International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Index Copernicus Value (2016): 79.57 | Impact Factor (2017): 7.296

Endometrial Cancer in Young Tunisian Women about four Cases

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Abstract: ***Objective: To report a series of 4 cases of endometrial cancer in young women and to study its peculiarities through our series and a recent review of the literature. Patients and methods: This is a retrospective study of the medical records of 4 cases followed for endometrial cancer at an age under 33 years. Results: the age of our patients was respectively 27, 27, 30 and 32 years old. Three patients had metabolic syndrome and one patient had a family history of cancer of the colon and pancreas. All our patients were childless. Persistent metrorrhagia and pelvic pain were the main circumstances of discovery. The diagnosis was made preoperatively by endometrial sampling under hysteroscopy in 2 cases and by histological examination after laparotomy for pelvic mass in 2 cases. The tumor was grade 1 or 2 endometrial carcinoma in 3 cases and carcinosarcoma in 1 case. Surgical treatment was oncological in 3 cases. Radiotherapy with or without chemotherapy was done in all cases. One patient died after 11 months of the discovery of her disease and the other 3 cases have a recurrence-free survival of more than one year. Conclusion: The endometrial cancer of young women is often diagnosed with some delay. This cancer differs from that of older women in several ways. The treatment has no particularity except for the desire to preserve fertility.***

Keywords: Endometrial cancer, young woman, management, prognosis

1. Introduction

Although endometrial cancer mainly occurs in menopausal women, it can hit younger patients (under 40 years) in 2 to 14% of cases as well [1,2]. The real problem of this pathology at that age is that it is rarely suggestive of malignant tumor,so that the diagnosis could be made late.However,in a review of the literature, the majority of cases of endometrial carcinoma of youngwomen were low-grade endometrioid carcinomas that present at low stages and are associated with favorable clinical outcomes [1]. The second problem, isthat most of these women of childbearing age want to preserve their fertility [1,2] Conventional treatment consists of total hysterectomy and bilateral adnexectomy with or without pelvic and / or aortic lymph node dissection. However, an alternative exists for these young women desiring pregnancies; conservative treatment in young women with endometrial adenocarcinoma grade 1 and FIGO stage Ia. [3]. The objective of this work is to report the diagnostic particularities mainly radiological, histopathological and therapeutic of endometrial cancer in young women.

2. Case Reports

Case 1:
A 30-year-old, obese patient (BMI = 36.6) with no notable pathological history consulting for pelvic pain. She is G1P0A1, with an unexplored sub-fertility. The patient reports leucorrhoea associated with pelvic pain that has been evolving for 6 months. An ultrasound was performed showing a heterogeneous echogenic 3cm thick endometrium. The patient underwentan endometrial sampling of the endometrium, which concluded that the endometrial endometrioid adenocarcinoma was well-differentiated grade 1 of the FIGO infiltrating endometrium. An MRI was performed showing an endometrial tumor process measuring 100x 30 mm extended to the isthmus, cervix and both parameters (proximal: 1/3 right, 2/3 left). In addition, there was no abnormality around the bladder and perirectal fat or pelvic lymphadenopathy, which classifies the tumor as FIGO's stage III B (Figure 1).

The patient received concomitant chemoradiotherapy. External radiotherapy at a dose of 45 Gray. Chemotherapy was based on cisplatin. Pelvic MRI (Figure 2) control was then performed showing a significant regression in tumor size with persistence of an intracavitary process of 70x 30 mm, without locoregional extension, associated with oval formation of the anterior wall of the uterus of 30 x 35 mm whose morphology and stable appearance are in favor of a uterine fibroid.

The patient therefore underwentoncologic surgery including total hysterectomy, bilateral adnexectomy and bilateral pelvic lymph node dissection. The histopathological examination of the surgical specimen concluded that, after chemotherapy, a viable residual tumor residue of a well-differentiated endometrioid adenocarcinoma type was evaluated at 5% of the total tumor volume. The tumor infiltrates the superficial part of the myometrium and extends to the isthmus. The six lymph nodes were free from metastasis. Currently she leads a life without recurrence with 3 years of follow up.

Case 2:
A 27-year-old patient, hypertensive and diabetic consulting our emergency for acute pelvic pain with metrorrhagia. The gynecological examination revealed the presence of a prolapsed mass of 150x 60 mm outside the vulva which was bleeding in contact. The evolution was marked by a

spontaneous heavy bleeding leading to a 3 g / dl drop in hemoglobin concentration. An emergency ultrasound showed then a possibility of uterine inversion (figure 3). Therefore, a diagnostic laparoscopy was performed showing a shifting aspect of the uterus and tubes to the vagina. The diagnosis of a uterine inversion was confirmed. So, we first removed the mass by simple excision and then we performed a laparotomy to reduce the uterine inversion which was not possible by laparoscopy. histopathological examination concluded for a uterine body adenosarcoma of 90x 80 mm. Pelvic MRI was completed at 2 months post-surgery, which showed a T2-mesoscale intracavitary tumor signaling process measuring 1.8 cm long axis (Figure 4).

The decision was to complete the surgery to be oncological and to perform total hysterectomy with ovarian preservation. The final pathological examination concluded that the uterine adenosarcoma was 3.7 cm tall. The tumor infiltrated the myometrium. It extended in height to the uterine isthmus and endocervix. The parameters were devoid of infiltration. Therapeutic management was to complete with radiotherapy and chemotherapy. Currently she leads a life without recurrence after a follow up of 14 months.

Case 3:
A 27-year-old nulliparous patient who was seen for metrorrhagia. She had a father who died at the age 46 of pancreatic cancer, and a maternal grandmother who died of colon cancer. The history of her disease was a year old marked by the installation of menometrorrhagia causing her a severe anemia poorly tolerated for which she was hospitalized. The examination on admission found a hypogastric sensitivity with the perception of a poorly limited mass at the level of the left iliac fossa. A pelvic ultrasound showed an enlarged uterus of 120x 40 mm polymyomatous with presence of three posterior fibroids, the largest of which measured 50x 40 mm. The decision of a laparotomy myomectomy was made. The exploration showed the presence of a low abundance ascites and a friable antero-posterior isthmic fibroma whose appearance was very suspect. A biopsy was performed showing a moderately differentiated grade 2 endometrioid adenocarcinoma of FIGO. Pelvic MRI was then performed showing a cervico-isthmic tissue mass measuring 80x 50x 50 mm extending into the uterine cavity with significant locoregional invasion to both parameters with suspect left pelvic lymphadenopaty. The tumor was class III C of FIGO (Figure 5).

She was treated with a first chemotherapy based on taxol and carboplatin. Due to the persistence of bleeding, locoregional radiotherapy for hemostatic purposes was started. An MRI post-chemotherapy was done and concluded a clear regression of the volume of the tumor process to almost 50%. The patient died of her disease becoming metastatic to the liver 11 months after the discovery of her pathology.

Case 4:
A young lady of 32 years G0P0A0 with a history of irregular menstrual cycles since her menarche. She consulted 14 months ago for pelvic pain and metrorrhagia that had been going on for more than a month. Her medical checkup showed a pallor and a morphological profile of a polycystic ovary syndrome with android obesity. Her supra-pubic ultrasound examination obstructed by obesity showed an irregular and thick endometrium at 30 mm. Therefore, a pelvic MRI was performed showing an intrauterine tumor process of 66 x 26 mm, an infiltration of more than a half of the myometrium and bilateral iliac lymphadenopathies strongly suspected(figure 6). The patient subsequently had a diagnostic hysteroscopy that showed an endometrial cancer pattern. This process extended throughout the uterine cavity and cervical canal. A directed endometrial biopsy was then performed and confirmed the presence of FIGO grade 2 endometrial endometrioid adenocarcinoma characterized by oncocyte differentiation. The tumor stage was evaluated as FIGO's III C1 after a negative extension assessment at the hepatic and pulmonary level. The therapeutic decision was then to start with a concomitant radiotherapy chemotherapy. A second MRI of control performed at the end of this first treatment showed a total regression of the uterine tumor process as well as the pelvic lymphadenopathies. A closing hysterectomy was finally done to her. The patient was reviewed a year later and her checkup done with pelvic MRI and thoracoabdominal CT showed no abnormalities.

3. Discussion

Most young patients with endometrial carcinoma have a particular clinical profile. They are often overweight with a BMI of between 25 and 30 or obese (BMI> 30) [4-7]. There are a range of othercontributing factors including diabetes, hypertension, nulliparity, infertility and irregular menstrual cycles, which is the case for 3 of our 4 patients.

Endometrioid adenocarcinoma is the most common histological type of endometrial cancer in young women. Most of these tumors (83% -100%) are FIGO's low grade [4, 5, 8]. Non-endometrioid endometrial tumors are rare in this age group, but can be seen in patients with Lynch syndrome, such as undifferentiated or dedifferentiated carcinomas and sarcomas [5, 9, 10]. It should be noted that undifferentiated carcinomas are aggressive tumors correlated with a high mortality rate [5, 9].In our series we had a case of carcinosarcoma and 3 cases of endometrioid carcinoma, one of grade 1 and 2 of grade 2. Carcangiu et al [11] concluded that young patients with Lynch syndrome often had non-endometrioid uterine tumors, including clear cell carcinoma, serous carcinoma and carcinosarcoma, as is the case with our second observation. Although most young women with endometrial cancer have low-grade tumors confined to the uterus [2], even in this case a search for synchronous or metastatic cancer is required. In the Duska et al review [2], the majority of women had stage I and grade I disease, but 19 of 95 (20%) had disease beyond the uterus. Coexistence with a malignant ovarian tumor is a worsen prognosis factor but its incidence is higher in young women compared to women over 45 [12]. In our series all 4 patients had locally advanced cancer but no metastases or coexisting ovarian cancer.

Endometrial cancer in young women has etiopathogenic particularities. In fact,hyperestrogenism and a genetic predisposition (lynch syndrome) are incriminated. Burleigh et al recently published a paper [13] whose objective was to

determine the proportion of young women with endometrial cancers that could be attributed to these factors. Out of 719 women included in the study, 57.5% met the criteria of the category of women with hyperestrogenism as is the case of the first and third observation. 8.25% met criteria for suspicion of Lynch syndrome, as is the case of our third observation and 34.25% classified as having no identified classical risk factors. There was no statistically significant difference in tumor grade at the time of diagnosis, the severity of the disease, and the response to hormone therapy. On the other hand, it had a significant difference in terms of the existence of a synchronous ovarian cancer. In fact, the prevalence of synchronous ovarian cancer was 21.0% in the "no risk factor" group, 23.1% in the "Lynch" group, and 6.6% in the "Hyperestrogenism" group. In our series the third belonged to the group of women in whom lynch syndrome was suspected; In view of her family history, she had a moderately differentiated endometrioid carcinoma grade 2. Once the diagnosis made, a local and remote extension assessment is required for this, using more and more sophisticated means of imaging. Transvaginal ultrasound may be effective for evaluating the depth of myometrial invasion, with a potential for 3D ultrasound [14], but it is unreliable for evaluating ganglionic extension. Contrast-enhanced MRI, which allows both assessment of local extension, with superior performance to transvaginal ultrasound, and lymph node with CT-equivalent performance, is the recommended baseline for the preoperative assessment of endometrial cancers [15] and for high-grade and type 2 cancers [16].

Young women desiring pregnancies may want fertility saving options hence the interest of a conservative treatment. The principle of an alternative protocol to hysterectomy is to propose an anti-gonadotropicprogestin treatment whose purpose is to ensure the regression of the lesions to allow a pregnancy under the guise of careful monitoring. There is no consensus regarding the ideal progestin agent. But the most commonly used agents were medroxyprogesterone acetate and megesterol acetate [17]. It is proposed for some selected patients with endometrial cancer endometrium confined to the endometrium and low grade, so likely to respond to hormonal therapy without compromising the prognosis of patients until childbearing is completed. After confirming the nature and grade of the tumor and excluding myometrial invasion and lymph node metastasis [3]. The4 cases of endometrial cancer among young women collected in our department did not meet the eligibility criteria for conservative treatment because they were discovered at advanced stages of the disease.

The data concerning the response to this treatment is controversial but some series reported encouraging results of complete regression and pregnancy [1,8,17]. The response rates vary in the range from 40% to 60%. [1,4]. The duration of progesterone treatment required for an adequate response is also variable. Most of patient receiving this treatment respond, in 2 to 3 months, but in some cases, it can take up to 6 months.The presence of persistent cytological abnormalities after 6 months of treatment indicate the failure of this treatment [18]. In a review of literature, a rate of 40% of recurrence have been reported [4, 18].Most of these patients require the use of assisted reproduction techniques [3,17].These patients undergoing in vitro fertilization are confronted with some difficultiesincluding obesity, polycystic ovarian syndrome and chronic anovulation. Therefore, before making a decision of a fertility preservation treatment,it is recommended to make sure that the woman don't have any other infertility factors and to evaluate the likelihood of conception [3].

There is another problem to take into consideration when treating endometrial cancer in young women; The ovarian preservation which avoid surgical menopause and its complications. This decision is difficult because synchronous ovarian carcinomas have been reported in up to 25% of young women with endometrial cancer. [1].

The determination of the absence of metastases into the ovary is very challenging and uncertain even if imaging explorations and per operative appearance are normal.

In summary, endometrial diseases that affect women of childbearing age are dominated by benign and functional pathologies, but we must know how to think of the possibility of malignant endometrial pathology in patients with gynecological symptomatology for the purpose of having early diagnosis. Most young patients with endometrial cancer have well-differentiated tumors. Patients often have early stage disease (80% -100% at stage I) and have an excellent prognosis [4, 5]. In our series all 4 patients were discovered at advanced stages of the disease. Several studies have noted that the presence of defective DNA distribution is a major prognostic factor [5,11,19]. In fact, there is an association between DNA repair defects and the presence of poor prognosis factors of endometrial carcinomas such as a high-grade tumor, the presence of myometrial invasion and lymphovascular invasion [11, 19]. The other factors correlated with poor prognosis are dominated by a low BMI and a non-endometrioid histological type [8].

4. Conclusion

Endometrial carcinomas in patients 40 years of age and younger are uncommon. These women of childbearing age want most of the time to preserve their fertility. Such pathology at this age have a diagnostic trap even by using the complementary radiological examinations. Conventional treatment consists of total hysterectomy and bilateral adnexectomy with or without pelvic and / or aortic lymph node dissection. However, a conservative therapeutic alternative exists for these young women desiring pregnancies until they finish childbearing. The majority of cases of endometrial carcinoma of young womenhave a good prognosis and therefore is preparing for a conservative treatment once diagnosed early, so it is necessary to know how to think of the possibility of malignant endometrial pathology in young patients, whose gynecological symptomatology is most of the time explained by benign and functional pathologies.

5. Conflicts of Interest

Without

References

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Figures

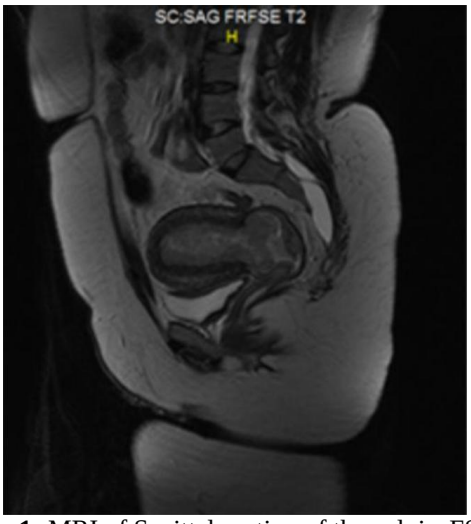

Figure 1: MRI of Sagittal section of the pelvis, FSET2-weighted showing T2W hypersignal endometrial tumor measuring 7 x 3 cm extending to the isthmus and cervix

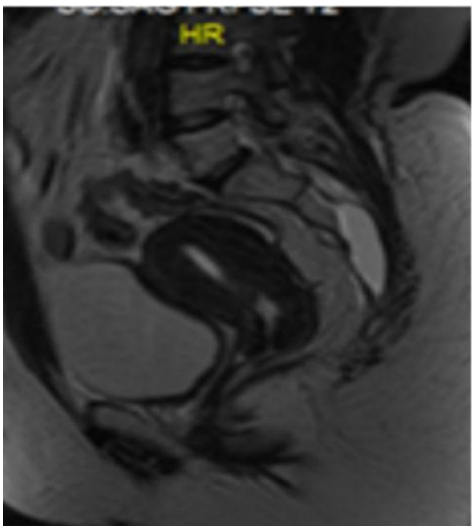

Figure 2: MRI of Sagittal section of the pelvis in T2 sequence showing an intracavitary tumor residue of 70 x 15 mm Without extension to the isthmus nor to the cervix

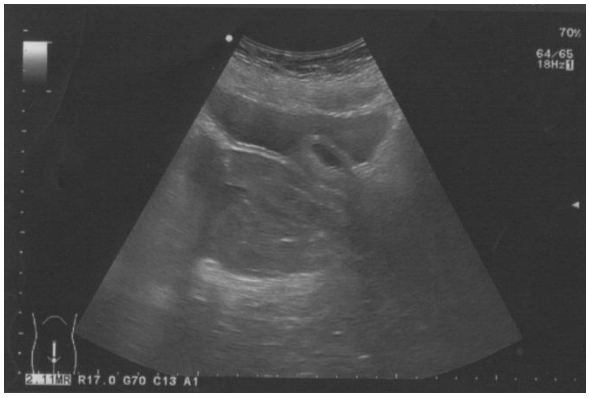

Figure 3: ultrasound aspect showing uterine inversion

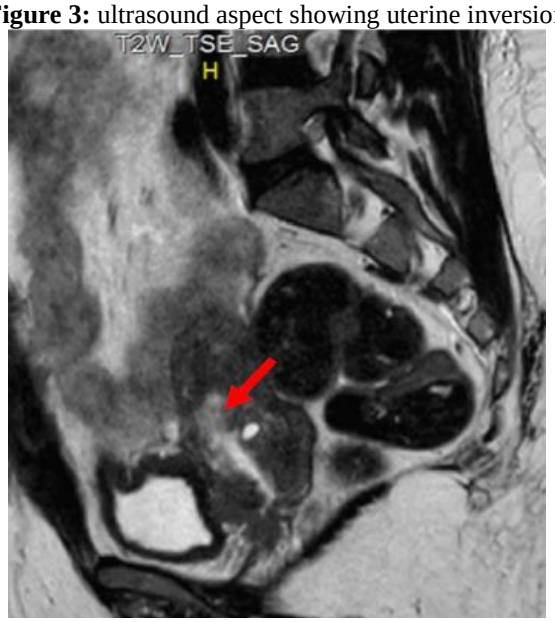

Figure 4: FSET2 pelvic MRI showing localized endometrial thickening of 18 mm (⟵) without extension to the myometrium

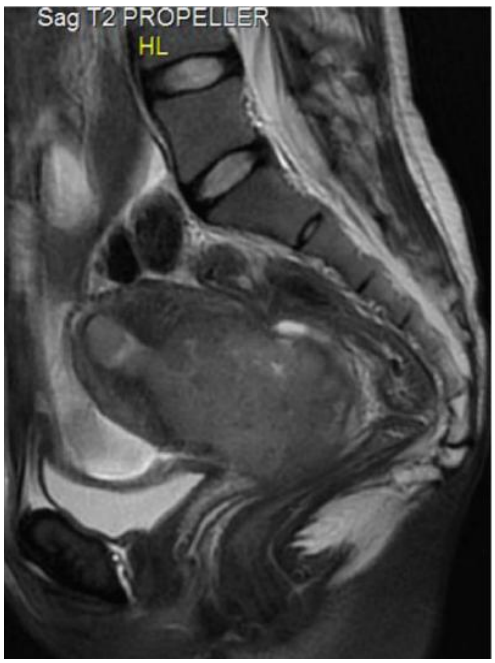

Figure 5: Pelvic MRI, FSET2 sagittal sequence showing a T2W hypersignal endometrial tumor measuring 90 x 50 mm extending to the isthmus and cervix.

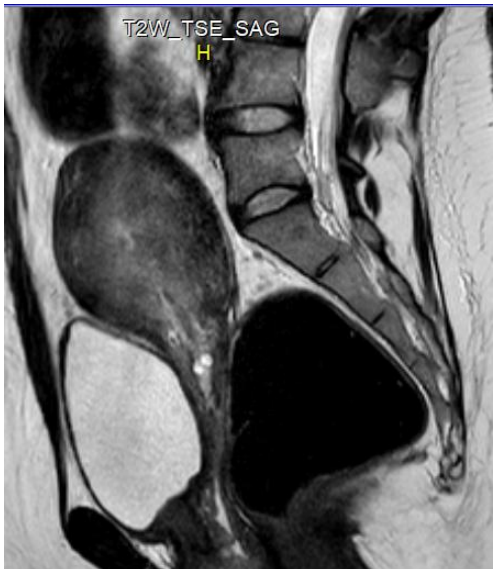

Figure 6: Pelvic MRI, FSET2 sagittal sequence showing an intermediate signal intensity endometrial tumor without myometrial invasion