Aggressive Angiomyxoma of the Vulva: A Case Report*

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ABSTRACT

Aggressive Angiomyxoma is a rare, slow growing, benign mesenchymal tumor arising from the pelvis and perineum which commonly affects women in the reproductive age group. Though benign, it is locally infiltrative with a marked tendency for local recurrence. We report a case of aggressive angiomyxoma of the vulva with translevator extension into the pelvic cavity in a 33 year old G2P2(2002). She presented with a left labial mass that recurred two years after excision was done. Debulking of the mass was carried out by abdominal and perineal approach. Histopathologic studies of the mass confirmed aggressive angiomyxoma. Long-term periodic follow-up with imaging studies was advised because of its high rate of recurrence in spite of negative tumor margins after wide excision.

Key words: Aggressive angiomyxoma, vulvar tumor

INTRODUCTION

Aggressive angiomyxoma is an uncommon, slow growing, benign,locally infiltrative mesenchymal tumor of the pelvic region. Since 2010, only less than 250 cases were reported worldwide (3) and this is the first reported case in our institution in the last 20 years. This paper will be discussing a case of aggressive angiomyxoma in a 33 year old, who presented with a vulvar mass that extended in the pelvic cavity.

CASE REPORT

H.A., 33 year old, G2P2(2002), sought consult at the gynecology outpatient department complaining of an enlarging vulvar mass. Four years prior patient underwent excision of a left labial mass at a district hospital; however histopathology of the mass was unknown. Two years prior to consult, patient noted recurrence of the left labial mass with associated increasing abdominal fullness and pelvic heaviness. There was no history of vaginal bleeding, vulvar pain nor changes in bowel and bladder habits. The patient's menstrual cycles ccurred regularly with a normal flow. There was no history of papsmear or oral contraceptive pills used. The patient denied any family history of malignancy or other heredofamilial diseases. She is a non-smoker and non alcoholic beverage drinker. Upon physical examination of the abdomen, there was palpable mass measuring 20 cm x 20 cm, cystic, movable, non tender from the hypogastrium to the left upper quadrant and the subxiphoid area. Genital examination revealed a well circumscribed left labial mass, soft, nontender with spongy consistency measuring 18 cm x 25 cm extending to the crural fold laterally; compressing the vaginal cavity medially and cephalad; with extension to the left gluteal fold presenting as a 10 cm by 10 cm soft non tender mass (Figure 1). The inguinal lymph nodes were not enlarged bilaterally. The initial impression was a pelvoabdominal mass with possible perineal extension/herniation.

Ultrasound of the abdomen revealed an isoechoic mass measuring 20 cm x 15 cm x 15 cm anterior to the uterus, extending to the vulvovaginal area. Contrast enhanced computed tomography (CT) of the abdomen revealed an enhancing mass within

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the left ischioanal fossa that extended through the pelvic floor musculature into the pelvis (Figure 2). The soft tissue mass is seen predominantly on the left side of the vaginal region extending inferiorly to the vulva and superiorly to the uterus at the level of L5 vertebra. The mass displaced and compressed the adjacent rectum and sigmoid colon to the right. This mass measured approximately 33cm x 10 cm x 17 cm (CC x W x AP). Another intraabdominal mass was seen in the region of the left upper abdominal quadrant and was noted to be predominantly cystic with enhancing septations. The lower portion of the mass was solid and measured 28 cm x 20 cm x 12 cm causing mass effect to the adjacent bowels displacing them to the right side.

Tumor debulking was done by abdominal and perineal approach. Intraoperative findings revealed a large tumor occupying almost the entire abdomen displaced to the left, on top of the intestines. The superior borders of the mass was noted to be just below the stomach and adjacent to the left lobe of the liver. Inferiorly, the mass was densely adherent to the left lateral border of the uterus, cervix and the bladder. The mass also had dense infiltration into retroperitoneum and was adherent to the rectum. The tumor was excised securing the integrity of the bowels, bladder and ureters. The surgical specimen was a soft, gelatinous mass with a glistening pink outer surface measuring 65 cm x 38.5 cm x 8.5 cm (Figure 3). Cut sections showed smooth, solid, tan to yellow soft fatty surface. Along with the tumor, the uterus with the left ovary and fallopian tube were removed. A 2 cm x 3cm submucous myoma was seen on cut section of the uterus (Figure 4). Upon closure of the abdomen, surgical drains were placed.

Excision of the vulvar mass was carried out by sharp dissection and electrocautery. Surgical specimen was an irregularly-shaped tan to brown rubbery tissue measuring 30 x 19 x 8.5 cm with portion of her labial skin (Figure 5). Cut sections showed smooth, solid, tan to yellow soft surface similar to the abdominal mass (Figure 6). Vulvar defect was approximated after placing a surgical drain which was removed on the 5th post operative day (Figure7).

The histopathological exam of the abdominal and vulvar specimens showed aggressive angiomyxoma. Histopathologic reports showed small, uniform, spindle shaped cells with poorly defined, pale eosinophilic cytoplasm and vesicular nuclei in a myxoid background. There are small thin walled capillaries showing perivascular hyalinization (Figure 8).

During follow-up 4 months postoperatively, the patient did not show any sign of recurrence (Figure 9). Yearly follow-up with physical examination was advised to the patient to monitor recurrence.

DISCUSSION

Aggressive angiomyxoma (AA) is a benign mesenchymal tumor of premenopausal women with peak incidence between 30 and 50 years (6). Classic presentation of the said tumor is a painless mass that has indolent growth. It has variable presentation involving the vulva, perianal region, buttock or pelvis. The greatest clinical dilemma of AA is high predisposition for local recurrence. Recurrence is local and reported in 36-72% of cases and usually manifests within 2 to 10 years. As to the patient, the vulvar mass recurred 2 years after excision was done.

Up to 80% of cases are wrongly diagnosed (7). Clinically, AA may be misdiagnosed as Bartholin cyst, lipoma, labial cyst, Gartner duct cyst, levator hernia or sarcoma. Smooth muscle tumors, canal of Nuck hernia, pelvic floor hernia, and vaginal prolapse also need to be considered in the differential diagnoses of a mass in the perineum. Histologically AA may mimic the following entities: angiomyofibroblastoma, fibroma, myxofibrosarcoma, myxoid leiomyoma, lymphangioma, neurofibroma, malignant mesenchymoma, malignant fibrous histiocytoma, myxolipoma, sclerosing mesodermal tumor, leiomyosarcoma, and embyonal rhabdomyosarcomas (4).

There is no agreement regarding the pathogenesis of aggressive angiomyxoma. This hormonally responsive tumor is thought to arise from primitive multipotent perivascular progenitor cells of the female lower genital tract display variable myofibroblastic and fibroblastic features (1). The tumor expresses desmin and smooth muscle actin

which are characteristic of myofibroblasts (9). A gene in the 12q12-15 region of chromosome 12, called high-mobility group protein isoform I-C (HMGIC), encodes proteins involved in the transcriptional regulation that renders the specialized mesenchymal cells of the pelvic-perineal region to display myofibroblastic features (9). The term "aggressive angiomyxoma" is due to the high local recurrence and its nature to infiltrate adjacent organs (2). These lesions can grow slowly into enormous sizes and infiltrate surrounding perivaginal and perirectal tissues (8). The neoplasm in this case grew into a large mass almost occupying the whole abdominal and pelvic cavity with infiltration to the retroperitoneum, uterus and rectum.

Aggressive angiomyxoma exhibits unusual growth patterns of translevator extension with growth around perineal structures (4). Extension from the perineum into the pelvis is common and often clinically unsuspected. The tumor tends to grow around the structures of the pelvic floor without penetrating the muscularis of the vagina or the rectum. These tumors have the tendency to displace rather than invade perineal structures (10). The hypothesis for the translevator extension of the mass in this case was through the round ligament. The mass from the labia majora passed through the deep inguinal ring entering the pelvis through the inguinal canal and continuing on to the pelvic cavity. CT and MR imaging can accurately reveal whether a tumor traverses the pelvic diaphragm. This determination is critical to choosing the surgical approach –either perineal, abdominal, or both – comprehensive enough to avoid leaving residual tumor. Imaging studies are important in preoperative evaluation since the tumor extension is often underestimated by physical examination (7).

Grossly, AA is a soft, well defined, sometimes polypoid mass, ranging in size from a few centimeters to 20cm or even more. The main feature is a shiny, homogenous, gelatinous appearance on cut sections (8). Microscopically the tumor is composed of widely scattered spindled to stellate-shaped cells with ill-defined cytoplasm and small round to oval hyperchromic nuclei with small centrally located nucleoli, embedded in a myxoid stroma. A significant special feature is the presence of variably sized vessels that range from small thin walled capillaries to large vessels with secondary changes including perivascular hyalinization and medial hypertrophy (8).

Several imaging modalities have been used to describe AA. On sonographic imaging, it appears as a hypoechoic or cystic mass. Computed Tomography scan typically demonstrates a mass with well-defined margins, slightly hypodense to muscle. This is due to loose myxoid stroma and high aqueous content of such tumor (7). On MRI, these neoplasms are usually hyperintense on T2 weighted images, likely related to high water content and loose myxoid matrix (9). On T1-weighted images, the tumors are isointense to muscle. Characteristically, the mass will have internal areas of swirled linear low-intensity signal on both T1-weighted and T-2 weighted images, thought to be related to fibrovascular stroma. Aggressive angiomyxomas demonstrate significant contrast enhancement, likely due to the high internal vascularity (6).

The first line of treatment for aggressive angiomyxoma is wide surgical excision, although achieving negative resection margins is difficult because of the infiltrative nature of the tumor and the absence of a well defined capsule (4). Organs such as the rectum and bladder to which the tumor may be attached are spared (9). Partial excision can be acceptable when high surgical morbidity is anticipated. Unfortunately recurrences can occur, even with negative surgical margins (7). Recurrences are reported from months to several years after excision. Local recurrences are treated with reoperation when possible and cannot be anticipated from tumor size nor cellularity (8).

Most of angiomyxomas show positivity to receptors of estrogen and progesterone. For this reason, hormonal treatment is believed to be a possible option for treatment. GnRH analogs have been used in some few cases of premenopausal women, but this tumor can regrow once the therapy is discontinued. The pre-operative reduction of tumors using analogs of GnRH can increase the chances of complete excision and reduce the morbidity of the surgical procedure. The length of GnRH agonist treatment is unknown at the moment, whether a short course or intermittent treatments are necessary (4). Our patient was not able to afford

the cost of treatment with GnRH analogs. Adjuvant hormonal treatment has also been described with Tamoxifen and Raloxifene with several degrees of success –from no response to complete remission of primary or recurrence of aggressive angiomyxoma. Radiotherapy and chemotherapy are poor treatment options because the tumor has low mitotic activity (6). Angiographic embolization may also help in subsequent resection by shrinking the tumor as well as making it easier to identify if from surrounding normal tissues (9). Generally, it is not conducted, as the tumors frequently have numerous feeding vessels. The role of biopsy of sentinel lymph nodes and lymphadenectomy is still unclear. Although there various treatment options, the recurrence rate is higher than 72% (7).

Currently there are no guidelines on the postoperative management of aggressive angiomyxoma. Because of high recurrence rate and potential morbidity associated with non-diagnosed recurrences, several authors have recommended periodic evaluations with physical exam and magnetic resonance for up to 15 years after the treatment (7). Early detection of recurrences can also be improved by inclusion of imaging studies in the follow-up protocol (7). Our patient was advised yearly follow-up at the outpatient department for 2 years and every 5 years thereafter. Prognosis is very good though some literature reported metastatic potential of aggressive angiomyxoma. Only two cases with metastatic disease have been reported. The first case occurred in a 63-year-old woman who presented with nonspecific abdominal symptoms and was found to have a pelvic AA with abdominal and lung metastasis. The second case occurred in a 27-year-old woman who developed several local recurrences after primary resection of an AA and subsequently died of multiple lung metastases (2).

By reviewing this case together with other reported cases, many physicians can gain better understanding of aggressive angiomyxoma. It is important to keep aggressive angiomyxoma as part of the differential diagnosis when patients present with painless vulvar mass. High index of suspicion is needed to make a clinical diagnosis.Current literature supports the current recommendations for treatment of angiomyxoma with a surgical resection and GnRH agonist treatment following resection. It is important to advise the patient for close follow-up with imaging of MRI or ultrasound since aggressive angiomyxoma has a high recurrence rate.

SUMMARY

This is a case of aggressive angiomyxoma in a 33 year old G2P2(2002) which presented as recurring left labial mass that extended in the abdominal cavity measuring 65 cm x 38 cm x 18cm. Wide excision of the mass was done by abdominal and perineal approaches. Histopathologic examination of the mass revealed an aggressive angiomyxoma. Periodic follow-up is warranted to monitor recurrence since aggressive angiomyxoma is known for its high propensity for tumor recurrence.

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APPENDIX

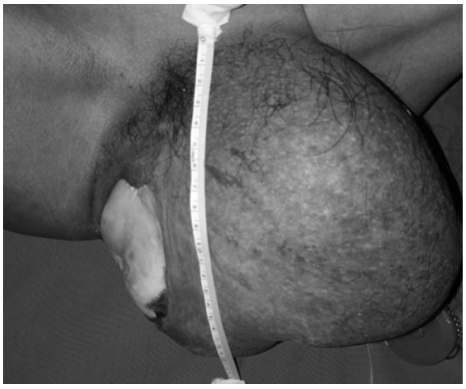

Figure 1. Preoperative appearance. Large mass located on the perineal and vulvar region

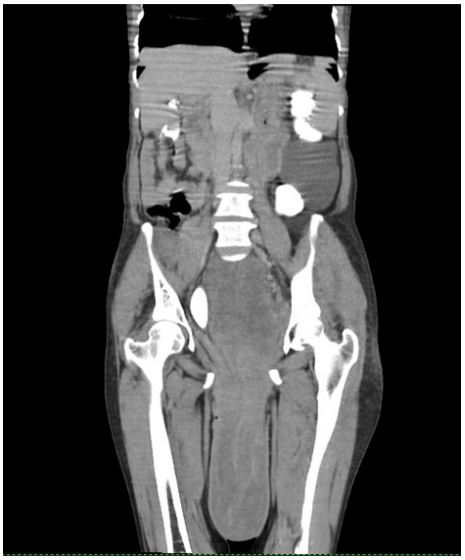

Figure 2. Contrast enhanced coronal CT scan image of abdomen and pelvis shows a large hypodense mass lesion herniating into the perineum.

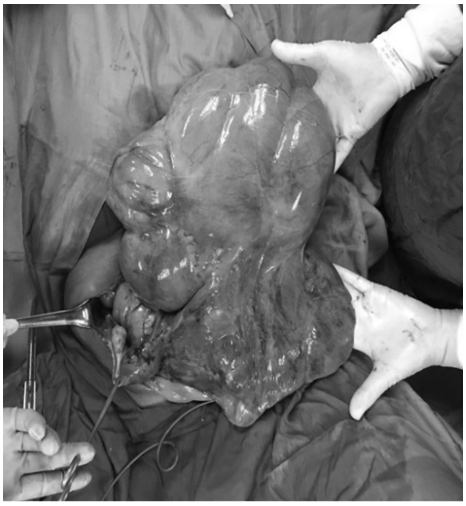

Figure 3. A 33 year old female with an enlarged vulvar mass diagnosed with aggressive angiomyxoma. Intra-operative photograph shows highly vascular fleshy mass.

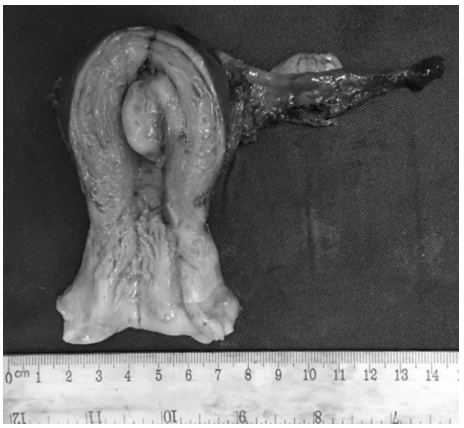

Figure 4. Cut section of the uterus showed posterofundalsubmucous myoma. Cervix, the myometrium, left ovary and fallopian tube were grossly normal.

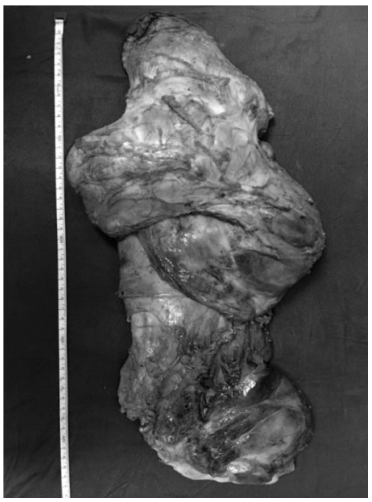

Figure 5. Gross appearance of the tumor, which measured 45cm x 30 cm x 13 cm with irregular external surface

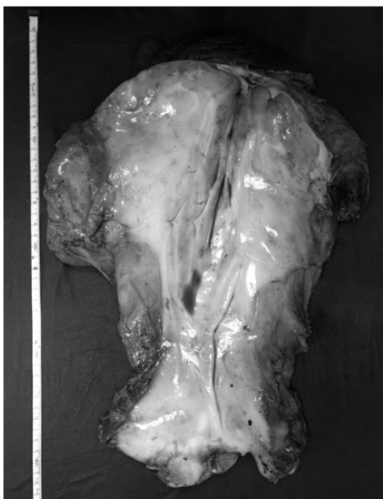

Figure 6. Cut section of the vulvar mass showed glistening gelatinous surface.

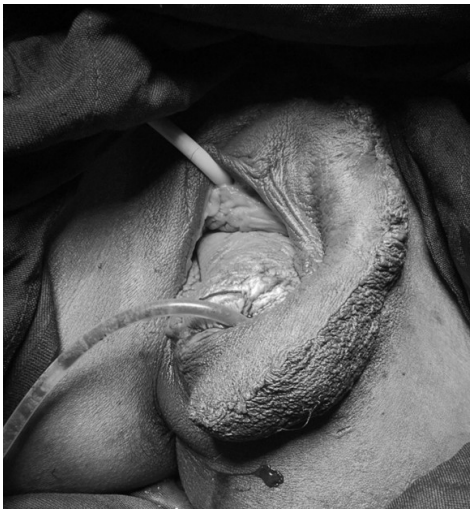

Figure 7. Post operative appearance. Approximation and suturing of the vulvoperineal region with application of suction drain

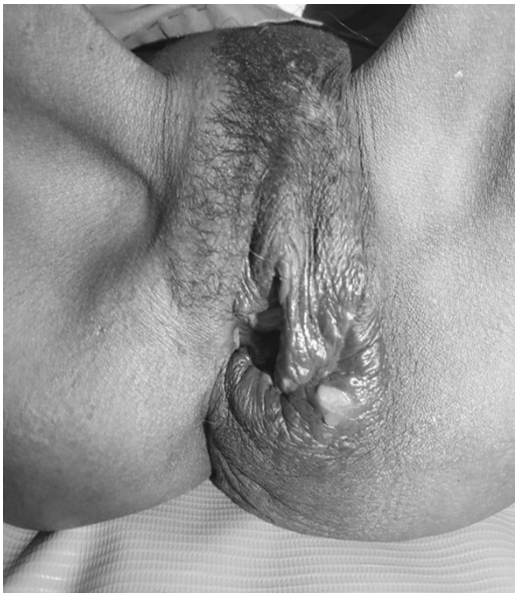

Figure 9. Four months postoperative appearance.

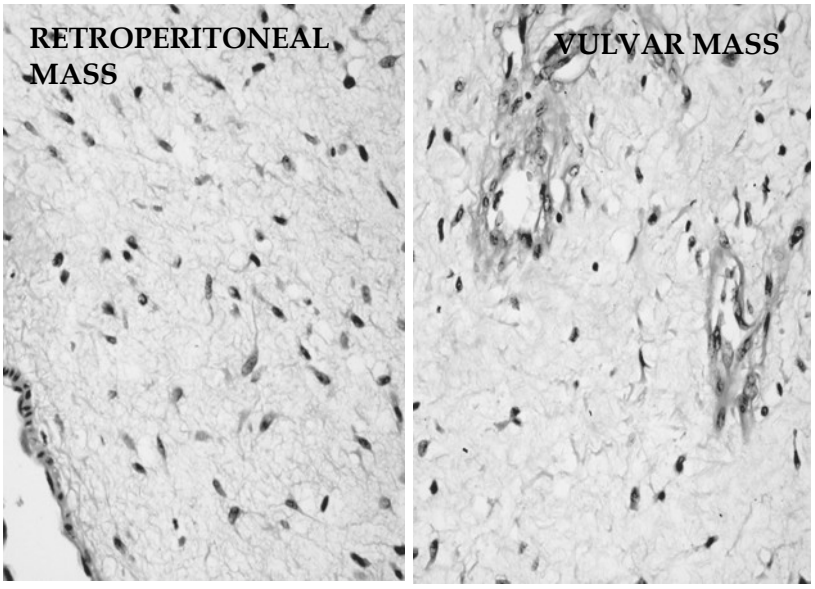

Figure 8. High power magnification showed small, uniform, spindle shaped to stellate with poorly defined, pale eosinophilic cytoplasm and bland, often vesicular nuclei in a myxoid background.