Angiomyofibroblastoma of the vulva: A diagnostic dilemma*

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ABSTRACT

Angiomyofibroblastoma (AMFB) is a rare, benign, well-circumscribed mesenchymal soft tissue neoplasm redominantly occurring in the vulvovaginal region among women of reproductive age (35-45 years old). Histologically, it is characterized by presence of alternating hypo and hypercellular areas containing spindle and round stromal cells admixed with blood vessels. At present, there are 137 cases reported since it was first described in 1992. Currently, there are no published cases of Angiomyofibroblastoma in the Philippines. This is a case report of a 31 year old, nulligravid patient who presented with unilateral labial enlargement which was noted to be painless and slow growing. The initial impression was that of a benign tumor of the labia. The mass was excised and histopathologic results were consistent with the microscopic findings of Angiomyofibroblastoma. Simple excision of the mass is the only treatment, as in this case, and is noted to have extremely low rate of recurrence.

The clinical importance to distinguish this unusual neoplasm from Aggressive Angiomyxoma and other mesenchymal malignant neoplasm with metastatic potential should be emphasized for appropriate management.

Keywords: Angiomyofibroblastoma, Mesenchymal Tumors, Vulva

INTRODUCTION

Angiomyofibroblastoma (AMFB) is a rare, benign, mesenchymal tumor that occurs mainly, but not exclusively, in the vulvar region of reproductive aged women.[1] More often, these tumors are encountered in the vulva. However, 10% to 15% occur in the vagina, occasionally in the perineum and the inguinal region while rare reports of fallopian tube lesions are also found.[2] Rare cases have also been reported to arise in the scrotum and the inguinal area in males.[3,4] This tumor is commonly seen in women of reproductive age as well as in perimenopausal women. The occurring average age of female is 45.8 years and is rather slow growing, from few weeks to 13 years, without pain.[5] There is female-to-male ratio found to be 10:1. In women, the vast majority of tumors are located in the vulva.[12]

Angiomyofibroblastoma was first described in 1992 as a new entity that occurred exclusively in the vulvo – vaginal area, predominantly of the vulva, of young to middle aged women.[6] Fletcher et al described 10 cases of previously unrecognized benign soft tissue tumor of the vulva that were misdiagnosed as Aggressive Angiomyxoma.[3] Since then, 137 cases of Angiomyofibroblastoma have been reported in the English medical literature.[12] Currently, there are no published case reports of this rare neoplasm in the Philippines.

This tumor is considered benign and of low recurrence rate after simple excision of the tumor. However, due to its rarity, misdiagnosis may happen. Correct identification of this tumor is important for appropriate management and rule out malignant neoplasms with widespread metastatic potential such as Aggressive Angiomyxoma. The knowledge of this tumor would help clinicians in avoiding significant delay in diagnosis, management and follow up.

This report presents a case of a 30 year-old, nulligravid who presented with a slow growing and painless tumor of the labia majora. The patient underwent local excision of the tumor and histopathological findings revealed presence of spindle to round shaped cells with alternating hypo and hypercellular areas admixed with thin walled capillary type blood vessels. These microscopic findings were consistent to that of Angiomyofibroblastoma.

CASE REPORT

This is a case of E.C., a 31 year-old, nulligravid, single, Filipino, Roman Catholic patient from Dasmariñas, Cavite. She consulted at the outpatient department of a tertiary institution for the first time last March 2017 with a chief complaint of a right labial mass.

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The patient was apparently well until three months prior to consult when she noted a non pruritic, non tender, erythematous, 2 x 2 cm lesion on the right lower labial area. No other symptoms were noted such as vaginal discharge, bleeding, discomfort noted. There were no dysuria, hypogastric pain noted. She did not take nor applied any medications. No consultation was done.

During the interim, patient noted a gradual increase in size but still no symptoms mentioned above were noted. The lesion was approximately 3 x 3 cm in size but remained non pruritic, non tender and erythematous. Due to further increase in size of the lesion, the patient sought consultation at a tertiary hospital and the primary impression then was Bartholin's duct cyst.

Past medical history revealed no history of hypertension, diabetes mellitus, bronchial asthma and other atopic diseases. No history of any cardiovascular, pulmonary, thyroid, hepatobiliary, gastroenterology or renal diseases noted. There were no other previous hospitalizations nor surgeries noted.

Patient noted no heredofamilial diseases such as hypertension, diabetes mellitus, bronchial asthma and other atopic diseases. No history of any cardiovascular, pulmonary, thyroid, hepatobiliary, gastroenterology or renal diseases noted. No cancer or the same symptomatology noted from other members of the family.

The patient is a college graduate and is a non smoker and non alcoholic beverage drinker. She has no preferred diet. She allegedly has no history of illicit drug use.

The patient had her menarche by the age of 12 years old. Her cycle was noted to be regularly occurring with 28-31 days interval and has a duration of approximately 5 days. She uses 6-8 regular pads, minimally soaked per day. She noted to have dysmenorrhea on the first day of her cycle and gradually decreases to null on the second to third day of menses. No other symptoms noted.

Patient allegedly still has no sexual contact or any related sexual relationship at the time examination. Patient has no history of any form of contraceptive use. She noted no history of any vaginal pruritus, discharge or any infections or diseases pertaining to the female reproductive tract. She has not undergone papsmear or any medical examination pertaining to the female reproductive tract. Patient noted this was the first time growth of any masses has occurred in the vulvo – perineal area.

Upon examination of the genitalia, there was a 5 x 5 cm well circumscribed, non tender, erythematous mass on the inner mid to lower portion of the right labia majora. The mass was well circumscribed, soft to doughy, with no ulcerations noted. Other parts of the external genitalia and contralateral labia were grossly normal. All other systemic examinations were unremarkable. No internal examination done. Rectal examination revealed good sphincteric tone. Rectovaginal septum was smooth with no masses or lesions. The uterine corpus was small and no adnexal masses palpated or tenderness noted. No inguinal lymphadenopathy noted.

The patient was subjected to have a transrectal/ translabial ultrasound on day 7 of cycle (Figures 1-3) and the primary consideration at that time was a benign vulvar mass, to consider Bartholin's Duct Cyst. The endometrium and cervix were noted to be unremarkable. The ovaries were noted to be polycystic.

Transrectal/Translabial Ultrasound (03/30/2017)

Uterine corpus: 4.8 x 2.4 x 2.4 cm anteverted
Cervix: 2.9 x 2.4 x 2.4 cm
Endometrium: 0.5 hyperechoic

Adnexae:
Right ovary: 3.2 x 3.7 x 2.2 cm vol= 13.2 ml
(+) more than 12 small peripherally located follicles with dense stroma
Left ovary: 3.3 x 3.0 x 2.1 cm vol= 11.0 ml
(+) more than 12 small peripherally located follicles with dense stroma

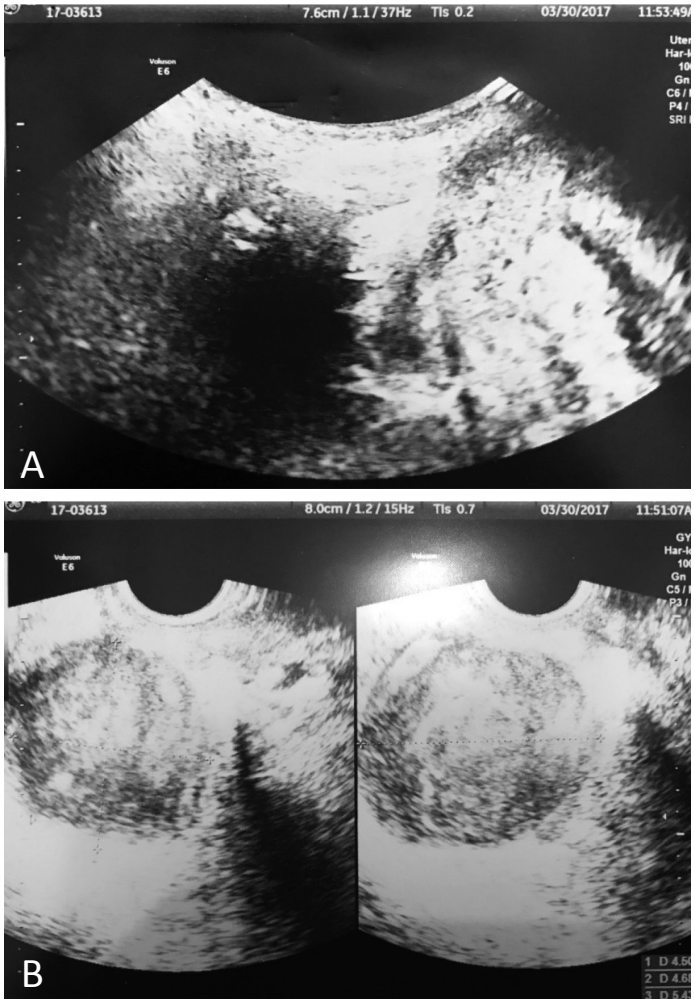
Others: Lateral and to the right of the lower third of the vagina is a 4.5 x 5.4 x 4.7 cm well circumscribed, heterogenous solid mass. There is no duct connection between the said mass and the urethral wall. No fluid on the posterior cul de sac.

Impression: Normal sized anteverted uterus with intact endometrium, Normal cervix, Polycystic ovaries, Labial mass, right, consider Bartholin's duct cyst.

Upon noting the transrectal ultrasound, the patient was advised to undergo elective excision of the labial mass. Approximately one week after consultation at the out patient department and upon patient's consent, she was scheduled and eventually underwent elective surgical excision of vulvar mass, right, under spinal anesthesia.

Intraoperatively, there was an asymmetrical external genitalia with a soft to doughy mass located from the 6 o'clock position to 11 o'clock position extending anterolateral to the urethra located at the right labia measuring 5.0 x 5.0 x 3.5 cm, ovoid and was well circumscribed, with a soft to doughy consistency covered by skin on all sides (Figure 4). On cut section, the mass was soft to doughy, cream tan in color and showed whorled like pattern with no areas of hemorrhage and necrosis. Postoperatively, the diagnosis was Vulvar Mass, Right probably benign.

Translabial Ultrasound (03/30/2017)



Figures 1A and 1B. Translabial Ultrasound revealed lateral and to the right of the lower third of the vagina is a 4.5 x 5.4 x 4.7 cm well circumscribed, heterogenous, solid mass.

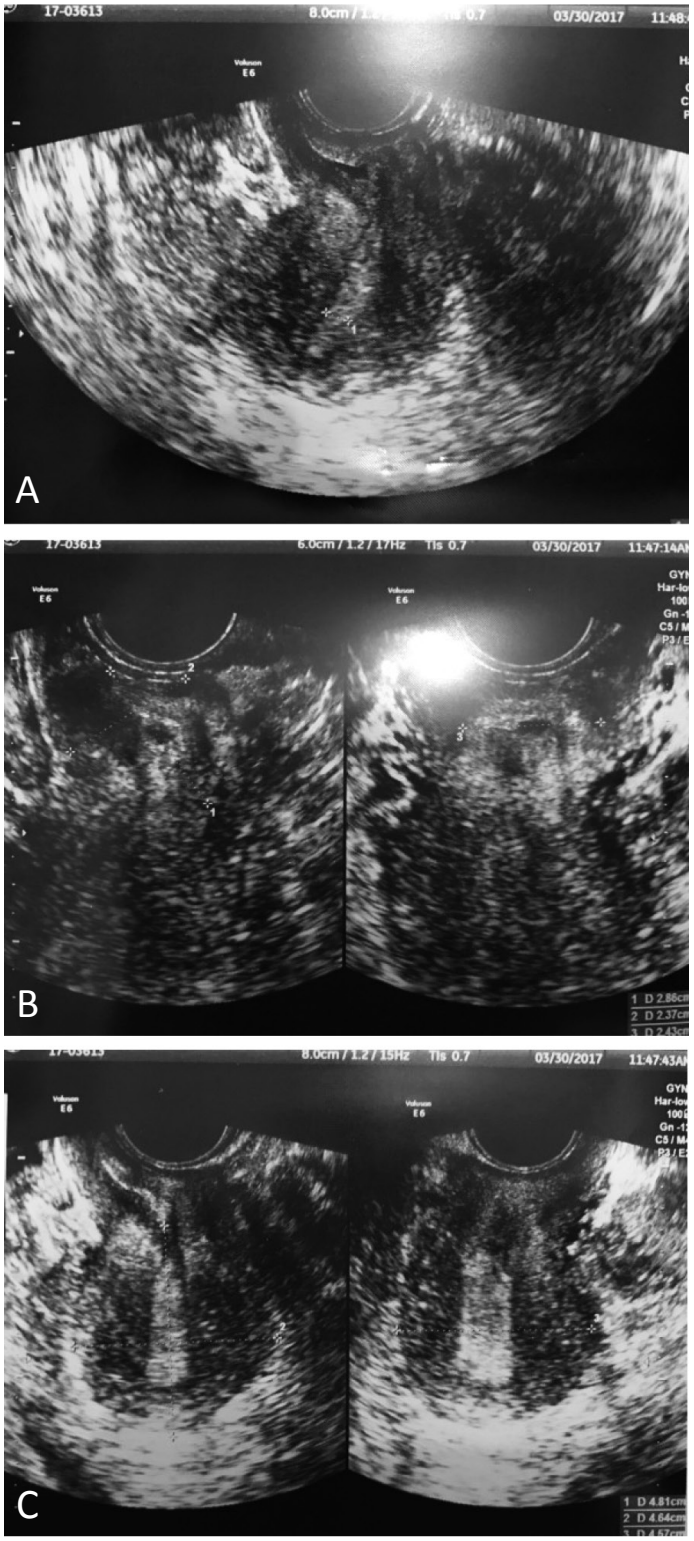
The sample was sent for histopathological examination. Multiple representative sections were taken and submitted for processing. Histological examination revealed a skin covered tissue showing hyper/hypocellular areas containing spindle and plump stromal cells admixed with blood vessels. The findings were compatible with the histologic features of Angiomyofibroblastoma, considering the presence of spindle cells admixed with thin walled blood vessels (Figure E).

The resection proved to be curative with no recurrence until the last follow-up in September 2017.

CASE DISCUSSION

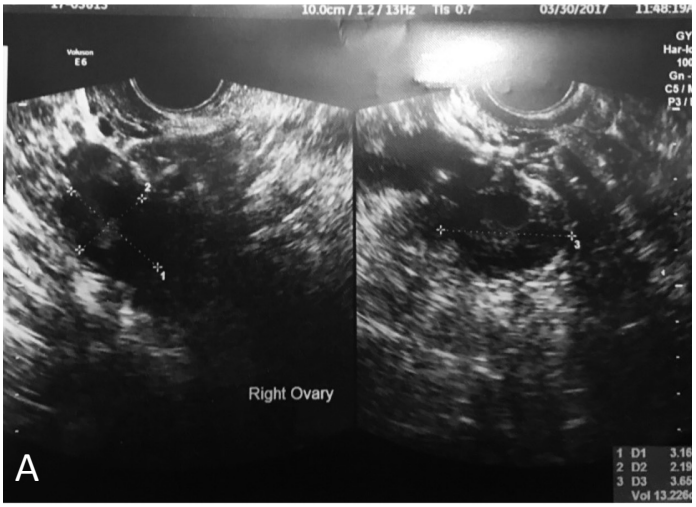
Angiomyofibroblastoma was initially said to be a vulva-specific neoplasm. However, there were several case reports showing it can also occur in the vagina, perineum and inguinal areas. It was hypothesized to be derived from mesenchymal cells in the subepithelial

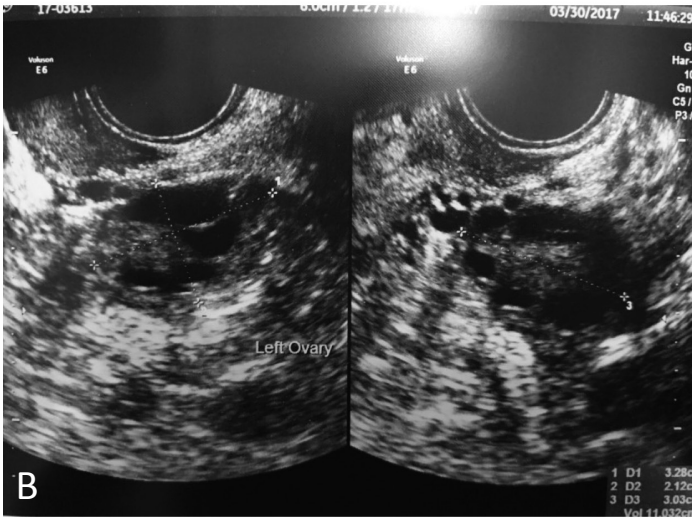
Transrectal Ultrasound (03/30/2017)



Figures 2A, 2B and 2C. Transrectal Ultrasound revealed normal sized anteverted uterus with intact endometrium and normal cervix.

myxoid stromal zone that extends from the endocervix to the vulva. Angiomyofibroblastoma is positive for estrogen and progesterone receptors. This represents the hormone responsive nature of this lesion and may explain why it





Figures 3A and 3B. Transrectal Ultrasound revealed polycystic ovaries.

Gross picture of the right labial mass

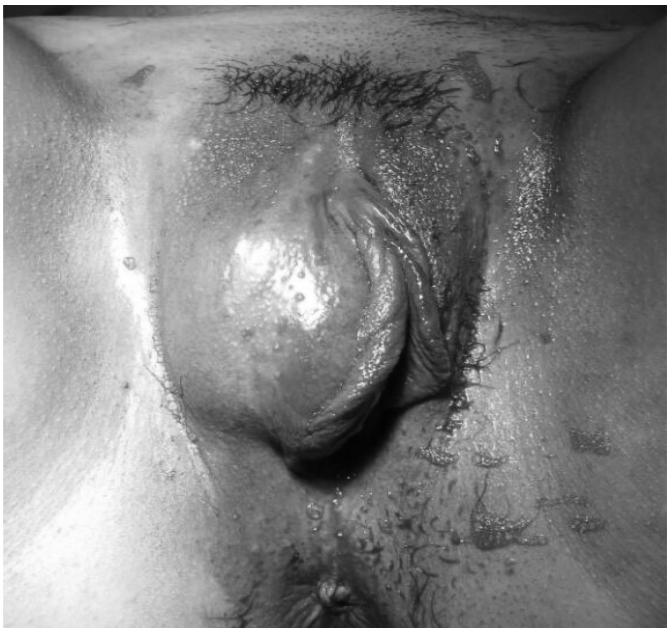


Figure 4 showed a gross photo of a well – delineated, sessile right labial mass measuring 5.0 x 5.0 cm prior to surgical excision.

Histopathologic pictures

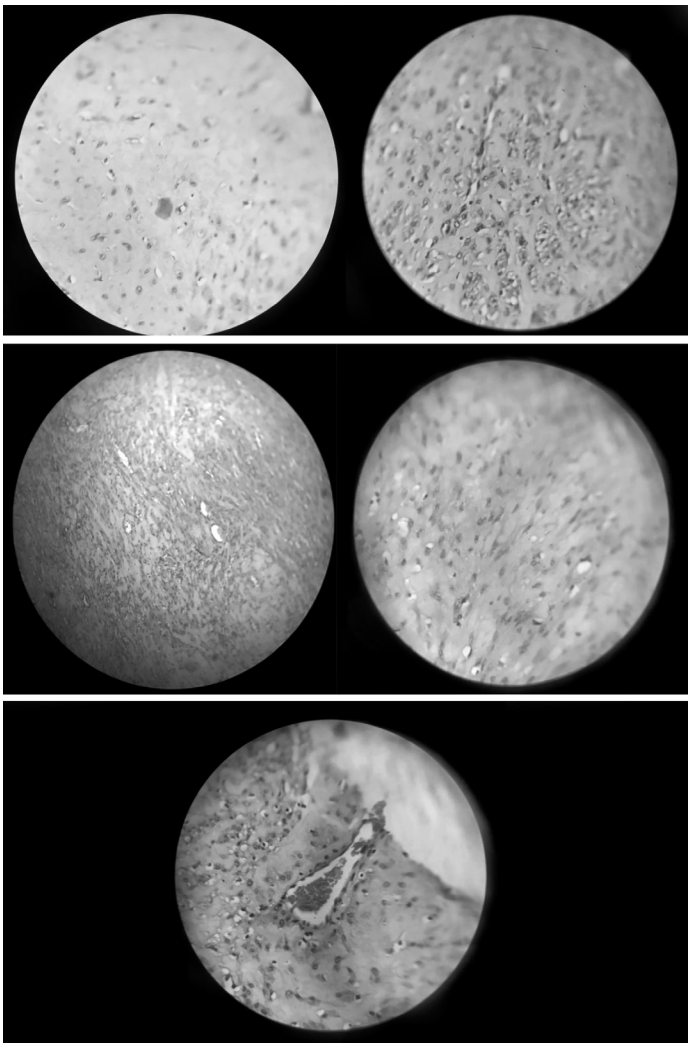


Figure 5. The following figures show the microscopic findings as round to spindle shaped cells (first and second photos) with hypo and hypercellular areas (third and forth photos) admixed with thin walled blood vessels (last photo).

Histopathology report (April 5, 2017)

PROCEDURE:
Excision of Vulvar Mass (APRIL 1, 2017)

Findings: Consistent with Angiofibromyoblastoma

The specimen labeled "VULVAR MASS RIGHT LABIA" consists of an irregularly shaped cream white to pinkish red, soft to doughy tissue with one side exhibiting whorled pattern surface measuring 5.0 x 5.0 x 3.5 cm. Cut sections show cream white homogenous solid surface.

is most common among reproductive aged women. This could also explain to some extent the predisposition of this tumor to arise in the lower genital tract since these hormone responsive receptors are normally found in the subepithelial stromal cells of the vulva and vagina.

Angiomyofibroblastoma was first described was in a study done in 1992 as a new entity that occurred exclusively in the vulvo – vaginal area, predominantly of the vulva, of young to middle aged women.[6] The authors described 10 cases of previously unrecognized benign soft tissue tumor of the vulva that were misdiagnosed as Aggressive Angiomyxoma.[3] Since then, only about 137 cases have been reported in the English medical literature.[12] Currently, there are no published case reports of this rare neoplasm in the Philippines.

We are presented with a case of a 31 year-old, nulligravid patient with a three month history of a slow growing painless mass on the right vulva with no other symptoms noted such as dysuria, dyspareunia, vaginal bleeding and discharge. Grossly the mass was observed to be, firm, movable and non tender. Because of the said gross features, indolent behavior of the mass, and absence of systemic as well as local symptoms, such as weight loss, bleeding, dysuria, urinary retention, change in bowel movement, malignancy was ruled out. The initial diagnosis was that of a benign vulvar mass, to consider Bartholin's gland cyst.

To rule out other possible benign lesions and possible extension of the mass to the internal genitalia, transrectal and translabial ultrasound was requested. The patient underwent elective surgical excision of the vulvar mass. Intraoperatively, it was described as well delineated, sessile and firm.

Clinically, most of the tumors present as slow growing, painless masses, and are often misdiagnosed as Bartholin gland cyst, hydrocele of the canal of Nuck, inguinal hernia, leiomyoma, or mesenchymal tumors, such as lipoma and liposarcoma, and aggressive angiomyxoma.[8,9] However, rare symptoms include dyspareunia, localized burning sensation and/ or mild tenderness of growing mass. Grossly, it is often described as well delineated, sessile, smooth, and mobile. Its texture is usually described as ruberry or firm. There are only five cases of pedunculated vulvar Angiomyofibroblastoma reported on English literature.[11]

Current journals noted that Angiomyofibroblastoma is indeed a diagnostic dilemma due to its gross features. Owing to its low incidence, Angiomyofibroblastoma and other vaginal soft tissue tumors can easily be confused clinically or sonographically with other, more common vaginal masses, such as Bartholin's cyst, rectocele, or urethral diverticulum.[12] No diagnostic modality has yielded high specificity and sensitivity in diagnosing Angiomyofibroblastoma. Sonographically, it was reported to be well demarcated with inhomogeneous echogenicity and multiple hypoechoic areas within an echogenic stroma.[12] In a study done in 2014, wherein the authors described two cases of Angiomyofibroblastoma out of 72 perineal tumors, they characterized it as solid cystic masses on the basis of ultrasonography. In contrast to these descriptions, the tumor found in this case was sonographically described as well circumscribed, heterogenous, solid mass.

The purpose of doing other diagnostic imaging such as Computerized Tomography (CT) scan and Magnetic Resonance Imaging (MRI) on vulvovaginal masses is to describe its contiguity and determine surgical planes. It is important to determine if these masses are locally infiltrative and to rule out possible attachment to the other structures, specifically, the urethra. However, several studies concluded that indeed other imaging modalities may be used, but still yield vague results. In a study done in 2012, Angiomyofibroblastoma on Computerized Tomography imaging most likely show moderate-to-strong enhancement, which may reflect the prominent vascularity of these tumors. In a study done in 2015, it was noted that the obtained Magnetic Resonance images did not add much information to what was already known based on the ultrasound studies. In the said study, the authors concluded that Magnetic Resonance imaging is not mandatory in the evaluation of soft tissue lesions of the lower genital tract such as Angiomyofibroblastoma. The authors also noted that ultrasonography is cost effective, widely available and extremely valuable in characterizing and distinguishing these tumors preoperatively to be able to plan for appropriate management. This held true with our patient. Use of translabial ultrasound was able to determine that the described mass had no duct connection with the urethral wall. Several studies have shown, however, that postoperative pathological examination of the surgical specimen remains the only way to definitively establish a diagnosis of Angiomyofibroblastoma.[12]

The treatment of choice is still local excision of the mass and is deemed curative. In the world medical literature, except for one case with sarcomatous transformation of Angiomyofibroblastoma in an 80 year old woman, there are currently no published reports of local recurrence or metastatic disease.[14,15]

In this case, the patient underwent surgical excision of the vulvar mass. The patient was then discharged the day after the surgical procedure and was advised for weekly, then eventually to monthly, follow up at the out patient department of the same tertiary institution. No recurrence was noted during the six months of the follow up period.

The specimen was sent for histologic examination.

Microscopically, there were round to spindle shaped cells with alternating hypo and hypercellular areas admixed with several capillary type, thin walled blood vessels. These microscopic findings were were similar microscopically with Angiomyofibroblastoma as described by several published cases. Characteristically, it shows round to spindle-shaped cells with alternating hypo and hypercellular areas, particularly around thin walled blood vessels. It was also noted that Angiomyofibroblastoma may have edematous stroma without extravasation of red blood cells from the blood vessels.

With regards to biologic behavior, all published reports suggest a benign clinical outcome in patients with Angiomyofibroblastoma. As previously stated, based on published reports, only one reported a case that underwent a sarcomatous transformation and no recurrence was noted.[8,15]

Conventional morphologic analysis is paramount in the recognition of genital Angiomyofibroblastoma. Immunohistology may assist in excluding other differential diagnoses. Differential diagnosis of mesenchymal tumors in the vulvovaginal area includes a wide array of lesions that are overlapping in both their morphology and immunohistochemistry. Their low incidence attributes to the significant dilemma in making the correct diagnosis. Aside from this, Angiomyofibroblastoma should be distinguished from Aggressive Angiomyxoma and other myxoid malignant tumours with widespread metastatic potential.

In a study done in Pakistan in 2012, it was noted that the differentiation of Angiomyofibroblastoma based on histological properties is conveyed on the two integral components: the stromal cells and the blood vessels. Grossly, it is well-circumscribed lesion and microscopically it is characterized by alternating hypercellular and hypocellular edematous legions with abundant blood vessels. There were noted plump round to spindle-shaped cells either in cluster or present in a linear array around numerous delicate capillary-sized vessels within a variable edematous to collagenous matrix. Nuclear atypia or mitotic figures are rare and the tumor cells tend to cluster around blood vessels. The histopathology of this case revealed the characteristic findings.

Other differential diagnoses that may be considered are Leiomyoma and Aggressive Angiomyxoma. In this case, the absence of arrangement of cells in a whorls and fascicles ruled out Leiomyoma. Other tumors that predominantly occur in the perineum may be confused with Angiomyofibroblastoma such as Fibroepithelieal Polyp, Cellular Angiofibroma, Superficial Myofibroblastoma, and Aggressive Angiomyxoma.

Fibroepithelial Stromal Polyp is usually exophytic, submucosal in location and are poorly circumscribed with frequent bizarre stromal cells. In contrast, Angiomyofibroblastoma are sessile, subcutaneous, well circumscribed and with bland cells. Cellular Angiofibroma are characterized by uniformly moderately cellular, uniformly moderately cellular, bland spindle cells with large thick walled vessels. Angiomyofibroblastoma has clusters of rounded, epithelioid cells, often around numerous small vessels with alternating hypercellular and hypocellular areas. On the other hand, Superficial Myofibroblastoma has stellate and spindled cells with inconspicuous vascularity. This may be distinguished from Angiomyofibroblastoma since the latter has perivascular epithelioid cells with prominent vascularity.

The most crucial issue was to determine if this case was that of a malignant and Aggressive Angiomyxoma (AAM). Aggressive Angiomyxoma is most likely to be confused with Angiomyofibroblastoma because both disease entities share many features including age at presentation, location, clinical manifestations, and pathological entities.

Clinically, Aggressive Angiomyxoma is also noted to occur in the vulvovaginal region predominantly among women of reproductive age. It may be an incidental finding due to its indolent course. However, grossly, Aggressive Angiomyxoma is usually poorly circumscribed due to its infiltrative nature and is nearly always >5-10 cm in size. Due to its infiltrative nature, patients may experience dull, aching pain on the mass, often with urinary symptoms such as dysuria and urinary retention. Patients may also present with dyspareunia and bleeding from the mass. Due to its propensity to grow more than 10 cm, pressure symptoms may also be experienced.[16] Histologically, it is a benign soft tissue tumor, with noted high risk of local recurrence as well as local infiltration that often results in entrapment of nerves and mucosal glands, thus making complete excision difficult.[2] Aggressive Angiomyxoma shows hypocellularity with sparse spindled or stellate cells and large thick walled vessels.

In this case, Angiomyofibroblastoma was distinguished from Aggressive Angiomyxoma by the former's clinical presentation as a slow growing, painless and asymptomatic mass, its gross feature as well circumscribed, sessile, mobile and soft to doughy consistency, and microscopic finding of presence of alternating hypo and hypercellular areas, admixed with small thin walled blood vessels. The microscopic findings of lack thick walled hyalinized vessels and extravasation of Red Blood Cells, together with absence of necrosis and mitosis were also features in favor of an Angiomyofibroblastoma.

Several studies have shown that immunohistochemistry reports are variable and thus it may not be reliable for separation. In a study done in Pakistan in 2011, the authors noted that that Aggressive

Angiomyxoma shares immunophenotypic similarities with Angiomyofibroblastoma. Hence, immunoreactivity does not appear to be helpful in distinguishing between these neoplasms. This was further supported by another study in 2016 wherein they noted that Desmin, Estrogen receptor and Progesterone receptor are no longer considered reliable markers for distinguishing Aggressive Angiomyxoma from Angiomyofibroblastoma. Since the immunohistological markers of Angiomyofibroblastoma are similar to those of Aggressive Angiomyxoma, differentiation between these two tumors is largely based on the appearance of the tumor morphologically.

In summary, Angiomyofibroblastoma is a rare benign mesenchymal tumour. Critical evaluation should be performed to rule out Aggressive Angiomyxoma, which requires the resection with wide tumor-free margins to prevent recurrence. Rapid and accurate diagnosis should be performed if possible, to prevent delay in appropriate management and follow up.

SUMMARY

Angiomyofibroblastoma is a rare but benign entity and often cause a diagnostic dilemma. Although the exact cause is unknown, it is curable with simple excision. A thorough histopathological examination of vulvar masses helps in differentiating angiomyofibroblastoma from other mesenchymal tumors occurring at this site. It is important to identify this type of tumor so that unnecessary follow-up and intervention post excision may be prevented. ■

REFERENCES

1. Canales BK, Weiland D, Hoffman N, Slaton J, Tran M. (2006) Angiomyofibroblastoma-like tumors (cellular angiofibroma). *Int J Urol.* 13:177-179.

2. Ibnerasa S, Yasmeen F, Shami N. Angiomyofibroblastoma of the Vulva. *Journal of the College of Physicians and Surgeons Pakistan.* 2012; Vol. 22(2):108-110.

3. Fletcher CD, Tsang WY, Fisher C, Lee KC, Chan JK. Angiomyofibroblastoma of the vulva. A benign neoplasm distinct from aggressive angiomyxoma. *Am J Surg Pathol.* 1992; 16:373-82.

4. Ockner DM, Sayadi H, Swanson PE, Ritter JH, Wick MR. Genital angiomyofibroblastoma: comparison with ag- gressive angiomyxoma and other myxoid neoplasms of skin and soft tissue. *Am J Clin Pathol.* 1997; 107:36-44.

5. Nielsen GP, Young RH. Mesenchymal tumors and tumor- like lesions of the female genital tract: a selective review with emphasis on recently described entities. *Int J Gynecol Pathol.* 2001; 20:105-27.

6. Jian W, Weiqi S, Xiaoyu T, Daren S, Xiongzeng Z, Renyuan Z. Clinicopathologic analysis of angiomyofibroblastoma of the female genital tract. *Chinese Med J.* 2000; 113:1036-9.

7. Takeshima Y, Shinkoh Y, Inai K. Angiomyofibroblastoma of the Vulva: A Mitotically Active Variant? Second Department of Pathology, Hiroshima University School of Medicine, Hiroshima and^Department of Obstetrics and Gynecology, National Ohtake Hospital, Ohtake, Japan.

8. Tochika N, Takeshita A, Sonobe H, Matsumoto M, Ko- bayashi M, Araki K. Angiomyofibroblastoma of the vulva: report of a case. *Surg Today.* 2001; 31:557-9.

9. Barat S, Tirgar-Tabari S, Shafaee S. Angiomyofibroblastoma of the vulva. *Arch Iran Med.* 2008; 11:224-6.

10. Indraccolo U, DeSanctis E, Liberati F, Ippolio M, Indraccolo SR. Giant angiomyofibroblastoma of the vulva. *Scott Med J.* 2008; 53:57.

11. Gianella, L. et.al., Pedunculated Angiomyofibroblastoma of the Vulva: Case Report and Review of the Literature. Division of Obstetrics and Gynaecology, Cesare Magati Hospital, Scandiano, 42019 Reggio Emilia, Italy. Received 1 June 2011; Accepted 21 July 2011.

12. Wolf Et Al. Ultrasound Plays A Key Role In Imaging And Management Of Genital Angiomyofibroblastoma: A Case Report. Department Of Obstetrics And Gynecology, Leipzig University, Liebigstrasse 20a, 04103 Leipzig. *Germanyjournal Of Medical Case Reports*. 2015; 9:248.

13. Wang X, Yang H, Zhang H, Shi T, Ren W. Transvaginal sonographic features of perineal masses in the female lower urogenital tract: a retrospective study of 71 patients. *Ultrasound Obstet Gynecol*. 2014; 43:702-10.

14. Nielsen GP, Young RH, Dickersin GR, Rosenberg AE. Angiomyofibroblastoma of the vulva with sarcomatous transformation. *Am J Surg Pathol.* 1997; 21(9):1104-8.

15. Zehra Neş, et.al. Angiomyofibroblastoma Of The Vulva: A Rare But Distinct Entity. From The Department Of Obstetrics & Gynecology And 2pathology, Marmara University Medical School, Istanbul, Turkey. *Acta Obstet Gynecol Scand.* 2000; 79:612-613

16. Barmon, D., et.al, Aggressive Angiomyxoma of the Vulva. Department of Gynecologic Oncology. Journal of Midlife Health. 2012.