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UTERINE TUMORS IN WOMEN: BIBLIOGRAPHIC DATA IN ALGERIA & AROUND THE WORLD

MOHAMED YASSINE AZZOUZ[1], NORA MIMOUNE[2,3*], RATIBA BAAZIZI[2], OUMAYMA BENADJEL[2] AND RACHID KAIDI[3]

[1]Faculty of Nature and Life Sciences, University of Blida 1, Blida, Algeria.
[2]High National Veterinary School (HNVS), Bab-Ezzouar, Algiers, Algeria.
[3]Institute of Veterinary Sciences, Laboratory of Biotechnologies related to Animal Reproduction, Algeria.
Email: nora.mimoune@gmail.com

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ABSTRACT

Among gynecological tumors, malignant uterine tumor (MUT) is the sixth most common cancer in women and the 15th most common cancer overall. There were approximately 382069 new cases and 89929 deaths attributed to this type worldwide in 2018. It was therefore the second and fourth leading cause of death from gynecological cancer in women in recent years and is expected to increase by more than 50% globally by 2040. Mortality rates are lowest in Central Asia, South and most of Africa. Survivors of MUT may experience treatment-related issues, including infertility, early onset of menopause, sexual problems, and lower limb lymphedema. WHO builds its own database from national modeling incidence estimates, using incidence ratios with a sampling method that relies on the calculation of a weighted or simple average of the most popular local rates applied to the population of a few regions or by an approximate estimate based on data provided by health establishments in neighboring countries. While in Algeria, existing statistical and epidemiological data and updated information on the pathology are insufficient. The objective of this work is to highlight the importance and the situation of the MUT in this country and to describe the different recent aspects (etiology, diagnostic and treatment) related to the disease.

Keywords: Uterus; malignant tumor; woman; statistics; etiology; diagnostic; treatment; Algeria.

INTRODUCTION

Gynecologic cancers are the leading cause of cancer death among women worldwide, and in modern societies, a significant number of these cancers affect a high proportion of women of childbearing age, who wish to preserve their fertility for future reproductive opportunities [1].

Among gynecological tumors, malignant uterine tumor (MUT) is the sixth most common cancer in women and the 15th most common cancer overall. There were an estimated 382069 new cases and 89929 deaths attributed to this type worldwide in 2018. It has thus been the second and fourth leading cause of gynecological cancer deaths in women in recent years [2] and is projected to increase by more than 50% worldwide by 2040 [3]. The Mortality rates are lowest in Central and South Asia and most of Africa [4]. Survivors of MUT may experience problems related to treatment, including infertility, early menopause, sexual problems, and lower limb lymphedema [5].

A study showed that Algeria experienced an increase of 40-60% in the prevalence of uterine cancer by socio-

demographic index from 1990 to 2017 [6], and the 5-years survival rate for severe tumors is low due to poor access to cancer care and an incomplete care setting [7].

The WHO builds its own database from national incidence estimates by modelling, using incidence rates with a sampling method that relies on the calculation of a weighted or simple average of the most recent local rates applied to the population of a few regions, or by rough estimation from data provided by health facilities in neighboring countries [8]. While in our country, existing statistical and epidemiological data and updated information on pathology are insufficient. Similarly, studies are currently being conducted to improve the management of MUT. In order to contribute to the elimination of this problem, we have carried out this study, which represents a modest contribution of knowledge regarding uterine cancers.

SITUATION IN ALGERIA

Global Situation

Complete statistics on gynecological tumors reported in Algeria are insufficient. The tables below represent some figures on uterine tumors in Algeria from the IARC.

Situation in Algiers

Table 3 represents some statistics relating to gynecological tumors in Algiers.

Table 1. Estimated total new cases in 2018 of gynecological tumors in all ages in Algeria [9]

Population	Number	Crude rates*	*ASR* (world)*
North Africa	12 244	10.3	11.7
Algeria	2 142	10.3	10.9

** Crude and age-standardized rates per 100,000 habitatnts*
ASR: Age-Standardized Rate

Table 2. Estimated number of new cases and deaths for each type of gynecological tumors in Algeria [9]

ICD	Cancer	Number	Mortality	Crude rate*	*ASR* (Monde) *
C00-97	**All cancers**	29 112	13 391	140,0	140,6
C53	Cervix	1 594	1 066	7.7	8.1
C54	Corpus uteri	436	73	2.1	2.3
C51	Vulva	76	27	0,37	0,36
C52	Vagina	36	16	0,17	0,18

** Crude and age-standardized rates per 100,000 habitants*
ASR: Age-Standardized Rate

Table 3. Main locations of gynecological tumors in Algiers in 2017 [10]

Location	Frequency	Relative frequency (%)	Gross impact	Standard impact
Breast	1605	38.4	88.4	82.2
Cervix	155	3.7	8.5	8.1
Ovary	152	3.6	8.4	8.3
Uterus	93	2.2	5.1	5

CLASSIFICATIONS OF GYNECOLOGICAL CANCERS

The Different References in Terms of Classifications of Gynecological Cancers

The various classifications of pelvic gynecological cancers have been modified from one day to the next in accordance with the improvement of medical knowledge and the evolution of practices in gynecological oncology [11].

There are now four main classifications of gynecologic cancers:

1. The classification of the International Federation of Gynecologic Obstetrics and Gynecology (FIGO), which became the first official sponsor of the annual report in 1958 [12];
2. The TNM classification of the International Union against Cancer created by Dr Pierre Denoix between 1943 and 1952 (UICC) was adopted in 1933 [13];
3. The American Joint Committee on Cancer (AJCC) classification in 1965, which tried to develop a classification for each type of cancer, to join the international classification (FIGO) in 1976 [14].
4. The WHO histopathological classification, last updated in 2014.

The currently published TNM System classifications have been approved by FIGO, UICC, and National Committees including the AJCC [15].

Table 4. FIGO 2009 pathology classification of endometrial cancers

FIGO 2009	TNM (2009)	Description	FIGO (1989)
Stage I*	T1	Tumor limited in the uterus	Stages I
IA	T1a	Tumor limited in the endometrium or not exceeding half the myometrium	IA-B
IB	T1b	Tumor invading half of the myometrium or more than half	IC
Stages II*	T2	Tumor invading the cervical stroma but not extending beyond the uterus	Stages IIA-B
Stages III*	T3 and/or N1	Local and / or regional extensions as follows:	Stages III
IIIA	T3a	serosa and / or appendages**	IIIA
IIIB	T3b	Vaginal and / or parametrial invasion**	IIIB
IIIC	N1	Regional lymph node involvement **	IIIC
IIIC1		pelvic lymph node	
IIIC2		lumboaortic ganglia +/-pelvic ganglia	
Stages IV*	T4 and/or M1	Extension to the vesical and / or intestinal mucosa, distant metastases	Stages IV
IVA	T4	Extension to the vesical and / or intestinal mucosa	IVA
IVB	M1	Distant metastases including intra-abdominal metastases and / or inguinal lymph nodes	IVB

*:Grade 1, 2 or 3; **: the results of peritoneal cytology must be reported separately and do not modify the classification (the classification of FIGO 1989 included the results of a positive cytology for stages IIIA).

The FIGO classification (Table 4) has been discussed and approved by the UICC, AJCC and World Health Organization (WHO) committees for the last 30 years and was reviewed in its latest version in 2009. These three classifications appear to be virtually identical and the goal of international collaboration is to have only one classification [16].

For instance, the Cancer Genome Atlas (CGA) has recently defined four clinically distinct types of endometrial cancer based on their overall mutation load, specific mutations, microsatellite instability, and histology [17].

Histomolecular Classification, Example of Endometrial Carcinomas

According to the classic dualistic model introduced by Bokhman in 1983, endometrial cancer was classified into two types. The histological prototype type for type I: low grade endometrioid tumors, mainly estrogen-related, strongly associated with obesity and other components of the metabolic syndrome, and type II: high grade non-endometrioid tumors [17,18]. This classification, also based on the incorporation of anatomopathological and molecular data, has been developed to best represent 2 major histogenetic pathways and 2 major prognostic groups (Table 5).

Table 5. The 2 main clinical-histomolecular types of endometrial carcinomas [19]

	Type I carcinoma	**Type II carcinoma**
Frequency (%)	Around 80	Around 20
Description model	Low-grade endometrioid carcinoma	Serous Carcinoma
Other tumors of the category	Grade 3 endometrioid carcinoma	Clear cell carcinoma Undifferentiated carcinoma Mixed carcinoma with >5% type II Carcinosarcoma
Carcinogenesis pathway	Hormone-dependent	Hormono-independent Chromosomal instability
Adjacent endometrium	Hyperplastic	Atrophic
Precursor	Atypica endometrial hyperplasia	Serous carcinoma in situ
Hormone receptor expression (%)	> 80	60-70
	Absent	Present
Other genetic alterations	Mutations *PIK3CA* (exon 9), *CTNNB1, KRAS, PTE*N Instabilité microsatellitaire	Mutations *PIK3CA* (exon20) Amplification *HER2* Surexpression de P16
Average age at diagnosis (years)	59	66
Stage I (%)	80	10
Survival (%)	> 80	40

Table 6. Classification of endometrial carcinomas into 4 molecular groups according to the TCGA study [19]

Group	Frequency	Main molecular characteristics	Most frequent histological types	Pronostic	Surrogate marker potential for routine use
Ultramute	7 %	Very high mutation frequency (C > A) POLE Mutations	Endometrioïd, of high grade	Very good	Mutation of *POLE*
Hypermute	28 %	High mutation frequency Microsatellite instability	Endometrioïd	Intermediate	Immunohistochemistry *MLH1, PMS2, MSH2, MSH6* (loss of expression)
Low number of copies	39 %	Low mutation frequency Mutations of CTNNB1	Endometrioïd	Intermediate	Immunohistochemistry *P53* (weak/focal marking)
High number of copies	26 %	Chromosomal instability Mutations of TP53	Serous endometrioid of Grade 1/2	Pejorative	Immunohistochemistry *P53* (intense and diffuse or completely absent marking)

Towards a New Model? The TCGA

In 2006, the National Cancer Institute and the National Human Genome Research Institute conducted different types of high-throughput molecular analyses on normal samples covering 33 types of cancers, the result was the molecular characterization of more than 20000 primary cancers of different histological types [20], and these studies identified 4 major tumor subtypes (Table 6)

ETIOLOGY

Uterine cancer (a term commonly used in oncology to refer to endometrial cancer) is typically a cancer of post-menopausal women, with peak prevalence around age 59, with a peak incidence between 50 and 70 years of age [21]. The main risk factors are:

Intrinsic Factors

Age

Age is an accentuating factor in the occurrence of cancers as genomic changes increase and accumulate over time [22].

Genetic origin

About 5% of cancers have a genetic origin. These hereditary predispositions may be responsible for the occurrence of cancers in several members of the same family [22]. The genetic factor associated with uterine cancer is mainly Lynch syndrome (2-4 to 11% of patients). It is related to the mutation of the MMR gene, involved in the repair of DNA mismatches. In this case, the cancer is characterized by the occurrence at an early age (before the age of 60), in patients with a lower IMC than in sporadic endometrial

cancers [23]. Cowden syndrome causes a mutation in the PTEN suppressor gene and determines a 13-19% lifetime risk of developing endometrial cancer [24].

Hormonal impregnation

When the endocrine system is disrupted, a hormonal imbalance appears in the body and promotes certain cancers. Indeed, a hypersecretion of estrogens can cause uterine cancer [22].

Overweight

Being overweight increases the risk of developing breast and endometrial cancer, mainly due to the storage of a portion of estrogens and the androgen aromatization in the adipose tissue [22, 25] .

Extrinsic Factors

Food

Differences between the diets followed by different populations, in terms of quantity and the relative proportion of the main food groups (vegetable, fat) have a major influence on the distributions of cancers [26].

Drugs

Drugs with carcinogenic effect in humans include antineoplastic drugs and drug combinations, hormones and hormone antagonists, and immunosuppressants. Tamoxifen use, especially in the case of breast cancer, predisposes to uterine cancer. In addition, contraceptive hormone therapy with combined estrogen-progestin therapy shows a protective effect [27].

Chronic infections

Experimental and biological evidence now indicates that a wide variety of infectious agents are one of the leading causes of cancer worldwide. Viruses are the main agents [28].

Ionizing Radiation

The carcinogenic effect of ionizing radiation (X, gamma, neutrons, beta and alpha) is definite for humans and is well established for doses of a few hundred milliSieverts (mSv) [29].

DIAGNOSIS OF TUMORS

Positive Diagnosis

Revealing signs

Emphasizes the frequent lack of anatomical-clinical correlation. Three elements are particularly suspected:

1. Hemorrhage (even) on anticoagulants,
2. Recent functional disorders persisting for more than 2 to 3 weeks and in any case an evolution towards aggravation, possibly interrupted by stages but without any real improvement,
3. Appearance of swelling [30].

Arguments in favor of diagnosis

The local arguments

They are clinically associated infiltration in typical cases with ulceration and hemorrhagic budding. Specific signs exist for certain localizations: painful and hemorrhagic inflammatory disease [31]. Local arguments exist in endoscopy for organs that are accessible to this means of investigation. If there is the slightest doubt, the examination is used to take the opportunity to perform biopsies or imaging [30].

Arguments linked to the context

They take into account age, a family context of orientation, a particular geographical origin, a predisposing pathology.

Biological arguments

They are usually of no help when the diagnosis is not immediately obvious. Tumor markers are elevated only when tumors are large or when they have spread [30].

Arguments of certainty

They are histological or cytological after biopsy. They are based on the malignant appearance of the cells and the invasion of normal tissues. They allow medical certainty and specify the strain. They are also of forensic interest [30, 32]. The purpose of the study is to precise:

- the histological nature of the tumor;
- its potential aggressivity;
- its prognosis;
- its ability to respond to increasingly specific treatments [33].

Morphological Diagnosis

Cytological or histological diagnosis requires good quality samples that are representative of the tumor and which have not been altered during collection or transport.

Examination of histological sections

The HE forms the basis for anatomopathological diagnosis (histological classification, grade, stage, limits). Other stains that reveal particularities of tumor cells or the stroma are often useful for diagnosis [34].

Immunohistochemistry

Immunohistochemistry with mono- or polyclonal antibodies is frequently used in tumor pathology. The use of combined antibodies, the choice of which is guided by histological study, makes it possible to determine in most cases the nature of slightly differentiated tumors and the primary origin of metastases.

- Antibodies can be used to determine the nature of the intermediate filaments of the
  - Cytoskeleton of cells. They have a specific distribution:
  - Cytokeratin filaments in epithelial cells,
  - Vimentin filaments in connective cells,
  - Desmin filaments in muscle cells,
  - Neurofilaments in nerve cells.

Thus a carcinoma is usually cytokeratin positive and vimentin negative, whereas a sarcoma has the opposite phenotype.

Surface markers are also specific for cell types: CD20 antigen (B lymphocyte), epithelial antigen membrane (epithelial cells), Neural Cell Adhesion Molecule (NCAM) (nerve cells and neuroendocrine cells).

Cytoplasmic markers that correspond to secretory products or functional molecules are also exploited: mucins in adenocarcinomas and chromogranin in neuroendocrine cells.

Antibodies directed against molecules with prognostic or therapeutic value are being increasingly used. Thus, the quantification of hormone receptors in the nuclei of adenocarcinoma tumor cells of certain organs provides information on the potential effects of antihormonal treatment [33].

Table 7. Immunoprofiling and histoprofiling of gynecological cancer types [35, 36, 37]

Tumor/condition	Histology/ Marker Panel	
Uterus, mesenchymatous	Leiomyomatous	*desmin, h-caldesmon, ocytocin, actineSm, ± CD10, Ki-67*
	Stromale	*CD 10, Ki-67, ± desmin, h-caldesmon, actin Sm*
Endometrial carcinoma	Endometrioid adenocarcinoma:	Similar to benign endometrial epithelium ; Endometrial hyperplasia; Squamous, morulous, mucinous metaplasia; Smooth luminal contours; Mild to moderate nuclear pleomorphism; ER, PR, vimentin positive; p53, p16, CEA negative (FIGO grades 1 and 2).
	C. serous :	No squamous, morose, mucinous metaplasia; Serrated luminous contours ; Slit-shaped spaces ; Cytological pleomorphism, numerous mitosis ; Possibility of cell exfoliation (hobnail) and psammoma body formation; Overexpression of p53, p16 and vimentin positive; ER, PR, CEA negative or weakly positive.
	C. with clear cells:	Hobnail cells, in tubular or papillary arrays, filled with glycogen. Hyaline stroma; Cytological pleomorphism; Vimentin positive; ER, PR, CEA negative or weakly positive; variable positivity p16 and p53.
	C.Mucinous	Cylindrical cells of endocervical type; mucin-rich cytoplasm ; Often low-grade.
	Carcinosarcoma	Mix of carcinomatous and sarcomatous components; Epithelial component generally of high grade,can be endometrioid (common), serous, clear cell, mucinous, undifferentiated or squamous. Sarcomatous component may resemble an endometrial (homologous) or non-endometrial (heterologous) stroma.
	C. squamous	Models range from the keratinization of individual cells to the formation of large masses of keratin.
	C. With transitional cell	Nested or papillary urothelial morphology, including lengthwise nuclear grooves
	C. undifferentiated	Non-distinctive appearance; Often composed of scattered leaves and nests with extended necrosis.

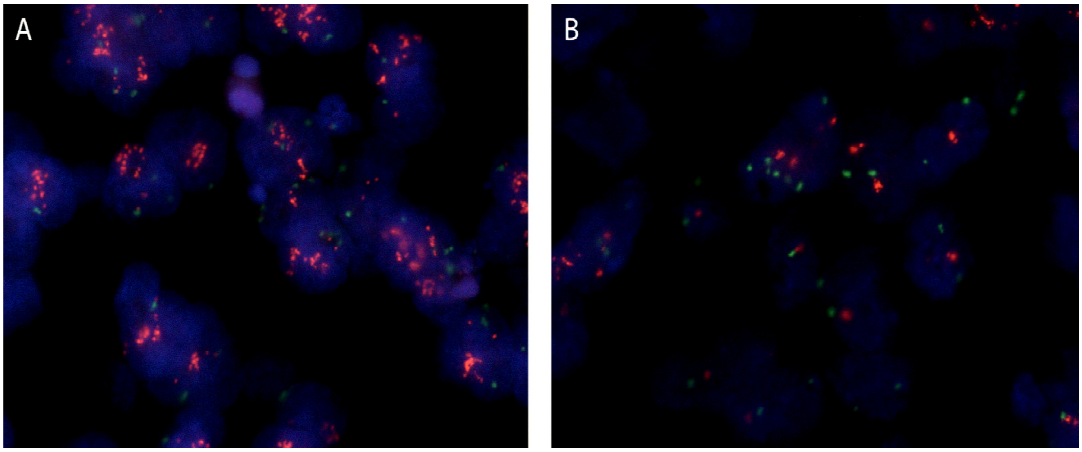

Fig. 1. Heterogeneity of gene amplification (HER2) in serous endometrial carcinoma by fluorescent in situ hybridization (FISH) [39]

The differentiated diagnosis between different types of uterine tumors includes several subtypes such as serous and clear cell carcinomas. Strategies for distinguishing between these entities are shown in Table 7, which represents a summary of histological and immunohistochemical profiles useful in the diagnosis and differential diagnosis of these tumor types and subtypes.

Molecular Diagnosis

Molecular pathology techniques are used to highlight molecular alterations in tumor cells. They can be performed on histological sections (e.g. in situ hybridization) or after the extraction of one of the molecular constituents from the tissue (Fig. 1).

These tools have diagnostic and prognostic value in certain malignant tumors, and can also help predict the response to targeted therapy (theranostics), detect residual disease after treatment, or diagnose an inherited predisposition to develop cancer.

Genetic alterations occur consecutively during the growth of a tumor. Some of these abnormalities are recurrent, meaning that the same type of abnormality occurs with high frequency in a given tumour type [38].

Differential Diagnosis

Most often it occurs between poorly differentiated tumors [37] and between dysplasia and benign tumors. In actual practice, it is necessary to know them in order not to get lost and thus reduce the frequency of late diagnosis [30]. Differential diagnoses also make use of molecular methods (Table 8).

Extended Diagnosis

Clinical

It specifies the location and dimensions of the tumor. The regional extension of the lymph nodes is then investigated and finally potential remote locations that are directly accessible for clinical examination: lymph nodes, skin, liver, pleural. Functional signs that may indicate the presence of metastases are also investigated [30].

Table 8. Antibody selection for poorly differentiated tumours at differential diagnosis [37]

Differential diagnosis	Antibody panel
carcinoma/sarcoma (epithelioid variants)	CAM5.2, AE1/AE3, S100, melan-A, HMB-45, CD45, CD3O, ALK, PLAP, CD117, desmin, CD34
Mesothelioma	AE1 / AE3, CK5 / 6, calrétinine, thrombomoduline, EMA, CEA, Ber EP4, MOC 31, TI F-1

By imaging

This type of examination can be useful to check for metastases prior to surgery and can help to clarify local and regional tumor extension. In some cases, when in doubt, the use of guided cytologic puncture might be considered [31].

By endoscopy

Allows to measure the surface extension of tumors accessible to this method of investigation and possibly to nearby organs.

Through surgical observation

Provides useful information on the invaded structures and the possible extension and specifies whether the resection is histologically complete or not, whether there is regional lymph node invasion or not, and whether there are capsular ruptures and/or neoplastic sites outside the lymph nodes.

The search for 2nd cancers (also called 2nd localizations) is systematic for certain types of locations: multifocal foci in the same organ [30].

Diagnostic Strategy

It requires a good knowledge of the advantages and limitations of each method. The objective of medical management of a cancer patient is to treat him or her in the best possible way and at the lowest possible cost. In the vast majority of cases, an anatomopathological diagnosis, with at least a tumor type, is necessary prior to treatment. However, this mostly requires an invasive procedure that has to be considered in relation to the risks and benefits for the patient. Some methods have a virtually certain diagnosis, but the inconvenience and risk of a histological confirmatory biopsy is not compensated by the expected benefit for the patient [33].

TREATMENT

Depending on the type and stage of the cancer, treatments may include surgery, which is often used, radiotherapy, hormone therapy or chemotherapy; the latter two are considered systemic treatments for metastatic or recurrent cancer [34]. These treatments can be used alone or in combination.

The goal is to achieve a complete cure, extend the patient's survival, and minimize disease-related symptoms [31].

Therapeutic Means

Surgery

It forms the basis of treatment [40], allows surgical staging and a decision to be made on postoperative strategy [41]. The standard treatment consists of a total hysterectomy without adnexal preservation [42]. Hysterectomy by vaginal access is the approach chosen whenever possible [43].

However, it does not allow inspection of the peritoneal surfaces and cytology cannot be retrieved. It is counter-indicated in cases of pelvic adhesions, prior surgical procedures in the pelvic region and inability to correctly position the patient for vaginal access. Other approaches are possible in the first place, such as the coelio-assisted vaginal approach, abdominal, coelioscopy and robotic-assisted coelioscopy [31].

Radiotherapy

Because of its documented efficacy in improving locoregional control and reducing recurrence rates of vaginal vault recurrence, radiotherapy has been used as an adjunct to surgery for the past 5 decades. Several randomized studies have established the role of adjuvant radiotherapy in reducing local recurrence in patients at risk of raising intermediate local failure.

External radiotherapy

Allows local control at the cost of some morbidity but does not influence overall survival.

Intracavitary brachytherapy

Appeared as an alternative to external radiotherapy because of its reduced overall morbidity. Trials are being conducted to determine the additional potential advantage of chemotherapy over radiotherapy, as well as to explore smaller doses of brachytherapy in the early stage of the disease [44].

Hormonotherapy

There are no standardised methods agreed upon. Most onco-gynecologists choose megestrol acetate as their first choice, but doses and durations are not standardized. Medroxyprogesterone acetate, depo-medroxyprogesterone acetate and combinations of tamoxifen and progesterone have also been suggested. Some authors suggest the use of cyclic therapy to induce monthly bleeding, most suggest continuous treatment that ultimately results in an atrophic endometrium, and others suggest treatment via an intrauterine device. Since progesterone is not well tolerated by many women, since breast sensitivity and weight gain are frequent complaints, it is probably best to use the smallest dose that will also successfully invert the neoplastic endometrium; the dose is likely to depend on the patient's IMC and tumor. Only women with grade 1 endometrioid adenocarcinomas and a disease clinically perceived as endometrial confinement with the best available radiologic modality should be considered for this treatment. Studies have suggested that histologic architectural complexity and high IMC are treatment failure predictors [45].

Chemotherapy

Chemotherapy for endometrial cancer has advanced over the last four decades and plays a role in the treatment of both advanced and recurrent endometrial cancer. Agents with established anti-tumor activity include doxorubicin, cisplatin and paclitaxel.

First-line chemotherapy

A combination of paclitaxel with the carboplatin analogue of cisplatin is currently the most commonly used combination for the first-line treatment of metastatic disease. Questions remain about the contribution of these therapies in adjuvant contexts, on the role of pharmacotherapy beyond first-line therapy, and the incorporation of targeted agents. Recent efforts have focused on the addition of other agents of interest such as

metformin, temsirolimus and bevacizumab [31, 46].

Second-line chemotherapy

There are very limited number of randomized trials of second-line chemotherapy in Phase II or III, most of the results are from non-randomized, but sometimes randomized, Phase II trials for ixabepilone, etoposide (VP-16), paclitaxel, oxaliplatin, doxorubicin, cisplatin, ifosfamide, methotrexate, topotecan, vinblastine and vincristine. Response rates have always been quite low. Ixabepilone, a synthetic analogue of epothilone B, was considered sufficiently promising in Phase II [46, 47].

Targeted therapy

In endometrial cancer, many trials of single-agent mTOR inhibitors are showing occasional patients with long-term benefit. Several studies have shown no association between tumor PTEN alterations or PI3KCA mutations and the clinical benefit of mTOR inhibitors [48]. One study shows the effect of the combination of everolimus and letrozole with an overall response rate of 32%. No significant toxicity was reported. Serous histology was the most powerful predictor of the non-response. Patients receiving metformin were observed to have an increased response rate to treatment [31].

Anti-angiogenic agents have consistently produced a modest response rate in endometrial cancer. However, Kandoth et al [20] observed toxicities including gastrointestinal and vaginal fistulas, intestinal perforation and venous thromboembolism and have been classified as adverse.

There is currently one trial of carboplatin/paclitaxel with or without trastuzumabcifying serous endometrial cancer with overexpression or amplification of HER2 [49, 50].

New approaches to immunotherapy based on immune checkpoints of antibodies in hyper and ultra-mutated tumors and the administration of tumor-specific drugs; small molecule inhibitors against the PI3K, AKT or mTOR pathways; Novel anti-angiogenic and cytotoxic agents such as epothilones against MSS and biologically aggressive high copies number, serous endometrial tumors are among the most promising developments in this disease [51].

Fertility Management

Infertility is also a characteristic of women under 40 with endometrial cancer, unlike their menopausal females, who are often referred to as (fertile). In a series of 11 patients (12%) were accidentally diagnosed with endometrial cancer during the infertility evaluation [52]. A large study in Korea reported an infertility rate of 38.3%, which was higher than that of the general population (10-15%) [53]. It is likely that in many of these cases, infertility is the result of anovulation, associated with high levels of uncontrolled circulating estrogen. Unfortunately, all data is retrospective and often limits the obtaining of hormonal information on patients unless specifically documented in the patient's record.

Treatment of the ovarian tumor should include dilation and curettage (D&C) to exclude underlying endometrial neoplasia.

The possibility of underlying grade 1 (or higher) underlying endometrioid adenocarcinoma should be considered when treating complex atypical hyperplasia (CAH) with hormones to preserve fertility.

Precautions should be taken to exclude carcinoma as a possibility, either via D&C (as a standard), slide examination by an expert pathologist, or both when considering treatment with hormones and preservation of the uterus.

The number of women with endometrial cancer who wish to preserve their fertility will continue to increase and prospective trials are currently in progress to establish a standard medication. In order to set a new standard of care in this regard, we need a better understanding of the molecular and genetic level of the mechanism of various progesterone formulations on endometrial cancer at the PR isoform level [45, 54].

CONCLUSION

Malignant uterine tumors are among the most common cancers of the genital tract with a potentially fatal nature. They mostly occur in postmenopausal women. The essential etiological factors are represented by menopause, nulliparity, infertility, hormonal disorders, certain metabolic and genetic diseases, without forgetting the heredity component. The diagnosis is made on the existence of bleeding (mainly), or abdominal pain. It is confirmed by the anatomo-pathological examination. The prognosis depends on many clinical and histological factors. The size of the tumor, its thickness, histological type and its differentiation, the time of consultation, lymph node invasion and metastases represent the most important prognostic factors. The treatment is based on the combination of surgery and radiotherapy, chemotherapy currently gives a better chance of survival.

CONPETIN INTERESTS

Authors have declared that no competing interests exist.

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