

CASE REPORT

# Atypical Vaginal Aggressive Angiomyxoma in a Virgin: A Case Report from South Jordan

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Abstract: Aggressive angiomyxoma is a locally invasive, rarely diagnosed mesenchymal tumor that predominantly affects the perineal region of women in their reproductive years. It is typically found in areas such as the vagina, vulva, and other pelvic soft tissues, but its presentation can be highly variable. We describe a particularly unique case of aggressive angiomyxoma, presenting in an atypical manner within the vaginal region of a 31-year-old virgin woman. This case is noteworthy for the unusual growth pattern of the angiomyxoma—located strictly within the vaginal epithelium, showing no signs of invasion into surrounding tissues, which is not typical of the aggressive nature of this type of tumor. The patient presented with a mass that protruded through the hymen, an uncommon presentation that led to initial speculation about the nature of the mass. The definitive diagnosis of aggressive angiomyxoma was made by meticulous histopathological examination after surgical excision of the mass. This case emphasizes the critical importance of considering aggressive angiomyxoma in the differential diagnosis of vaginal masses, particularly those that do not exhibit invasive characteristics. The case also highlights the need for increased awareness among clinicians about the potential for atypical presentations of this rare tumor, to facilitate timely and accurate diagnosis, and to guide appropriate management strategies. This report contributes to the growing body of literature on aggressive angiomyxoma, highlighting the variability in its presentation and the need to heighten suspicion in atypical cases.

Keywords: aggressive angiomyxoma, vaginal cyst, vaginal tumor, mesenchymal tumor, case report

#### Introduction

Vaginal cysts display various histological characteristics, categorized by their epithelial lining. We present a distinctive case of a posterior vaginal cyst in a virgin patient diagnosed with aggressive angiomyxoma (AA) who underwent postoperative resection.

AA, classified by the World Health Organization as a tumor of uncertain differentiation, 1 is a rare and locally invasive mesenchymal tumor that is most commonly seen in women of reproductive age. Although AA occurs predominantly in the perineum, it can also develop in the vagina, vulva, and other pelvic soft tissues. 2 In particular, AA has a high local recurrence rate, ranging from 30% to 70%. 3 Despite more than 500 reported cases and approximately 300 related articles since its first description in 1983, 2.4 AA remains relatively underexplored, and histopathological examination after surgical resection is crucial for an accurate diagnosis.

At the initial clinical evaluation, the diagnosis of AA can be challenging prior to excision,<sup>3</sup> as it is often mistaken for more common superficial lesions such as vaginal cysts, Bartholin cysts, leiomyomas, pedunculated polyps, lipomas, Gartner duct cysts, or levator hernias. Additionally, angiomyxoma is clinically difficult to distinguish from other mesenchymal tumors that occur in the vulvovaginal region. The slow tumor growth rate often results in patients presenting with asymptomatic, painless masses that have developed over periods ranging from 2 months to 17 years.<sup>5</sup> Furthermore, imaging studies, including ultrasound and computed topography [CT] scanning, help determine the location and extent of the tumor, but do not always allow accurate classification and characterization. Consequently, the large, bulky nature and deep tissue involvement of AA are rarely recognized until radiographic imaging and surgical resection are performed.

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Surgery is the main treatment for angiomyxoma, with the aim of complete surgical resection. Effective treatment of angiomyxoma requires a balance between thorough surgical excision to prevent recurrence, which is common, and the preservation of function and aesthetics. In this regard, insights from the treatment of vulvar cancer are informative. Giannini et al discussed the transition from radical en bloc resections to more conservative surgeries, such as wide local excisions and sentinel lymph node biopsies, to minimize morbidity without compromising treatment efficacy. Similarly, for AA, adopting a surgical approach that thoroughly excises the tumor while preserving surrounding tissues can improve patient outcomes.

This case report presents a particularly unique case of AA, manifesting as a well-localized mass within the vaginal epithelium of a 31-year-old woman. The tumor exhibited an atypical growth pattern, showing no signs of invasion into the surrounding tissues, which is unusual for this type of tumor. Considering the evolving principles of personalized surgical care, this case underscores the importance of individualized treatment strategies and comprehensive diagnostic evaluation in the management of rare gynecological tumors.

## **Case Report**

## Patient Information and Complaint Presenting

A 31-year-old unmarried woman presented to the clinic of a government hospital in southern Jordan, reporting a mass that had protruded through her hymen over the past year, a concern that she had hesitated to address due to cultural and religious customs. However, the increasing size of the mass, which caused significant discomfort, led her to seek medical help. She did not report any urinary or intestinal symptoms, pelvic pain or pressure, abnormal vaginal discharge, vaginal bleeding, or dysmenorrhea. The patient reported no significant medical or relevant family history of the disease.

## Clinical Findings

On physical examination, the mass was initially concealed during pelvic examination, but presented as a non-tender 5-cm cystic bulge upon straining. Due to the patient's virginity, a speculum examination was not feasible, so a transabdominal ultrasound was performed, which revealed a normal-sized uterus and unremarkable ovaries. The conservative nature of our community presented challenges in performing a transvaginal ultrasound. Following ultrasound, which showed no significant findings, a CT scan was conducted. However, CT was performed without contrast enhancement, as no abnormalities were detected on initial scans. Considering the young age of the patient, the radiologist prioritized differential diagnoses that were more common and benign, resulting in an incomplete assessment. Consequently, the CT scan yielded inconclusive results.

Choosing additional evaluation under anesthesia, the patient and her family provided their written informed consent, which included documentation of the case and potential injury to the hymen during mass excision.

# Diagnostic Evaluation

Examination under anesthesia revealed a 5×5-cm mass on the posterior vaginal wall, stretching the hymenal ring (Figure 1).

# Therapeutic Intervention

#### Surgical Technique

The rectovaginal septum was not invaded, and the mass was surgically removed with meticulous closure of the vaginal mucosa. A longitudinal incision was made in the posterior vaginal wall and the mass was excised using both sharp and blunt dissection methods. Redundant portions of the vaginal mucosa that enveloped the cyst were also excised. The vaginal mucosa was then closed with absorbable sutures.

#### Pathological Findings

Macroscopic examination after excision revealed a 4×2.5×1.5 cm specimen with a hard gelatinous consistency. Under a microscope, a fibrovascular tumor with thick-walled hyalinized blood vessels and a myxoid stroma with stellate to

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Figure I Mass extruding from introitus.

spindle cells and bland nuclei was observed (Figure 2A–C). The free excised margins were clear of the tumor. An immunohistochemical analysis showed cells that were positive for both progesterone and estrogen receptors, which is consistent with an aggressive androgenic anabolic steroid angiomyxoma tumor. Due to the unusual clinical presentation, the specimen was reviewed by two pathologists for confirmation.

#### Adverse and Unanticipated Events

The patient experienced an uneventful postoperative recovery and no complications occurred during or after the surgical procedure. She was discharged on the third day. The patient was informed of a potential local recurrence, although no adverse or unanticipated events were reported during the treatment or follow-up period.

#### Follow-Up and Outcomes

At the six-month follow-up, pelvic magnetic resonance imaging (MRI) exhibited no local recurrence, and subsequent pelvic examinations showed no significant findings. The patient remained recurrence-free at the one-year follow-up; the patient expressed a desire for hymenorrhaphy to avoid stigmatization. During the next 2.5 years, she married, successfully conceived, and delivered vaginally with no evidence of tumor recurrence during pregnancy.

#### Discussion

Considering the variable differential diagnosis of vaginal wall masses, a preliminary diagnosis can be made based on the patient's history and physical examination. Conducting outpatient pelvic examinations for an unmarried woman in a conservative community can be difficult due to cultural and religious constraints. Therefore, imaging techniques such as CT or MRI are essential in preoperative evaluation to identify the origin of the mass and to determine its extent in relation to the surrounding organs, <sup>7</sup> particularly when ultrasound results are indeterminate, as in our case.

MRI is the recommended modality for preoperative assessment and monitoring of AA recurrence of to its characteristic swirling pattern and high, relatively homogeneous signal intensity on T2-weighted images.<sup>8</sup> This pattern is distinguished by hyperintense and hypointense bands clustered in layers and vortices, creating a "laminated" or "swirled" look. In contrast, the variable CT appearance of AA, which can range from hypodense regions relative to the muscle to mainly cystic masses without distinguishing characteristics, could explain the initial diagnostic error in our case. Wang

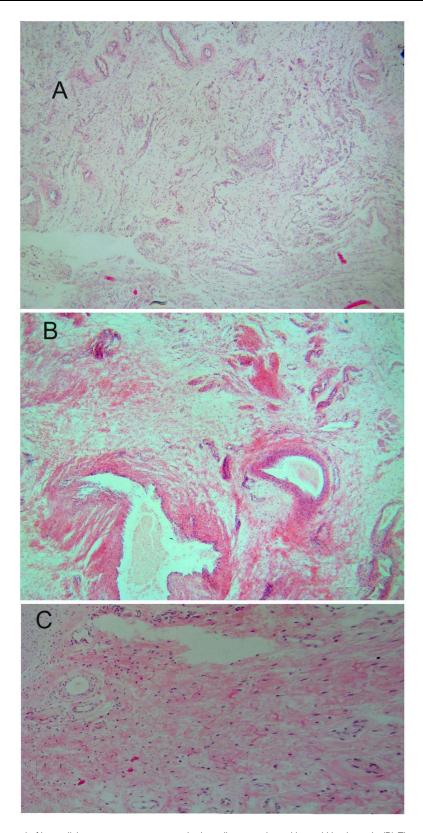


Figure 2 (A) The tumor composed of hypocellular areas contains numerous haphazardly arranged, variably sized blood vessels. (B) The stroma is distinctly myxoid with intermixed, wispy collagen fibrils; scattered, smooth muscle bundles. Perivascular rings of condensed collagen may be a prominent feature. (C) The tumor cells are cytologically bland and have a spindled, ovoid, or stellate appearance with ill-defined cytoplasmic borders. Nuclear chromatin is evenly dispersed with minimal to no cellular atypia. Mitotic figures are rare.

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et al observed that competent radiologists can identify AA with ultrasound and MRI; however, CT scans may not be as useful. In their study, none of the 24 patients who underwent CT examinations were diagnosed with AA. Despite this finding, the importance of relying on various imaging modalities in assessing the tumor spread into surrounding tissues cannot be overlooked.

AA generally have a locally invasive and infiltrating growth pattern in the surrounding tissues.<sup>7,9</sup> Some sources describe their behavior as displacing adjacent organs rather than truly invading them.<sup>8</sup> However, in our patient, the mass was well-defined and limited to the superficial soft tissue, which is unusual. Despite these differences, histopathology confirmed the diagnosis. Uncommon cases, such as that of our patient, where the mass is easily resected without invading neighboring structures,<sup>10</sup> may be confused with angiofibroblastoma due to morphological similarities.<sup>2,11</sup> To prevent misdiagnosis, Wang et al recommended wide lesion excision to assess invasion and aid pathologists in confirming diagnosis.<sup>10</sup>

Histological examination is the gold standard for diagnosing AA. It reveals spindle, ovoid, or stellate cells with low mitotic figures embedded in the myxoid stroma featuring fine, wavy collagen fibrils. A distinctive characteristic is the myxoid stroma, which has numerous blood vessels of varying sizes. <sup>10,11</sup> Fine smooth muscle fibers are frequently seen near blood vessels, a characteristic feature of AA. While AA lacks specific immunohistochemical markers, it typically exhibits diffuse and focal desmin immunoreactivity, along with diffuse positivity for vimentin and CD34. Smooth muscle immunoreactivity (SMA) highlights the presence of myoid bundles, while immunostaining for the S-100 protein was absent. <sup>4,11,12</sup> Neoplastic cells in AA commonly express estrogen and progesterone receptor positivity, <sup>9</sup> in correlation with its prevalence in women of reproductive age. <sup>13</sup>

The differential diagnosis of aggressive angiomyxoma includes other vulvovaginal mesenchymal tumors, including fibroepithelial stromal polyps (the most common type), angiofibroblastoma, superficial angiomyxoma, myxoid lipomatous tumors, myxoid leiomyoma, and botryoid rhabdomyosarcoma. Angiofibroblastoma often appears as a well-defined lesion in superficial soft tissue, usually less than 5 cm in size, without involving nearby glands or nerves, resulting in no reported recurrences. Histologically, angiofibroblastoma is characterized by alternating areas of low and high cellularity, featuring cytologically benign, plump, or epithelioid cells, frequently clustered around blood vessels, and occasionally containing multinucleated giant cells with linearly arranged nuclei. Blood vessels are thin-walled, capillary-shaped vessels. Mitotic activity is minimal, similar to that in aggressive angiomyxoma. 4,9,10

Superficial angiomyxoma typically develops in the dermis or subcutaneous tissue as a poorly circumscribed lesion of less than 5 cm in size and shows a distinct lobular or multinodular structure. Histologically, it is myxoid and vascular but lacks the large-caliber vessels seen in AA. Its immunophenotype is nonspecific, typically negative for estrogen and progesterone receptors, but it may show immunoreactivity for S100.<sup>4,9</sup>

The fibroepithelial stromal polyps appear as indistinct lesions of different sizes in the superficial tissue. Histologically, it exhibits a fibrous, edematous, and myxoid stroma characterized by thin-walled blood vessels and high mitotic activity. Its immunophenotype is similar to that of angiomyxoma.<sup>4,9</sup>

Recent research suggests that the gonadotropin-releasing hormone analog (GnRHa) may be a viable noninvasive alternative for primary cases of aggressive angiomyxoma with positive margins or recurrent AA.<sup>7,13,14</sup> In certain cases, treatment with adjuvant GnRHa has shown efficacy in reducing the risk of recurrence and treating residual disease. <sup>13–16</sup> In our case, the patient, who had negative margins after resection, adhered to the imaging follow-up plan without hormonal treatment.

The minimal mitotic activity of the tumor makes radiation therapy and chemotherapy less suitable alternatives. <sup>10,16</sup> A limited number of studies have reported the efficacy of radiotherapy in the management of recurrent cases. <sup>4</sup> However, there are no reports supporting the use of chemotherapy as suggested treatment protocols for AA.

Primary treatment for aggressive vaginal angiomyxoma is complete tumor resection through surgery, with the objective of reducing the likelihood of recurrence. The accuracy of the evaluation of tumor extent prior to surgery enhances the results by facilitating the complete eradication of the tumor or the reduction of its residual size. However, Chan et al found that patients with negative resection margins have a comparable likelihood of remaining disease-free compared to those with positive resection margins (50% vs 40% in 10 years). Due to its locally invasive nature in adjacent muscle or adipose tissue and its proximity to important nearby organs such as the bladder, rectum, and vagina,

achieving complete resection of AA can be challenging. This difficulty is compounded by the potential increase in postoperative morbidity and the impact on fertility preservation, which remains a priority, as this tumor is commonly seen among women of reproductive age. In these situations, whereby significant surgical morbidity is expected, incomplete removal may be acceptable, despite the preference for complete surgical excision. 17,18

According to Gulino et al, wide surgical excision is essential to achieve tumor-free margins and to reduce the high recurrence rates associated with AA. Their review of the literature over the past decade indicates a post-operative recurrence rate between 36% and 72%, indicating the importance of long-term attention. 18 In generally, this approach was consistent with our management of this patient, which involved a successful surgical excision of a wellcircumscribed mass that did not invade surrounding tissues, followed by a careful pathological examination.

Panici et al highlighted that lymphadenectomy plays a significant role in the prognosis of vulvar squamous carcinoma, where nodal status and the number of resected nodes play a significant role.<sup>19</sup> Our patient did not show involvement of lymph node spread and since lymph node metastasis is rare in AA, the principle of minimal unnecessary lymphatic dissection applies.

A literature review revealed two reports of cases of recurrent vulvar AA that underwent bilateral inguinal and pelvic lymph node dissection, but no information was available on whether these patients experienced subsequent relapse. Another case preferred to use a GnRHa for vulvar AA with enhanced lymph nodes on CT, despite the fact that the nodes were not palpable clinically and considering the local invasive nature.<sup>20</sup> These examples illustrate how the management of aggressive angiomyxoma should be tailored to minimize potential post-surgical morbidity.

A sentinel lymph node biopsy should be considered in cases of suspected lymph node involvement, to avoid unnecessary treatment. The importance of thorough surgical excision and pathological examination is underlined by the following principles. In the management of rare gynecological tumors, it is critical to ensure clear margins and an accurate diagnosis to minimize recurrence and improve patient outcomes.

In this case, we did not assess the inguinal lymph nodes due to the patient's young age and the possibility of other more common benign vaginal lesions in the differential diagnosis, as discussed above. Additionally, the preoperative CT scan, performed without contrast, was inconclusive and the finding was not anticipated for the same reasons. This represents a limitation in our diagnostic approach. Future cases should include a thorough evaluation of the inguinal lymph nodes, as well as alternate imaging modalities, such as MRI, which has been shown to be more helpful at determining the extent of AA and guiding the surgical approach. The possibility of misdiagnosis and insufficient staging, emphasized in previous research, emphasizes the need for complete imaging and evaluation of the lymph nodes.

The recurrence rate has been documented to be as high as 70%, with the majority of recurrences occurring within a two-year period. However, recurrence can manifest at any time, ranging from several months to up to 20 years after initial therapy. 5,18 Imaging, particularly MRI as the preferred modality, is recommended for close clinical surveillance and detection of recurrences. Recurring lesions have an appearance similar to that of a primary tumor.<sup>3</sup> Incomplete resection, combined with the invasive nature of the tumor and the involvement of neighboring tissues and the visceral peritoneum, is the main cause of relapses. No clinical or histological markers reliably predict tumor recurrence, apart from positive surgical margins. 18 To minimize the rate of recurrence, postoperative medication and consistent follow-up are essential. Administration of estrogen receptor modulators (such as tamoxifen and raloxifene), aromatase inhibitors (such as letrozole) for postmenopausal women, and GnRHa for patients in reproductive age with positive estrogen receptor status after surgery can substantially decrease the rate of recurrence. However, the potential adverse effects of hormonal treatment must also be considered.

Given the lack of a definitive treatment for this highly recurrent and locally infiltrating tumor, the management of AA requires a multidisciplinary team consisting of gynecologists, radiologists, and pathologists to ensure a precise diagnosis, effective treatment, and a follow-up care plan. This effort is essential to optimize patient outcomes.

## Conclusion

When evaluating a vaginal mass in young women, it is important that both the gynecologist, during the clinical examination, and the radiologist, during the imaging review, include AA in the differential diagnosis before proceeding Dovepress Al-Kharabsheh et al

with any surgical intervention. This approach will minimize the risk of misdiagnosis and help develop personalized treatment and follow-up plans. Furthermore, the pathologist should maintain a high index of suspicion in women with vaginal masses, even in the presence of an atypical clinical presentation.

#### **Abbreviations**

AA, aggressive angiomyxoma; CT, computed topography; MRI, magnetic resonance imaging; SMA, Smooth muscle immunoreactivity; GnRHa; gonadotropin-releasing hormone analog.

## **Data Sharing Statement**

All supporting documents have been submitted along with the case report.

## **Ethics Approval**

This case report has been approved by the Ethical Committee of Mutah University [Reference number: 1622024] and the patient has provided written informed consent.

### Consent for Publication

Written informed consent was obtained from the patient with permission for documentation of the case and publication.

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## **Author Contributions**

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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#### **Disclosure**

The authors declare that they have no competing interests in this work.

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