Aggressive angiomyxoma of the vulva: A case report and review of the literature*

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Background: Aggressive angiomyxoma is a distinctive soft tissue tumor of the pelvis and perineum of adult women associated with a high risk of local recurrence.

Case: A case of an aggressive angiomyxoma of the vulva in a 55-year-old woman is reported. The tumor was gelatinous, polypoid and 2x1.8x1.5 cm in size. Histologically, stellate and spindled cells were embedded in a loosely collagenized matrix with scattered vessels of varied caliber. No mitoses were evident. It was found that the tumor cells were immunoreactive to vimentin and estrogen receptor, but negative to factor VIII and S–100 protein. The cell proliferation was analyzed by the mean AgNOR counting and mitotic count which showed very low activity.

Conclusion: Aggressive angiomyxoma of the vulva must be distinguished from the more common benign and malignant myxoid tumors including myxoma, myxoid liposarcoma, myxoid variant of malignant fibrous histiocytoma and other soft tissue tumors with secondary myxoid changes.

Keywords: Aggressive angiomyxoma, myxoid tumors, vulva

Background

Aggressive angiomyxomas (AA) are rare, slow-growing, soft (often gelatinous) and benign tumors, which are, predominantly, located on the perineum of reproductive age women. Steeper and Rosai first described its histologic characteristics and its tendency to local infiltration and recurrence in 1983. It can be mistaken both clinically and on microscopy for several other conditions such as myxoma, myxoid liposarcoma, myxoid variant of malignant fibrous histiocytoma and other soft tissue tumors with secondary myxoid changes. It is important to diagnose this condition because the tumor is locally infiltrative and requires wide excision and follow up. Although most reported cases are in women, a small number have been reported in men. The line of differentiation is not firmly established, but a fibroblastic/myofibroblastic origin has been proposed.

Case

A 55-year-old woman was presented with a polypoid mass in right labium minus for two years, which has been gradually increased in size since a week. The polypoid mass was non tender having a soft consistency with normal overlying skin. The tumor that clinically thought to be a Bartholin gland cyst was totally excised. The mass was measured as 2x1.8x1.5 cm. The outer surface was smooth and the cut surface had a gelatinous pale appearance. The cervix and vagina were healthy. The uterus was normal in size.

Microscopic examination revealed a non-encapsulated but relatively well-circumscribed neoplasm composed of a loose matrix with wavy
collagen and scattered vessels of varying caliber (Figure 1). The background stroma stains positively with alcian blue (pH 2.5). The neoplastic cells exhibited spindled or stellate morphology with relatively scant eosinophilic cytoplasm (Figure 2). Their nuclei were ovoid, contained finely dispersed chromatin with one or two small eosinophilic nucleoli. A few multinucleated cells were identified. Microcystic degeneration was focally present. Mitoses and lipoblasts were not observed. There is no evidence of any atypia or malignancy in the sections examined. The neoplastic spindle-shaped cells were stained intensely for cytoplasmic vimentin, actin, desmin and few cells estrogen positive (Figure 3). Others antibody such as S–100 protein, CEA, desmin, cytokeratin, progesterone and factor VIII expression were not identified in any tumoral cells. The mean AgNOR counting showed very low activity (1.69). The patient had no evidence of recurrence 7 years after surgery.

Discussion

Aggressive angiomyxoma (AA) is an uncommon and distinctive, mesenchymal tumor with a predilection for the pelvis and perineal regions in females and less frequently in males. The title of AA was chosen in view of the neoplastic nature of the blood vessels, locally infiltrative and recurrent nature perhaps due to incomplete excision.

The age distribution is wide, with the peak incidence at 31 to 35. On gross examination these tumors are characteristically soft, bulky masses with a smooth external surface, measuring between 3 and 60 cm in greatest dimension. The microscopic appearance of these neoplasms is characterized by a mixture of spindle or stellate cells in a loosely myxoid stroma. This stroma contains collagen fibers and a prominent vascular component containing large, thick-walled vessels. Hemorrhage and cysts is not a feature of AA, although microcystic change may be seen in microscopy as in our case. Our patient was 55 years old and the size of the tumor was smaller than 5 cm contrary to the majority of other tumors reported. However, the histological findings such as spindled or stellate cells containing finely dispersed chromatin and

![Figure 1](image1.png)

Figure 1. A loose matrix with wavy collagen and scattered vessels of varying caliber (100XH&E)

![Figure 2](image2.png)

Figure 2. The neoplastic cells exhibited spindled or stellate morphology with relatively scant eosinophilic cytoplasm (200XH&E)

![Figure 3](image3.png)

Figure 3. Neoplastic spindle-shaped cells stained intensely for cytoplasmic vimentin (100XDAB)
a loose matrix stained with alcian blue (pH 2.5), were considered in favor of the AA.

The line of differentiation is not firmly established, but recent immunostaining and ultrastructural studies indicated that this neoplasm derives from a primitive mesenchymal cell normally found in the lower female genital tract, which is capable of fibromyofibroblastic differentiation. Since its initial description in 1983 by Steeper and Rosai, significant progress in the differential diagnosis of myxoid tumors has been achieved (Table 1).

Cytogenetic and molecular analysis revealed clonal karyotypic abnormalities including chromosomal translocation involving chromosome 12 associated with rearrangement of the HMGIC gene and it was proposed that AA is molecularly belonging to the benign group of mesenchymal tumors showing multiple aberration region involvement. HMGIC expression in aggressive angiomyxoma is of value in the distinction of difficult cases from its histological mimics.

Because of its propensity to occur in female patients during the reproductive years, it is possible that aggressive angiomyxoma is a hormonally responsive neoplasm. The neoplastic cells of aggressive angiomyxoma exhibit fibroblastic and myofibroblastic features and appear to be hormonally influenced. It was proposed that; in those tumors with positivity for estrogen and progesterone receptors, medical management with a GnRH agonist seems able to control the disease. But estrogen and progesterone immunoreactivity can not be used to distinguish aggressive angiomyxoma and its histological mimics due to the possible positivity of dermal fibroblasts in normal vulvar skin and stromal cells in a variety of vulvar lesions (Table 2).

<table>
<thead>
<tr>
<th>Macroscopy</th>
<th>Stromal mucin</th>
<th>Vessels</th>
<th>Other</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>5 -60 cm</td>
<td>Present, between collagen fibers</td>
<td>Variable calibers</td>
<td>Genital, perineal, pelvic regions</td>
</tr>
<tr>
<td>Superficial angiomyxoma</td>
<td>Small size, multinodular, poorly circumscribed</td>
<td>Abundant</td>
<td>Lack the large caliber vessels</td>
<td>Lobular architecture, mixed inflammatory infiltrate, squamous or basaloid cells</td>
</tr>
<tr>
<td>Angiomyofibroblastoma</td>
<td>Small size well marginated, non infiltrative</td>
<td>Minimal</td>
<td>Abundant vasculature lack the large caliber vessels</td>
<td>Highly cellular, vascular, rare extravasation of red blood cells</td>
</tr>
<tr>
<td>Myxofibrosarcoma</td>
<td>Abundant</td>
<td>Culvilinear branching capillaries</td>
<td>Multinucleated atypical cells</td>
<td>High</td>
</tr>
<tr>
<td>Myxoid liposarcoma</td>
<td>Abundant</td>
<td>Plexiform, thin-walled</td>
<td>S100 protein (+)</td>
<td>High</td>
</tr>
<tr>
<td>Myxoid neurofibroma</td>
<td>Abundant</td>
<td>Hyalinized blood vessels</td>
<td>More uniform cellular</td>
<td>None</td>
</tr>
<tr>
<td>Cellular angiofibroma</td>
<td>Small size, &lt; 3 cm</td>
<td>Minimal</td>
<td>Matre adipocytes, collagen bundles</td>
<td>None</td>
</tr>
</tbody>
</table>

| Table 2. Different hormone positivity in AA according to certain authors |
|---------------------------------|---------------------------------|
| Silverman et al.                | Androgen +                      |
| Fetsch et al.                   | Estrogen + and progesterone +   |
| Htwe et al.                     | Estrogen – and progesterone +   |
| Fishman et al.                  | Estrogen + and progesterone -   |

It often recurs and there is no correlation between the size of the tumors and the chance of recurrence. The tumor has widely been known that have no potential to metastasize. But some recent reports are contrary to this knowledge.
AA is a locally aggressive neoplasm and it must be distinguished from benign proliferations with a low risk for recurrence, as well as from fully malignant myxoid tumors. The differential diagnoses range from benign tumors such as myxolipoma, myxoid neurofibroma and myxoid leiomyoma to myxofibrosarcoma, myxoid variant of liposarcoma, leiomyosarcoma, malignant fibrous histiocytoma and botryoid rhabdomyosarcoma. This neoplasm may also be clinically misdiagnosed as vaginal polyposis, myxoma, lipoma, vulvar mass, vulvar abscess, Bartholin's cyst, Gardner's duct cyst, vaginal cyst, vaginal prolapse, pelvic floor hernia, fibromatosis and other benign and malignant soft tissue tumors of the pelvis and perineum. The diagnosis of angiomyxoma may be difficult to establish. The distinctively striking vascular component in aggressive angiomyxoma helps in ruling out most of the above mentioned neoplasms as differentials. Within the stroma, prominent vasculature is present and reminiscent of that seen in the myxoid liposarcomas. The absence of lipoblasts in aggressive angiomyxoma helps to differentiate it from a liposarcoma.

The optimal treatment for AA is wide local excision with tumor free margin, as this tumor is locally invasive and tends to infiltrate deep into pelvic soft tissues. Pre-operative knowledge of tumor extent is important in determining surgical approach and MR imaging features of AA are characteristic. It is associated with frequent recurrences, probably secondary to incomplete removal. Also these neoplasms can have a multifocal occurrence, which might explain the recurrences in some of the neoplasms, especially those with negative surgical margins. Generally recurrences occur within the first 3 years. Our patient was free of recurrence 7 years after the initial surgery.

We conclude that AA is a rare, benign mesenchymal tumor occurring in young females of reproductive age group and is quite site specific. But it should be distinguished from benign myxoid tumors with a low risk of local recurrence. Therefore, long term follow-up and careful monitoring with imaging techniques are necessary before the possibility of a recurrence can reasonably be dismissed. Recurrence of the tumor may be avoided by wide local excision based on correct histopathological diagnosis.

References