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(CASE REPORT)

Diagnostic pitfalls in vulvar masses: A case report of recurrent aggressive angiomyxoma and a brief review of literature

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Abstract

Aggressive angiomyxoma (AAM), is a rare, slow-growing mesenchymal tumor that frequently mimics benign vulvar lesions, leading to delayed or missed diagnosis. We report the case of a 29-year-old woman presenting with a painless, progressively enlarging left vulvar mass. The lesion had been excised two years prior and was presumed to be a benign cyst; however, it gradually recurred over the subsequent months. The patient denied systemic symptoms but reported discomfort with sitting and ambulation. Laboratory findings were unremarkable, and physical examination was inconsistent with a simple cyst, prompting a broader differential diagnosis. Magnetic resonance imaging (MRI) demonstrated a well-circumscribed, lobulated 8 × 6 × 2 cm mass with high T2 signal intensity and a characteristic laminated ("swirled") internal architecture, displacing adjacent structures without evidence of invasion.

Given concern for recurrent AAM, a multidisciplinary team proceeded with wide local excision, achieving negative margins, followed by adjunctive gonadotropin-releasing hormone (GnRH) agonist therapy to reduce the risk of recurrence. Histopathologic evaluation revealed a gelatinous, hypocellular tumor, and immunohistochemical (IHC) findings confirmed the diagnosis of angiomyxoma.

At 18-month follow-up, there was no evidence of recurrence. This case highlights the importance of maintaining a broad differential diagnosis for vulvar masses to avoid misdiagnosis of AAM, as well as the value of a multidisciplinary approach and adjunct hormonal therapy in optimizing patient outcomes.

Keywords: Aggressive angiomyxoma; Mesenchymal tumor; Gonadotropin-releasing hormone; Recurrence; Hormonal therapy

1. Introduction

Aggressive angiomyxoma (AA) is an exceptionally rare, locally infiltrative mesenchymal tumor that predominantly arises in the pelvi-perineal region of women during their reproductive years. [1] First described by Steeper and Rosai in 1983 as a distinctive type of gynecologic soft-tissue neoplasm, this entity has been documented in fewer than 350 cases in the English medical literature to date. [2]

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Although classified as a benign tumor with virtually no metastatic potential, the term "aggressive" denotes its profound propensity for deep local invasion and high rates of postoperative recurrence, which can occur up to 15 years after the initial excision. [3] Clinically, AAM often presents insidiously as an asymptomatic, slow-growing mass, frequently misdiagnosed as a common benign condition such as a Bartholin's gland cyst, lipoma, or vulvar hernia. [4] This diagnostic ambiguity often leads to inadequate initial surgical management and subsequent disease recurrence. Furthermore, the strong expression of estrogen and progesterone receptors in most of these tumors highlights a hormone-dependent growth pattern, opening avenues for targeted medical therapies. [5]

We present a challenging case of a recurrent aggressive angiomyxoma of the vulva in a young woman, illustrating the critical importance of a multidisciplinary approach, combining complete surgical resection with adjuvant hormonal therapy to optimize long-term outcomes.

2. Case Presentation

2.1. Clinical Presentation

A 29-year-old female, gravida 2 para 2, presented with a progressively enlarging, painless mass in the left vulvar region. She reported a history of surgical excision for a similar lesion two years prior, which was then diagnosed as a benign cyst. The mass had slowly recurred over the preceding 12 months, and she sought medical attention for its increasing size, which caused discomfort while sitting and walking, and a noticeable bulge at the introitus. [1,2] There was no history of urinary or bowel symptoms, and she reported no systemic symptoms such as fever or weight loss.

2.2. Physical Examination, Imaging, and Differential Diagnosis

On physical examination, a large, soft, non-tender, and poorly defined mass was palpated in the left labia majora, extending towards the perineum. It was non-fluctuant and did not transilluminate. There was no palpable inguinal lymphadenopathy. Personal and family history were non-contributory. Laboratory workup, including complete blood count and serum tumor markers, was unremarkable. MRI of the pelvis revealed a well-defined, lobulated mass measuring approximately 8 x 6 x 5 cm, exhibiting high signal intensity on T2-weighted images with a characteristic "swirled" or "laminated" internal pattern, and progressive enhancement on post-contrast images. The mass displaced the adjacent vaginal wall but did not show signs of local invasion. [1,4,7] The clinical and radiological differential diagnosis included a Bartholin's gland cyst, a lipoma, an angiomyofibroblastoma, and a recurrent aggressive angiomyxoma. [2,5]

2.3. Multidisciplinary Tumor Board Discussion and Management Plan

The case was discussed at the multidisciplinary tumor board, which included gynecologic oncologists, radiologists, and pathologists. The central discussion focused on the high rate of local recurrence for aggressive angiomyxoma, particularly in this young patient with a history of prior resection. The team concluded that achieving a complete surgical excision with negative margins (R0 resection) was the primary treatment goal to minimize further recurrence. Given the patient's age and the tumor's typical hormone receptor positivity, the board also considered the potential role of adjuvant hormonal therapy to reduce the long-term risk of recurrence. The recommended next step was a wide local excision of the mass via an abdominoperineal approach.

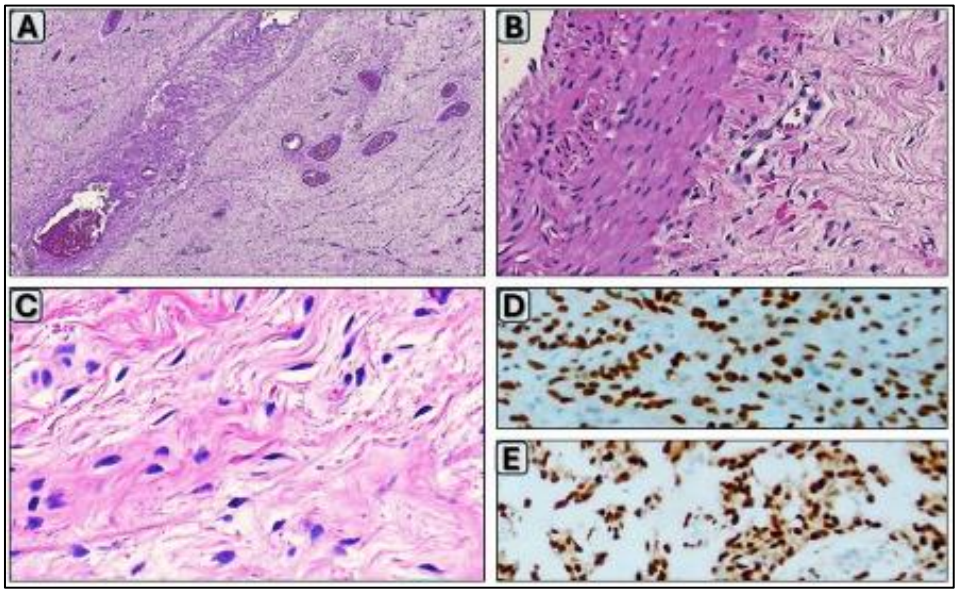
2.4. Special Studies and Pathology

The surgical specimen was submitted for histopathological examination. Grossly, the mass was an unencapsulated, gelatinous tumor. Microscopically, it was a hypocellular lesion composed of bland spindle and stellate cells set in a prominent myxoid stroma, with numerous variably-sized, thin- and thick-walled blood vessels. There was no significant nuclear atypia or mitotic activity. IHC studies demonstrated strong positivity for estrogen receptors (ER), progesterone receptors (PR), and vimentin, with focal positivity for desmin. The tumor cells were negative for S-100 protein. Given the morphological and IHC features, the diagnosis of recurrent AAM was confirmed. Molecular studies were considered and could be performed but were not deemed necessary for diagnosis in this case.

2.5. Treatment, Outcome, and Follow-up

The patient underwent a wide local excision of the vulvar mass. The surgery was performed to achieve clear margins, as confirmed by the final pathology report. Her postoperative recovery was uneventful. In accordance with the tumor board's recommendations and the tumor's hormone receptor positivity, she started on a course of a gonadotropin-releasing hormone (GnRH) agonist as adjuvant therapy. At her 18-month follow-up visit, the patient remained

asymptomatic, with no clinical or radiological evidence of tumor recurrence on surveillance MRI. She continues to be followed closely with regular clinical examinations and annual pelvic MRI scans.



1A**:** Low-power view showing hypocellular lesion composed of bland spindle and stellate cells set in a prominent myxoid stroma with numerous variably-sized, thin- and thick-walled blood vessels (H&E X20); 1B**:** High-power view showing thickened vascular wall (H&E X40); 1C**:** High-power view showing bland spindle and stellate cells in a prominent myxoid stroma. No significant nuclear atypia or mitotic activity (H&E ×60); 1D: Tumor cells positive for ER; 1E: Tumor cells positive for PR

Figure 1 Microscopic features of aggressive angiomyxoma (AAM)

3. Discussion

3.1. Background (History, epidemiology, risk factors, and WHO classification):

AAM was first described by Steeper and Rosai in 1983 as an infiltrative, benign-appearing myxoid and vascular tumor with a high risk of local recurrence. [6] Aggressive angiomyxomas are rare soft-tissue tumors, with only a few hundred cases reported in the literature. It predominantly affects women, with a reported female-to-male ratio of approximately 6.6:1. [5,6] The tumor most commonly occurs in women of reproductive age; however, cases have been documented across a broad age range from 16 to 70 years, with peak incidence during the fourth decade of life. [7,8]

The exact etiology remains unknown, and no definitive hereditary, environmental, or occupational risk factors have been identified. Nevertheless, the frequent expression of estrogen and progesterone receptors suggests a hormonally responsive tumor. [8] In addition, HMGA2 gene rearrangements have been reported in a substantial proportion of cases, although their precise role in tumor development and progression remains uncertain. [5,8]

In the WHO 5th edition, aggressive angiomyxoma is classified under benign tumors of uncertain differentiation. [9] The pelvis, perineum, and vulva are the most common locations of this neoplasm. [5,8] Despite its benign histologic features, it is considered "aggressive" because of its locally infiltrative behavior, deep tissue extension, and high rate of local recurrence. [8]

3.2. Pathogenesis, Pathophysiology

The precise histogenesis of AAM remains elusive. However, it is postulated to originate from multipotent perivascular stromal cells in the lower genital tract that can differentiate into myofibroblasts and fibroblasts. [1] A defining molecular hallmark in a significant proportion of AAM cases is the chromosomal translocation or rearrangement involving the 12q13-15 region, leading to the aberrant expression of the High Mobility Group AT-hook 2 (HMGA2) gene. [10] This genetic alteration promotes cellular proliferation and tumorigenesis.

Additionally, the pathogenesis is heavily influenced by the hormonal milieu; the near-universal expression of ER and PR receptors in neoplastic cells drives tumor growth, particularly during pregnancy, and provides a mechanistic rationale for using GnRH agonists as an effective medical intervention. [5]

3.3. Comparative Analysis of Our Case with Existing Literature. (Clinical, radiology, pathology, lab, diagnosis, management and outcome)

The clinical trajectory of our patient closely mirrors the classical presentation detailed in existing literature yet underscores the persistent challenge of managing recurrent disease. Consistent with comprehensive reviews, such as the retrospective analysis of 87 cases by Sun et al., our patient presented in her third decade with a progressively enlarging, painless vulvar mass that had previously been misdiagnosed and inadequately excised. [4]

The MRI findings in our case, specifically the characteristic "swirled" or "laminated" internal pattern with high T2 signal intensity, perfectly align with established radiological criteria, which are crucial for delineating the tumor's deep local extent prior to surgery. [11] While historical paradigms advocated for radical surgery to achieve clear margins, contemporary literature, including the series by Haldar et al., suggests that the recurrence rates remain high (approximately 30% to 40%) even with R0 resections. [3] Consequently, there has been a paradigm shift toward fertility-sparing, wide local excision combined with medical management.

Our multidisciplinary decision to employ adjuvant GnRH agonist therapy echoes the successful strategies reported in recent literature, demonstrating that hormonal manipulation can effectively suppress residual microscopic disease and prevent subsequent relapses in strongly receptor-positive tumors. [5,12]

4. What Have We Learned from This Case?

This case translates several critical diagnostic and therapeutic concepts into actionable clinical insights. Foremost, it highlights the necessity for a high index of suspicion; any progressively enlarging or recurrent vulvar mass, especially those previously deemed "simple cysts," must raise suspicion for aggressive angiomyxoma. Clinicians must recognize that physical examination often significantly underestimates the true extent of these infiltrative lesions. Therefore, pelvic MRI should be considered the gold-standard imaging modality for evaluating deep tissue involvement and guiding surgical planning. [11]

Therapeutically, this case reinforces the evolving knowledge that surgical excision alone is frequently insufficient for long-term cure due to the tumor's unencapsulated nature. The integration of IHC profiling, specifically testing for ER, PR, and HMGA2, is not merely academic but directly dictates management. By identifying hormone receptor positivity, clinicians can leverage GnRH agonists either as neoadjuvant therapy to reduce tumor volume prior to surgery, or as adjuvant therapy to mitigate the high risk of recurrence. [12] Ultimately, the management of AAM demands a multidisciplinary approach and rigorous, long-term surveillance, as recurrences can manifest over a decade later.

Abbreviations

- Aggressive angiomyxoma (AAM)
- Immunohistochemical (IHC)
- Gonadotropin-releasing hormone

5. Conclusion

Aggressive angiomyxoma of the vulva is a rare but formidable clinical entity characterized by deceptive initial presentations and a relentless tendency for local recurrence. We report this case to emphasize the critical need for accurate preoperative radiological assessment and meticulous histopathological diagnosis in the management of recurrent vulvar masses. This report adds value to the medical community by illustrating the successful integration of complete surgical resection with adjuvant GnRH agonist therapy in a young patient, highlighting a modern, fertility-sparing, and multidisciplinary approach. By sharing these clinical insights, we aim to enhance awareness among gynecologists, pathologists, and surgeons, ultimately reducing misdiagnoses, minimizing surgical morbidity, and improving the long-term oncological outcomes for women affected by this challenging neoplasm.

Compliance with ethical standards

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All authors make the following declarations:

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- Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might be interested in the submitted work.

Statement of informed consent

Informed consent for the publication of this case was obtained from the patient.

Data access statement

All relevant data are included in the paper.

Author contributions

All authors contributed equally to producing this manuscript.

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