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Aggressive Angiomyxoma of the Vulva: Libyan Female Case Report

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Authors' contributions

This work was carried out in collaboration between all authors. Author NE operating surgeon, collected the materials, authors JB and NE conducted a literature search and prepared first draft, authors JB and FA provided the pathological report and figures. Author FA summarized the case history and prepared final draft. All authors read and approved the final manuscript.

Case Study

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ABSTRACT

Aims and Background: Aggressive angiomyxoma is rare tumor of pelvic and perineal organs, occurring usually in women of reproductive age, and carrying a high tendency to local infiltration and relapse. Most literature about Aggressive angiomyxomaconsists of isolated case reports.
Presentation of Case: We reported a case of 41-year-old Libyan woman complaining of a slow and progressive growth of a right vulvar labia major a pedunculated tumor with long a stalk was detected, measuring of 12.0x8.0 cm. Wide surgical resection of the tumor were performed. Histopathology diagnosed a large aggressive angiomyxoma with uninvolved resection margins. Patient remains without recurrence at 8.0-months follow-up.
Discussion and Conclusion: Non Aggressive angiomyxomais rare but should be excluded in any large vulval mass. We expect that awareness accompanied with wide free safe margin excision has important role to prevent the recurrence of tumor.

Keywords: Aggressive angiomyxoma; vulval; pedunculated tumor; immunohistochemistry staining.

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ABBREVIATIONS

MRI, Magnetic resonance image; WHO, World health organization, ER, Estrogen receptor, PR, Progesterone receptor, SMA, Smooth muscle actin.

1. INTRODUCTION

The vulva is the part of the female genital tract located between the genitocrural folds laterally, the mons pubis anteriorly, and the anus posteriorly. Embryologically, it is the result of the junction of the cloacal endoderm, urogenital ectoderm, and paramesonephric mesodermal layers. This hollow structure contains the labia majora, labia minora, clitoris, vestibule, urinary meatus, vaginal orifice, hymen, Bartholin glands, and Skene ducts. Different epithelia, from keratinized squamous epithelium to squamous mucosa, cover the vulva. The labia minora are rich with sebaceous glands but have few sweat glands and no hair follicles. The epithelium of the vestibule is neither pigmented nor keratinized and contains eccrine glands [1] Fig. 1. Benign tumors of the vulva are relatively uncommon and may show nonspecific clinical features. Therefore, a biopsy is often needed to exclude a malignant neoplasm and to indicate proper treatment. They may first be seen by physicians of various specialties, including dermatologists and gynecologists, and often require a multidisciplinary approach [2,3].

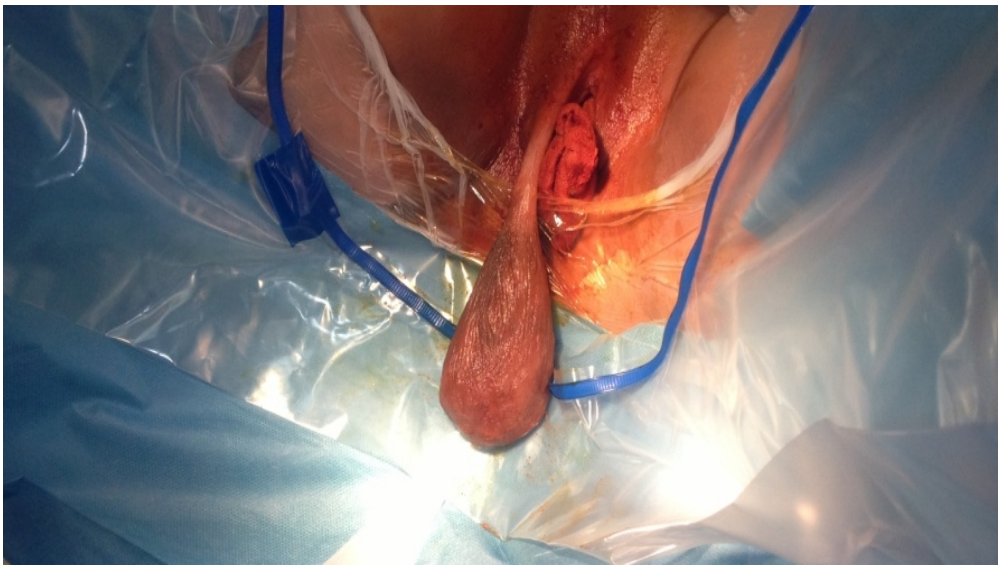

Fig. 1. A well-defined polypoidal pedunculated mass was measuring 12 cm×8.0 cm with an attached stalk and overlying normal skin

Aggressive angiomyxoma (AA) is a rare neoplasm with unknown etiologic factors [1,4-7]. The name angiomyxomawas chosen because of the similarity to myxoma and the notable vascular component. The term Aggressive angiomyxoma was not coined until 1983 but similar tumors were described as early as in the 1860s. World health organization (WHO) start to classified aggressive angiomyxoma under Tumors of uncertain differentiation of locally aggressive behavior and the high potential for local recurrence. The reported local

recurrences varied from 9% to 72% during long-term follow-up [8], with only 2 cases have been reported as metastatic disease [9], that might be due to sarcomatous transformation. Aggressive angiomyxoma is a benign soft tissue neoplasm [7]. It involves mainly the lower pelvis, more specifically perineum, vulva, and vagina of adult women in the reproductive age, with a peak incidence in the fourth decade of life [10].

The majority of patients present with a slow-growing mass which is otherwise asymptomatic. Observed accompanying symptoms and signs are regional pain, a feeling of local pressure, or dyspareunia. Tumor size is often underestimated by physical examination. Most aggressive angiomyxoma are big, often more than 10 cm in largest diameter. These tumors are macroscopically lobulated and may adhere to surrounding soft tissue. AA is often clinically misdiagnosed for a Bartholin cyst. Radiographically, aggressive angiomyxoma is isointense or has low signal intensity on T1-weighted MRI, and has a whorled pattern of high signal intensity on T2-weighted MRI. These tumors' show contrast enhancement, reflecting theirinherent vasculature, and tend to displace and grow around structures rather than infiltrate them [8,10].

Microscopically, the cellularity of tumor is generally low to moderate cells with scarce mitotic Figures. However, the infiltration into fat, muscle, and nerves might be seen. The immunohistochemistry staining can be used to confirm the histological diagnosis of AA, most AA is positive for desmin, smooth muscle actin, vimentin, estrogen and progesterone receptor. Some tumors are positive for CD34, whereas S100 is invariably negative [8]. Radical surgery with wide margins is the treatment of choice [11]. Because most tumors are large, grow infiltrative and blends with adjacent soft tissue, and are located in close proximity to vital organs such as bladder and rectum, wide excision is not always possible and/or may cause significant morbidity. In such situations watchful waiting may be advisable because these tumors may be stable with no or very limited growth over long periods. Several reported attempts using chemotherapy and radiotherapy as part of the treatment for aggressive angiomyxoma have been disappointing, probably due to the low mitotic activity (growth fraction of cells). Most aggressive angiomyxoma expresses oestrogen and progesterone receptors and is likely to have a hormone-dependent growth. Because of this, treatment with GnRH agonists has been administered to aggressive angiomyxoma patients, and some case reports with dramatic responses to such GnRH agonists have been reported [1,11].

2. CASE PRESENTATION

A 41-year-old Libyan lady, Para four, presented with apolypoidal, slow-growing painless mass for one yearduration, arising from the right labia majora. Patient was admitted in November 2012, and clinical examination showed a large skin covered non-tender, pedunculated polypoidal mass involving the middle part of right labia majora. The soft doughy tumor mass attached to vulve by long stalk Fig. 1. General examination and all systemic review of the patient were normal. Her laboratory investigations, chest X-ray, and abdominal and pelvic ultrasonography were normal. Speculum examination for vagina and cervix were also normal. The preoperative diagnosis of the patient was mostly benign soft tumor of vulval and surgical excision of the tumor with deep safety marginwas immediately done under general anesthesia.

The whole procedure was successful and the tumor with it stalk was resected. Tumor specimen was weighting 160 gram, and measuring 12.0×8.0cm Fig. 2. Cut surface was a

homogenous gray, gelatinous and some prominent blood vessels could be seen but without areas of hemorrhage or necrosis. The microscopic examination revealed polypoid tumor covered by normal skin Fig. 3, and composed of hypocellular myxomatous tissue enclosed wavy bundles of collagen and clustered blood vessels, some of which have dilated lumina and others have hyalinized wall Fig. 4. The myxomatous tissue was composed of spindle and stellate-shaped cells (fibroblast, myofibroblast). These cells had eosinophilic cytoplasm and lacked significant nuclear pleomorphism and mitosis.Additionally, there were few inflammatory cells Figs. 3 and 4. The surgical margin was negative. Most importantly, immunohistochemical staining indicated the positive expression of CD34, and SMA and focal positive of ER and PR while S-100 was negative in the tumor cells, which confirm the diagnosis of aggressive angiomyxoma Figs. 5 (A and B).

Fig. 2. The pedunculated tumor was weighting 160 gm

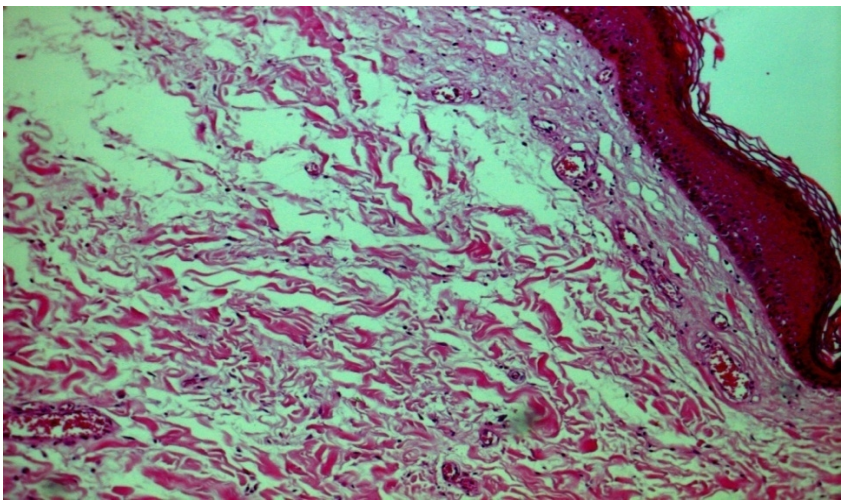

Fig. 3. Tumor covered by normal skin and enclosed wavy collagen fibers and variable walled blood vessels (H and E×200)

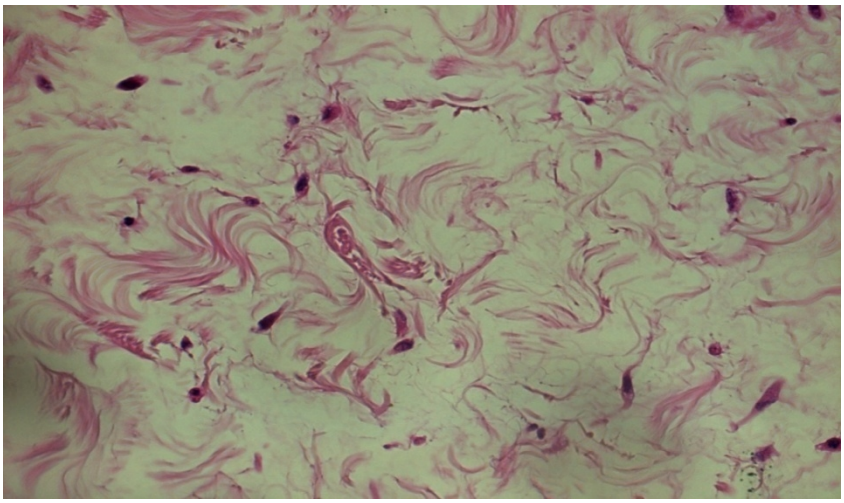

Fig. 4. The neoplastic cells exhibited spindled or stellate morphology with eosinophilic cytoplasm and embedded within myxoid matrix (H and E×400)

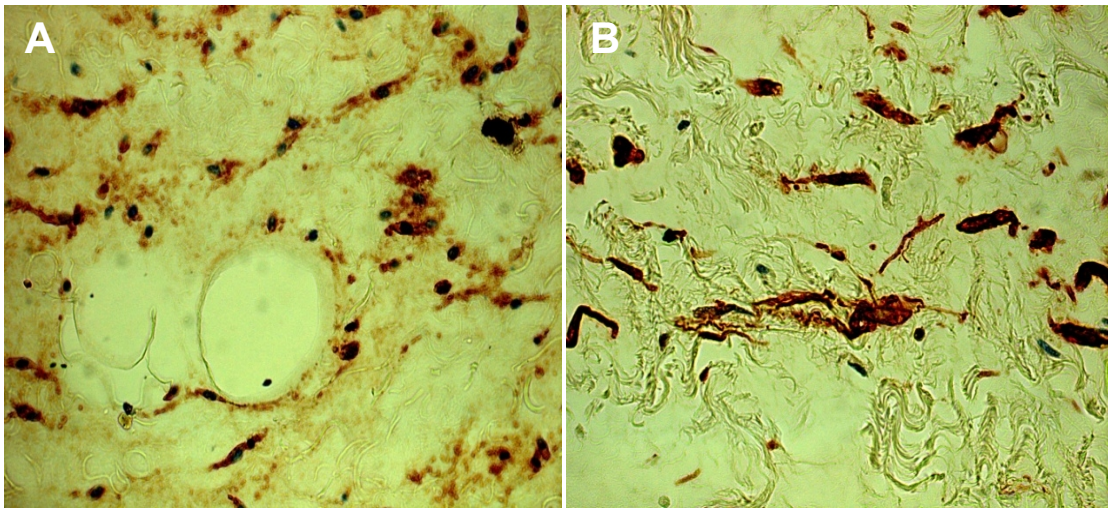

Fig. 5. Aggressive angiomyxoma shows neoplastic spindle-shaped cells stained intensely (A) for cytoplasmic CD34 and (B) for cytoplasmic SMA (400XDAB)

3. DISCUSSION

Steeper and Rosai in 1983 were the pioneers in described the aggressive angiomyxoma asa distinct clinicopathologic entity [7]. Since then less than 250 cases of this rare tumor have been reported in world literature [4]. The first cases of aggressive angiomyxoma in black African women was reported in 2009 [12]. Approximately 95% of the cases occurs in females in reproductive age, and the sex ratio (Female: Male) is about 6:1 [8,9]. The tumors tend to be very large and the maximum diameter of aggressive angiomyxoma is about 10cm. This tumor usually arise in the pelvis and perineal regions, with vulvar region being the most common site of involvement [13], however, a few cases of aggressive angiomyxoma outside

the pelvis have also been reported. The present case study was also adult female in reproductive age, who presented with a relatively large pedunculated mass in the right labia majora.

According to Steeper and Rosai [7] and Nucci and Fletchr [10], the patients are usually asymptomatic due to the slow and insidious growth pattern of the tumor with locally aggressive behavior of the tumor and its tendency to recur locally. In contrast to other benign soft tissue tumors, excision with wide tumor-free margins should be performed for aggressive angiomyxoma, rather than local excision. The current case study had insidious asymptomatic onset, and excision of the lesion was complete and after 7 months has been no yet evidence of any local recurrence.

Fibroepithelial polyp, angiomyofibroblastoma, angiofibroma and smooth muscle tumors need to be considered in the differential diagnoses of a polypoid mass in the perineum [10]. A careful microscopically and immunohistochemistry evaluation helps in differentiating this tumor from the other soft tissue tumors occurring in this region [10,14]. The diagnostic hallmark of aggressive angiomyxoma is presence of loose collagenous matrix rich by vessels of varying caliber and contain spindled and/or stellate cell that usually positive for IHC stain of smooth muscle actin, CD34, estrogen and progesterone receptor, whereas S100 is invariably negative. About fourth of the cases also show cytokeratin positivity that may indicate on epithelial component [8,15,16]. Our findings have been on line with these observations. Based on IHC results of this study and other previous studies of we can stated, that the neoplastic cells of aggressive angiomyxoma might be, have myofibroblastic differentiation. Aggressive angiomyxoma shows higher levels of SMA expression and steroid receptors (ER and PR) than angiomyofibroblastoma, angiofibroma and myxoma. Fibroepithelial polyp differ from aggressive angiomyxoma by being negative for SMA. Aggressive angiomyxoma cells differ from Botryoid rhabdomyosarcoma cells by being negative for Myogenin protein [2,8].

Adjuvant therapy could be necessary. Angiographic embolization may shrink the tumor preoperatively, allowing the tumor to be completely removed [11]. Hormonal manipulation may be used in recurrent cases or residual tumors [16]. Due to the specificity of treatment in aggressive angiomyxoma, accurate diagnosis prior to surgery is critical.Whether treatment is only surgical or followed by hormone therapy, it is clear that aggressive angiomyxoma requires close, long-term follow-up to monitor for disease recurrence and that the individualization of each case is essential for adequate management. Patient in this current case study presentation has been yet without recurrence at 8.0-months follow-up.

4. CONCLUSION

Aggressive angiomyxoma is rare benign tumor of vulva and presents with local aggressive clinical behavior, notorious for local recurrence and extremely rare to metastasize.

While wide surgical excision remains the mainstay of treatment, some adjuvant treatment modalities have also been tried to reduce tumor recurrence. To the best of our knowledge this case report is the first ever report of aggressive angiomyxoma in Libyan women.

CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

ETHICAL APPROVAL

All authors hereby declare that the proposed studyhas examined and approved by the Research Council of Misurata Cancer Center.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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