International Journal of Academic Health and Medical Research (IJAHMR)
ISSN: 2643-9824
Vol. 5 Issue 2, February - 2021, Pages: 79-82

A Rare Tumor Distinct From Uterine Cancer: Carcinosarcoma, About Ten Cases And Review Of The Literature

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Abstract: *Uterine carcinosarcomas or malignant mixed Müllerian tumors are rare and aggressive tumors with a poor prognosis, and represent less than 5% of all malignant tumors of the uterine body. They are more common in black patients. The aim of this study is to specify the epidemiological characteristics of our patients, to identify the diagnostic, clinical as well as radiological problem, and to discuss the therapeutic management of this type of rare tumors, through the ten cases collected in the service. of gynecology and obstetrics 1 of the CHU Hassan 2 in Fez.*

Keywords : Carcinosarcomas ,uterine, body, radiological

Introduction

Uterine carcinosarcomas or mixed mullerian malignant tumors are rare and aggressive tumors in postmenopausal women, often discovered following postmenopausal metrorrhagia associated in some cases with pelvic pain. They represent less than 5% of malignant uterine tumors.

They are characterized by a double epithelial and mesenchymal tumor contingent, which can be homologous (Leiomyosarcoma, endometrial stromal sarcoma, or fibrosarcoma) or heterologous (chondrosarcoma, liposarcoma, rhabdomyosarcoma). The origin of CS is currently being debated with two main hypotheses (1). On the one hand, that of a totipotent stem cell that differentiates in the epithelial and connective sense, the most probable hypothesis, and on the other hand, the coexistence of two different and independent cellular contingents. They were long considered to be uterine sarcomas, whereas their prognosis depends mainly on their carcinomatous component.

The preoperative diagnosis especially on the endometrial biopsy guided by HSC, sometimes the biopsy curettage of the endometrium or the biopsy of externalized lesions is essential in order to optimize the treatment which is essentially surgical, namely a total hysterectomy with bilateral adnexectomy and omentectomy associated with pelvic, iliac and lumboortic lymph node dissection.

The prognosis is unfavorable compared to adenocarcinoma and sarcoma, even at an early stage with an overall 5-year survival rate not exceeding 45%. The main prognostic factor is tumor extension at diagnosis.

The high rate of local and distant relapses after surgery implies defining an effective complementary care: RTH, chemotherapy Prospective studies are difficult to conduct, long and rarely randomized, small in number due to the rarity of the pathology.

Our work is a descriptive, single-center, retrospective study based on 10 cases of patients with uterine carcinosarcoma followed by the obstetric gynecology department 1 of the Hassan2 University Hospital in Fez from 2013 to 2018.

METHODS

The aim of this study is to review our experience with uterine carcinosarcomas, analyze their clinical and histopathological characteristics, discuss the diagnostic and therapeutic difficulties associated with them, assess their prognosis and compare our series with data from the literature.

Our study relates to 10 cases of uterine carcinosarcomas collected in the department of gynecology and obstetrics I at CHU Hassan II in Fez. It is a retrospective study that spans a period of 6 years from January 01, 2013 to December 31, 2018, all the patients had a mammogram and a breast ultrasound, with an extension assessment: chest x-ray, abdominal ultrasound, determination of CA15.3, the histopathological diagnosis was established by biopsy or by extemporaneous examination, the immunohistochemical study was carried out

Result:

The Gyneco-Obstetrics I department of CHU Hassan II of Fez collected 10 cases of uterine carcinosarcomas over a period of 6 years (from 2013 to 2018) out of 18 cases of type 2 endometrial cancer during this period, which corresponds to 55% of all endometrial tumors operated on. The extreme ages of our patients were 50 and 80 years old. The most affected age group was 50-60 years and the average age of patients was 64 years. That said, the 50-60 year old age group has the maximum number of cases, i.e. 53.5

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In our series, we were able to see in 90% of patients the existence of metrorrhagia, mostly from the endocervix

In our series, 100% of the patients underwent a pelvic MRI showing a large endometrial tissue tumor process with invasion of more than half of the myometrium. The existence of areas of intralesional necrosis is also very specific. This examination revealed in three of our patients iliac lymphadenopathy, and in one of her inguinal lymphadenopathy, and involves the staging of FIGO. The preoperative FIGO staging is done by pelvic MRI objectifying stage I in four patients, or 40% of cases, stage II in two patients, or 20% of cases, and stage III in two patients, or 20% of cases, and finally the IV stage in two patients, in 20%.

The 1st stage of surgery consisted of cytoreductive surgery in 100% of the cases of our study on uterine carcinosarcomas, based on total hysterectomy with bilateral annexectomy and omentectomy. Lymph node dissection was performed in 80% of patients (fairly uniform distribution of stages I to IV). Lumbar aortic dissection is associated with pelvic dissection in 20% of cases. Omentectomy, peritoneal biopsies as well as peritoneal cytology are not performed routinely. Surgery is optimal (R0) in 80% of patients.

Discussion

Carcinosarcomas are rare tumors, they represent less than 5% of endometrial cancers according to epidemiological data from the National Cancer Institute [2] in the United States and the Royal Mardsen Hospital in Great Britain [3]. In France, 300 new uterine cases per year.

This is a tumor in postmenopausal women, its incidence increases with age. However, there are very rare cases of uterine CS in young women.

In our study, the patients who presented with uterine carcinosarcomas were all postmenopausal with an age greater than 50 years, which is consistent with the data in the literature.

Uterine carcinosarcomas remain a histological type which is part of uterine sarcomas, and which represent a double histological component, in the literature the frequency of histological subtypes of uterine sarcomas varies according to the series and includes uterine carcinosarcoma. (Board)

Séries	Nombre depatient	LMS		CS		SSE		Autres		Période
		N	%	N	%	N	%	N	%	
Koivisto-Korander et al. 2008[149]	100	39	39	40	40	21	21	0	0	1990–2001
SAMPATH et al. 2009[147]	3650	920	25	1877	52	544	15	309	8	1985-2005
Champetiere t al. 2010[145]	111	49	44	45	41	17	15	0	0	1996-2007
Notre série	10	1	10	10	100	5	50	0	0	2013-2018

Pelvic ultrasound is not very specific, it can show a large heterogeneous uterus, a uterine mass without being able to specify the malignancy or a pelvic mass for which it is difficult to specify the adnexal or uterine origin.

Endovaginal ultrasound coupled with color Doppler shows a richness of the vascularization which, unlike other lesions, is not synonymous with malignancy and does not distinguish between fibroma and sarcoma [4]. But it could be interesting when discussing the diagnosis of an invasive tumor.

In our series, the diagnosis of carcinosarcoma was evoked in 100% of cases by pelvic ultrasound, showing an enlarged uterus with a heterogeneous echogenic endocardial image, dopplerized in some patients. Doppler ultrasound results have been reported in 5 out of 10 patients, and in the 5 there is hyper vascularization. IR has not been calculated.

Some studies, including that of Kim et al [5], found 4 ultrasound aspects which were admittedly not very specific but which should suggest the diagnosis of endometrial stromal sarcoma:

- • A polypoid mass with myometrialenodular extension.
- • An intra-mural mass with ill-defined contours
- • A large heterogeneous intracavitary mass with irregular boundaries.

The cornerstone of the preoperative diagnosis of uterine tumors is endometrial sampling. It is also possible to carry out in consultation during the examination under speculum, the biopsy of a lesion delivered by the cervix for the forms of polyploid carcinosarcomas with endocavitary development. Curettage after dilation, which requires general anesthesia has long been considered the gold standard for removing endometrial mucosa but it is currently much less practiced, it is reserved for cases where sufficient equipment cannot be obtained on an outpatient basis, due to cervical stenosis for example.
However, blind endometrial biopsy can miss a malignant lesion. Only hysteroscopy with an oriented biopsy allows reliable screening. Hysteroscopy explores the entire uterine cavity, diagnoses focal lesions, and takes directed biopsies. It completes the preoperative assessment by looking in particular for an extension to the endocervix.
In our series, a diagnostic hysteroscopy with biopsy of the mass was performed in 70% of the patients to explain the postmenopausal metrorrhagia, which thus made it possible to establish the histological type of uterine carcinosarcoma in 50% of cases. The sensitivity of endometrial biopsy or curettage after dilation to detect sarcomatous elements is lower than that of endometrial carcinomas because they allow only simple abrasion of the endometrial mucosa, which does not allow the diagnosis of sarcomas deriving from the uterine muscle. or mesenchyme

The surgery includes at least for carcinosarcoma a total hysterectomy, bilateral adnexectomy, resection of any macroscopic tumor lesion as needed as well as pelvic iliac and lumboortic lymph node dissection. Omentectomy, and peritoneal biopsies and peritoneal cytology are more random in surgical procedures. The initial clinical and morphological assessment underestimates the stage of the disease.
The diagnosis can be suspected preoperatively in a particular context (rapid growth of a uterine mass in a postmenopausal patient) or proven during a histological sample, the diagnosis can also be evoked intraoperatively, in front of the atypical macroscopic appearance of a fibroid. But the relevance of the extemporaneous examination, in particular in the context of leiomyosarcomas, remains low (sensitivity of 20%). [6].
The recent development of a new FIGO classification specific to uterine carcinosarcoma has made it possible to adapt surgical methods according to the histological type. The objective is to achieve a surgical treatment meeting the usual requirements of cancer surgery, with surgery without microscopic tumor residue, without tumor fragmentation. [7]
Pelvic and lumbar aortic dissection is essential in the quality of surgical staging for the apparently early stages. In the study by Park (2010) [6], 31.7% of 71 stage I and II patients were reclassified to stage III on a positive dissection. Three patients had exclusive lumbar aortic lymph node metastases (7%, 3/41) without pelvic lymph node involvement, and 50% of positive pelvic dissection was associated with lumbar aortic lymph node involvement. Lymph node metastases were actually confirmed after dissection in only 3 out of 7 cases of doubtful lymphadenopathy on preoperative imaging. It is interesting to note in this study that the practice of peritoneal biopsies and omentectomy did not lead to the change in stage. Lymph node dissection also appears to have a positive impact on survival in several retrospective studies, it would reduce the risk of death for stages I to III by 36% in the Nemani series [8], and for all stages. , a decrease from 33% to 46% according to studies by Garg [9] and Bansal [5].
Optimal cytoreductive surgery for the advanced stages (III and IV) remains a fundamental objective in uterine localization, which was shown by the study of Tanner (2011) [15].
Surgery is R0 in 57% of cases, R + with a residue <1cm in 20% of cases and> 1cm in 23% of cases.
In carcinosarcomas, ectopic localizations are very frequent. Thus, in the study by Podczaskiet Al, an ectopic extension was observed in 39% of the 52 patients with a prior stage I tumor.
These extensions are most often ganglionic (from 18% to 35%) or peritoneal. In the specific case of carcinosarcomas, hysterectomy and adnexectomy will be systematically associated with pelvic lymphadenectomy (or lumbar aortic in case of adenomegaly), omentectomy and multiple peritoneal biopsies.
In the event of stage III uterine carcinosarcoma (ovarian or lymph node involvement), hysterectomy with bilateral adnexectomy remains the standard procedure associated with the removal of any metastatic sites and lymphadenectomy.
In case of stage IV carcinosarcoma (bladder, rectal, peritoneal involvement, distant metastases), surgery is discussed; nevertheless, hysterectomy with first bilateral adnexectomy seems indicated when it is technically feasible
A recent study by PECTASIDES et al on 29 patients with uterine carcinosarcoma, to assess the effect and toxicity of the combination of doxorubicineliposomalpegylate (called Doxil), carboplatin and paclitaxel, found that this combination appears to have an impact on advanced or recurrent carcinosarcoma, with an acceptable toxicity profile. [6].
In our study, chemotherapy was administered in 2 patients. Only 22% of patients with early-stage uterine carcinosarcoma received chemotherapy, the third patient scheduled for this treatment died 20 days after her surgery and before starting her chemotherapy course.

It is currently fairly well established that external beam radiation therapy reduces the risk of pelvic relapse, although its impact on survival remains controversial. There are no randomized phase III studies whose reference arm is surveillance and whose primary objective is survival. The only Phase III trial is that of Reed. Adjuvant pelvic radiotherapy is compared with monitoring for stage I and II uterine sarcomas (42% carcinosarcomas). The main focus is pelvic relapse and long-distance relapse. Only the cumulative incidence of local relapse at 5 years is approximately halved ($p = 0.0013$). On the other hand, the distant relapse was not modified ($p = 0.2569$).

Pelvic radiotherapy alone decreases the risk of local relapse by 17% at 5 years but does not appear to have an impact on survival. However, there are no prospective studies comparing radiotherapy to surveillance and whose primary objective is survival. In our series, six patients underwent adjuvant external radiotherapy (60% of cases), one of which received brachytherapy after external radiotherapy. In our case series, 60% of our patients received radiotherapy, mostly at a dose of 50 GY in 28 fractions. A patient received dam brachytherapy on the vaginal slice at a dose of 5GY per weekly session.

In the end, surgery is the basis of the therapeutic management associated with pelvic radiotherapy. The place of chemotherapy is not clearly defined outside of stages IIIA, IIIC and IVA. The standard chemotherapy is discussed between 5 schemes, poly chemotherapies based on Platinum or Ifosfamide

Consclusion :

Uterine carcinosarcoma or malignant mixed mullerian tumors are rare and aggressive tumors in postmenopausal women with a poor prognosis whatever the stage.

Treatment is currently very little influenced by prognostic factors since we can offer adjuvant treatment even for stages I. Optimal surgery including pelvic and lumbar aortic lymph node dissection remains the basis of the management of uterine carcinosarcomas. Both chemotherapy and radiotherapy have not shown any benefit in adjuvant settings.

The challenge is to define the postoperative therapeutic strategy and its most effective modalities. But the main constraint still remains the rarity of the pathology. The inclusion times are long and the cohorts small.

The originality of our retrospective series is that it studied the impact of changing practices on survival. Since the 2000s, treatment has intensified, with more patients receiving radiotherapy alone or as part of a sequential treatment combining chemotherapy and brachytherapy. Despite this, we were unable to observe any significant improvement in survival. The cohort is small and the follow-up is low for the last patients included.

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