Uterine sarcoma: An unusual but high lethal disease of gynecological malignancies

Wen-Ling Lee[a,b], I-San Chan[c,d], Peng-Hui Wang[c,d,e,f,*]

[a]Department of Medicine, Cheng-Hsin General Hospital, Taipei, Taiwan, ROC; [b]Department of Nursing, Oriental Institute of Technology, New Taipei City, Taiwan, ROC; [c]Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [d]Department of Obstetrics and Gynecology, National Yang-Ming University, Taipei, Taiwan, ROC; [e]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, ROC; [f]Department of Medical Research, China Medical University Hospital, Taichung, Taiwan, ROC

Uterine sarcoma, a high lethal gynecologic malignancy, due to its rarity, heterogeneous characteristics, unknown etiology, and highly divergent genetic aberration, is still a biggest challenge in the current cancer treatment.[1–3] There is a lack of consensus on risk factors for occurrence and predictive poor outcomes as well as optimal therapeutic choices. Therefore, we are happy to introduce an article published in the January issue of the *Journal of the Chinese Medical Association*, on the identification of the predictive factors to determine the prognosis of the uterine sarcoma and effectiveness therapy of various treatment modalities.[4] The authors retrospectively evaluated 42 patients (23 uterine leiomyosarcoma [LMS], 12 endometrial stromal sarcoma [ESS], and 7 malignant mixed Mullerian tumor [MMMT]) and found the overall survival rate was 57.1%, and elder age, MMMT histology, > 20 mitotic counts/10 high power field [HPF], and ≥ 50% necrosis rate of the tumor were associated with worst prognosis. By contrast, different treatment strategies seemed to be not associated with prognosis in patients with uterine sarcoma. We congratulated the success of the publication. However, this study shows some limitations and is worthy of discussion.

At first, uterine sarcoma tumor types according to the World Health Organization classification include LMS, ESS, and undifferentiated sarcoma.[1–3] MMMT (carcinosarcoma) is no longer considered as sarcoma due to their different spreading pattern as by a dedifferentiated or metaplastic form of endometrial cancer, in which the sarcoma components retain epithelial features (e.g., conversion theory supported by many molecular studies with similar chromosomal aberrations, cytogenetic aspects, concordant loss of heterozygosity, identical *p53* and *K-ras* mutations, and matching X-inactivation patterns in both carcinoma and sarcoma components).[3] In addition, complete staging surgery, which includes lymphadenectomy, is not recommended in the management of an early stage uterine sarcoma, especially LMS; however, it may be much more acceptable in the management of the similar stage of uterine cancer (endometrial cancer),[5–8] because the standard treatment for early uterine LMS is only hysterectomy with/without bilateral salpingo-oophorectomy.[3] However, for MMMT, complete staging surgery is much more important, since there are high percentages of MMMT with lymph node metastases.[3] Therefore, it is not appropriate to include MMMT as uterine sarcoma for analysis.

Second, the data of histo-pathological parameters provided by Dr. Momtahan's study seemed to be very much confusing. Conventional leiomyosarcoma is diagnosed when at least 2 of 3 features are present: moderate to severe cytologic atypia, mitotic index greater than or equal to 10 mitotic figures per 10 HPFs, and tumor cell necrosis.[9] Therefore, it is very strange to find that there were 34.8% of LMS (n = 8) with mitotic count <10; in addition 13% (n = 3) without tumor necrosis. Furthermore, histopathological parameters in ESS also need our attention. For ESS, mitotic activity is strikingly apparent and often >10 per 10 high-power fields, and necrosis is usually present, but Dr. Momtahan's study showed that mitotic index seemed to be usually lower than those published everywhere, since near three-fifths of ESS has mitotic index <10, and half of cases did not have tumor necrosis.[4]

Third, the conclusion of the authors seemed to be much more confusing to the audience. As shown by authors, MMMT was the most aggressive tumor with the shortest survival time. However, we found 100% of patients with MMMT with a 2-year survival compared with 83.3% of patients with ESS and 69.6% of LMS. In addition, the authors wrote postoperative adjuvant radiotherapy resulted in a better survival, compared with chemotherapy alone or combination with radiotherapy, and concluded adjuvant radiotherapy resulted in a better survival, compared with surgery alone in early stage. In fact, the authors did not provide how many patients were treated with postoperative adjuvant therapy. In addition, is it true that this recommendation can fit all histological types of uterine sarcomas? There is no agreement about postoperative adjuvant therapy for uterine sarcoma, regardless of whether early or advanced stage the uterine sarcoma is. In fact, the National Comprehensive Cancer Network Guidelines suggested that stage I low-grade ESS did not need any adjuvant therapy.[10] For stage I high-grade ESS, observation or considering chemotherapy (category 2B) was recommended.[10] For uterine LMS, a guideline of the German Society of Gynecology and Obstetrics (DGGG) and the Austrian Society of Gynecology and Obstetrics (OEGGG) suggests radiotherapy should not be carried out after complete resection of a stage I/II uterine LMS, and adjuvant chemotherapy should not be generally administered, and it may be administered in individual cases after carefully weighing up the potential drawbacks/benefits with the patient depending on the presence of certain risk factors, such as higher stage tumor.[11]

*Address correspondence. Dr. Peng-Hui Wang, Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, 201, Section 2, Shi-Pai Road, Taipei 112, Taiwan, ROC. E-mail addresses: phwang@vghtpe.gov.tw; pongpongwang@gmail.com (P.-H. Wang).

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

Journal of Chinese Medical Association. (2020) 83: 213-214.

Received December 7, 2019; accepted December 7, 2019.

doi: 10.1097/JCMA.0000000000000242.

Taken together, although we published Dr. Momtahan' study addressing the prognosis and treatment strategy of patients with uterine sarcomas, due to presence of many aforementioned potential bias, the interpretation of the authors' data and results, as well as conclusion should be much more concerned. Due to rarity and extremely little experience in the management of women with uterine sarcoma,[12–15] we welcome more and more studies to explore this topic.

ACKNOWLEDGMENTS

This article was supported by grants from the Ministry of Science and Technology, Executive Yuan, Taiwan (MOST 106-2314-B-075-061-MY3), and Taipei Veterans General Hospital (V108C-085). The authors appreciate the support from Female Cancer Foundation, Taipei, Taiwan.

REFERENCES

1. Yen MS, Chen JR, Wang PH, Wen KC, Chen YJ, Ng HT; Taiwan Association of Gynecology Systematic Review Group. Uterine sarcoma part III-targeted therapy: the taiwan association of gynecology (TAG) systematic review. *Taiwan J Obstet Gynecol* 2016;**55**:625–34.
2. Horng HC, Wen KC, Wang PH, Chen YJ, Yen MS, Ng HT; Taiwan Association of Gynecology Systematic Review Group. Uterine sarcoma part II-uterine endometrial stromal sarcoma: the TAG systematic review. *Taiwan J Obstet Gynecol* 2016;**55**:472–9.
3. Wen KC, Horng HC, Wang PH, Chen YJ, Yen MS, Ng HT; Taiwan Association of Gynecology Systematic Review Group. Uterine sarcoma part I-uterine leiomyosarcoma: the topic advisory group systematic review. *Taiwan J Obstet Gynecol* 2016;**55**:463–71.
4. Momtahan M, Emami F, Aslani FS, Akbarzadeh-Jahromi M. Evaluation of treatment results and prognostic factors of uterine sarcoma: a single-center experience. *J Chin Med Assoc* 2020;**83**:84–8.
5. Turan T, Kimyon Comert G, Turkmen O, Ureyen I, Fadiloglu E, Karalok A, et al. Therapeutic value of lymphadenectomy and adjuvant radiotherapy in uterine corpus confined endometrioid-type cancer. *J Chin Med Assoc* 2018;**81**:714–23.
6. Li YT, Horng HC, Wang PH. The role of complete staging surgery for pure endometrioid-type endometrial cancer. *J Chin Med Assoc* 2018;**81**:663–4.
7. Shih YC, Lin IC, Wang PH. Hysteroscopic resection for women with FIGO IA grade 1 endometrioid-type endometrial cancer. *Taiwan J Obstet Gynecol* 2019;**58**:304–5.
8. Deura I, Shimada M, Azuma Y, Komatsu H, Nagira K, Sawada M, et al. Comparison of laparoscopic surgery and conventional laparotomy for surgical staging of patients with presumed low-risk endometrial cancer: the current state of japan. *Taiwan J Obstet Gynecol* 2019;**58**:99–104.
9. Devereaux KA, Schoolmeester JK. Smooth muscle tumors of the female genital tract. *Surg Pathol Clin* 2019;**12**:397–455.
10. Koh WJ, Greer BE, Abu-Rustum NR, Apte SM, Campos SM, Cho KR, et al.; National Comprehensive Cancer Network. Uterine sarcoma, version 1.2016: featured updates to the NCCN guidelines. *J Natl Compr Canc Netw* 2015;**13**:1321–31.
11. Denschlag D, Ackermann S, Battista MJ, Cremer W, Egerer G, Follmann M, et al. Sarcoma of the uterus. Guideline of the DGGG and OEGGG (S2K level, AWMF register number 015/074, February 2019). *Geburtshilfe Frauenheilkd* 2019;**79**:1043–60.
12. Comert GK, Turkmen O, Kar I, Yucel O, Kilic C, Boran N, et al. Hormone therapy following surgery in low-grade endometrial stromal sarcoma: is it related to a decrease in recurrence rate? *J Chin Med Assoc* 2019;**82**:385–9.
13. Cheng CH, Su B, Ding DC. Rare case of undifferentiated uterine sarcoma with neuroectodermal differentiation and osteoclast-like giant cells. *Taiwan J Obstet Gynecol* 2018;**57**:442–6.
14. Lee WL, Lee FK, Wang PH. Hormone therapy and low-grade endometrial stromal sarcoma. *J Chin Med Assoc* 2019;**82**:445–6.
15. Togami S, Kawamura T, Fukuda M, Yanazume S, Kamio M, Kobayashi H. Clinical management of uterine cervical Mullerian adenosarcoma: a clinicopathological study of six cases and review of the literature. *Taiwan J Obstet Gynecol* 2018;**57**:479–82.