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Case Report

Huge abdominal and perineal aggressive angiomyxoma: A misdiagnosed case report and literature review

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Abstract: Aggressive angiomyxoma (AA) is a distinctive soft tissue tumor with a high risk of local recurrence. Clinicians must be aware of this rare tumor pre-operatively. Excision is the preferred method of AA treatment. The case report presents a case of a 36-year-old woman who was difficulty in walking due to a non-painful tumor in the abdomen and perineum. She was misdiagnosed as abdomen neurofibroma for more than 10 years, and an operation was performed in 1997. However, the tumor was incompletely resected because its huge volume accompanies with extensive infiltration and bleeding. The tumors in her abdomen and perineum were growing gradually, and the latter became a large lump which impeded her daily life. In 2008, the perineal tumor was incompletely resected, which weighed 10725 g. The severe hemorrhage had been ceased by Gonadotropin-Releasing Hormone treatment. She is alive till now. Details of the history and operative procedures are presented. An AA diagnosis was made by microscopy immunohistochemically. Long-time misdiagnosis and improper treatment are the important reasons for making it impossible to be radically resected. Pathological and immunohistochemical examination are important for avoiding misdiagnosis. For this case, there is a remaining tumor in her abdomen. A special project including further follow-up and treatment will be taken out.

Key words: Aggressive angiomyxoma; Misdiagnosis; Operation.

Introduction

Aggressive angiomyxomas (AA) is a kind of rare, slow-growing, soft (often gelatinous) and benign tumor, which is, predominantly, located on the perineum. It has tendency to local infiltration and recurrence in sites that frequently in the pelvis and perineum of the reproductive age women (1). The incidence ratio of AA in females to males is 6.6:1. The age distribution is wide ranging from 18 to 63 years old with the peak incidence at 31 to 35 (2). The misdiagnosis of AA often occurs. It can be mistaken clinically as several other diseases such as myxoma, myxoid liposarcoma, the myxoid variant of malignant fibrous histiocytoma and other soft tissue tumors with secondary myxoid changes. It is important to diagnose this condition because the tumor is locally infiltrative and requires wide excision and follow-up (3). The line of differentiation of AA is not firmly established, but its fibroblastic /myofibroblastic origin has been proposed. However, its rarity, frequent misdiagnosis, and issues in its management probably merit reporting of every case. We present a case of AA concerning the abdomen and perineum of a 36-year-old woman who was misdiagnosed with neurofibroma at 1997. Besides, details of the history and the operative procedure are given. Then, the literature was reviewed and management was discussed.

Case report

A 36-year-old female was faced with a swelling in the low abdomen and perineal region for more than 10 years, and the tumor was growing up gradually since four years ago (Figure 1).

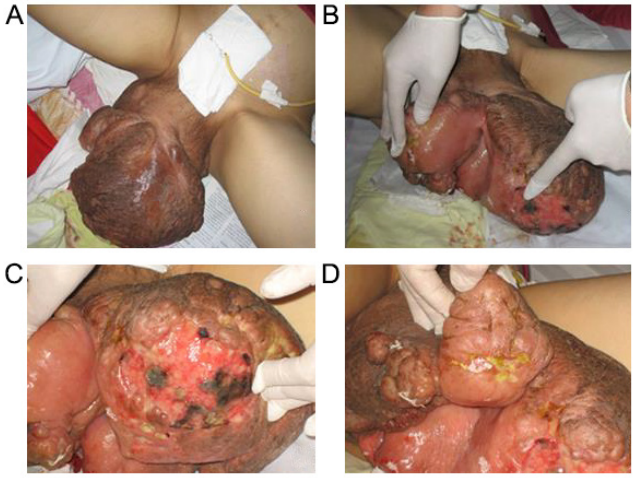

Figure 1. Physical examination revealed a globular, semisolid and rubbery tumor, with the size of 25 cm × 25 cm × 30 cm in the abdomen and 32.5 cm × 27.5 cm × 12 cm in her perineum with the pedicle thickness of 12 cm, arising from the bilateral labium majus. The middle of it is the vagina. C. A. Outside the tumor; B. Inside the tumor; C. Tumor with partial necrosis; D. The necrosis and secretion in the tumor.

She was diagnosed with neurofibroma and received a laparotomy for tumor resection in the abdomen and retroperitoneal region on March 4, 1997. The tumor was resected incompletely because of deep stromal invasion, and the pathological examination shows neurofibroma. After that, cystostomy and bilateral ureteral ostomy to skin were performed in 1999 and 2003 respectively. In 2008, the tumor in her perineal region was growing

up rapidly in the last six months, which impeded her walking progressively. Physical examination revealed a globular, semisolid and rubbery mass, with the size of 25 cm × 25 cm × 30 cm in the abdomen and 32.5 cm × 27.5 cm × 12 cm in her perineum with the pedicle thickness of 12 cm, arising from the bilateral labium majus (Figure 1A-D). It was non-tender and covered with the purple normal skin. Besides, rough protuberances appear on its surface. CT scans showed a mass of soft tissue originating from the right side of the vulva, without infiltration. Lower abdomen MRI shows a huge pelvic mass, according to her history, when considering the reoccurred neurofibroma (Figure 2).

Laboratory blood examination had shown that: WBC, 14.35 × 10^9/L, lymphocytes: 7.4%, the neutrophil percentage: 88.3%, red blood cells: 1.76 × 10^9/L, Hb: 36 g/L, hematocrit: 14%, absolute neutrophil: 12.67 × 10^9/L; blood biochemistry: albumin 28.7 g/L, uric acid: 581 umol/L, and urine: urine protein +, and interleukin 3+. She was transfused with RBC 14.5U and plasma 2250 ml, and then her Hb reached 93g/L. Tumor markers were negative. To reduce the tumor load and to preserve as much of the external genitalia as possible, the tumor on her labia was excised using a modified and combined technique. The standard elliptic incision appeared on the right labia, and the right distal opening of the vagina was extirpated when an inverted incision existed with a smaller elliptic incision that allowed the surgeon to reach the pedicle more proximally and distantly than taking the standard approach. The left labia incision was similar to that of the right. Excision was then achieved simply by clamping the thick pedicle bit by bit. The resected tumor with the weight of 10725 g and the size of 32.5 cm × 27.5 cm × 12 cm, was externally lobulated, grayish white and glistening. The operation continued for 126 minutes, when about 1300 ml of blood was lost, and a total of 5U blood cells and 600 ml plasma were transfused. The cut section of the tumor was gelatinous. After extirpating the external tumor, the inverted incision was closed by separated mattress sutures with 3/0 Vicryl suture materials. No drain was used; no wound contracture or dehiscence occurred and recovery was complete without any complication. The cut surface of the resected tumor had the grey, diffuse gelatinous, myxoid and semitranslucent gross appearance, with small hemorrhagic focuses but no cystic spaces. During hospitalization, the infusion of red blood cells in patients is featured with a total of 26 U and plasma of 22450 ml. Microscopic examination revealed a low-grade spindle cell lesion comprising the areas of hypocellularity amidst myxoid change and interspersed by numerous rounded thick and thin walled vessels. At few places, vessels showed extravasation of RBC's. There was no evidence of pleomorphism, mitotic activity or necrosis. urologists and pathologists held that a diagnosis was made by immunohistochemically examination (Figure 3): the soft tissue region is the myxoid background, with muscle spindle-like cells that appear with CD34 (+), SMA (+), EP (±), PR (++), Desmin (±), S-100 (-) and myoglobin (-). The hardware region consisted of the spindle fiber region-like cells, showing fascicular and weaving-like arrangement of red stained cytoplasm, when the mitotic phase was not found. It is featured with CD34 (-), SMA (+), EP (++), PR (+), Desmin (+++), S-100 (-) and myoglobin (-).

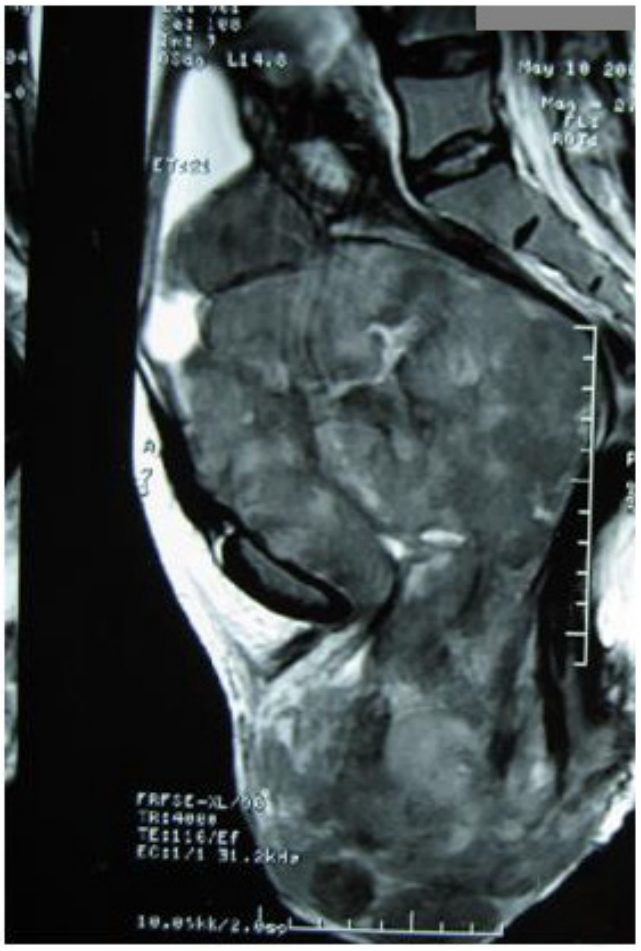

Figure 2. MRI image showed that there was huge mass abnormity in the pelvic cavity and outside genitals. To be specific, the tumor reaches anterosuperior iliac spine in the top, and vaginal orifice in the bottom. It looks like a dumb-bell shape.

Discussion

Aggressive angiomyxoma is an independent, rare and soft tissue tumor with local infiltration, and it is easy to relapse. Furthermore, it was first reported in 1983 by Steeper et al. (4). Approximately two years later, Begin et al. published their experience with 9 examples, in-

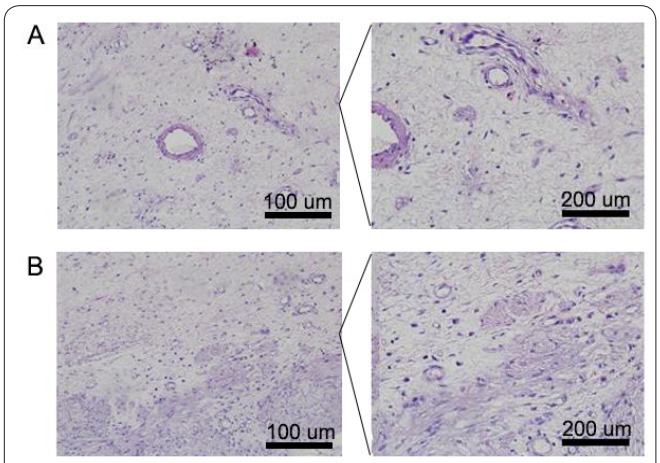

Figure 3. Immunohistochemically examination. A. The soft tissue region is the myxoid background, with spindle-like cells in it. B. The necrosis region is composed by the spindle fiber region-like cells, showing fascicular and weaving-like arrangement of red stained cytoplasm, without mitotic phase.

cluding the first report of this entity in males (5). The sites of involvement for this tumor exist in the vulva, vagina, inguinal area, buttock, peritoneum, head and bladder neck of women and other parts such as scrotum of men (3). As the tumors are often large, contiguous involvement of several sites is common. The origin of it is controversial. All of the reported cases of AA in the vulva have as painless, slow-growing, polypoid and cyst-like masses in females between the ages of 15 and 77 years. The peak incidence of AA is at the age of 31-35 (6). Our case extends this age range. The tumor diameter is generally 3 ~ 5 cm, when the largest is up to 20 cm (7), while AA in our case is considerably larger than this, regardless of the tumor in the abdomen. The perinal part is up to 32.5 cm. However, the resected tumor weight of our case is less than that reported by Chen et al, when it arises from the right labium majus and extends into the retroperitoneum with the weight of 19.8 kg (8), but in our case, a partial tumor in the abdomen could not be resected because of wide infiltration, and she was misdiagnosed for 14 years, which is rare to our knowledge.

As reported, misdiagnosis of AA occurs in 82% of cases (9). The disease after the first prosecution of cases was diagnosed as "neurofibromatosis" for many years in accordance with the "neurofibromatosis" treatment and poor clinical efficacy. The tumor grew up and was in line with the AA of clinical features. These tumors have an overall lobulated architecture with relatively sharp margination in some areas when adhering to, or infiltrating to fat and fibrous tissue or muscle. In our case, the long standing chronic mass appears with pain in the perineal labial or pelvic region, pressure-like and pulsating sensations, dyspareunia, increased mass effect with heavy lifting, urinary frequency, and diffusely infiltrative margins in the lower abdomen, the pelvic region and the perineal labial, consistent with the report (5), and it is easy to be misdiagnosed as neurofibromatosis.

Clinically, the differential diagnosis includes the vulval abscess, Bartholin abscess, Gartner's duct cyst, vaginal cyst, vaginal mass or polyp, vaginal prolapse, pelvic floor hernia, obturator and levator hernia, vulval lipoma, pedunculated vulval leiomyoma, and vulvar hypertrophy with lymphedema. Computed tomography (CT) may help delineate AA, but CT appearances are not as characteristic as magnetic resonance (MR) images (10). Histomorphologically, the differential diagnosis includes fibroma, myxoid fibrosarcoma, lymphangioma, neurofibroma, malignant mesenchymal and mixed mesodermal tumors, sclerosing hemangioma, botryoid pseudosarcoma, fibroangioma, embryo-nal rhabdomyosarcoma, angiomyofibroblastoma, and cellular angiofibroma (11). However, AA is the only myxoid tumor with a prominent vascular component (12).

Immunohistochemically, AA cells may stain for actin, desmin, vimentin, estrogen receptors and progesterone receptors, but are negative for S-100 protein, carcinoembryonic antigen and keratin. It has recently been suggested that special staining detecting abnormal architectural chromatin protein-high mobility group protein HMGA2 expression may be useful in the diagnosis of AA, and the residual disease is identified (13). Microscopically, these tumors have low to moderate cellularity. The neoplastic cells usually exhibit spindled or stellate morphology with relatively scant eosinophilic cytoplasm in a myxoid background. Large and medium sized blood vessels with a variety of secondary changes including medial hypertrophy and fibrointimal proliferation are scattered throughout the tumor. Mitosis may appear. Small scattered bundles or fascicles of smooth muscles may be evident. The evidence of infiltration can be seen by the entrapment of fat, muscle and medium sized nerve bundles.

To diagnose AA, one must eliminate malignant lesions like myxoid liposarcoma and myxofibrosarcoma which are extremely similar. The vascular pattern of myxoid liposarcoma which has thin walled capillaries with small arcs and that of myxofibrosarcoma which shows less frequent thick walls with wider arc capillaries, make it different from AA, where the blood vessels are numerous, open and more rounded.

Angiomyofibroblastoma which has the similar appearance and site predilection can be ruled out on the basis of higher cellularity, abundance of vessels, plump stromal cells and absence of extravasation of RBC's. Immunohistochemistry shows positivity for desmin, vimentin, smooth muscle actin and the specific muscle antigen. In our case, the diagnosis was based on the microscopic findings: low grade spindle cell lesion comprising the areas of hypocellularity amidst myxoid change, interspersed by numerous rounded thick and thin walled vessels; and immunohistochemistry has supported the diagnosis.

The main treatment of AA is surgical resection. Before surgery, if the operation involves the possibility of this disease, in the intraoperative frozen biopsy should be sent, while if the pathology of return appears for this disease, the local excision line should be widened. As the disease has no distant or lymph metastasis, it is not necessary to have local lymph node dissection. If the disease was not taken into account, and intraoperative frozen biopsy was not conducted, when it was diagnosed, to perform second surgery for removing the tumor as far as possible and reducing the residue tumor and the relapse rate was strong suggested. The gonadotrophin-releasing hormone (GnRH) agonist is a possible alternative means of treating recurrences (14), and it can be used as neoadjuvant therapy before the surgery of reducing the tumor volume and reducing complications (15, 16). On the other hand, GnRH agonists also have some disadvantages such as menopausal symptoms and bone loss, especially associated with long-term therapy (17). In our case, she had to accept transfuse blood treatment because of serious anemia caused by urinary bladder hemorrhage. Later, she agreed with Goserelin Acetate SR Depot subcutaneous injection monthly. At the first month after she accepted the treatment, the bleeding in her bladder aggravated, but was ceased since the second month. In the six-month treatment, the severe hemorrhage had not occurred and the tumor had shrunk to some extent till she no longer used this drug three months later for she could not afford the expensive fee. She is alive till now and is accepting another circle of GnRH treatment.

Removal of AA is sometimes difficult because of its infiltrative nature, as in our case. Perhaps for this reason, recurrence occurs in 70% of cases, but even patients with clear resection margins cannot avoid deve-

loping to recurrence. Nonetheless, excision (multiple in the case of recurrences) with wide tumor-free margins, as advocated by Elchalal et al in 1992, is still the most common treatment. However, it is now considered that incomplete resection is acceptable when high operative morbidity is anticipated and preservation of fertility is an issue. Our case received laparotomy tumor resection and retroperitoneal tumor resection on March 4, 1997, and the complexity of the rumor's diffusely infiltrative margins made it difficult to be removed. Thus, she also accepted long-term follow-up with MRI or CT scans (18, 19), and then a gradually increasing history was revealed for 14 years. Though the GnRH agonist is a possible alternative means of treating recurrences (14), radiation therapy and chemotherapy are less suitable due to low mitotic activity (14).

In conclusion, this case is reported because this entity has the individual standing as it is rarely misdiagnosed for 14 years, and rarely seen in sites, volume and weight, with very few cases reported in literature. Besides, it has to be differentiated from benign myxoid tumors. Then, it should be differentiated from malignant myxoid tumors because it lacks the metastatic potential, and any adjunctive therapy is not useful.

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Conflict of interest
None.

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