



## Case series

# A case series of aggressive angiomyxoma: Using morphologic type and hormonal modification to tailor treatment

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## ABSTRACT

Aggressive angiomyxoma is a rare tumour type with a predilection for the female pelvis, high rates of estrogen and progesterone receptor positivity and local recurrence. A retrospective chart review of patients with aggressive angiomyxoma treated at 2 cancer centres is presented.

Nine patients were identified with a mean age of 41. Five patients had deeply invasive tumours that were difficult to surgically resect. Four patients had pedunculated tumours with less complex resections. In only two cases was aggressive angiomyxoma considered before resection: one due to classic magnetic resonance imaging findings and one with a preoperative biopsy. Four patients had positive margins after resection, with only one having persistent disease. Two patients were treated with gonadotropin-releasing hormone (GnRH) agonists resulting in tumour regression in one and no recurrence in the other. In this case series, aggressive angiomyxoma presented in deeply invasive and pedunculated forms. Previously reported high rates of recurrence were not observed in this group, perhaps secondary to easier resection in the pedunculated forms. GnRH agonists were successfully used as adjuncts to surgery. Evidence in this case series could be used to provide tailored treatment to patients with aggressive angiomyxoma.

## 1. Introduction

Since first described by Steeper and Rosai, aggressive angiomyxoma has been reported in multiple single case reports and some case series (Steeper and Rosai, 1983; Yalinkaya et al., 2003). This tumour is characterized by spindle cells in myxoid stroma with blood vessels of varying caliber, limited mitoses and projections of tumour into the surrounding tissue (Steeper and Rosai, 1983). On MRI imaging, this tumour has a characteristic appearance with T2 brightness and a whorled appearance attributed to stretching of the fibrovascular stroma and disorganized vascular stroma. This tumor tends to grow around and displace structures without penetrating them.

Most commonly presenting in the female pelvis, this tumour is called “aggressive” due to frequent local recurrence rather than a propensity for distant metastatic disease, although three metastatic cases have been described (Steeper and Rosai, 1983; Blandamura et al., 2003; Geng et al., 2012; Siassi et al., 1999). Not recognized initially, it is increasingly apparent that this tumour is often hormonally modifiable with

predilection for reproductive-aged women, high estrogen and progesterone receptor (ER/PR) positivity, response to anti-hormonal treatments and growth in pregnancy (McCluggage et al., 2000; McCluggage et al., 2006).

We present this case series focusing on radiographic features, two distinct presentation types, lower rates of recurrence and the use of anti-hormonal adjuvant therapy.

## 2. Methods

Nine female patients with aggressive angiomyxoma treated at two tertiary cancer centers between 1996 and 2019 were identified. Ethics approval was obtained prior to review. A literature search was performed for the keyword “aggressive angiomyxoma” in MEDLINE (Ovid), EBM Reviews, HealthSTAR, PubMed, CINAHL, MEDLINE (Ebsco) as well as grey literature sources.

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### 3. Patient characteristics

Patients were aged 22–56 years old; median age of presentation was 41. No patient had a medical comorbidity that impacted their surgical management plan. Four of nine (44%) patients had previous pelvic surgery including hysterectomy. Five (55.5%) were parous. Demographic information is summarized in [Table 1](#).

### 4. Presentation

All patients had slow symptom development with at least 12 months of symptoms (mean 26 months). The most common presenting sign was increasing size of the mass although three had pain and one had friction-related bleeding. One patient presented to the emergency department when the angiomyxoma prolapsed from her vagina. The remaining patients presented to outpatient primary care.

Due to the rarity of this tumour, the majority of cases were initially suspected to be more common gynecologic presentations. Two were thought to be canal of Nuck cysts, one a lipoma, one a pelvic organ prolapse and three benign masses. Two had a diagnosis or suspected diagnosis of aggressive angiomyxoma prior to resection.

There were two distinct presentations in this group. See [Table 2](#) for a summary of patient presentations. Five patients had deep, infiltrative disease with the bulk of the tumour not appreciated on physical exam. The second presentation, in three patients, was of a pedunculated mass from the vulva or vagina.

The mean size in maximal dimension was 9.7 cm. Of the infiltrative presentations, two tumours threatened the integrity of critical structures by growth or resection. One distorted the urethra and clitoris, and another progressed deeply and superiorly to wrap around the pubic bone.

### 5. Preoperative investigations

Due to the propensity of this tumour to be mistaken for more common entities, seven of the nine patients were initially treated by general gynecologists or general surgeons. These patients had limited preoperative investigations. For two cases mistaken for canal of Nuck cysts, ultrasound or CT was used to rule out communication with the abdominal cavity.

Two patients were initially managed by oncologic surgeons. MRI work-up by a general gynecologist led to gynecologic oncology referral after imaging identified aggressive angiomyxoma in the differential diagnosis, due to the stereotypical whorled appearance. [Fig. 1](#) shows this patient’s classic findings. The other, managed by surgical oncology, was identified on a preoperative biopsy.

**Table 1**  
Patient Demographics.

Case	Age	Medical History	Abdominopelvic Surgical History	Obstetric History	Social History
1	56	NA	NA	NA	NA
2	35	Obesity	Cesarean section, appendectomy	G2P2	Cigarette smoker
3	34	Palpitations	Nil	G3P3	Nil
4	41	Asthma	Tubal ligation, appendectomy	G0P0	Nil
5	22	Nil	Nil	G0P0	
6	41	Anxiety, depression	Nil	G0P0	Cigarette smoker
7	39	Thrombophilia	Cesarean section, appendectomy	G4P1	Social alcohol use
8	56	Dyslipidemia	Cesarean section, tubal ligation, total abdominal hysterectomy	G3P2	Social alcohol use
9	49	Nil	Nil	G4P3	Nil

### 6. Resection

[Table 2](#) summarizes disease characteristics and treatment results. Seven of nine (78%) cases were initially managed by non-oncologic surgeons and 5/7 (71%) had positive margins after the initial resection. Four patients had another resection with gynecologic oncology and three of these achieved negative margins.

The three pedunculated masses were more easily resected, but two did have positive margins. One went on to have another resection without evidence of persistent disease, the other elected to trial anti-hormonal therapy with a gonadotropin-releasing hormone (GnRH) agonist with no evidence of residual disease on follow-up MRI.

In the infiltrative cases, the tumours were larger and more deeply involved than appreciated on exam. In these cases, the resection often ended prematurely without surety of complete resection due to morbidity of a more radical procedure and uncertainty of pathology. The margins in these cases were involved or indeterminate.

For the patient managed by surgical oncology, the tumour involved the pubic bone and ischiorectal fossa. Preoperative doxorubicin and external beam radiation were used in an attempt to decrease the size of the tumour but no size reduction was recorded. Nonetheless, the surgery was extensive, requiring resection of a portion of the pubic bone with hardware for pelvic stability, as well as reconstruction of the vagina and abdominal wall. The margins were negative after this resection, at the cost of significant short and long-term morbidity related to radiation side-effects, orthopedic revision and iatrogenic menopause.

Taken as a group, 5/9 (56%) patients had negative margins at the completion of surgical management with the remaining four electing to proceed with watchful waiting or anti-hormonal therapy.

### 7. Anti-hormonal management

In the four patients who had ER status performed and recorded, the results were all positive. Two ER positive patients with positive margins went on adjuvant anti-hormonal therapy. One patient, 39 years old at diagnosis, received goserelin acetate for 18 months. After that time period, she elected to undergo surgical menopause with a hysterectomy and bilateral salpingoophorectomy in order to discontinue this medication. This patient did have suspected residual tumour on MRI that slowly decreased in size with this treatment but was still present at time of discharge from specialist care five years later. Another patient with positive margins, diagnosed at age 49, received 18 months of leuprolide acetate. This was subsequently discontinued due to logistical difficulties for the patient to receive injections and eventual menopausal status. Two other patients were recently menopausal at the time of their diagnosis and treatment and did not receive additional anti-hormonal treatment.

### 8. Recurrence

The follow-up period in this group was a mean of 31 months, median of 23 months and range of 0–77 months. Three patients were followed for five or more years. One patient did not have subspecialist follow up and no patient was re-referred back to the cancer centers after discharge.

Despite four patients with positive surgical margins, only one was found to have persistent disease in her follow-up period of 66 months. She was maintained on a GnRH agonist until oophorectomy, with ongoing disease regression over 58 months. The other three patients with positive resection margins did not recur over a mean follow up of 22 months. Two of these patients had a low estrogen and progesterone milieu as one patient received leuprolide acetate until menopause and the other was menopausal at diagnosis. The remaining five patients with negative margin status also did not have tumour recurrence over a mean of 29 months. The patient with extensive resection and preoperative doxorubicin and radiation did not experience recurrence in 5 years of follow-up and did not receive any adjuvant treatment.

**Table 2**  
Summary of presentation and management.

Case	Time with symptoms (months)	Presenting symptom(s)	Size (cm)	Neoadjuvant treatment	Surgical procedure(s)	Margin status	Hormonal medical management	Recurrence	Follow-up (mo)
1	Unknown	Vulvar Mass	Not available	Nil	1. Vulvar wide local excision – General Gynecology 2. Hemi-vulvectomy – Gynecologic Oncology	Pos Neg	Menopausal	Nil	60
2	12	Buttock mass; pain	10 × 9.5 × 7.3	Doxorubicin and 3000cGY in 10 fractions	1. Resection of aggressive angiomyxoma, resection of portion of pubic bone and vagina with reconstruction – Surgical Oncology	Neg	Radiation induced premature ovarian failure	Nil	77
3	12	Pedunculated vulvar mass	8.7 × 5.5 × 4.5	Nil	1. Vulvar wide local excision – General Gynecology	Neg	Nil	Nil	0
4	12	Perineal Mass; pain	14 × 3.0 × 2.5	Nil	1. Perineal wide local excision - General Gynecology	Pos	Nil	Nil	16
5	12	Not available	Not available	Nil	1. Vulvar wide local excision – General Gynecology 2. Simple hemi-vulvectomy – Gynecologic Oncology	Ind Neg	Nil	Nil	6
6	48	Pedunculated vulvar mass	6.2 × 5.4 × 4.1	Nil	1. Vulvar wide local excision – General Gynecology 2. Vulvar wide local excision – Gynecologic Oncology	Pos Neg	Nil	Nil	1
7	18	Vulvar mass; pain	11 × 9.5 × 2.1	Nil	1. Vulvar wide local excision – General Gynecology 2. Vulvar wide local excision – Gynecologic Oncology	Pos Pos	Goserelin acetate for 18 months	Persistent disease	66
8	12	Pedunculated vaginal mass	2.3 × 2.0 × 0.8	Nil	1. Vaginal excision - Urogynecology	Pos	Menopausal	Nil	23
9	84	Vulvar mass	16 × 7.5 × 5.5	Nil	1. Radical Vulvectomy – Gynecologic Oncology	Pos	Luprolide acetate for 18 months then menopausal	Nil	26

## 9. Discussion

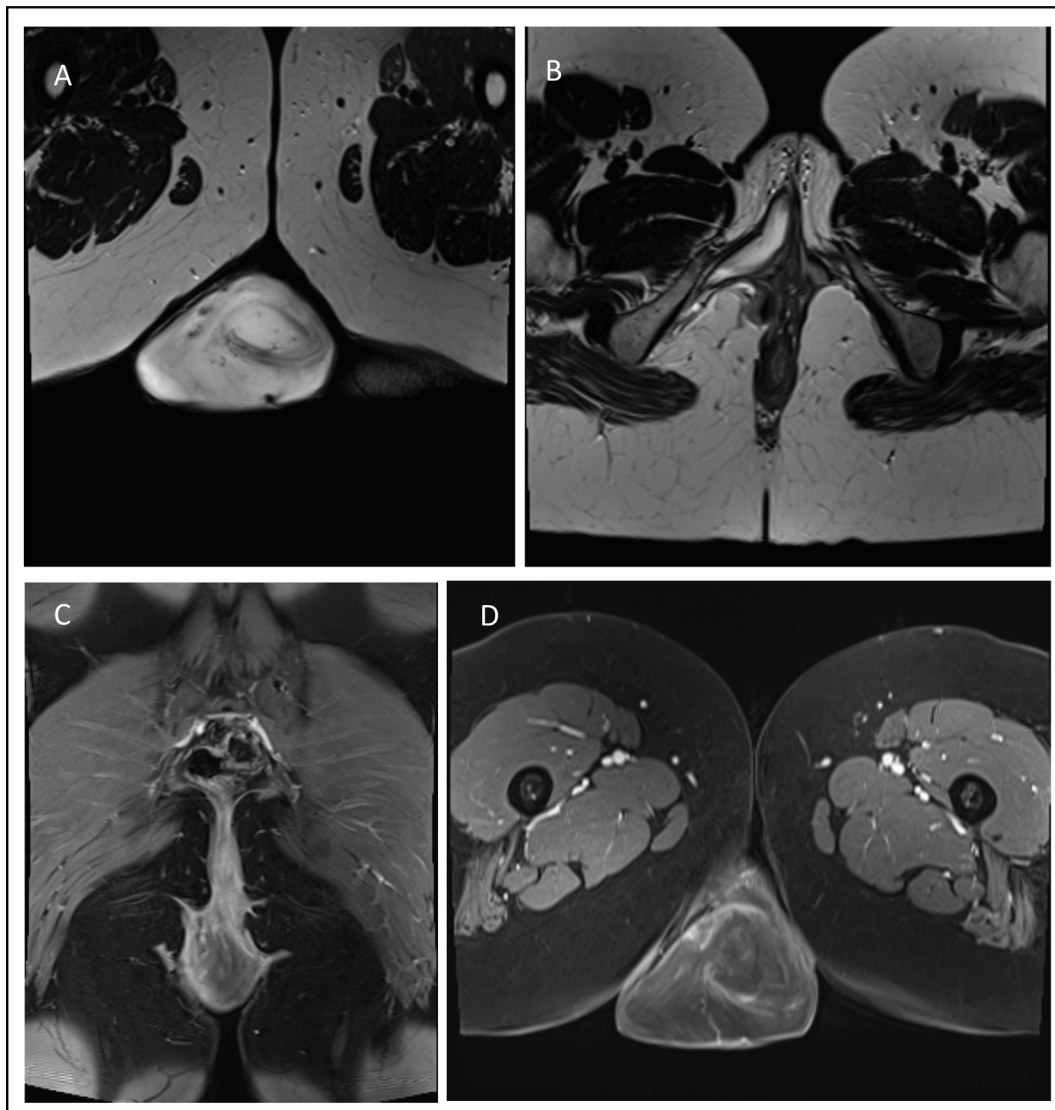
Aggressive angiomyxoma is a very rare tumour presenting most commonly in the soft tissues of the female pelvis and perineum during reproductive years (Steeper and Rosai, 1983). Due to its rarity, randomized prospective trials are not feasible and management has been based on case reports and case series. This review contributes to the literature regarding presentation type, prognosis and the role of adjunctive hormonal therapy. Previously, management algorithms for this tumour have been proposed and we present evidence to further refine and define best treatment strategies (Schwartz et al., 2014; Han-Geurts et al., 2006; Sourrouille et al., 2015).

We found two very distinct types of presentations in our group: pedunculated and infiltrative. The pedunculated and infiltrative forms have been described previously however, one third of our patients had a pedunculated presentation, which is higher than in case reports published thus far (Yalinkaya et al., 2003). We suspect this may be related to reporting bias as the infiltrative cases are more difficult to resect and may be overrepresented in the literature. Aggressive angiomyxoma must be considered in the differential diagnosis of any pedunculated vulvar mass. Our series suggests that pedunculated forms could be considered for less intensive follow-up. It appears that negative margin status is more likely to be achieved (66% in our group) compared with only half of the deeply invasive group. Resection in the pedunculated group was also achievable with a wide local excision of the vulva instead of a larger, disfiguring procedure more frequently required in the infiltrative presentations.

This tumour has been labeled aggressive for its propensity for local recurrence. The available literature describes a recurrence rate of 47% with the majority occurring within three years (Chan et al., 2000). The recurrence rate in this series, however, was only 10%, significantly lower than previous reports. We speculate that this may be partially driven by the larger number of pedunculated cases as noted above, which are less likely to recur. There is also a possibility that some

recurrences were missed as not all patients were followed for three or more years. One-third of the patients, however, were followed at least five years. There were no subsequent re-referrals after discharge of patients from subspecialist care, recognizing that some patients may have moved (one recorded) or passed away from other causes (one recorded). Lastly, the reduced rate of recurrence may be attributed to the use of hormonal modifying treatments, as described in detail below.

Increasing evidence demonstrates potential hormonal modifiability of this tumour. It presents commonly in reproductive years, the majority of tumours express ER/PR, and reports have shown response to anti-hormonal treatment (Fucà et al., 2019; Xu et al., 2020). Two patients had GnRH agonists employed in their follow-up. One had no recurrence and the other had continued regression of her disease on this treatment. Of the three patients observed without medical management, two were post-menopausal at the time of their diagnosis and neither had recurrence after resection. The third patient experienced radiation-induced premature ovarian insufficiency and did not have recurrence despite having an extensive tumour. The lower associated estrogen and progesterone levels may have contributed to the absence of recurrence and adjuvant radiation has been described in some cases with improved control over surgery alone (Han-Geurts et al., 2006). Based on information from this series, and from other reports, anti-hormonal therapy must be strongly considered in patients who are pre-menopausal at the time of their diagnosis with risk factors for recurrence including infiltrative disease and/or positive margins after resection. This treatment has the potential to spare a patient from having a disfiguring, multi-stage resection or recurrence. It is possible that recently post-menopausal patients may not need this adjuvant therapy, but rather watchful waiting in their low estrogen state. Although no cases of neoadjuvant anti-hormonal use were presented in our series future consideration could be given to pre-operative anti-hormonal treatment based on other reports.



**Fig. 1.** A: Axial T2 sequence demonstrating the pedunculated T2 bright mass with classic swirl appearance and multiple internal T2 dark vessels; B: Axial T2 sequence further superiorly demonstrating the T2 hyperintense mass insinuating the right clitoral anatomy, without direct invasion; C: Axial T1 fat saturated post contrast sequence demonstrating enhancing pedunculated mass; D: Coronal T1 fat saturated post contrast sequence demonstrating enhancing pedunculated mass.

## 10. Conclusion

Aggressive angiomyxoma remains a rare tumour with frequent initial misdiagnosis but it is essential for gynecologic oncologists to be aware of its presentation and treatment. The distinct pedunculated and infiltrative presentations appear to behave differently. Based on our case-series, pedunculated masses resected with negative margins may be considered for less intensive follow-up, freeing up healthcare resources and minimizing patient burden. Recurrence likelihood may be overstated in the literature based on infiltrative-predominant case reports. GnRH agonists and other anti-hormonal treatments are promising options in the event of recurrent disease, positive margins or low likelihood of complete resection. As with any rare tumour, concerted multicenter collaborative efforts are required to gain more information on optimal care management, however, information from this series lends support to assessment of morphologic type and hormonal modification to tailor treatment approach.

### Contributions

All authors reviewed the article for its content and editing. JK contributed to the literature review, data collection, preparation, and editing of the article. VC contributed to the literature review and article

editing. LS contributed to the ethics submission and article editing. SS provided radiologic expertise and contributed to article editing. GN contributed to oversight and editing of this case series.

### Declaration of Competing Interest

None declared.

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