Smooth Muscle Tumors of the Uterus

UTERUSUN DÜZ KAS TÜMÖRLERİ

Hüsnü GÖKASLAN*, Tanju PEKIN**, Emine AY***,Zehra Neşe KAVAK****, Funda EREN*****

* Assis.Prof., Dept. of Obstetrics and Gynecology, Medical School of Marmara University
** Assoc.Prof., Dept. Dept. of Obstetrics and Gynecology, Medical School of Marmara University
*** Resident, Dept. of Obstetrics and Gynecology, Medical School of Marmara University
**** Prof., Dept. of Obstetrics and Gynecology, Medical School of Marmara University
*****Assis.Prof., Dept. of Pathology, Medical School of Marmara University, Istanbul, TURKEY

Summary

Objective: Our aim was to find out the incidence of the smooth muscles of the uterus among the patients admitted to the hospital with uterine mass or the presumed diagnosis of leiomyoma. To elucidate the reasons for inaccurate clinical or pathologic diagnosis which hinders to offer the patients a standard and optimum treatment in smooth muscle tumors of the uterus.

Methods: The clinical files and the medical records of 653 women who had admitted to our hospital between January 1989 and May 2003 with uterine leiomyoma or uterine mass followed by the operation with this preoperative diagnosis were reviewed. These records were compared with the final pathological diagnosis reviewing the registeries of pathology department.

Results: Among 653 women operated, 2 cellular myoma on the benign side of the spectrum and 3 mixed müllerian tumor and 4 leiomyosarcoma on the malignant side were diagnosed. One was endometrial stromal sarcoma. 490 leiomyoma could be matched with the reports recorded by the pathology department.

Conclusions: The incidence of malignant smooth muscle tumors in hysterectomies done in a university clinic is very rare (1.38%).The incidence, clinical presentation, diagnosis and treatment of uterine smooth muscle tumors are all controversial and so investigational. These data also suggested that the incidence was also infrequent among the rapidly growing masses of the uterus.

Key Words: Uterus, Smooth Muscle, Tumor

T Klin J Gynecol Obst 2004, 14:27-31

Özet

Amaç: Amacımız, hastaneye uterus kitlesi veya leiomyom olduğu düşünülerek yatırılan hastalar arasında uterusun düz kas tümörlerinin sıklığını bulmaktır. Ayrıca, uterusun düz kas tümörleri olan hastaların standard ve optimum bir şekilde tedavi edilmelerini engelleyen klinik ve patolojik kesin tanı koyamama nedenlerini ortaya çıkarmaktır.

Yöntemler: Ocak 1989 ve Mayıs 2003 tarihleri arasında hastanemize uterus leiomyomu veya uterus kitlesi nedeniyle yatırılarak ameliyat edilen 653 kadının hastanın klinik ve tıbbi kayıtları gözden geçirildi. Bu kayıtlar, patoloji bölümündeki kayıtlar incelenerek kesin patolojik tanılarla karşılaştırıldı.

Bulgular: Ameliyat edilen 653 hasta arasında yelpazenin selim tarafında yer alan 2 selüler myom ve yelpazenin habis tarafında yer alan 3 miks müllerian tümör ile 4 leiomyosarkom tanısı konuldu. Bir olgu ise endometrial stromal sarkomdu. Patoloji bölümünde kayıt edilen raporlarla karşılaştırıldığında 490 leiomyom eşleştirilebildi.

Sonuçlar: Bir üniversite kliniğinde yapılan histerektomiler arasında habis düz kas tümörleri sıklığı son derece azdır (%1.38). Uterus düz kas tümörlerinin sıklığı, klinik belirtileri, tanı ve tedavisi bütün olarak tartışmalıdır ve dolayısıyla araştırma konusudur. Bu veriler aynı zamanda uterusta hızlı büyüyen kitleler arasında da sıklığın az olduğunu göstermektedir.

Anahtar Kelimeler: Uterus, Düz kas, Tümör

T Klin Jinekol Obst 2004, 14:27-31

Smooth muscle tumors of the uterus form a wide spectrum of diseases from benign, leiomyoma, to the most malignant lesion, leiomyosarcoma. The limits between the disease entities are vaguely distinguished and the criteria for the diagnosis either clinically or even pathologically are not very well established. Therefore, the smooth muscle tumors of the uterus pose a great difficulty in the clinical practice.

The most malignant form of the lesions, sarcomas of the uterus, is rare. It comprises only 3-5% of all uterine tumors. The annual incidence ranges between 1.2 and 2.3 cases per 100 000 women. They are more common in black women

than in white women. The mean age of the cases with leiomyosarcoma is the mid 50's. The most common symptom is the rapidly enlarging uterus. Vaginal bleeding is another symptom. Preoperative diagnosis is very hard due to the difficulty to take biopsy from the lesion before the surgery. Advanced disease carries an extremely poor prognosis being an appreciable number of these patients in stage I disease (1).

We investigated the incidence of the smooth muscle tumors of the uterus in our university clinic to obtain an information about the frequency of the malignant forms in a referral hospital. Another aim was to elucidate the incidence of the malignant forms among the patients admitted to the clinic with the primary symptom of rapidly enlarging mass of the uterus.

Methods

All the patients who have admitted to the Obstetrics and Gynecology Clinics of the School of Medicine of University of Marmara and undergone surgery with the preoperative diagnosis of uterine myoma between December 1989 and May 2003 were included in the study. Age and clinical findings were already recorded in the files. The records of all the patients for physical and pelvic examination with ultrasounds were also reviewed. These clinical records were matched with the registries of the Pathology Department of our university to check the incidence among pathology specimens. The frequency of the presenting symptoms and the incidence of the malignant smooth muscle tumors were given in percentages.

Results

The mean age of 653 patients included in the study was 47 (32-68). One hundred sixty (30%) patients were postmenopausal. The most frequent symptom was menometrorhagia. Pelvic pain and discomfort and presence of a mass in the lower abdomen were other symptoms and signs. The lesions of some patients were discovered during routine pelvic examination (Table 1).

In 593 patients, abdominal hysterectomy was the preferred method of treatment while vaginal hysterectomy was done in 60 patients. According to the pathology results, 4 leiomyosarcoma (0.61%), 3 mixed mesodermal tumor and 2 cellular myoma were diagnosed. One was found as endometrial stromal sarcoma and it was not included to the evaluation since it was not arising from the smooth muscle of the uterus. There was no STUMP (smooth muscle tumor with low malignant potential) diagnosed in the group. In this group, the incidence of leiomyosarcoma was 0.61%. All of the leiomyosarcoma cases were postmenopausal while only the patient with endometrial stromal sarcoma was premenopausal at the age of 39.

Table 1. Distribution of patients according to symptoms

SYMPTOMS	NO. OF PATIENTS (n=653)	%
MENOMETRORHAGIA	359	55
PELVIC PAIN	131	20
RAPIDLY GROWING MASS	91	14
ASYMPTOMATIC	72	11

Two of the leiomyosarcomas were diagnosed by frozen section during the surgery while one was diagnosed following simple hysterectomy. One case was diagnosed by sharp and deep curettage before the definitive surgery as low- grade sarcoma from the material removed. The frozen section diagnosis was also the same and the patient was treated with only TAH & BSO and cytologic washings which was negative for malignancy. However, the actual diagnosis after the surgery was reported as high-grade leiomyosarcoma. The mixed mesodermal tumors were diagnosed by frozen section while endometrial stromal sarcoma was discovered after the surgery.

The most common symptom was rapidly growing mass in leiomyosarcoma cases while the others declared menometrorhagia. The patients whose malignancies diagnosed during surgery had undergone total abdominal hysterectomy with bilateral salpingo-oophorectomy and bilateral pelvic lymph node dissection.

In the registries of pathology, 490 leiomyoma could be found but there were only two leiomyosarcoma recorded. Instead, two cellular myoma were pathologically diagnosed. Three cases of mixed mesodermal tumor were verified by the records of pathology.

Discussion

The frequency of the smooth muscle tumors of the uterus in our hospital which is a referral center for a very densely populated area is relatively rare. The total incidence of smooth muscle tumors in this series is 1.4%. The incidence of leiomyosarcoma which is the most malignant form of smooth muscle tumors among hysterectomies performed for presumed uterine leiomyoma is 0.61%. Its incidence in uterine leiomyomas is estimated to be between 0.13 to 0.29%. However, Leibsohn et al. claimed that the exact incidence of leiomyosarcoma uteri removed with a preoperative diagnosis of benign uterine leiomyoma had not been previously reported. In their study, after the hysterectomy in the 1429 patients with presumed benign disease, the histologic diagnosis of leiomyosarcoma was 0.49%. However, it was demonstrated that the presence of leiomyosarcoma in the hysterectomy specimens increased steadily from the fourth to the seventh decades of age and in the sixth and seventh decades it was reported as 1.4% and 1.7% respectively (2). In our series, the histopathologic diagnosis of leiomyosarcoma among hysterectomy specimens presumed uterine leiomyoma is 0.40%. Therefore, leiomyosarcoma incidence in our hospital can be considered relatively low according to this study. This may be partly explained with the difficulty of the diagnosis before the surgery, so the patient usually can not be directed to a cancer center as in other cancers which the preoperative diagnosis was possible. Most of these patients generally undergo a regular operation with a presumed diagnosis of uterine myoma in general hospitals.

All of our leiomyosarcoma patients were postmenopausal and the most common presenting symptom was rapidly growing mass. Leibsohn et al. in their series demonstrated that between the ages of 40 and 60 years, 1% of women presumed uterine leiomyomas producing symptoms that necessitated hysterectomy had had leiomyosarcoma postoperatively (2). On the contrary, Parker et al. found that the total incidence of uterine sarcoma (leiomyosarcoma, endometrial stromal sarcoma and mixed mesodermal tumor) among patients operated on for leiomyoma was extremely low. Moreover, the incidence of sarcoma among patients having surgery for “rapidly growing” leiomyoma (0.27%) or among those who met published criteria for rapid growth (0%) did not substantiate the increased risk of sarcoma in these women (3). Silverberg et al. found that the major symptom in 34 patients with leiomyosarcoma was abnormal vaginal bleeding but none of these had rapidly growing mass (4). Liao et al reported that the clinical symptom of the uterine sarcoma was nonspecific (mostly vaginal bleeding) and the prognosis was poor. The patients with leiomyosarcoma were relatively younger and had better prognosis but the rate of preoperative diagnosis was low (5). In contradiction to this, Barker et al. reported that out of 21 leiomyomas which were rapidly growing 10 were leiomyosarcoma (6). Schwartz et al. found 4 out of 21 leiomyosarcoma operated had a rapidly growing mass as a presenting symptom (7). For rapid growing, the criteria has been set forth by Butram and Reiter was the growing of the uterus to the size of more than six weeks of gestation in a year (8). Therefore, a mass increasing its size in a short interval in a postmenopausal woman should always raise the suspicion of malignant uterine smooth muscle tumor.

The diagnosis during surgery by frozen section is usually inconclusive. The final diagnosis is always liable to be changed after the permanent sections examined as were in our two cases with the diagnosis of cellular myoma. These were reported as leiomyosarcoma by frozen section probably due to over-diagnosis.

Four hundred ninety cases of leiomyoma could be extracted from the pathology files which is remarkably less than the numbers of clinical files. The difference is probably related with the specimens evaluated in other pathology laborato-

ries in the early years either by the patient or physician preference. An alternative explanation might be that the presumed diagnosis of leiomyoma was discovered during surgery as totally different situation such as ovarian or adnexial mass.

The final pathological diagnosis may not sometimes be straigthforward and the limits between the lesions from benign to malignant are not clearly defined. Nowadays, mitotic count and the rate of necrosis are the most reliable criteria for differentiation. Recently, the expression of some oncogenes has gained importance for the differentiation between leiomyoma and leiomyosarcoma. Having demonstrated first that p 53 mutations were very common in leiomyosarcoma, De Vos et al. claimed that one of the most important differences between leiomyoma and leiomyosarcoma was acquiring p 53 mutation (9,10). Wang et al. also suggested that p 53 and desmin expression could be utilized as an additional criteria for diagnosis (11). It was shown that the abnormal expression of ovarian steroid receptors, p 53 and Ki-67 were associated frequently with leiomyosarcoma (12,13). Mittal et al. proposed that Ki-67, p 53 and progesterone could be useful in differentiating STUMP (Smooth muscle tumor with unknown malignant potential) and cellular myoma (14). Amant et al. have recently published that pTEN mutations involved into the development of carcinosarcomas (15).

The treatment is not very well established for uterine sarcomas. The gold standard for the surgical procedure of uterine sarcoma in case of tumor limited to the uterine corpus is hysterectomy & bilateral salpingo-oophorectomy. Omentectomy and lymphadenectomy should be performed in carcinosarcoma. In other histologic subtypes, lymphadenectomy should be performed only in patients with enlarged nodes discovered at the time of surgical procedure (16). Fait et al. recommended abdominal hysterectomy with or without bilateral salpingo-oophorectomy (17). However, Ayhan et al. in Hacettepe hospital experience showed the existence of a substantial risk of lymph node metastasis, so advised a complete surgical staging in the management of uterine sarcomas, particularly in MMMT type (18). Friedrich et al. emphasized that the primary treatment should have consisted of an operation as radical as possible (19). Hill et al. reported the importance of surgical resection for leiomyosarcoma patients and the value of other treatment modalities was largely limited to surgical failures (20).

In conclusion, the incidence, clinical presentation, diagnosis and treatment of uterine smooth muscle tumors are all controversial and so investigational. Since the only effective mean of therapy is the optimum surgery, the diagnosis is the most important issue. We believe that the benefits of treatment would increase accordingly in this awful disease as the precision in diagnosis improved.

REFERENCES

1. Disaia PJ, Creasman WT. In sarcoma of the uterus. Clinical Gynecologic Oncology. Sixth edition. Mosby Inc. 2002: 173-5.
2. Leibsohn S, d'Ablaing G, Mishell DR Jr, Schlaerth JB. Leiomyosarcoma in a series of hysterectomies performed for presumed uterine leiomyomas. Am J Obstet Gynecol 1990 Apr; 162(4): 968-74.
3. Parker WH, Fu YS, Berek JS. Uterine sarcoma in patients operated on for presumed leiomyoma and rapidly growing leiomyoma. Obstet Gynecol 1994 Mar; 83(3): 414-8.
4. Silverberg S. Leiomyosarcoma of the uterus. A clinicopathologic study. Obstet Gynecol 1979; 38: 613-28.
5. Liao Q, Wan J, Han J. Clinical and pathological analysis on 106 cases with uterine sarcoma. Zhonghua Fu Chan Ke Za Zhi 2001 Feb; 36(2):104-7.
6. Barker J, Smith E, Spazk C, Hinshaw W, Clarke-Pearson D, Creasman WT. Leiomyosarcoma of the uterus. Clinicopathologic study of 21 cases. Gynecol Oncol 1985; 21: 220-7.
7. Schwartz L, Diamond M, Schwartz P. Leiomyosarcomas: Clinical presentation. Am J Obstet Gynecol 1993; 168: 180-3.
8. Buttram V, Reiter R. Uterine leiomyomata. Etiology, symptomatology and management. Fertil Steril 1981; 36: 433-5.
9. de Vos S, Wilczynski SP, Fleishhacker M, Koeffler P. p 53 alterations in uterine leiomyosarcomas versus leiomyomas. Gynecol Oncol 1994 Aug; 54(2): 205-8.
10. Nordal RR, Kristensen GB, Stenwig AE, Trope CG, Nesland JM. Immunohistochemical analysis of p 53 protein in uterine sarcomas. Gynecol Oncol 1998 Jul; 70(1): 45-8.
11. Wang M, Xu Y, Zhang T. Smooth muscle neoplasms of the uterus- a 51 cases study. Zhonghua Bing Li Xue Za Zhi 1996 Oct; 25(5): 263-5.
12. Zhai YL, Kobayashi Y, Mori A, Orii A, Nikaido T, Konishi I, Fujii S. Expression of steroid receptors, Ki – 67, and p 53 in uterine leiomyosarcomas. Int J Gynecol Pathol 1999 Jan; 18(1): 20-8.

13. Bodner K, Bodner-Adler B, Kimberger O, Czerwenka K, Leodolter S, Mayerhofer K. Anticancer Res 2003 Jan – Feb; 23(1B): 729-32.
14. Mittal K, Demopoulos RI. MIB-1(Ki-67), p 53, estrogen receptor and progesterone receptor expression in uterine smooth muscle tumors. Hum Pathol 2001 Sep; 32(9): 984-7.
15. Amant F, dela Rey M, Dorfling CM, van der Walt L, Dreyer G, Dreyer L, Vergote I, Lindeque BG, Van Rensburg EJ. pTEN mutations in uterine sarcomas. Gynecol Oncol 2002 Apr; 85(1): 165-9.
16. Morice P, Rodrigues A, Pautier P, Rey A, Camatte S, Atallah D, Pomel C, Lhomme C, Haie-Meder C, Duvillard P, Castaigne D. Surgery for uterine sarcoma: review of the literature and recommendations for the standard surgical procedure. Gynecol Obstet Fertil 2003 Feb; 31(2): 147-50.
17. Fait T, Freitag P, Zivny J. Sarcoma of the uterus. Ceska Gynekol 1998 Aug; 63(4):318-21.
18. Ayhan A, Tuncer TS, Tanir M, Yüce K, Ayhan A. Uterine sarcoma: the Hacettepe hospital experience of 88 consecutive patients. Eur J Gyneacol Oncol 1997; 18(2):146-8.
19. Friedrich M, Villena-Heinsen C, Mink D, Hell K, Schmidt W. Leiomyosarcomas of the female genital tract: a clinical and histopathological study. Eur J Gyneacol Oncol 1998; 19(5): 470-5.
20. Hill MA, Mera R, Levine EA. Leiomyosarcoma: a 45-year review at Charity Hospital, New Orleans. Am Surg 1998 Jan; 64(1): 53-60.

Geliş Tarihi: 28.08.2003

Yazışma Adresi: Dr.Hüsnü GÖKASLAN
Marmara Üniversitesi Tıp Fakültesi
Kadın Hastalıkları ve Doğum AD
İSTANBUL
husnugokaslan@ yahoo.com