Aggressive deep angiomyxoma - a case report and review of the literature

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Summary

Background: Aggressive deep angiomyxoma (AA) is locally infiltrative, non-metastasizing neoplasm that typically occurs in the pelvis and perineum in women of the reproductive age. Local recurrence is high despite apparently complete surgical resection. *Case:* The authors describe a case of AA in the pelvis in a 27-year-old woman. She underwent one invasive diagnostic procedure and three surgical interventions during four months, due to diagnostic problems and very early recurrence of the disease. Follow-up one year later revealed no recurrence. *Conclusion:* The present case confirms that AA are locally aggressive and notorious for local recurrence. Such an early recurrence of AA has not been described in available literature.

Key words: Aggressive angiomyxoma; Surgery; Recurrence.

Introduction

Aggressive (deep) angiomyxoma (AA) was described for the first time in 1983 as an aggressive myxoid mesenchymal benign tumor that affects adult women and involves mostly pelvic and vulvoperineal area [1]. Occurrence of the tumor is rare [2]. Typically, the tumor grows slowly, and it has potential for local infiltration, which is associated with frequent local recurrence. The primary treatment is surgical resection. Even in the case of radical intervention, the risk of recurrence is high [2].

Case study

In November 2010, the patient, a 27-year-old nullipara, underwent in another facility laparoscopy due to suspicion of a tumor of the right adnexa. A tumor was detected during preventive gynecological examination. Upon examination the patient was complaining of mild pain and edema in the right gluteal area. During laparoscopy, no significant findings were revealed in the inner genitalia or abdomen, and therefore the procedure did not continue further. However, follow-up ultrasound confirmed the presence of isoechogenic and slightly hypoechogenic homogeneous mass with poorly-defined margins, with dimensions 11 cm by 6 cm. Examination with computed tomography (CT) was recommended. CT scan confirmed presence of oval, septal, cystoid lesion with maximum size of 12 cm by 6 cm. CT showed postcontrast enhanced image, the tumor was pressing on the bladder, uterus, and rectosigmoid colon. Radiologist recommended biopsy and histological examination of the tumor. During the CT-guided biopsy (Figure 1) in November 2010, only small fragments of normal smooth muscle were obtained. After the procedure, the patient was sent to the department for consultation and more testing. Ultrasound examination confirmed presence of tumor in the pelvis; the blood flow characteristics were typical for benign tumor. On the basis of the CT findings and previous sonographic results, the diagnosis of retroperitoneal tumor was established. The second laparoscopy was suggested and surgery was carried out in December 2010. The tumor was found to be located in the retroperitoneal area below the level of iliac blood vessels. Its direction was toward the obturator foramen and toward the pelvic bottom. It was irregular in shape, soft and rubbery in consistency. The tumor's cut surface was homogeneous, glassy, and yellow-white, and it lacked any necrosis or hemorrhage. On slicing the specimen, the tumor tissue stuck tenaciously to the knife. The tumor was removed completely, and it was sent for pathologic examination (Figure 2). Through inspection of the abdominal cavity, the finding was normal. Histological examination (Figure 3) showed mesenchymal tumor composed of bland-appearing, spindle-shaped, and stellate cells embedded in abundant myxoid stroma. In addition, the lesion contained a prominent vascular component with numerous vessels displaying often a medial hypertrophy and vascular grouping. Nuclear atypia and mitoses were absent. In the tumor margin, infiltration of the pelvic skeletal muscle tissue was visible focally. Immunohistochemically, the tumor cells expressed vimentin, desmin, alpha-smooth muscle actin, estrogen receptor, and progesterone receptor. Based on these findings, a diagnosis of AA was rendered. The high-risk of recurrence of the tumor, even after its radical removal, was explained to the patient. During the first follow-up exam, one month after surgery, the patient complained of pressure pain while in a sitting position, otherwise she denied other discomfort. Ultrasound showed early recurrence of the disease. It confirmed the presence of another tumor sized 9 cm x 6 cm. The condition and the methods of treatment were explained to the patient and the patient agreed to undergo another surgical intervention. The third laparoscopy was performed in February 2011. During surgery, an artificial lesion on the bladder was detected. The tumor was found to be located deep in the pelvis bottom. Due to anatomical changes caused by the first surgery and pathologic findings and intraoperative complications, the intervention was converted into laparotomy. The tumor was situated in the paravesical direction, toward the pelvis bottom. It had spread into rectovaginal space, almost to the anal canal. The tumor had size of 11 cm x 5 cm x 3 cm, it was excised radically, and intraoperatively the diagnosis of AA with the typical histological structure was confirmed. In the margins of the excision, infiltration of the tumor into skeletal

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Fig. 1

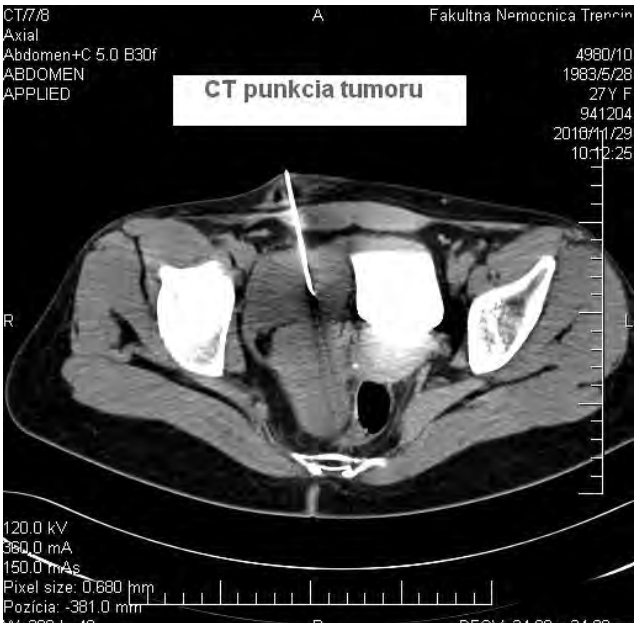

Fig. 2

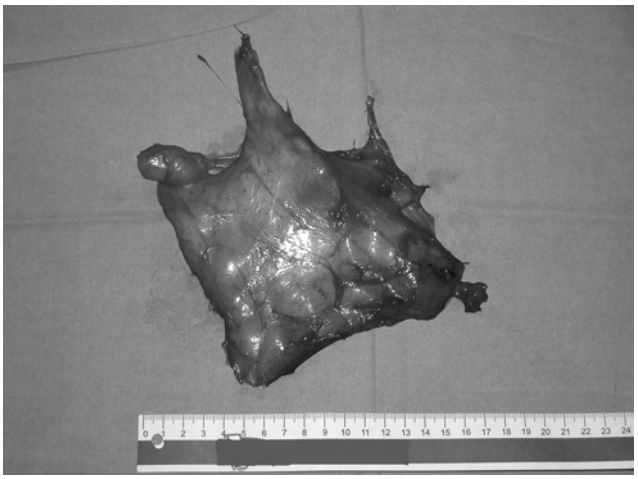

Figure 1. — Aggressive (deep) angiomyxoma. CT-guided tumor puncture.
Figure 2. — Aggressive (deep) angiomyxoma. Macroscopic appearance of the tumor after its laparoscopic removal.

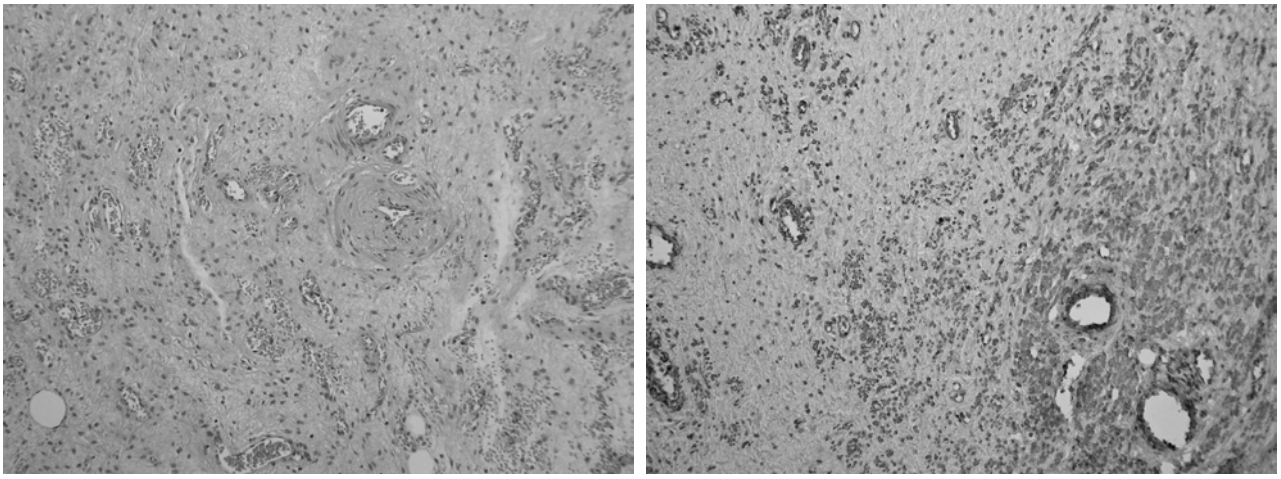

Figure 3. — Aggressive (deep) angiomyxoma, histologic, and immunohistochemical findings. (A) bland-appearing cells embedded in myxohyaline stroma, and numerous vessels; (B) immunohistochemical positivity for desmin visible as brown-colored cytoplasm of the cells (hematoxylin-eosin stain and ABC technique, respectively; original magnification x100).

muscle and fatty tissue was observed. At present, one year after the last surgery, the patient is free of the disease. However, she still reports mild discomfort in the lesser pelvis. She describes this discomfort as a pressure pain which comes and goes.

Discussion

AA is a mesenchymal tumor occurring mostly in pelvis, retroperitoneum, vagina, vulva, and gluteal region [3]. Etiopathogenesis of the lesion is unknown. According to available data, the disease occurs in patients from the age of six to 77 years, and its occurrence culminates during the fourth decade of a woman's life [4]. The occurrence of AA was reported also in male patients; however, in females it is seven times more frequent [4]. Because of the slow growth and slow infiltration rate, in most patients, the disease is asymptomatic and the tumor may reach the size of more than ten cm [3]. One article reports a gluteal AA reaching the size of 60 cm by 40 cm [5]. The authors from Bratislava described a case in which AA of the pelvis and vulva reached the size of 34 cm x 14 cm x 10 cm and weight of 2,040 grams [6]. Patients suffering from the disease report localized pain, dyspareunia, and sensation of pressure. Although it is generally understood that the tumor does not represent potential for metastases, development of metastases in lungs was reported in two cases [7, 8]. Recent reports describe rare, uncommon localization of the primary tumor [9-12]. Diagnosis of suspicious AA is generally established with difficulties due to the fact that this lesion occurs rarely. An appearance of AA by clinical examination is polypoid and cystic. Usually different types of lesions are considered, such as Bartholin's gland cyst, hernia, pelvic cyst, lipoma or fibroma. Ultrasound shows

the homogenous hypoechogenic mass, however, it usually underestimates the actual size of the tumor. Examination by CT or by magnetic resonance imaging (MRI) is more useful, since it provides information about the translevator spread of the tumor, and its distance from the anal sphincter, urethra, and the wall of the urinary bladder [2]. Correct diagnosis can be established only on the basis of results of histological examination [2, 6]. The typical morphology of the lesion includes bland-appearing, spindle or stellate cells lying in abundant myxoid matrix, and prominent vascular component with numerous abnormal vessels [1]. Immunohistochemically, the tumor is positive for desmin, and often for alpha-smooth muscle actin and CD34 (smooth muscle and myofibroblastic markers). Immunohistochemical reactivity for estrogen and progesterone receptors is frequent, and, in some male cases, expression of androgen receptor was observed [13]. Molecular genetic studies revealed that rearrangement of transcription factor HMGA-2 on chromosome 12q15 appears to be typical for AA [13]. Imaging methods are important also for planning of surgical management of the disease. Even with adequate surgical treatment, in 30% - 70% of the patients, there is the risk of recurrence of the tumor at different time intervals. Salman reports recurrence of vulvar AA eight years after the primary therapy [3]. Resection with wide margin of normal tissue was a preferable means of treatment in the past. According to current reports, the risk of the recurrence in females with negative resection margins is statistically the same as in females with the tumor cells on the edge of the resection [12, 14]. Authors from the Netherlands described seven cases treated in one facility within 20 years, three of them were pregnant at the time of diagnosis [15] and all of them were treated surgically. Excision with positive margin was performed in five patients. Recurrence of the tumor within two to ten years was reported in three patients. These patients were treated by selective embolization and by surgical reinterventions. No recurrence of the tumor was reported within two to 20 years after this treatment. Angiographic embolization is not considered to be effective, since the blood supply to the tumor is provided by numerous small blood vessels and imaging techniques usually fail to determine which blood vessel is the "primary" [2]. There are no reports available which evaluated the relation between the size of the primary tumor and the risk of recurrence. Nowadays, in cases with high-risk of perioperative complications, partial surgical therapy is considered to be acceptable means of management of the tumor [2]. It is difficult to achieve a negative margin of the surgical resection line because of the aggressive infiltration growth of the tumor and the lack of the tumor encapsulation. Haldar achieved a negative resection line in the group of seven patients only in one case, and recurrence of the tumor was reported in two females with the positive resection line [2]. AA originates from sex-steroid hormone dependent cells of the pelveoperineal soft tissue, as indicated by its frequent positivity for estrogen and progesterone receptors (including this case). It was proved that in selected cases, hormonal therapy can be effective [2, 3, 5]. Flores described the case of the patient with a vulvar AA sized 15 cm x 10 cm [16]. Since the histological findings of the resection line were positive, the patient was treated with radiation therapy, and for six months she received hormonal therapy with gonadoliberin agonists (aGnRH). Three years after the primary therapy, there was no recurrence of the tumor in this patient. Effectiveness of the therapy with aGnRH was described in the patient with AA of the vulva, in which the tumor residuals disappeared completely after this therapy had been applied for postoperative residuals or for secondary recurrence of the tumor [17, 18]. In the case of the presented patient, positive hormonal receptors were also found, and therefore, in the case of another recurrence of the tumor, therapy with aGnRH is planned. When the hormonal receptors are found to be positive, therapy with tamoxifen, raloxifen or with aromatase inhibitors may be considered [13, 19]. To lower the risks of recurrence of the tumor, it is not recommended to apply radiation therapy or chemotherapy postoperatively because AA is a neoplasm with a low proliferation rate [3]. Nowadays long-term follow-up without adjuvant therapy is the preferred means of postoperative management of the disease. Unfortunately, it is not possible to plan the strategy of treatment on the basis of evidence-based medicine, since the current literature presents only case reports or studies of small series of cases [2, 5, 6].

Conclusion

AA is a rare benign tumor invading soft tissues. Primary treatment is surgical resection without subsequent treatment. Due to the high-risk of recurrence of the tumor, long-term follow-up is required. Preoperatively, it is recommended to use imaging diagnostic methods, since the tumor may occupy large pelvic space, and it may invade surrounding anatomical structures. The patient must be informed about the risks of the radical surgical intervention. This report presents a case of the patient who experienced recurrence of the AA in the retroperitoneal area of the pelvis one month after the surgical intervention. The authors believe that such an early recurrence of AA has not been described in available literature.

References

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

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

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

[4] Dierickx I., Deraedt K., Poppe W., Verguts J.: "Aggressive angiomyxoma of the vulva: a case report and review of literature". *Arch. Gynecol. Obstet.,* 2008, *277,* 483.

[5] Ohene-Yeboah M., Bewtra C.: "Aggressive angiomyxoma in African women: a report of two cases". *West. Afr. J. Med*., 2009, *28,* 333.
[6] Sasko A., Ferančíková Z., Korbel' M., Danihel L'., Ondruš B., Holomáň M. *et al*.: "Aggressive angiomyxoma in the pelvic region and adjacent tissues and organs in a woman. Case report and literature review". *Čes Gynek.,* 1996, *61,* 240.
[7] Siassi R.M., Papadopoulos T., Matzel K.E.: "Metastasizing aggressive angiomyxoma". *N. Engl. J. Med.,* 1999, *341,* 1772.
[8] Blandamura S., Cruz J., Vergara L.F., Puerto I.M., Ninfo V.: "Aggressive angiomyxoma: a second case of metastasis with patient's death". *Hum. Pathol*., 2003, *34,* 1072.
[9] Pai C.Y., Nieh S., Lee J.C., Lo C.P., Lee H.S.: "Aggressive angiomyxoma of supraclavicular fossa: a case report". *Head Neck,* 2008, *30,* 821.
[10] Sylvester D.C., Kortequee S., Moor J.W., Woodhead C.J., Maclennan K.A.: "Aggressive angiomyxoma of larynx: case report and literature review". *J. Laryngol. Otol.,* 2010, *124,* 793.
[11] Skálová A., Zámečník M., Michal M., Opatrný V.: "Aggressive angiomyxoma presenting as polyp of uterine cavity". *Pathol. Res. Pract*., 2000, *196,* 719.
[12] Choi Y.D., Kim J.H., Nam J.H., Choi C., Na K.J., Song S.Y.: "Aggressive angiomyxoma of the lung". *J. Clin. Pathol.,* 2008, *61,* 962.
[13] McCluggage W.G.: "Recent developments in vulvovaginal pathology". *Histopathology*, 2009, *54,* 156.
[14] Chan I.M., Hon E., Nqai S.W., Nq T.Y., Wong L.C.: "Aggressive angiomyxoma in females: is radical resection the only option?". *Acta Obstet. Gynecol. Scand*., 2000*, 79*, 216.
[15] 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.
[16] Flores E.L.N., Blanco M.A.A., Vadillo J.F., Ortiz H.C.: "Angiomixoma agresivo de la vulva. Informe de un caso y revisión de la bibliografía". *Ginecol. Obstet. Mex*., 2009, *77,* 487.
[17] 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.
[18] Fine B.A., Munoz A.K., Litz C.E., Gershenson D.M.: "Primary medical management of recurrent aggressive angiomyxoma of the vulva with a gonadotropin-releasing hormone agonist". *Gynecol. Oncol*., 2001, *81,* 120.
[19] Ding D.C., Hsu S., Hsu Y.S., Chen H.T.: "Aggressive angiomyxoma of the vulva in a young female: a brief case report". *Eur. J. Obstet. Gynecol. Reprod. Biol*., 2008, *140,* 128.

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