and remained disease-free on follow-up. This series highlights the diagnostic role of histology and immunohistochemistry, underscores the importance of distinguishing angiomyxoma from histological mimics, and broadens the clinical spectrum by documenting a rare intestinal case.

Keywords: Desmin, Mesenchymal tumour, Spindle cells, Vulvovaginal

INTRODUCTION

Angiomyxomas are uncommon mesenchymal tumours predominantly observed in the perineal, vulvovaginal, and pelvic regions of females [1]. The usual presentation is around the fourth decade. These tumours are rare in males, with reported cases involving the scrotum, perineal, and inguinal regions [2]. Clinically, angiomyxomas often present as slow-growing, painless masses, which may lead to misdiagnosis as other benign or malignant soft-tissue tumours [3]. Diagnosis is mainly based on the histological diagnosis after surgical resection [3,4]. Histopathological evaluation remains the cornerstone for diagnosis [3]. Grossly, the tumour presents as an ill-defined gelatinous mass. Microscopically, it is a hypocellular tumour with spindle to stellate-shaped cells embedded within a loose myxoid matrix and numerous thin-walled blood vessels [3,4]. Immunohistochemistry further aids in diagnosis, with frequent positivity for vimentin, desmin, CD34, and hormone receptors such as oestrogen and progesterone receptors [3].

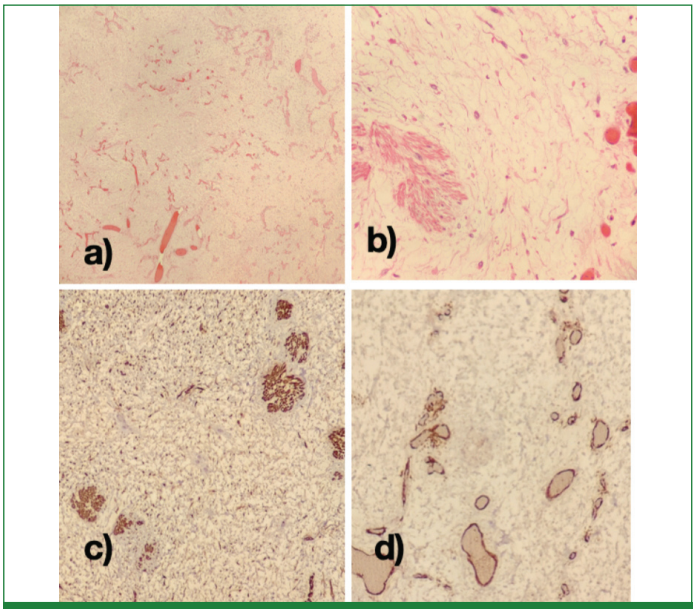
In this study, we present a case series of angiomyxomas, highlighting their diverse clinical presentations, characteristic histopathological features, and immunohistochemical profiles. Through this series, we aim to underscore the diagnostic challenges and emphasise the role of histopathology and immunohistochemistry in differentiating angiomyxomas from other morphologically similar lesions. This case series discusses three cases: two involving the vulvovaginal region in females and one affecting the small intestine in a male.

CASE REPORTS

Case 1:

A 35-year-old female presented with a pedunculated mass in the labia majora, gradually increasing in size over the past six months. Radiological imaging revealed a well-defined soft-tissue mass in the same location. Surgical excision was performed, and the specimen was submitted for histopathological evaluation.

Grossly, the mass measured 15×12×3 cm, appeared glistening, and exhibited firm consistency with gelatinous areas. Microscopically, the [Table/Fig-1] was ill-defined and hypocellular, composed of spindle to stellate cells embedded in a loose myxoid stroma. Numerous dilated, thick-walled blood vessels were present, along with smooth muscle bundles. There was no evidence of necrosis, nuclear atypia or increased mitotic activity.



[Table/Fig-1]: a,b) Magnifications of 100x,200x in microscope of angiomyxoma of the vulva, respectively.(H & E); c) Immunohistochemical staining of Desmin (100x) positivity in the tumour cells; d) Immunohistochemical staining of CD34 (100x) highlighted blood vessels.

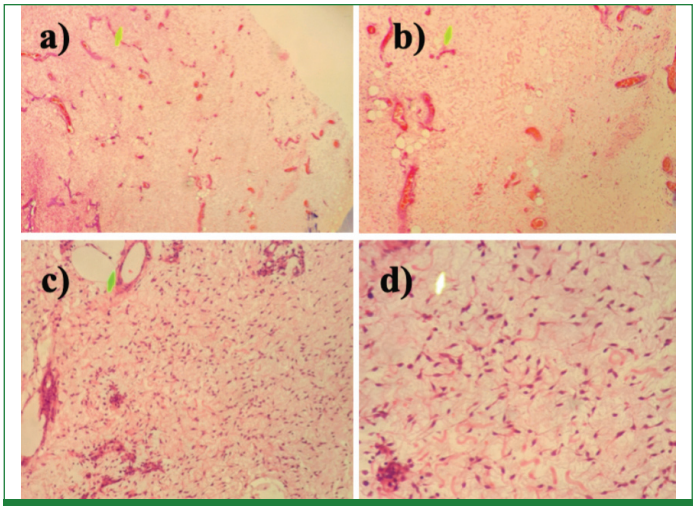
The differential diagnosis included angiomyxoma, angiomyofibroblastoma, and angiofibroma. Angiomyofibroblastoma was excluded due to the absence of alternating hypercellular and hypocellular areas, a typical feature of this entity. Immunohistochemically, CD34 highlighted blood vessels, Desmin marked smooth muscle bundles, and Oestrogen Receptor (ER) positivity was noted in the stromal cells. The Ki-67 proliferation index was low (~1%). Based on the hypocellular morphology, the presence of spindle and stellate cells in a myxoid stroma, and immunopositivity for Desmin and ER, a diagnosis of angiomyxoma was established.

Angiofibroma was ruled out due to the myxoid stroma, absence of fibrous or collagenous areas, and ER positivity. Although HMGA2 is considered a highly specific marker for angiomyxoma, it could not be performed due to its unavailability. The patient was followed up and remained asymptomatic.

Case 2:

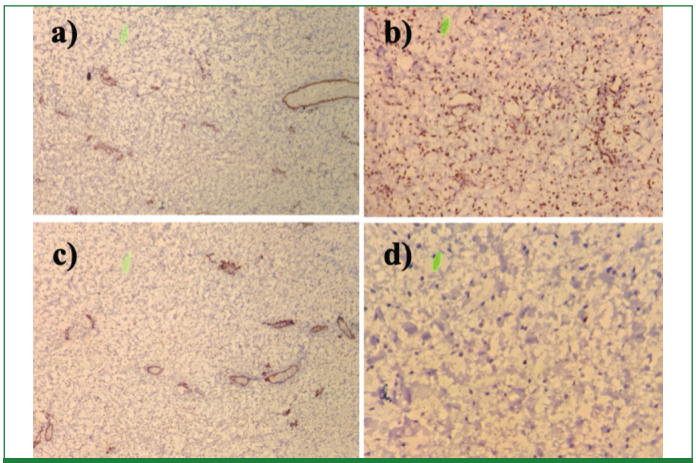
A 22-year-old female presented with a pedunculated mass in the labia majora gradually increasing in size over the past three months. Radiological evaluation showed a well-defined soft-tissue mass in the same location. The lesion was surgically excised and submitted for histopathological examination.

Grossly, the tumour measured 9×5×4 cm and appeared ill-defined, firm, and gelatinous. Microscopic examination [Table/Fig-2] showed an ill-defined hypocellular lesion composed of spindled and stellate cells in a myxoid stroma with numerous thick-walled blood vessels. No necrosis, nuclear atypia, or increased mitosis was observed.



[Table/Fig-2]: Magnifications of 40x, 200x, 400x in microscope of angiomyxoma of the vulva, respectively.(H & E) Microscopically, the lesion was hypocellular, composed of spindle and stellate cells in a myxoid stroma. Numerous dilated thick-walled blood vessels were identified, along with areas of smooth muscle bundles.

The differential diagnosis included angiomyxoma, angiomyofibroblastoma, and angiofibroma. Angiomyofibroblastoma was excluded due to the absence of alternating hypercellular and hypocellular areas. Immunohistochemically [Table/Fig-3], Desmin was positive in the stromal cells and muscle bundles; ER was positive in the stromal cells. CD34 highlighted blood vessels. The Ki-67 proliferation index was low (~1%). Based on these findings, a diagnosis of angiomyxoma was confirmed. Angiofibroma was excluded due to the myxoid nature of the stroma, lack of collagenous areas, and ER positivity. HMGA2 staining could not be performed due to its unavailability. The patient remained asymptomatic during follow-up.

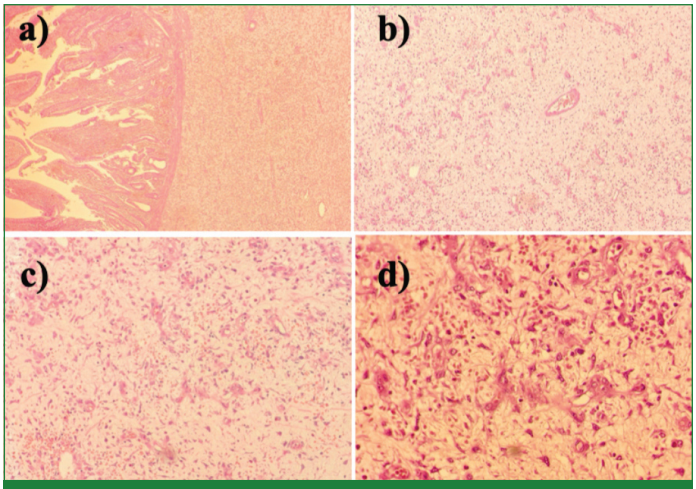


[Table/Fig-3]: Immunohistochemical staining of: a) Desmin (100x) positivity in the tumour cells; b) ER (100x) positivity in the tumour cells; c) SMA (100 x) highlighted muscle bundles; and d) Ki67 (200x) around 1% in angiomyxoma of the vulva, respectively.

Case 3:

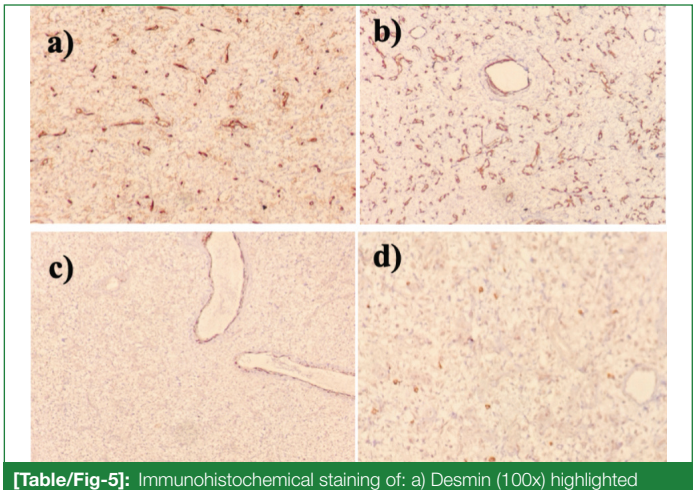
A 49-year-old male presented with acute abdominal pain of one-day duration. Clinical evaluation suggested small intestinal obstruction, likely secondary to intussusception. Radiological imaging revealed a well-defined intraluminal mass in the small intestine, with a provisional differential diagnosis of lymphoma or neuroendocrine tumour. The patient underwent surgical resection of the affected small intestinal segment. The resected specimen was submitted for histopathological examination.

Gross examination of the resected ileocolic segment (35 cm in length) revealed a pedunculated, submucosal, tan-white firm polypoid lesion with focal glistening areas measuring 5×3×2 cm in the ileum. Microscopic evaluation [Table/Fig-4] showed a submucosal tumour composed of spindle and stellate cells within a myxoid matrix. Numerous thick-walled blood vessels were noted, along with inflammatory infiltrates comprising eosinophils, lymphocytes, and mast cells.



[Table/Fig-4]: Magnifications of 100x, 400x in microscope of angiomyxoma in the small intestine, respectively (H & E); Microscopically, the submucosal lesion consisted of spindle and stellate cells in a myxoid matrix with numerous thick-walled blood vessels and inflammatory infiltrates, including eosinophils, lymphocytes, and mast cells.

Immunohistochemical studies [Table/Fig-5] demonstrated Desmin positivity highlighting perivascular smooth muscle bundles, CD34 positivity highlighting blood vessels, SMA highlighting perivascular smooth muscle bundles. CD117 was negative in tumour cells but positive in scattered inflammatory cells. The principal histological differential was inflammatory fibroid polyp; however, this was excluded due to the absence of the characteristic “onion-skin” arrangement of spindle cells around blood vessels. Additionally, CD34 staining did not exhibit the typical concentric perivascular pattern seen in inflammatory fibroid polyps.



[Table/Fig-5]: Immunohistochemical staining of: a) Desmin (100x) highlighted perivascular myoid bundles; b) CD34 (200x) highlighted blood vessels; c) SMA (100x) highlighted myoid bundles; and d) CD117 (100x) negative in the tumour cells but positive in inflammatory cells in angiomyxoma in the small intestine, respectively.

Based on these morphological and immunohistochemical findings, a diagnosis of angiomyxoma of the small intestine was rendered. The patient remained asymptomatic on follow-up.

DISCUSSION

Angiomyxomas represent uncommon mesenchymal neoplasms with a marked predilection for the perineal, vulvovaginal, and pelvic regions in females, while remaining exceptionally rare in males where they typically involve the scrotal, perineal, and inguinal areas [1,2]. Our case series encompasses three distinct presentations that collectively illustrate both the typical and unusual manifestations of these tumours: two conventional vulvar presentations in females and one extraordinary case involving the small intestine in a male patient.

The clinical presentations of the first two cases closely align with established patterns. Both patients were young females presenting with gradually enlarging pedunculated masses in the labia majora, consistent with the characteristic slow-growing, painless nature of these lesions reported by Fetsch JF et al., and Steeper TA and Rosai J [3,5]. The age distribution in our female cases (22 and 35 years) falls within the typical range described in larger series, though slightly younger than the fourth decade peak commonly cited [1]. The gross appearance of our specimens, measuring 15×12×3 cm and 9×5×4 cm, respectively, demonstrated the characteristic gelatinous, ill-defined nature described in previous reports [3,4]. Radiological findings in both cases revealed well-defined soft-tissue lesions, consistent with imaging characteristics described by Outwater EK et al., for angiomyxomas [4].

Histopathologically, our cases exhibited the pathognomonic features of angiomyxoma, including hypocellular spindle to stellate cells embedded within a loose myxoid matrix accompanied by numerous thick-walled blood vessels, mirroring the morphologic criteria established by Fetsch JF et al., [3]. The absence of necrosis, nuclear atypia, and mitotic activity in our specimens corresponds to the benign cytologic features typically observed in these tumours [5]. Our immunohistochemical findings, including desmin and ER positivity with low Ki-67 proliferation indices (~1%), align with the characteristic immunophenotype described in the literature [3,6]. The hormone receptor positivity observed in our cases supports the established association between angiomyxomas and hormonal influences, as reported in previous studies [7].

The differential diagnosis considerations in our vulvar cases required careful distinction from angiomyofibroblastoma and angiofibroma [Table/Fig-6] [2,3,8,9]. Unlike angiomyofibroblastoma described by previous authors [8], our cases lacked the alternating hypercellular and hypocellular areas, abundant plump stromal cells, and perivascular cellular concentration that characterise this entity. The strong CD34 positivity around vessels in our cases further supported the angiomyxoma diagnosis, contrasting with the typically focal CD34 expression seen in angiomyofibroblastoma. Similarly, the absence of the hypercellular spindle cell fascicles characteristic of angiofibroma as described in the literature [9], combined with the myxoid rather than collagenous stroma, excluded this diagnostic possibility.

Tumour type	Histological features	Immunohis-tochemistry	Clinical features
Aggressive angiomyxoma	Hypocellular myxoid stroma with spindle/stellate cells; thick-walled blood vessels [3]	Desmin+, SMA+, vimentin+(3), CD34+, ER/PR+ (in females) [2]	Deep-seated, infiltrative; high recurrence [3]
Angiomyofibroblastoma	Alternating hypercellular and hypocellular areas; perivascular stromal cells [8]	Desmin+, ER/PR+, SMA+, vimentin+ [8]	Well-circumscribed; vulvovaginal region [8]
Cellular Angiofibroma	Cellular spindle cells with prominent hyalinised vessels; collagenous stroma [9]	CD34+, Desmin-/weak+ [9]	Slow growing [9]

[Table/Fig-6]: Differential diagnosis of aggressive angiomyxoma in vulvovaginal region [2,3,8,9].

Our third case represents a remarkably rare manifestation, with angiomyxoma arising in the small intestine and presenting with acute intussusception. This presentation is extraordinarily uncommon, with only scattered case reports in the literature describing similar occurrences [10,11]. The 49-year-old male patient's acute presentation with small bowel obstruction contrasts sharply with the typical indolent growth pattern seen in conventional locations. Previous authors have reported similar rare presentations [10,11], emphasising the diagnostic challenge posed by angiomyxomas in atypical locations. Despite this unusual site and presentation, our tumour retained the characteristic histologic features, including the spindle and stellate cell morphology within a myxoid matrix and the presence of thick-walled vessels.

The primary differential consideration for our intestinal case was inflammatory fibroid polyp [Table/Fig-7] [1-3,10-14], a diagnosis that required careful exclusion given the overlapping myxoid appearance and inflammatory infiltrate. However, our case lacked the pathognomonic "onion-skin" arrangement of spindle cells around blood vessels that characterises inflammatory fibroid polyps as described in the literature [12]. The CD34 staining pattern did not exhibit the characteristic concentric perivascular pattern typical of this entity, further supporting the angiomyxoma diagnosis despite its unusual location.

Feature	Angiomyxoma	Inflammatory Fibroid Polyp (IFP)
Nature	Benign, infiltrative mesenchymal tumour [1-3]	Benign, localised reactive lesion [12]
Common sites	Perineal, pelvic region (rare in intestine) [1-3,10,11]	Gastrointestinal tract (stomach >small intestine >colon) [12]
Clinical presentation	Obstruction, mass effect (e.g., intussusception) [10,11]	Obstruction, bleeding, intussusception [12]
Gross appearance	Gelatinous, ill-defined, infiltrative [1-3]	Polypoid, firm, well-circumscribed [12]
Histological features	Hypocellular, spindle/stellate cells in myxoid matrix with thick-walled vessels [1-3]	Fibromyxoid stroma with eosinophilic infiltrates, onion-skin pattern [12]
Inflammatory component	Minimal, non-specific inflammatory cells [1-3]	Prominent eosinophilic infiltrate with plasma cells and lymphocytes [12]
Vascular pattern	Numerous thick-walled blood vessels [3]	Thin-walled vessels with perivascular onion-skin spindle cell arrangement [12]
Immunohistochemistry		
CD34	Positive in tumour cells and blood vessels (diffuse) [3]	Positive in perivascular cells (concentric pattern) [12]
Desmin	Positive [3]	Usually negative [12]
Smooth Muscle Actin (SMA)	Positive in perivascular myoid bundles [3]	Variable positivity [12]
CD117 (c-KIT)	Negative [3]	Negative in spindle cells; positive in mast cells [12]
S100	Negative [3]	Negative [12]
HMGA2	Positive [3]	Negative [12]
ER/PR (Hormone receptors)	Often positive in stromal cells [2,3,14]	Negative [12]
Recurrence risk	High (especially in pelvis/vulva) [1-3,13,14]	Rare [12]

[Table/Fig-7]: Differences between angiomyxoma and inflammatory fibroid polyp [1-3,10-14].

Treatment considerations for our cases follow established principles, with complete surgical excision remaining the mainstay of therapy [13]. The propensity for recurrence, particularly in females and with larger tumours as noted by previous studies [5], necessitates

careful long-term follow-up. Our first case, measuring 15×12×3 cm, represents a relatively large tumour that may carry increased recurrence risk. The potential role of hormonal therapy in managing recurrent disease, as described in the literature [14], may be relevant given the hormone receptor positivity observed in our cases. However, this was not required in our patients who remained asymptomatic during follow-up periods.

Our case series reinforces the diagnostic challenges posed by angiomyxomas, particularly in distinguishing them from morphologically similar lesions. The combination of characteristic histologic features and appropriate immunohistochemical markers remains essential for accurate diagnosis. The rare intestinal presentation in our third case expands the recognised spectrum of these tumours and highlights the importance of considering angiomyxoma in the differential diagnosis of myxoid lesions regardless of anatomic location.

CONCLUSION(S)

In conclusion, angiomyxomas are rare mesenchymal tumours primarily found in the perineal, vulvovaginal, and pelvic regions of females, and are uncommon in males. Accurate diagnosis is dependent on histopathological and immunohistochemical analysis. Surgical excision remains the primary treatment; however, a significant risk of recurrence exists, particularly in females. Management may also involve hormonal therapy to help reduce tumour size and recurrence risk.

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