EJGO European Journal of Gynaecological Oncology

Five cases' female aggressive angiomyxoma experience

A.W. Le[1], Z.H. Wang[1], X.Y. Dai[1], T.H. Xiao[1], R. Zhuo[1], R. Yuan[2]

[1] Department of Obstetrics and Gynaecology, the Nanshan Affiliated Hospital of Guangdong Medical College, Shenzhen
[2] Department of Obstetrics and Gynaecology, The First Affiliated Hospital of Chongqing Medical University, Chongqing (China)

Summary

Objective: The aim of the present study was to investigate the clinical and pathological features of female aggressive angiomyxoma (AAM), as well as its diagnosis and prognosis. *Materials and Methods:* The medical information of five AAM patients aged from 20 to 52 years was retrospectively collected between December 2011 and January 2015, and the clinical and pathological features, diagnostic methods, and prognosis were analyzed. *Results:* Clinical manifestations were different for each patient, including pelvic cystic mass detected by B-scan ultrasound in patient 1, low abdominal pain in patient 2, vaginal prolapse in patient 3, vaginal bleeding after sexual intercourse in patient 4, and vaginal mass found by physical examination in patient 5. Three patients had vaginal masses and the other two had pelvic or abdominal masses. Enhanced CT or MRI revealed a mass with a spiral-like or stratified structure. The tumor cells were characterized by identical morphology, presented as stellate-shaped, oval, or spindle-shaped cells revealed by pathological studies, with a large amount of mucosal matrix, expanded thin envelope, and thick-walled blood vessels. The masses were soft, and usually had no obvious envelope or partial envelope (including complete envelope in two patients, partial envelope in one patient, and no envelope in two patients). All patients underwent surgeries; one of them had recurrent tumor and underwent secondary surgery. *Conclusion:* Although AAM is a benign tumor, it has high recurrent rate and requires follow-up. Surgery is the main therapeutic method, the extended dissection is not emphasized, and gonadotropin-releasing hormone agonist treatment could be considered.

Key words: Aggressive angiomyxoma; Pathological examination; Treatment.

Introduction

Aggressive angiomyxoma (AAM) is a rare mesenchymal tissue-derived mass, often found in women at childbearing age; the incidence ratio between men and women was reported to be 1:7 [1], and most common sites of AAM were vulva, vagina, and pelvic cavity [2]. The formal nomenclature was decided in 1983 by Steeper *et al.* [3], and it was classified as "undefined differentiated benign tumor" by World Health Organization in 2012 [4]. Since no obvious or specific clinical symptom or manifestation was reported, the misdiagnosis rate was as high as 80% [5], and it was often misdiagnosed as fibroma, lipoma, Bartholin cyst, or femoral hernia with the postoperative recurrence rate of 33–83% [6]. In general, AAM has not been well acknowledged by clinicians. Published clinical information is missing and AAM per se has no specific clinical manifestation or imaging features. In the present study, the medical records of five AAM patients were retrospectively collected, to investigate the clinical and pathological features, differential diagnosis, and prognosis of AAM based on the literature review.

Materials and Methods

The medical records of five AAM patients were retrieved between December 2011 and January 2015 and the clinical and pathological features, diagnosis, and prognosis were analyzed. A retrospective analysis was adopted in the present study; the information regarding age, gender, symptoms, physical signs, imaging examination results, treatment, and pathological examination results of the patients was collected.

Software SPSS 16.0 was used for statistical analysis. The gross specimen was measured at the maximum radial line. The measurements were reported as means ± SD; the categorical data were presented as percentage and ratio.

Results

The age of onset was 32.37±19.65 years in the present study, including three patients at menopause transition period or post-menopause period, and two patients at their childbearing age. Clinical manifestations were different for each patient, including pelvic cystic mass detected by B-scan ultrasound in patient 1, low abdominal pain in patient 2, vaginal prolapse in patient 3 (Figures 1, 2), vaginal bleeding after sexual intercourse in patient 4, and vaginal mass found by physical examination in patient 5. The locations of AAM were vagina in three patients and pelvic and abdominal cavity in two patients.

Imagining examination included ultrasound and computed tomography (CT) scanning. The ultrasound exami-

Revised manuscript accepted for publication December 21, 2015

Eur. J. Gynaecol. Oncol. - ISSN: 0392-2936
XXXVIII, n. 5, 2017
doi: 10.12892/ejgo3511.2017

7847050 Canada Inc.
www.irog.net

Figure 1. — Case 3 vulva appearance of aggressive angiomyxoma.

Figure 2. — Case 3 aggressive angiomyxoma.

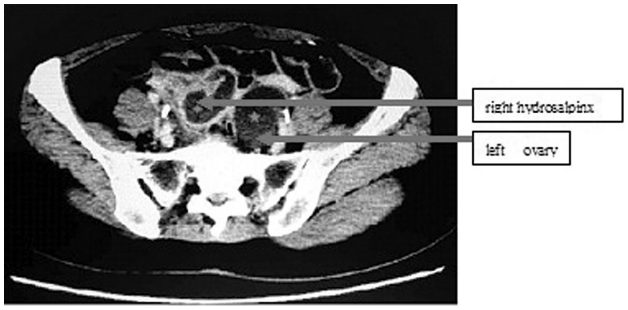

Figure 3. — Case 2 CT plain and enhanced scanning of pelvis.

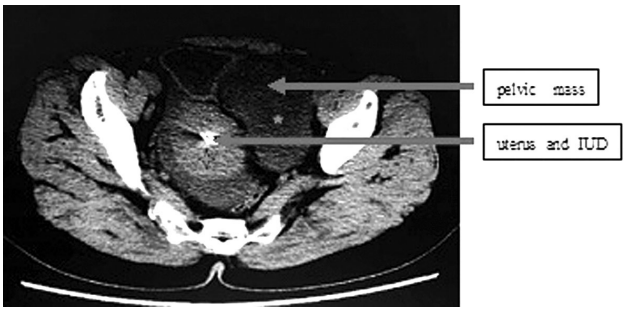

Figure 4. — Case 2 enhanced CT scanning.

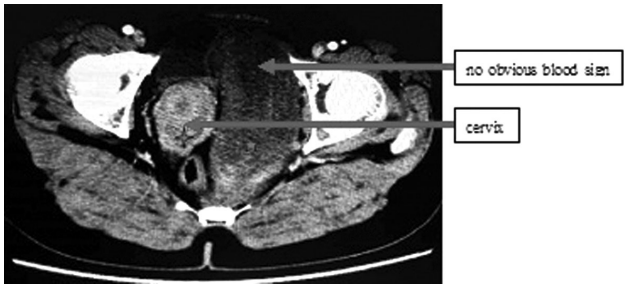

Figure 5. — Case 2 enhanced CT scanning.

nation for four patients indicated three solid masses (75%) with blood flow featured by color Doppler flow imaging (CDFI), and one cystic mass. CT examination was performed in two patients, and a spiral-like or stratified structure was revealed; one of them showed weak enhancement in the solid mass and the other had no significant alteration on images (Figures 3-5). Magnetic resonance imaging (MRI) was conducted in one patient, and a spiral-like or stratified structure was revealed, indicating the abundant blood supply. The definitive diagnosis was not made preoperatively in all five patients. Two patients were diagnosed by intraoperative frozen-section pathological studies, and the other three were diagnosed by postoperative paraffin pathological studies. The final diagnosis was confirmed by paraffin pathological studies.

All patients received surgical treatment, including five primary operations and one secondary operation. The masses in three patients were completely removed by surgery. However, the masses in the other two patients had tight adhesions to adjacent tissues or organs; hence, they were not completely removed. The patients were followed up for six to 43 months.

Patient 1 was not diagnosed with AAM during her first surgery; the tumor was recurrent 20 months after operation and considered as encapsulated effusion, which was treated with peritoneocentesis and discharged around 700 ml of thick, clear liquid. The second surgery was performed when the mass volume increased again and was detected by B-scan ultrasound. A cyst measuring 18×10 ×9 cm was observed during surgery, which closely adhered

to small intestine and sigmoid colon, and the cyst wall was composed of the lateral wall of the pelvic cavity, pelvic floor, bladder wall, and intestinal wall, which could not be removed. Therefore, the partial cyst wall was examined by pathological studies after cyst drainage. The mass volume was less than five cm, and the patient was followed up to date.

Patient 2 underwent laparoscopic exploration, left accessory resection, right fallopian tube resection, large pelvic tumor resection, pelvic adhesion lysis, pelvic floor gauze packing, and vaginal gauze packing. The mass was located anterior to the left ureter, interior to the umbilical ligament, posterior to the bladder, and lateral to uterine, vagina, and rectum. The mass volume was 23×20×10 cm and weighed 500 grams. The vaginal masses of the other three patients were removed through vagina.

All patients were followed up, and only one patient had recurrence. The diagnosis was finally made by postoperative pathological studies. The size and shape of tumors varied among patients, with an average diameter of 11.21 ± 6.03 cm. The masses were soft and the sections appeared yellow white or pink. The masses generally had no obvious envelope or partial envelope (including complete envelope in two patients, partial envelope in one patient, and no envelope in two patients). Some tumors presented as gel or mucosal content and infiltrated to the surrounding fat, fibers, or muscle tissues. AAM shared almost identical morphology under the microscope, presented as stellate-shaped, oval, or spindle-shaped cells revealed by pathological studies, with a little nontransparent cytoplasm. No nuclear atypia or nuclear division was found; collagen fibers could be observed between tumor cells. The blood vessels of various sizes with expanded thin wall or thick wall could be observed within tumors, accompanied by a large amount of mucosa. S-100 was negative in all five patients, and smooth muscle actin (SMA) was positive in three of them.

Discussion

Disease onset

AAM often occurs in women at their childbearing age. It can be found at ages between six and 77 years, with the peak onset at 30–40 years [7, 8]. A retrospective study based on 106 patients [9] reported that AAM could be found in the pelvic cavity, anal area, vulva, vagina, and uterus, and rarely found in colon, jejunum, throat, lung, and orbital cavity [6]. In the present study, the age of patients with AAM ranged between 20 and 52 years. AAM was located in the pelvic cavity in two patients and vagina in three patients. The metastasis of AAM was found in two patients and one of them died [2].

The nonspecific heterogeneous low-echo signal of AAM was detected by ultrasound examination; the tumor generally had a thin envelope with internal separations, and some of the tumors had blood flow signal [10, 11]. In the present study, four patients had a blood flow signal detected before operation, and one of them had quite abundant blood flow signal. The signal attenuation of AAM was less than that of muscle tissue by CT scan; since the internal separation usually had enhanced signal, the special spiral-like or stratified structure was revealed in some patients. The signal intensity equivalent to muscle signal was found in T1W1 and enhanced signal in T2W2 by MRI inspection; the stratification and spiral-like structure was revealed after enhancement. In the present study, three patients showed spiral-like or stratified structure by CT examination and two patients out of four showed spiral-like or stratified structure by MRI inspection, which was suggestive of preoperative diagnosis. In addition, CT and MRI indicated the location and range of tumors, and provided reference for optimal surgical treatment.

AAM usually has no envelope and unclear boundary with adjacent tissues [9]. The tumor size ranges between one and 60 cm, usually larger than ten cm, and is pink or gray in color. AAM is a large-sized, homogenous, solid, jelly-like structure with luminescence; vascular congestion, hemorrhage, or fibrosis is found in some part of the tumor [12]. AAM shows almost identical morphology under the microscope, presents as stellate-shaped, oval or spindle-shaped cells revealed by pathological studies, with a little nontransparent cytoplasm. No nuclear atypia or nuclear division is found; collagen fibers can be observed between tumor cells. The blood vessels of various sizes with expanded thin wall or thick wall can be observed within tumors, accompanied by a large amount of mucosa. The specific histological biomarker has not been reported yet. Vimentin and desmin diffuse staining was found in most of the tumor cells; some of them were SMA positive and S-100 negative. In the present study, S-100-positive cells were found in all five patients and SMA-positive cells were found in only 60%, indicating that AAM might not have a specific histological biomarker. It was reported by Kenny-Moynihan *et al.* that X chromosome was lost in 40% metaphase cells, whereas the adjacent blood cells showed normal karyotype, implying that chromosome loss in tumor cells might be associated with malignancy [13].

Differential diagnosis includes the following: 1) myxoid liposarcoma − it often occurs in the limbs, and retroperitoneal or subcutaneous tissue. A large number of bud branch vessels can be found in mucosal tissues, mixed with primary immature mesenchymal cells, and a large number of ring-like lipoblasts, S-100 positive, and fat tissue stain positive; 2) angiomyofibroblastoma − the location is similar to myxoid liposarcoma, though usually shallow with diameter less than five cm. The tumor has a clear boundary, and is full of interstitial fibers. Hemorrhage is very rare, with no mucosal changes or interstitial edema; 3) superficial angiomyxoma − is mainly located in the trunk, limbs, head dermis or subcutaneous tissue. The tumor usually has

a thin envelope and is full of mucosal matrix scattered with blood vessels, with less cellular components. Histological studies show that tumor cells are desmin, estrogen receptor (ER), and progesterone receptor (PR) negative; 4) mucinous tumor − it occurs in the elderly and is often found in the thigh, with lack of blood vessels; the tumor usually has a clear boundary with the adjacent tissues. The recurrence is very rare after dissection; 5) mucinous nerve fiber tumor − in peripheral nerve tumors, the nucleus of the tumor cells has no prominent vascular component [2-5].

Treatment and prognosis

The major therapeutic modality is surgery, although partial dissection or extended dissection mode is still controversial. Previous studies indicated no significant difference in the recurrence rate between complete dissection and partial dissection. The lymph nodes need not be dissected, since no remote or lymphoid metastasis is observed. The ideal target is to remove the tumor completely; however, the fertility-preserving surgery should be considered for patients with a desire to be pregnant [10]. It was reported that the incomplete removal of the tumor might be associated with postoperative recurrence, and extended dissection was believed to be helpful if the diagnosis was clear and well defined [14, 15]. However, the recurrence rate was still as high as 72% for patients who underwent extended dissection and the dissection edge had no lesions [16]; therefore, the operation range was suggested to be conservative [17, 18]. In the present study, the surgeries were performed in all five patients with AAM, although the extended dissection was not carried out. Four out of five patients had no recurrence, and only one patient underwent secondary surgery for recurrence. Most of AAM tumors were ER and PR positive, and occurred during pregnancy; therefore, AAM was considered to be hormone dependent [19].

It was reported that GnRH-α and other female hormone antagonists could cause tumor shrinkage or disappearance [20]; however, the effect and recurrence of long-term hormonal treatment are yet unclear [19]. On the contrary, the menopausal symptoms and bone loss could be the concern for long-term hormonal treatment [21]. Therefore, the five patients in the present study were not given hormonal treatment.

Radiotherapy was used for patients with recurrent tumor and no recurrence within two to three years afterwards [22]. However, radiotherapy has an adverse effect on fertility and hence should be used with extreme care. In addition, the malignant transformation by radiotherapy is another potential risk. With no nuclear division in tumor cells of AAM, chemotherapy is not recommended. The interventional therapy and chemo-targeted therapy were not recommended either, given the abundant blood supply usually found in most AAM tumors [2, 4].

In general, the preoperative diagnosis of AAM is usually difficult; the spiral-like and stratified structure revealed by preoperative CT and MRI scan might be helpful in diagnosis, at least suggestive for the region of surgery. The tumor should be completely removed to avoid any residues and hence reduce postoperative recurrence. Major therapy is surgical treatment; postoperative GnRH-α therapy as an adjuvant therapy can also be considered. Regular postoperative examination is suggested and close follow-up is usually needed.

Acknowledgement

This research was supported by a grant from the Research Fund of the Shen Zhen City Technology Creative Committee (No. JCYJ2014041109115144).

References

[1] Jingping Z., Chunfu Z.: "Clinical experiences on aggressive angiomyxoma in China (report of 93 cases)". *Int. J. Gynecol. Cancer*, 2010, *20*, 303.

[2] Elkattah R., Sarkodie O., Otteno H., Fletcher A.: "Aggressive angiomyxoma of the vulva: a précis for primary care providers". *Case Rep. Obstet. Gynecol.*, 2013, *2013*, 183725.

[3] Steeper T.A., Rosai J.: "Aggressive angiomyxoma of the female pelvis and perineum: Report of nine case of a distinctive type of gynecologic soft tissue neoplasm". *Am. J. Surg. Pathol.*, 1983, *7*, 463.

[4] Sutton B.J., Laudadio J.: "Aggressive angiomyxoma". *Arch. Pathol. Lab. Med.*, 2012, *136*, 217.

[5] Haldar K., Martinek I.E., Kehoe S.: "Aggressive angiomyxoma: a case series and literature review". *Eur. J. Surg. Oncol.*, 2010, *36*, 335.

[6] Iyibozkurt A.C., Yasa C., Schmieta D.E., Gungor-Ugurlucan F., Topuz S., Berkman S.: "Aggressive angiomyxoma of the pelviperineum: surgical treatment through a perineal incision". *J. Minim. Invasive Gynecol.*, 2011, *18*, 541.

[7] Salman M., Kuzey G., Dogan N.U., Yuce K.: "Aggressive angiomyxoma of the vulva recurring 8 years after initial diagnosis". *Arch. Gynecol. Obstet.*, 2009, *280*, 485.

[8] Piura B., Shaco-Levy R.: "Pedunculated aggressive angiomyxoma arising from the vaginal suburethral area: case report and review of literature". *Eur. J. Gynaecol. Oncol.*, 2005, *26*, 568.

[9] Haldar K., Martinek I.E., Kehoe S.: "Aggressive angiomyxoma: a case series and literature review". *Eur. J. Surg. Oncol.*, 2010, *36*, 335.

[10] Jingping Z., Chunfu Z.: "Clinical experiences on aggressive angiomyxoma in China (report of 93 cases)". *Int. J. Gynecol. Cancer*, 2010, *20*, 303.

[11] Xubin L., Zhaoxiang Y.: "Aggressive angiomyxoma of the pelvis and perineum: a case report and review of the literature". *Abdom. Imaging*, 2011, *36*, 739.

[12] McCluggage W.G.: "A review and update of morphologically bland vulvovaginal mesenchymal lesions". *Int. J. Gynecol. Pathol.*, 2005, *24*, 26.

[13] Kenny-Moynihan M.B., Hagen J., Richman B., McIntosh D.G., Bridge J.A.: "Loss of an X chromosome aggressive angiomyxoma of female soft parts: a case report". *Cancer Genet. Cytogenet.*, 1996, *89*, 61.

[14] Sun N.X., Li W.: "Aggressive angiomyxoma of the vulva: case report and literature review". *J. Int. Med. Res.*, 2010, *38*, 1547.

[15] Kiran G., Yancar S., Sayar H., Kiran H., Coskun A., Arikan D.C.: "Late recurrence of aggressive angiomyxoma of the vulva". *J. Low. Genit. Tract Dis.*, 2013, *17*, 85.

[16] Haldar K., Martinek I.E., Kehoe S.: "Aggressive angiomyxoma: a case

series and literature review". *Eur. J. Surg. Oncol.*, 2010, *36*, 335.
[17] Han-Geurts I.J., van Geel A.N., van Doorn L., den Bakker M., Eggermont A.M., Verhoef C.: "Aggressive angiomyxoma: multimodality treatments can avoid mutilating surgery". *Eur. J. Surg. Oncol.*, 2006, *32*, 1217.
[18] Sutton B.J., Laudadio J.: "Aggressive angiomyxoma". *Arch. Pathol. Lab. Med.*, 2012, *136*, 217.
[19] Shinohara N., Nonomura K.: "Medical management of recurrentaggressive angiomyxoma with gonadotropin-releasing hormone agonist". *Int. J. Urol.*, 2004, *11*, 432.
[20] Lee C.W., Yoon J.H., Park D.C., Lee S.J.: "Aggressive angiomyxoma of the vulva treated by using a gonadotropin-releasing hormone agonist: a case report". *Eur. J. Gynaecol. Oncol.*, 2011, *32*, 686.
[21] McCluggage W.G., Jamieson T., Dobbs S.P., Grey A.: "Aggressive angiomyxoma of the vulva: Dramatic response to gonadotropin-releasing hormone agonist therapy". *Gynecol. Oncol.*, 2006, *100*, 623.
[22] Suleiman M., Duc C., Ritz S., Bieri S.: "Pelvic excision of large aggressive angiomyxoma in a woman: irradiation for recurrent disease". *Int. J. Gynecol. Cancer*, 2006, *16*, 356.

Corresponding Author:
R. YUAN, M.D.
Department of Obstetrics and Gynaecology
The First Affiliated Hospital of
Chongqing Medical University
No. 1 Yixueyuan Road, Yu Zhong District
Chongqing City 400016 (China)
e-mail: leaiwen@126.com