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IMPORTANCE OF EARLY DIAGNOSIS OF SARCOMA

Uterine sarcomas (US) are a clinically and histologically heterogeneous group of very rare tumors of mesenchymal origin. They represent approximately 4% of malignant tumors of the uterus and <1% of those of the female genital tract [1]. They are characterized by an aggressive behavior and a poor prognosis. However, prognosis mostly depends on its histological variant. Effective preoperative diagnostic procedures for these sarcomas have not been well defined yet. However, molecular tests have recently become a very common approach in the diagnosis and prognosis of US [1].

The diagnosis of US is always a challenge. For uterine tumors not suspected to be malignant pre- or intraoperatively, their fragmentation can lead to pelvic–abdominal tumoral dissemination, which increases the rate of disease recurrence and shortens the progression-free survival. It is important to highlight the fact that an occult US is diagnosed in 1 out of 1,124 hysterectomies, when the indication for this procedure is a benign gynecological disorder, heavy bleeding or myomas [2]. It is to note that the most common US is the leiomyosarcoma (LMS) (1-2%), that has its “benign equivalent” - the leiomyoma, which is the most common benign tumor in women. Sometimes it is quite difficult to differentiate, either clinically (through complementary tests) or histologically, a benign tumor from a malignant one. For this precise reason it is crucial to make an accurate diagnosis which is a key factor for a focused clinical approach and effective treatment. Moreover, a correct diagnosis helps to avoid additional and often unnecessary (or inappropriate) tests which not only increase the costs of cure but also delay the initiation of treatment.

Improving the detection rate of patients at risk of sarcoma before they undergo surgery is of utmost importance, as it enables to plan the type of surgery as well as helps to avoid iatrogenic sterility or early / premature menopause. Considering this, intraoperative frozen section biopsy may be useful to perform a differential

diagnosis of an atypical uterine mesenchymal tumor, leaving the histological subtyping for later.

In case of patients with unfulfilled reproductive desire and uncertain diagnosis, we could opt for a conservative treatment and avoid iatrogenic sterility. Furthermore, even in cases of high suspicion or even confirmation of malignancy, fertility-preserving surgery could be considered in selected patients with great reproductive desire as long as they are cases with FIGO stage IA of low-grade endometrial stromal sarcoma (LG-ESS) and adenosarcoma without sarcomatous overgrowth.

US in premenopausal women is another clinical challenge because ovariectomy might be the treatment scenario. Fortunately, ovarian metastasis of a US is <5% [3]. In any case, ovary-sparing procedures should only be considered in young premenopausal women, depending on tumor hormonal receptor status, and extensive counselling is advised [4]. There is no evidence to preserve the ovaries in young patients with high-grade endometrial stromal sarcoma (HG-ESS), undifferentiated sarcoma (UUS) and adenosarcoma. However, bilateral oophorectomy can be avoided in premenopausal women with macroscopically normal ovaries and LMS and LG-ESS in stage I, hence excluding or significantly reducing the negative impact that surgical menopause would have on quality of life.

The treatment approach towards a US will be conditioned by the accurate diagnosis. When the diagnosis is preoperative, it is recommended that the hysterectomy be performed through a laparotomic method to avoid fragmentation of the surgical specimen, since it is the most important iatrogenic prognostic factor. The laparoscopic or robotic method should only be used when it is possible to carry out a complete removal of the uterus without the need of its fragmentation. Fragmentation, in the case of an uncertain diagnosis, will negatively affect the prognosis of the disease. For this reason, the use of electromorcellators should be limited only to selected cases and specific information should be provided regarding the use of containment systems that limit the spread of tumor cells. Fragmentation of the intracorporeal sample, being considered a strong independent prognostic factor,

significantly decreases the likelihood of healing ^[5]. Thus, having certainty in the diagnosis prior to surgical treatment (whenever possible) is crucial for the possible success in the healing process. In case of incidental diagnosis, e.g. after myomectomy or hysterectomy, it is advisable to perform an imaging study to exclude metastatic disease, since more than 30% of these patients will present metastatic changes in the liver, lungs or upper abdomen. Lymphadenectomy is often not part of the surgical strategy ^[6], and unnecessary if pre-surgical diagnosis is correctly performed.

Regarding adjuvant treatment, the benefit of chemotherapy, as an additional treatment of sarcomas, is limited. For this reason, chemotherapy is only recommended in high risk patients, suffering from LMS, HG-ESS and UUS where the disease is confined to the uterus or when the disease is advanced but the uterus has been completely resected ^[7].

Frequently, in cases when diagnosis is imprecise, we are unable to give an adequate prognosis and/or follow-up to patients. For instance, in cases of HG-ESS, extrauterine extension is common at the time of diagnosis. Indeed, more than 50% of patients will present in advanced stages and have a tendency toward early recurrence (<1 year) which may affect lymph nodes, bones, peritoneum, lung, intestine and skin. Cases like these, will limit both the prognosis and the information one can provide to the patient. On the other hand, while HG-ESS are generally highly aggressive, LG-ESS has a benign behavior. Another example is the smooth muscle tumor of uncertain malignant potential (STUMP) which has an uncertain malignant potential. Currently, the pathologic diagnostic criteria for STUMP are not unified and a consensus is needed in order to differentiate STUMP from other smooth muscle tumors - which appears to be very challenging.

In conclusion, confirmation of a primary malignant uterine mesenchymal neoplasia and its histopathological type through the evaluation by an expert team of gynecological pathologists is essential to establish both the definitive diagnosis and its most appropriate treatment and prognosis. When we face US patients, we must have in mind 3 questions:

Could US have been suspected/diagnosed earlier?

Could the surgical procedure have been performed better?

Last but not least, what can we change?

All these questions can only be answered when we have a prior histological diagnosis.

References

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