Aggressive Angiomyxoma of Vulva a Rare Condition: Case and Literature Review

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ABSTRACT

Aggressive angiomyxoma (AA) is a rare, benign mesenchymal tumor predominantly affecting women of reproductive age. Despite its benign nature, AA exhibits locally infiltrative growth and a high propensity for recurrence. We report a case of a 40-year-old female presenting with recurrent vulvar swelling, managed through wide excision and adjuvant radiotherapy. The histological evaluation confirmed AA. This manuscript discusses the clinical presentation, diagnostic imaging, histopathology, and management approaches, focusing on surgical excision and adjunct therapies. Literature findings highlight the need for a multidisciplinary approach and follow-up to ensure favorable outcomes.

Keywords: Aggressive Angiomyxoma of the vulva, vulva tumor, labial tumor, perineal mass

INTRODUCTION

Aggressive angiomyxoma (AA) is categorized by the World Health Organization (WHO) as "Tumors of uncertain differentiation" due to its benign nature and ability to grow locally and recur (1). The condition was first described by Steeper and Rosai in 1983 and is characterized by slow growth, local invasiveness, and a high recurrence rate (2). It predominantly affects the pelvis and perineum of women, although cases in men have been documented (3). Given its rarity and nonspecific clinical presentation, AA is often misdiagnosed as other soft tissue tumors, leading to delayed intervention (4). Patients should be routinely followed up for at least 2 years postoperatively for early diagnosis of recurrence, thereby reducing the risk of morbidity (5). This case report illustrates the management of recurrent AA and emphasizes the importance of accurate diagnosis, tailored treatment, and close follow-up.

Case Presentation:

A 40-year-old woman, Para 1, was admitted to our gynecological ward being referred from a peripheral regional referral facility; she presented with progressive left labial swelling for two years. The size of the swelling was increasing during or just after her menses. It was associated with discomfort when walking due to its size. The swelling was associated with pain, and it impaired her sexual activities. The swelling developed an ulcer at the distal end, which was not bleeding easily or itching. She reported having a normal micturition pattern and a normal bowel movement. This was the third episode of swelling in the left vulva. The first episode occurred about 16 years ago, and the second one was about 6 years ago. In both episodes, excision of the tumor was done, and a biopsy for histology was taken on both occasions, but the patient was told that there was no pathology.

Physical examination revealed a pedunculated vulva mass on the left labia majora measuring 22 x 12 x 11 centimeters with a thick stalk and ulcer on its distal end. The mass was soft, mobile, and non-tender (Figure 1a). There was no palpable inguinal or left supraclavicular lymph node. Based on the clinical presentation, a provisional diagnosis of vulvar lipoma, Fibroma, Lip fibroma, Agiomyofibroblastoma, and Leioyomyoma was reached.

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Incisional biopsy, which was taken at the ulcer involving normal tissue, showed nonspecific inflammatory cells. Chest X-ray revealed a normal chest radiogram. Magnetic Resonance Imaging (MRI) of the pelvis with contrast showed a left vulvar mass/tumor that is infiltrating the ipsilateral vagina wall, cervix, uterus, and ischiorectal fossa.

She was scheduled for extensive excision of the vulva. Total excision of the tumor was carried out under spinal anesthesia, and this was followed by a single dose of radiotherapy 72 hours postoperatively.

The gross examination of the excised mass showed a fungating tumor covered by skin measuring 21x 12 x 10 cm. The cut section showed a whitish tumor with gel-like material and cystic areas (Figure 1b).

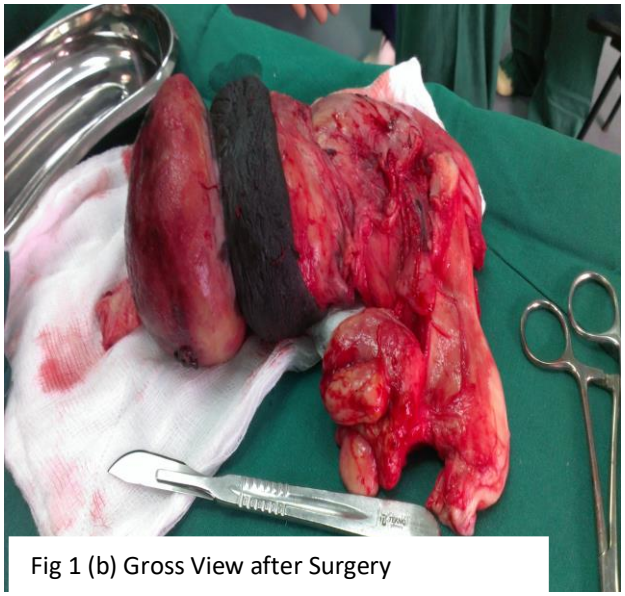

Fig 1 (b) Gross View after Surgery

Figure 1(a): Gross appearance of vulva mass showing a pedunculated tumor with ulceration at the distal end

Histological analysis confirmed AA, which has characteristic features of myxoid stroma, bland spindle cells, and vascular proliferation (Fig 2). Surgical management involved wide excision with clear margins, followed by single-dose radiotherapy. Postoperative recovery was uneventful, and the patient was discharged with instructions for close follow-up.

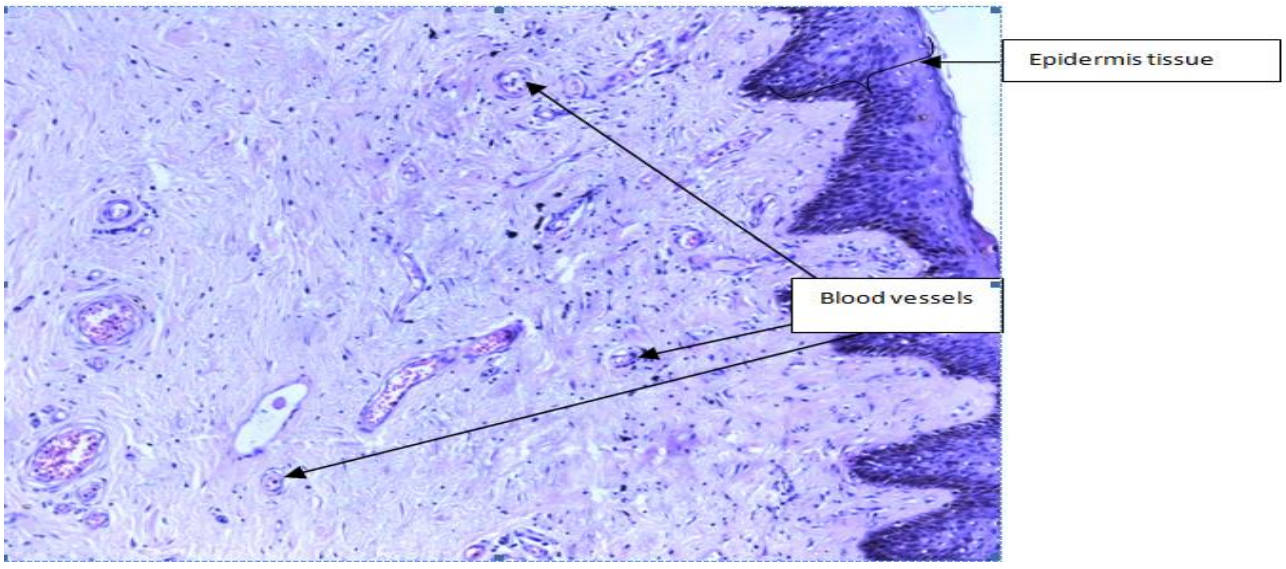

Figure 2: Histological findings Magnification x 10

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LITERATURE REVIEW

Aggressive angiomyxoma (AA) is an uncommon soft tissue tumor categorized by the World Health Organization as a locally aggressive mesenchymal tumor. Initially reported by Steeper and Rosai in 1983, its incidence remains low, with most cases reported in women of reproductive age (2). AA predominantly arises in the pelvic and perineal regions, exhibiting a slow-growing but infiltrative nature. Due to overlapping clinical features, it is commonly mistaken for more benign conditions like Bartholin cysts or lipomas (7).

The etiology of AA is unclear, but it is frequently linked to hormonal influences, as evidenced by the presence of estrogen and progesterone receptors in many tumors (8). This hormonal sensitivity suggests a potential therapeutic role for gonadotropin-releasing hormone (GnRH) agonists, particularly in recurrent or inoperable cases (9). Recurrence rates for AA range from 9% to 72%, with intervals varying between months and decades, underscoring the need for long-term follow-up (10).

Imaging modalities, particularly MRI, play a critical role in diagnosing and planning the surgical management of AA. MRI typically reveals a well-defined mass with low signal intensity on T1-weighted images and a high-intensity whorled pattern on T2-weighted images (11). Histopathologically, AA consists of hypocellular myxoid stroma with scattered spindle and stellate cells, minimal mitotic activity, and prominent vascular components (12). Immunohistochemical staining for desmin and vimentin further supports the diagnosis (13).

AA management strategies prioritize complete surgical resection with wide margins to minimize recurrence risk. However, achieving clear margins is challenging due to the tumor's infiltrative growth into adjacent soft tissues (14). Adjuvant therapies, such as radiotherapy and GnRH agonists, have been explored in cases where surgical resection alone may be insufficient (15). Notably, GnRH agonists have demonstrated tumor size reduction preoperatively, enhancing surgical outcomes (16).

Recent studies highlight the potential of combining surgical and non-surgical therapies to optimize outcomes. Advances in imaging techniques and molecular diagnostics will likely refine treatment protocols and improve prognostic assessment (17). Despite these advances, AA remains a diagnostic and therapeutic challenge, warranting further research into its pathogenesis and long-term management.

AA diagnosis relies heavily on imaging and histopathology. Ultrasound often shows a heterogeneous lesion, while MRI provides superior delineation of tumor extent. Typical findings on MRI include a low-signal-intensity mass on T1-weighted images and a high-signal-intensity whorled pattern on T2-weighted images (11). Histologically, AA comprises spindle and stellate cells in a myxoid matrix with prominent vascular structures and minimal pleomorphism (12).

Recent advances in molecular pathology have identified the high mobility group protein A2 (HMGA2) gene as a frequently overexpressed marker in aggressive angiomyxoma (13). Immunohistochemical studies have shown strong nuclear expression of HMGA2 in AA tumors, suggesting its role in tumorigenesis and recurrence. Additionally, estrogen and progesterone receptor positivity further support the hormone-dependent nature of these tumors (6). Other markers such as CD34, desmin, and smooth muscle actin (SMA) are variably expressed and assist in differentiating AA from other soft tissue neoplasms (14).

Surgical excision remains the cornerstone of AA management, aiming for clear margins while preserving adjacent structures (17). However, the infiltrative nature of AA often complicates complete resection. Gonadotropin-releasing hormone (GnRH) agonists have shown promise as neoadjuvant or adjuvant therapy due to the tumor's hormonal responsiveness (16). Radiotherapy, though less commonly used, has been effective in some selected recurrent cases (20). Given the high recurrence rates, close surveillance post-treatment is critical post-treatment (10).

DISCUSSION

Our patient's presentation and management align with the existing literature on AA. Her recurrent episodes highlight the tumor's indolent yet persistent nature (10). Surgical excision achieved symptomatic relief and

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tumor control, while adjuvant radiotherapy was employed to minimize recurrence risk (20). This case underscores the importance of comprehensive imaging and histological evaluation to guide treatment planning. Emerging therapies, such as laparoscopic surgery, including hormonal and targeted treatments, offer potential avenues for improving outcomes in recurrent or unresectable cases (16, 18, and 22).

This patient had recurrences following surgical excision alone, whereby combined therapeutic approaches have variable positive outcomes. The surgical approach alone has demonstrated 30% and 72% recurrence rates, largely due to difficulty achieving clear margins (8). In contrast, the incorporation of adjuvant gonadotropin-releasing hormone (GnRH) agonists, such as goserelin or leuprolide, has been associated with a marked reduction in recurrence, with reported rates dropping to 10%–30% (6, 21). Radiotherapy, though less commonly used due to the tumor's low mitotic index, has proven effective in select recurrent cases, reducing recurrence to below 20% when combined with surgery (20,17). Additionally, preoperative hormonal therapy may downsize the tumor, enhancing the likelihood of achieving tumor-free margins and thereby lowering postoperative recurrence risk. Overall, combination therapies integrating surgical and medical modalities offer the most favorable recurrence profiles and are increasingly advocated in clinical practice.

Due to scarcity, this patient did not benefit from newer molecular tests. Recent advances in molecular pathology have identified the high mobility group protein A2 (HMGA2) gene as a frequently overexpressed marker in aggressive angiomyxoma. HMGA2, a transcriptional regulator involved in mesenchymal proliferation, is often rearranged in AA cases, particularly through chromosomal translocations involving 12q15 (13). Immunohistochemical studies have shown strong nuclear expression of HMGA2 in AA tumors, suggesting its role in tumorigenesis and recurrence. Additionally, estrogen and progesterone receptor positivity further support the hormone-dependent nature of these tumors (6). Other markers such as CD34, desmin, and smooth muscle actin (SMA) are variably expressed and assist in differentiating AA from other soft tissue neoplasms (14). Detecting these molecular markers has improved diagnostic accuracy and opened avenues for targeted therapy, particularly in patients with recurrent or inoperable tumors. Continued investing in molecular diagnostic approaches in low- and middle-income settings is critical for developing personalized treatment strategies for future patients.

Conclusion Aggressive angiomyxoma is a rare but challenging tumor due to its local invasiveness and high recurrence rate. Accurate diagnosis through imaging, molecular, and histopathology tests, combined with multidisciplinary management, is essential. Surgical excision with clear margins remains the mainstay of treatment, supplemented by hormonal or radiotherapeutic strategies in select cases. Long-term follow-up is paramount to detect and manage recurrences promptly.

Key Take-Home Messages

- Aggressive angiomyxoma is a rare, benign tumor with significant local recurrence potential.
- Diagnosis relies on imaging modalities such as MRI and confirmatory histopathology.
- Surgical excision with clear margins is the primary treatment, supplemented by adjuvant therapies.
- Long-term follow-up is crucial due to the tumor's propensity for recurrence.

Conflict of interest

The authors had no conflict of interest

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Consent:

The patient and her guardians granted us permission to publish this case report and its associated images.

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Limitation: This single case report cannot be generalized in management to other patients

Author contributions:

JGK was involved in patient care and manuscript writing. PJTW was involved in manuscript editing. IM carried out histopathology studies and was involved in manuscript editing.

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