Case Report

Varied Clinical Presentations of Aggressive Angiomyxoma of the Vulva: A Rare Entity

Lajya Devi Goyal; M.D.[1], Priyanka Garg; M.D.[1], Suresh Goyal; M.D.[2], Surbhi Bansal; M.D.[1], Manjit Kaur Rana; M.D.[3]

1 Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, Bathinda, India
2 Department of Urology, All India Institute of Medical Sciences, Bathinda, India
3 Department of Pathology, All India Institute of Medical Sciences, Bathinda, India

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Abstract

Objective: Aggressive Angiomyxoma (AA) of the vulva is a slow-growing mesenchymal tumour with a tendency to local invasion and recurrence.

Case report: We report two cases of vulvoperineal masses that were diagnosed to be Aggressive Angiomyxomas after surgical excision. Both patients presented to the Gynaecology OPD of All India Institute of Medical Sciences, Bathinda, Punjab, India, in 2020 and 2022 with complaints of a mass coming out of introitus of three years duration and 14 years duration, respectively. The first patient was managed by surgical excision of the mass via abdominoperineal approach, while the second patient underwent vaginal hysterectomy along with the removal of the mass. Both patients were given GnRH analogues after the surgery to avoid any further recurrences and have been in remission on follow-ups so far.

Conclusion: Due to its rare occurrence, clinicians should consider the possibility of AA while encountering patients with vulvovaginal masses to avoid misdiagnosis and delayed management.

Keywords: Angiomyxoma; Vulva; Aggressive; Recurrence; Mesenchymal Tumor

Introduction

Aggressive angiomyxoma (AA) of the vulva is a benign, locally invasive mesenchymal tumor originating from myxoid cells of connective tissue. It was first mentioned by Steeper and Rosai in 1983 (1). It is a soft tissue neoplasm having a propensity for women of reproductive age group, with its peak incidence in the third to fifth decade of life. Although the entity is slowly growing, it is locally infiltrative and has a low propensity to metastasize. It is often misdiagnosed owing to its rarity, resulting in delayed management in such patients. The diagnosis is usually made retrospectively on histopathology examination following surgical excision. Once diagnosed, the accepted treatment modality includes wide local excision with tumor-free margins. Recently, the administration of GnRH (Gonadotropin releasing hormone) agonists for tumors that express estrogen and progesterone receptors have been tried as a therapeutic manipulation to prevent future recurrences (2). It persuades for a long-term follow-up due to its high chances of recurrence ranging from 30% to 82% (3). We describe two cases of AA with

Correspondence:
Dr. Priyanka Garg
Email: priyanka.garg.u@gmail.com

different clinical presentations successfully managed by wide local excision followed by GnRH agonists.

Case report

Case 1: A 36-year-old female, Para 1 Live 1, presented in Gynecology OPD in the year 2020 with a complaint of a mass coming out of introitus for the last three years. It was insidious in onset, non-tender, and partially reducible on pushing into the vagina. The size of the mass increased on straining, coughing, and prolonged standing. There was a history of vaginal surgery for the same mass two years back, where the mass could not be excised entirely, and a biopsy of the mass suggested chronic inflammatory changes. After one year of this surgery, the patient went to a private practitioner, where the surgery was reattempted to remove the mass via an abdominoperineal approach. Still, the attempt failed, and it could not be removed. There was no history of any sexually transmitted infection (STI) or perineal trauma. There was no relevant past or family history. On general examination, her vitals were normal and systemic examination was unremarkable. On per-abdomen examination, the mass was not palpable. Local examination revealed a 10*9 cm left labial swelling, which increased on straining with a positive cough impulse. Ultrasound showed a normal sized uterus with an elongated heterogenous hypoechoic lesion on the left side of the pelvic cavity extending along the left lateral wall of the vagina. Further, MRI (magnetic resonance imaging) was done, which showed a 4.6 x 5.7 x 8.7 cm lobulated lesion in the left peri-vesical space extending inferiorly along the left anterolateral aspect of the vagina up to the introitus, maintaining fat planes with adjacent structures (Figure 1).

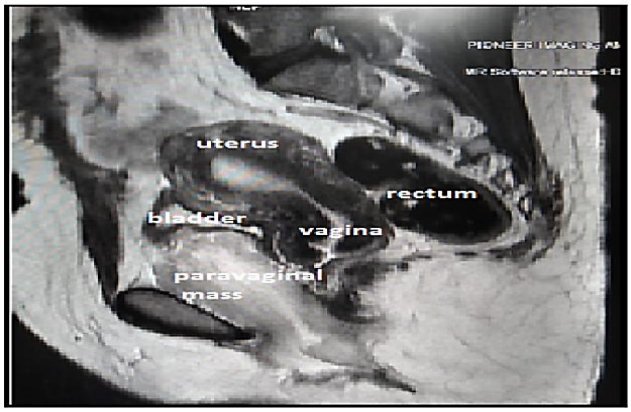

Figure 1: MRI (Sagittal section) showing 4.5*5.7*8.7 cm para-vaginal mass in the left peri-vesical region

After obtaining informed consent, the patient was planned for exploratory laparotomy via abdominoperineal approach after consultation with a urologist. Intra-operatively, the space of Retzius was entered where a soft brownish mass abutting the left side of the urinary bladder was identified. The size of the mass increased by giving pressure from the vulvar side. The mass was dumbbell-shaped, which was protruding out through a defect in the left levator-ani muscle reaching up to the left wall of the vagina. The mass was gradually dissected from the urinary bladder (medially), anterior abdominal wall (anteriorly), peritoneum (posteriorly), and lateral pelvic wall (laterally). A longitudinal incision was given on the mucocutaneous junction on the left vagina, and the mass was mobilized from surrounding areas and delivered out through the perineal incision. The defect in the levator-ani muscle was repaired. Grossly, it was a rounded, non-encapsulated soft tissue mass of 12 x 10.5 x 3.5 cm (Figure 2).

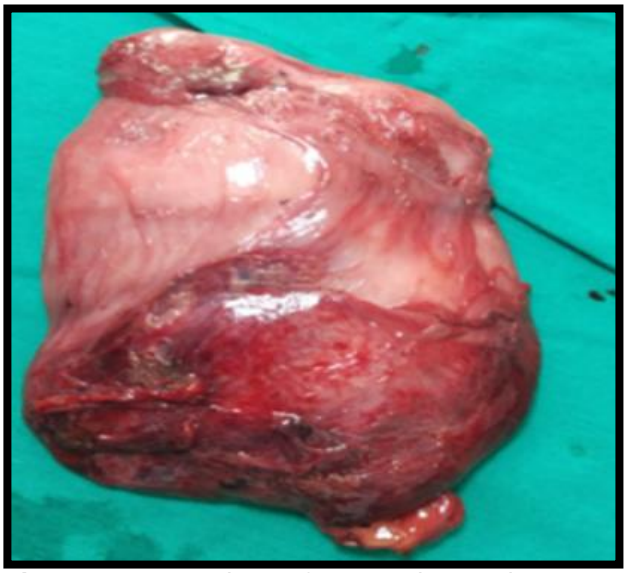

Figure 2: Gross photo of Aggressive Angiomyxoma after excision

The cut section showed a homogenous mass with a glistening grey-to-white surface. Histopathology revealed a benign mesenchymal tumor suggestive of angiomyxoma (Figure 3). On immunohistochemistry, the tumor was positive for estrogen and progesterone receptors. The patient was given a GnRH analogue injection and discharged satisfactorily. She has been coming for a follow-up for three years, and no recurrence has been reported.

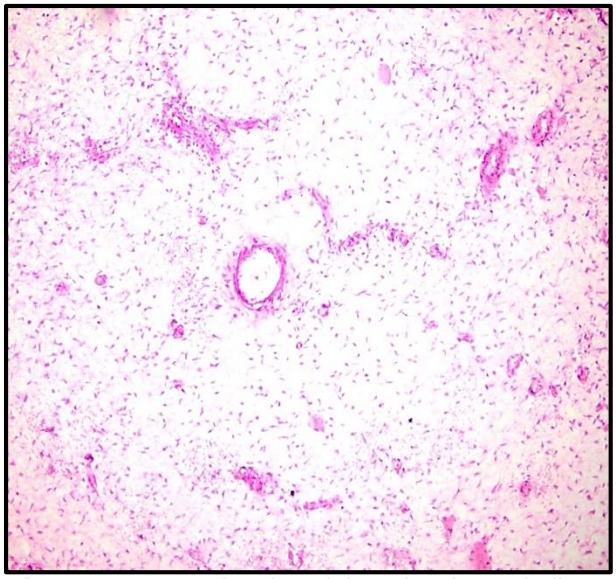

Figure 3: H & E (10X) staining showing spindle to stellate-shaped cells in the myxoid stroma with irregularly distributed thin and thick-walled blood vessels

Case 2: A 45-year-old female, Para 5 Live 5, presented in gynecology OPD in the year 2022 with chief complaints of something coming out of her introitus for a long duration of 14 years associated with foul-smelling discharge per vaginum. She had uneventful normal vaginal deliveries. Her past and family history were non-significant. She went to a local surgeon eight years ago, where she was planned for surgery. However, the surgery was deferred on the operating table after anaesthetising the patient, owing to the complicated appearance of the mass. Since then, the patient had not visited any doctor and opted for home remedies for the same. On presenting to us, local examination showed a sizeable irregular growth arising from the anterolateral and posterior lip of the cervix measuring approximately 14 X 10 cm, lying outside the vagina. A decubitus ulcer was also present on the growth. On making the patient strain, a third-degree cervical descent was also seen (Figure 4). On per vaginal examination, the uterus was retroverted with multiparous size with free fornices. After informed consent, the patient was planned for vaginal hysterectomy and pelvic floor repair. The specimen was sent for histopathology examination, which reported angiomyxoma with tumor cells positive for estrogen and progesterone receptors on immunohistochemistry. The patient was given an Injection of Leuprolide (GnRH analogue) in the post-operative period and discharged in a stable condition.

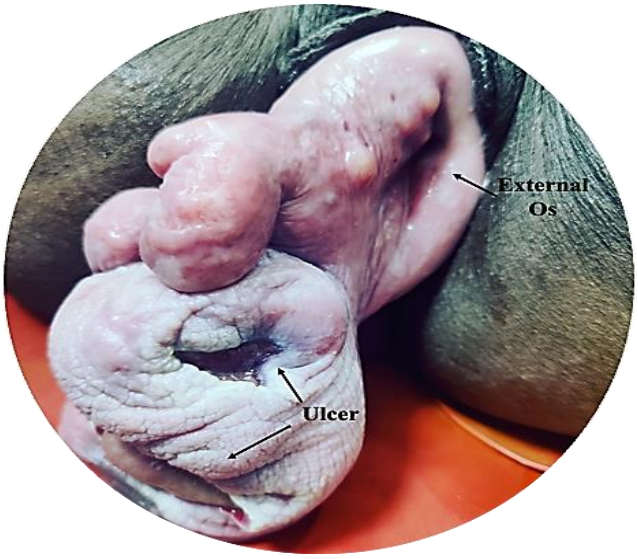

Figure 4: Third-degree cervical descent with irregular growth arising from anterolateral and posterior lip of the cervix with decubitus ulcer

Discussion

AA is a rare benign soft tissue neoplasm involving the female pelvis, with the most common location being the vagina, vulva, perineum, and buttocks (1). The term "aggressive" points to the blood vessels' neoplastic nature and its locally invasive property with a high risk of local recurrence (2). Although slow growing, it infiltrates the paravaginal and pararectal spaces, causing displacement of the adjacent structures (4). It is generally found in females of reproductive age group. However, rare cases have been reported in children, perimenopausal women, and even in males with a female-to-male ratio of 6.6:1 (5, 6).

Even though the pathogenesis of AA is still a question of research, a translocation at chromosome 12 with a consequent aberrant expression of HMGI-C (high mobility group protein isoform I–C) protein with a role in DNA transcription has been reported recently. Thus, localizing HMGI-C in neoplastic stromal cells by immunohistochemistry can be used to assess the margin status after excision and subsequently as a marker for any residual disease (7).

The patient usually presents with a painless, slow-growing mass in the genitofemoral region, which is often soft to touch and easily compressible, with sizes varying from 3 cm to as large as 60 cm.[2] The true extent of the tumor is often underestimated on close examination because the clinically visible tumor is only part of the deeper tissues of the pelvis and

retroperitoneum. The most significant AA reported to date is of a 38-year-old woman with a tumor size of 57 x 47 x 23 cm (8). Non-specific symptoms such as dull aching pain, localized pressure, dysuria, retention of urine, or painful coitus may occur.

The diagnosis of AA is often tricky due to its rare occurrence. It can be confused with vulvar lipoma, abscess, vaginal, Bartholin's or Gartner's duct cyst, leiomyoma with cystic degeneration, or a levator-ani muscle hernia (9). On ultrasound, it usually appears as a hypoechoic cystic mass. Angiography depicts it as a hyper-vascular mass. The trans-levator and trans-diaphragmatic extent can be visualized on both CT (computed tomography) and MRI. On CT, a well-defined hypo-attenuated enhancing mass is seen with a swirled pattern. T1 MRI shows an isointense signal with muscles but a high-intensity signal on T2 MRI due to its loose myxoid matrix and high water content. Wu et al. elucidated that MRI is more specific than CT in ascertaining the tumor's relation to surrounding pelvic structures, thus making MRI the investigation of choice for diagnosis and follow-up of recurrent cases (7).

The final diagnosis is revealed on the histopathology. Grossly, it appears as a soft, smooth, and bulky mass without a capsule. Due to its local extension, it may develop projections and become irregular in shape (in our case, it was dumbbell-shaped). On the cut surface, it has a homogenous yet gelatinous consistency with the occasional presence of areas of congestion and hemorrhage. The histology further depicts stellate and spindle-shaped neoplastic cells with thin cytoplasmic processes in the background of the loose myxoid matrix. This loose myxoid matrix comprises hyaluronic acid and wavy collagen fibers, which stain pale pink on eosin (10, 11). The striking feature of AA is prominent vasculature ranging from a tiny capillary to large thick-walled blood vessels without any anastomotic channels, ruling out other histological differentials like fibrohistiocytoma, myolipoma, leiomyoma, and others (12). Another way to distinguish AA is through immunohistochemistry. AA reveals high positivity for desmin, vimentin, and ER PR and is negative for S-100 protein (3).

AA is benign, but some anecdotal past cases have reported pulmonary and mediastinal metastasis (3, 13). As traditionally, the gold standard management of AA continues to be the wide surgical excision with tumor-free margins. As these tumors lack a true capsule, achieving negative margins becomes challenging. Also, a review of 100 cases demonstrated that patients left with positive margins had equal chances of recurrences than those with negative margins (14). Due to the intrinsic low mitotic activity of AA, radiotherapy, and chemotherapy are not effective treatment options. Also, because of multiple feeding vessels, embolization or chemo-embolization is unsuitable as an alternative approach (12, 15). Therefore, one should aim for complete resection of the tumor, although an incomplete surgery is acceptable when extensive surgery anticipates high morbidity. A relatively newer treatment modality is the administration of GnRH agonists as an adjuvant to incomplete resection and a neoadjuvant treatment for recurrent cases. They help to reduce the tumor bulk, preferably for ER & PR positive tumors, but data corroborating their use is still scanty (15). Due to the presence of ER PR-positive receptors, there is the possibility of pregnancy promoting the growth of tumors. However, the effect of pregnancy on the relapse risk is still unknown. The recurrence rate is highly variable, ranging from 30% to 80%. A maximum number of recurrences have been reported within the first three years of surgical excision, necessitating a long-term follow-up by both clinical and MRI examination (16).

Conclusion

Our report highlights that the possibility of AA should be considered whenever a patient presents with a vulvovaginal mass, as inaccurate diagnosis may lead to repeated and failed surgeries, causing undue morbidity to the patient. Wide surgical excision is the preferred treatment modality, and a combined abdominoperineal approach is sometimes needed for complete resection of the tumor with negative margins. Due to the high propensity for local invasion, yearly follow-up is recommended to detect early recurrences.

Conflict of Interests

Authors declare no conflict of interests.

Acknowledgments

Informed consent was obtained from the patient for publishing this case report. Authors have no conflict of interest.

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