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Case Report

Clinicopathologic and treatment features of aggressive angiomyxoma: a case report

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Abstract: Objective: The present study is to accumulate clinicopathologic and treatment data on aggressive angiomyxoma (AA), a rare tumor. Methods: Various clinical findings were analyzed in 9 patients with AA at Affiliated Tumor Hospital of Xinjiang Medical University from 1996 to 2016. Results: Nine patients (8 females and 1 male) were included in the present study, with an age range from 14 to 63 years (median age, 33.4 years). The sites of tumor in 6 cases were perineum and vagina, right breast, left pelvic peritoneum and right groin (male). Gross examination showed that the tumor was solid and soft, with unclear boundary but no capsule. The cut surface was gray and jelly-like. According to microscopic examination, the tumor had invasive growth, and small fusiform or star-shaped cells being dispersed in a myxoid background, enclosing several capillary structures with a thin wall. The initial treatment was localized excision. Follow-up showed that 2 patients died from cardiovascular and cerebrovascular disease, 2 patients had local recurrence, 2 patients were withdrawn, and others had neither local recurrence nor distant metastasis. Follow-up time was 3-25 years. Conclusion: AA is a rare tumor that occurs predominantly in females. Local resection is appropriate to manipulate the tumor, and local recurrence is common.

Keywords: Aggressive angiomyxoma, pathologic analysis, surgical treatment

Introduction

Aggressive angiomyxoma (AA) is a very rare gynecologic tumor that is classified as "tumors of uncertain differentiation" in the latest WHO classification [1]. Although almost all AA cases are benign, these neoplasms usually present a locally infiltrative nature and high rates of recurrence [2].

AA is most frequent in adult females during the period of childbearing age, and the tumor size generally ranges about 1-60 cm. AA mostly occurs in pelvis, perineum, buttocks, or groin area, with a prevalence ratio of 6.6:1 (females:males) [3, 4]. According to previous reports, there are fewer than 400 cases in total, and only 5 reports have shown more than 10 cases. In the present study, 9 patients with AA were admitted to our hospital. The follow-up period is 25 years. Their clinical, pathologic, treatment and follow-up data are reported here.

Case report

Subjects

A total of 9 patients with AA (age of the first visit was 14-63 years) were diagnosed and treated in the Department of Gynecological Surgery at the Affiliated Tumor Hospital of Xinjiang Medical University between 1996 and 2016, including 8 females and 1 male. Greatest diameter of the tumor ranged from 1 cm to 14 cm. Among the 9 cases, 6 patients had the tumor perineum and vagina, 1 patient in right breast, 1 patient in left pelvis, and 1 patient in right groin (male). All procedures performed in the current study were approved by the Ethics Committee of Xinjiang Medical University. Written informed

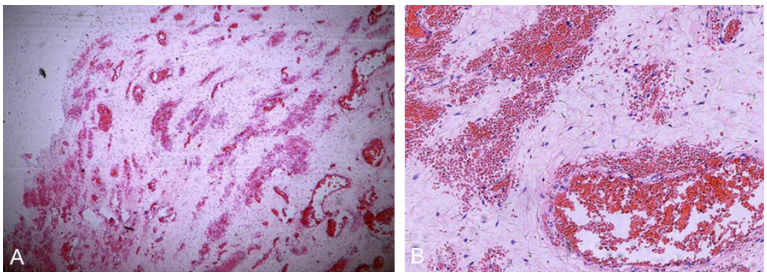

Figure 1. Invasive growth, with small fusiform, or star-shaped cells that are dispersed on a myxoid background, enclosing several capillary structures with a thin wall. A. Magnification, 40×; B. Magnification, 200×.

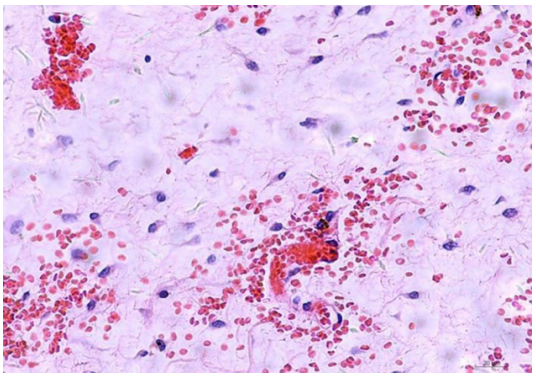

Figure 2. Tumor cells are star-shaped, oval or short spindle-shaped, with sparse cytoplasm and no nuclear atypia. Magnification, 400×.

consent was obtained from all patients or their families.

Pathologic features

According to gross pathology, 9 tumors were solid and soft, with unclear boundary but no capsule. The cut surface was gray and jelly-like. The length of the tumors ranged about 1-14 cm, and larger tumors could be seen within sheet-like bleeding and cystic degeneration.

According to hematoxylin and eosin staining, the tumors had invasive growth, small fusiform or star-shaped cells dispersed on a myxoid background enclosing several capillary structures with a thin wall (**Figure 1A** and **1B**). Tumor cells were star-shaped, oval, or short spindle-shaped, with sparse cytoplasm, and no nuclear atypia (**Figure 2**).

Immunohistochemical results were as follows: CD34 (blood vessels +), DES (+), HHA-35 (+), PR (-), S-100 (-), VIM (-), SMA (blood vessels +) (**Figure 3A-E**).

Treatment

The 9 patients were first treated with locally expanded resection, and the margin of 8 cases was negative. One patient with AA at major vestibular glands had a positive margin, and gonadotropin-releasing hormone agonist (GnRH-a) was administered for 6 cycles after surgery.

Follow-ups

By June 2016, all of the cases were followed up for 3-25 years. Among them, 2 cases were lost, and 2 cases had local recurrence and died of cardiovascular disease finally. Patients with positive margin and recurrence were followed up as follows:

Case 1: The patient with AA in the major vestibular gland underwent her first surgery at 38 years old in March 2013, and the surgical margin was positive. Without any treatment, 3 × 3.3 cm lesions appeared in operative position after 2 months. Because the margin of the second surgery was still positive, she received GnRH-a for 6 cycles after the second surgery. No recurrence was observed during the follow-up of 3 years.

Case 2: The patient with AA in right breast (3 times of recurrence) underwent her first surgery at 34 years old in April 1985. In October 1996, she was diagnosed with the first relapse in right breast, and received simple mastectomy. In September 2006, she was diagnosed with the second relapse in the right chest wall and armpit, and received tumorectomy and right axillary lymph node biopsy. Because the masses removed from the right chest wall and armpit were both AA (but the axillary lymph node had chronic inflammatory reaction), she accepted local radiation therapy. In March 2007, she was diagnosed with the third relapse in the right chest wall, and accepted tumorectomy. After tumor resection, the patient was transferred to medical treatment, because of acute myocardial infarction. Then, she died of heart failure in August 2010.

Case 3: The patient with left iliac retroperitoneal AA underwent her first surgery at 55 years old in September 1998. In April 2006, she was diagnosed with local relapse and received left

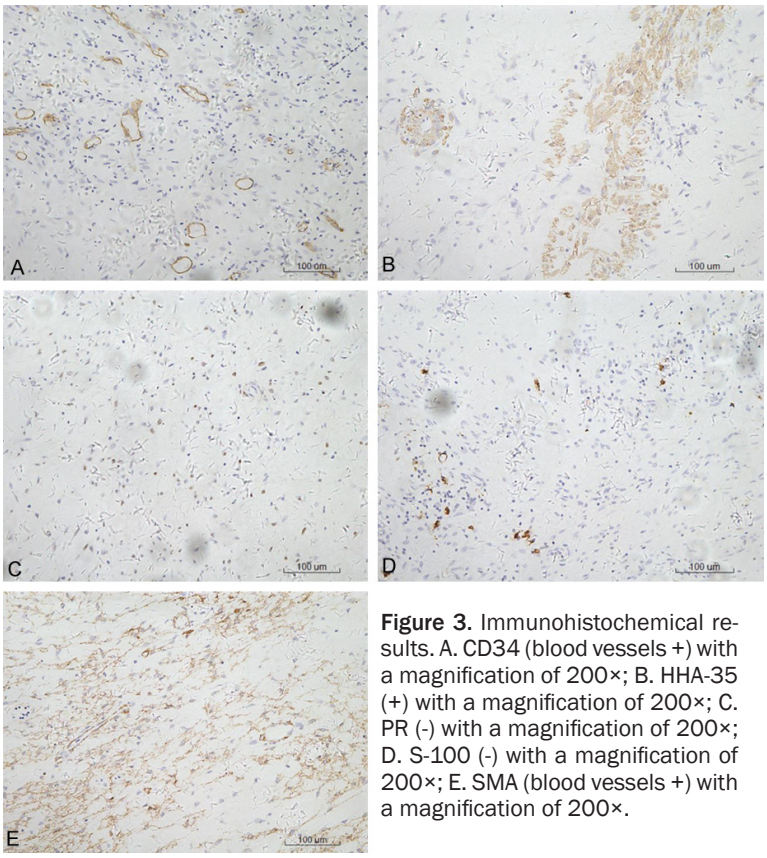

Figure 3. Immunohistochemical results. A. CD34 (blood vessels +) with a magnification of 200×; B. HHA-35 (+) with a magnification of 200×; C. PR (-) with a magnification of 200×; D. S-100 (-) with a magnification of 200×; E. SMA (blood vessels +) with a magnification of 200×.

iliac fossa tumor resection and partial bowel resection. She was followed up until February 2014, and died of cerebrovascular accident.

Discussion

We reporrt cases of AA in vulva and/or vagina, urethra, pelvis, breast and groin area. Their structures are similar, with papillary gland cysts, femoral hernia, lipoma, and fibroma, and these tumors often infiltrate to peripheral tissues. For the reasons given above, difficult diagnosis and severe hemorrhage have occurred during the operation. Therefore, it is essential to assess the relationship between tumor and surrounding tissues by computed tomography or magnetic resonance imaging before operation [5].

The pathologic characteristics of the cases are similar to other reports. The characteristics will be helpful to distinguish AA from superficial angiomyxoma, angiomyofibroblastoma and other soft tissue tumors. According to immunohistochemistry, the expression of some markers is positive in tissues of AA, such as desmin, vimentin, smooth muscle actin, and less commonly, estrogen and progesterone [6, 7]. Therefore, diagnosis of AA through hematoxylin and eosin staining will be beneficial to select the appropriate immunohistochemical markers in practice.

Therapies of AA include surgery, GnRH-a, arterial embolization, and radiation therapy. However, radiation therapy and chemical therapy are used in rare cases, because proliferation and division of tumor cells are not significant, limiting responses to radiation and chemical therapy. In the present study, case 1 had the second relapse in her right armpit, and we used local radiotherapy. However, AA still recurred after 10 months. It is confirmed that radiotherapy is not helpful. It is also reported that relapsing patients have non-recurrence with radiotherapy after 2-3 years [8]. Nevertheless, radiotherapy needs to be used with care, because it not only affects fertility, but also develops a risk of sarcoma. In the present study, 1 patient who received radiation therapy had recurrence after 10 months, this being inconsistent with other reports.

Surgery is utilized in most cases to remove tumor as completely as possible [9]. In the present study, case 3 had AA at vestibular gland, which was not excised completely in the first operation. The tumor reoccurred 2 months later. Therefore, positive or negative surgical margin is one impacting factor for the prognosis. Now, emerging therapies to minimize mutilating surgery include hormonal therapy and angiographic embolization of the mass [4].

Immunohistochemical study confirms that Estrogen receptor (ER) and/or Progesterone repeptor (PR) were positive in the present study. Janaampaio [10] et al. report a 25-year-old woman with AA in the vaginal area and the tumor grew rapidly within 1 week after pregnancy, suggesting that the tumor may be hormone-

dependent. It is reported that GnRH-a drugs or other anti-estrogen drugs (tamoxifen) can mediate shrinkage until disappearance of tumors [11]. In the present study, the 37-year-old patient whose margin is positive received vulvar tumor resection. The edge was still positive, and ER and PR were positive according to immunochemistry. The patient received GnRH-a drug for six courses, and follow-up showed no recurrence after 3 years. Therefore, thorough resection of tumors\and endocrine therapy are suitable for women who intend to maintain fertility afterwards.

In the present study, recurrence rate of AA is about 33-83%, and the earliest recurrence occured 2 months after surgery. In addition, 71% of the cases occured within 3 years after surgery, and 94% occured within 7 years. In the present study, two cases had recurrence. One case had the recurrence after 8 years; the other case had a recurrence 3 times, and the second recurrence had soft tissue transferring at the same lateral axillary.

In conclusion, the most frequently reported AA cases are single-case reports, because of its low incidence. Extensive local resection surgery is the preferred treatment for AA. However, GnRH-a may be an appropriate treatment regimen for patients with recurrence.

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Disclosure of conflict of interest

None.

Abbreviations

AA, Aggressive Angiomyxoma; ER, Estrogen Receptor; PR, Progesterone Repeptor.

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