Aggressive Angiomyxoma of Vulva: Case Report

VULVANIN AGRESİF ANJİOMİKSOMASI

Seyit Temel CEYHAN, MD,[a] İskender BAŞER, MD,[a] Ömer GÜNHAN, MD,[b]
Sadettin GÜNGÖR, MD,[a] Ümit GÖKTOLGA, MD,[a] Ali YILMAZ, MD[a]

Departments of [a]Gynecology and Obstetrics, [b]Pathology, GATA, ANKARA

Abstract

Aggressive angiomyxoma (AA) is a rare mesenchimal tumor mostly involves female pelvis and perineum in the reproductive age group with tendency to common recurrence and local invasiveness.

A 44-year old woman diagnosed as Bartholin duct cyst and underwent surgical excision. Pathology report described as non-neoplastic cyst without lining epithelium. Six months after surgery; pelvic examination revealed a size of 6 x 6 cm mass with deep stromal invasion on the left side. MRI scan confirmed the presence of a large ill-defined mass consisting entirely of myxomatous tissue and patient undergone second surgery. Tumor resected incompletely because of deep stromal invasion. Pathology report described as aggressive angiomyxoma. Monthly injections of GnRH agonist commenced (Goserelin acetate 3.6 mg, Zoladex® Depot 3.6 mg sc implant, AstraZeneca). After 3 months, patient was asymptomatic. MRI scan was repeated, which showed a drastic decrease in size of the lesion with scarring and also complete resolution of the myxomatous tissue was seen without any evidence of residual AA.

Occuring predominantly in premenopausal woman, rapidly growing during pregnancy and immunoreactivity to estrogen receptor and progesterone receptor provide a rationale for the management of AA with GnRH agonists. GnRH agonist therapy may help complete resection of large tumors and provide avoidance to radical surgery when administered pre-operatively. Post-operative administration may be usefull for the treatment of residuel tumors or recurrences. Eventhough many questions waiting for the answer such as dose, duration and side effects of therapy, we think that GnRH agonists will be more popular in near future for the treatment of AA.

Key Words: Myxoma; vulva; goserelin

Özet

Agresif anjiyomiksoma (AA), reprodüktif yaş grubunda kadın pelvis ve perineumunu tutan, yaygın rekürrens ve lokal invazyon eğilimi olan, oldukça nadir görülen bir mezenkimal tümördür.

Kırk dört yaşında bir kadın Bartholin kanal kisti tanısıyla opere edildi. Patoloji, spesmeni döşeyici epiteli olmayan non-neoplastik kist olarak rapor etti. Cerrahiden 6 ay sonra, pelvik muayenede, sol vulvar bölgede 6 x 6 cm boyutunda derine doğru invazyon gösteren kitle saptandı. Manyetik rezonans görüntülemede (MRG) iyi sınırlı, geniş miksomatöz doku izlendi ve hastaya ikinci kez cerrahi uygulandı. Derin stromal invazyon nedeniyle tümör inkomplet olarak rezeke edildi. Patoloji sonucu agresif anjiyomiksoma olarak rapor edildi. Hastaya aylık GnRH agonisti (Goserelin asetat 3.6 mg, Zoladex® Depot 3.6 mg subkütan implant, AstraZeneca) enjeksiyonuna başlandı. Üç aylık tedavi sonrası kontrolde hastanın semptomu yoktu. MRG tekrarlandığında, lezyonun boyutunun skar oluşumuyla ileri derecede gerilediği ve herhangi bir rezidüel AA bulgusu olmaksızın miksomatöz dokunun komplet rezolusyona uğradığı gözlendi.

AA'nın daha çok premenopozal dönemde görülmesi, gebelikte hızlı büyümesi, östrojen ve progesteron reseptörleri içermesi, yönetiminde GnRH agonistlerinin kullanılmasının mantığını oluşturmaktadır. GnRH agonistleri pre-operatif uygulandığında büyük tümörlerin tam rezeksiyonuna yardımcı olabilir ve radikal cerrahi girişimden kaçınma imkanı sağlayabilirken, post-operatif uygulama rezidüel tümörlerin ya da rekürrenslerin tedavisinde etkili olabilir. Tedavinin süresi, dozu, yan etkileri gibi cevaplanmayı bekleyen bir çok soru olmasına rağmen, yakın gelecekte GnRH agonistlerinin AA tedavisinde daha populer olacağını düşünüyoruz.

Anahtar Kelimeler: Miksoma, vulva, GnRH agonisti

Turkiye Klinikleri J Gynecol Obst 2007, 17:61-64

Aggressive angiomyxoma (AA) was first described by Steeper and Rosai in 1983.[1] This rare mesenchimal tumor mostly involves female pelvis and perineum in the reproductive age group. This tumor termed as AA because of its common recurrence and local invasiveness.[2] In very occasional cases, metastasis has been described.[3] Misdiagnosis of AA as other female pelvic soft tissue mesenchimal tumors is not rare and clinicians must be aware of this rare tumor pre-operatively because of determining degree of infiltration. Surgical management of primary or recurrent tumor may be prob-

Geliş Tarihi/*Received:* 22.06.2006 **Kabul Tarihi/*Accepted:*** 11.09.2006

Yazışma Adresi/*Correspondence:* Seyit Temel CEYHAN, MD
GATA,
Department of Gynecology and Obstetrics, ANKARA
stceyhan@gata.edu.tr

lematic because of that reason, some medical management methods might be needed. In this case we reported gonadotropin-releasing hormone (GnRH) agonist treatment after surgery in the management of AA.

Case Report

A 44-year old gravida 2, para 2 woman was referred to our gynecology out-patient department with a history of recent onset swelling on the left side of vulva. She diagnosed as Bartholin duct cyst and underwent surgical excision first on 24th of May 2004. Pathology report described as non-neoplastic cyst without lining epithelium. Six months after surgery; patient invited for check up and pelvic examination revealed a diffuse swelling on the left side. Magnetic resonance imaging (MRI) scan confirmed the presence of a large ill-defined mass consisting entirely of myxomatous tissue with high signal intensity. Patient undergone second surgery on 13rd of December 2005. Tumor resected incompletely because of deep stromal invasion by vaginal approach. This time pathology report described as AA and she referred to gynecological oncology department. Monthly injections of GnRH agonist (Goserelin acetate 3.6 mg, Zoladex ® Depot 3.6 mg sc implant, AstraZeneca) commenced. After 3 months, patient was asymptomatic. The MRI scan was repeated, which showed a drastic decrease in size of the lesion with scarring and also complete resolution of the myxomatous tissue was seen without any evidence of residual AA.

Pathological Findings

Macroscopically; tumoral tissue was 8 cm in highest diameter. It is ill defined, polypoid, gelatinous mass.

Histopathological examination revealed a hypocellular myxomatous tumor composed from spindle fibroblastic cells (Figure 1). There is no cellular atypia or mitosis. There are numerous large caliber vessels having thickened wall in tumor.

Spindle fibroblastic cells were immunoreactive to muscle specific actin. Nuclear Ki-67 and cytoplasmic vascular endothelial growth factor receptor (VEGFR) immunoreactivity were positive only in the endothelial cells of vessels (Figure 2).

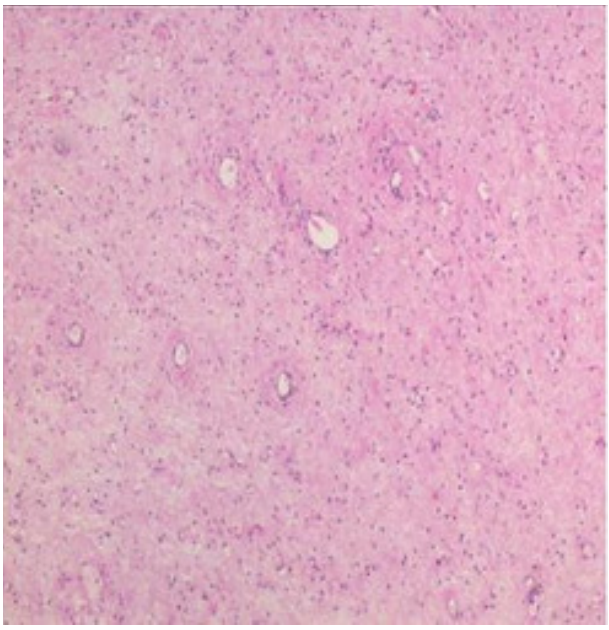

Figure 1. Hypocellular myxomatous tumor composed from spindle fibroblastic cells (Hematoxylen-Eosin x 100).

Discussion

AAs are very rare tumors and frequently clinically mistaken for cysts of the Bartholin duct or for

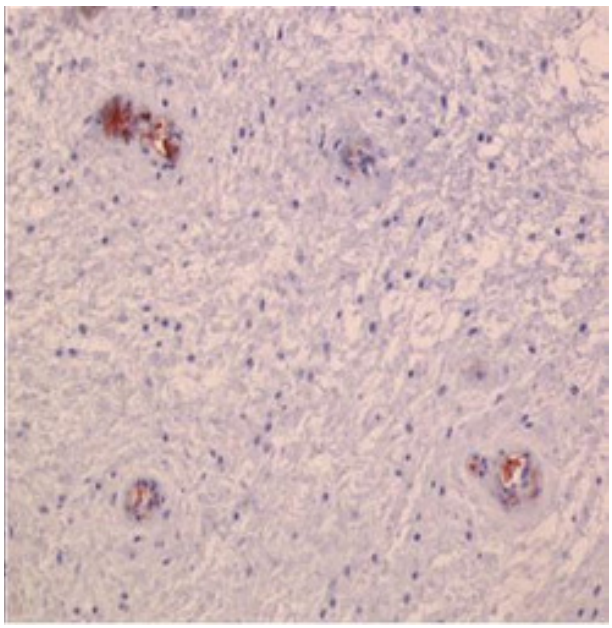

Figure 2. Vascular endothelial growth receptor (VEGFR) immunoreactivity were positive only in the endothelial cells of vessels (Immunohistochemistry x 200).

abscesses, vaginal cysts, lipomas, vulvar masses or abscesses, vaginal cysts or hernias,[4] as we assumed as the Bartholin duct cyst in this case. Differential diagnosis of AA is important because of its tendency for recurrence. The true size of the tumor was often significantly underestimated by physical examinations.[5] The treatment of choice is wide local excision which was performed in our case. The local recurrence rates in the range of 50-70% for AA in reports[1,6,7] and recurrence could occur after 10-15 years of primary excision. Close long-term follow up is important for these patients in order to asses for local recurrence. MRI scanning of the pelvis is usefull for determining the extent of disease, the suitability for surgery and following up patients with AA.[8] Experiences of radiologist is crucial for evaluation of AA on MRI scan.

Pathologically, AAs are nonencapsulated gelatinous tumors with infiltrative edge. Histologic examination shows hypocellular tumor with small ovoid, spindled or stellate cells that exhibit minimal, if any, nuclear atypia. Mitotic figures are not common. Numerous blood vessels are present and vary from thin-walled, capillary-like vessels to large vessels with thick muscular walls.[9] There is no specific immunohistochemical marker of AA yet. Tumor cells uniformly express vimentin and heterogeneously express muscle-specific actin and desmin. AA has no immunohistochemical reactivity for alpha-smoot muscle actin, myoglobin, cytokeratin, type IV collagen, CD 68 or S-100.[4] In this case, tumor showed immunohistochemical reactivity to muscle specific actin, Ki-67 and VEGFR as emphasized above.

Occuring predominantly in premenopausal woman, rapidly growing during pregnancy and immunoreactivity to ER and PR provide a rationale for the management of AA with GnRH agonists. GnRH agonists initially stimulate pituitary gland and increase production of follicle-stimulating hormone (FSH) and luteinising hormone (LH) than desensitize and decrease production of them with resultant hypoestrogenic state. Several authors reported drastic decrease in size of AA following GnRH agonist therapy.[8,10,11]

GnRH agonist therapy may help complete resection of large tumors because of shrinkage and provide avoidance to radical surgery when administered pre-operatively. It can also be an alternative if patient is reluctant to radical surgery or when surgery is not feasible. Post-operative administration may be usefull for the treatment of residuel tumors or recurrences. On the other hand, GnRH agonists also have some disadvantages such as menopausal symptoms and bone loss especially associated with long-term therapy.[12] Resistance to GnRH agonists is another worry. Duration of GnRH agonist therapy remains unclear and furthermore concern is that withdrawal of the medication may also result in re-growth of the tumor.

In conclusion, clinician should be aware of AA when face off a perineal tumor. If pre-operative diagnosis is possible MRI study necessary for the determining complete extent and location. Today, wide surgical excision seems to be treatment of choice if possible. Close long-term follow-up is crucial to detect recurrence. Even-though many questions waiting for the answer such as duration of therapy, side effects and long-term outcomes. We think that GnRH agonists will be more popular in near future for the treatment of AA.

REFERENCES

1. Steeper TA, 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;7:463-75.
2. Shahid N, Ahluwalia A, Sahasrabudhe N, Davenport A. Aggressive angiomyxoma of the vagina: A rare differential diagnosis of a lateral vaginal wall cyst. J Obstet Gynaecol 2005:25:622-3.
3. Blandamura S, Cruz J, Faure Vergara L, Machado Puerto I, Ninfo V. Aggressive angiomyxoma. Asecond case of metastasis with patient's death. Hum Pathol 2003;34: 1072-4.
4. Magtibay PM, Salmon Z, Keeney GL, Podratz KC. Aggressive angiomyxoma of the female pelvis and perineum: A case series. Int J Gynecol Cancer 2006;16:396-401.
5. Fetsch JF, Laskin WB, Lefkowitz M, Kindblom LG, Meis-Kindblom JM. Aggressive angiomyxoma: A clinicopathologic study of 29 female patients. Cancer 1996;78:79-90.
6. Begin LR, Clement PB, Kirk ME, Jothy S, McCaughey WT, Ferenczy A. Aggressive angiomyxoma of the pelvic soft parts: A clinicopathologic study of nine cases. Hum Pathol 1985;16:621-8.

7. Granter SR, Nucci MR, Fletcher CD. Aggressive angiomyxoma: Reappraisal of its relationship to angiomyfibroblastoma in a series of 16 cases. Histopathology 1997;30:3-10.
8. McCluggage WG, Jamieson T, Dobbs SP, Grey A. Aggressive angiomyxoma of the vulva: Dramatic response to gonadotropin-releasing hormone agonist therapy. Gynecol Oncol 2006;100:623-5.
9. McCluggage WG. A review and update of morphologically bland vulvovaginal mesenchymal lesions. Int J Gynecol Pathol 2005;24:26-38.
10. Fine BA, Munoz AK, Litz CE, Gershenson DM. Primary medical management of recurrent aggressive angiomyxoma of the vulva with a gonadotropin-releasing hormone agonist. Gynecol Oncol 2001;81:120-2.
11. Shinohara N, Nonomura K, Ishikawa S, Seki H, Koyanagi T. Medical management of recurrent aggressive angiomyxoma with gonadotropin-releasing hormone agonist. Int J Urol 2004; 11:432-5.
12. Lethaby A, Vollenhoven B, Sowter M. Efficacy of pre-operative gonadotropin hormone releasing analogues for women with uterine fibroids undergoing hysterectomy or myomectomy: A systematic review. BJOG 2002;109: 1097-108.