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Research Article

Adult Granulosa Tumors of the Ovary about 12 Cases

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Abstract

Tumors granulosa cells are part of the sex cord tumors. They represent less than 5% of ovarian cancers. Their prognosis is quite favorable in relation to their diagnosis often at an early stage.

The authors present a retrospective series of 12 cases of granulosa cell tumors, over a period of 7 years (2008-2015) collated at the National Institute of Oncology in Rabat.

The average age of patients was 53 years, 67% were postmenopausal and the majority was multiparous. The abdominal pelvic ultrasound was performed in all women. Tumor markers, having estradiol, inhibin was performed in 2 patients with against no patients received the dose of anti-Müllerian hormone. According to the FIGO classification, 6 patients (50%) were classified as stage I, 4 patients (33.33%) stage II, 1 patient (8.33%) stage III and 1 patient (8.33%) stage IV. Surgery is the hub of the therapeutic arsenal, the majority of patients (10 cases) underwent a radical treatment. Chemotherapy was given in 6 cases. Patients were followed with a mean of 20 months (1-122 months). The evolution was marked by two cases of recurrence, 1 of which underwent surgical recovery and one patient underwent palliative chemotherapy.

Keywords: Cancer of the ovary granulose; Hyperestrogenism; Inhibin; Treatment

Introduction

The granulosa cell tumors of the ovary are rare tumors of the ovary, were described for the first time by Rokitansky in 1855 [1]. They represent about 5% of malignant ovarian tumors.

They belong to the group of mesenchymal tumors and sex cord ovary as classified by the World Health Organization (WHO).

Typically, they are divided into two forms, adult and child according to their histological appearance, the adult form a majority 95% of cases and especially for women over 50 years, the juvenile form mainly concerned children or women less than 30 years.The granulosa cell tumors have the distinction of being the majority of secreting and hyper oestrogéniques case. They are considered tumors with low malignant potential and a favorable prognosis compared to epithelial ovarian tumors. Their main feature is the late recurrence.

Our goal, from a retrospective study of 12 cases of granulosa cell tumors conducted at the National Institute of Oncology (INO) between 2008 and 2015, was to try to identify elements of clinical, radiological, biological and pathological diagnostic direction and define how to take care and supervision.

Materials and Methods

This is a retrospective study over a period of 7 years, from February 2008 to January 2015, conducted at the National Oncology Institute in Rabat.

During this period, we collected 12 cases of granulosa cell tumors of the ovary.

Our study focused on the analysis:

1. From the epidemiological profile of patients: mean age, parity, hormonal status.
2. Discovery of Circumstances.
3. Of particular clinical symptomatology and para clinical specialties of these tumors.
4. From their staging, according to FIGO classification.
5. From established treatment, according to each stage.
6. For their histology and that of the endometrium.
7. Their evolution and recurrence.

Results

The age of the patients ranged between 40 and 76 years with an average of 53ans. The peak incidence is between 40 and 53 years. 67% of our patients were postmenopausal.

Parity in our series ranges from 0 to 8 with an average of 3.4. Almost half of our patients were multiparous.

For gynecologic obstetric history, a patient presented with primary infertility (8.3%). Hormonal contraception was found in 3 cases (25%). No patient had a family history of ovarian cancer.

Functional signs were dominated by bleeding in postmenopausal women (67% of cases), and pelvic pain in women of childbearing age (50% of cases). The increase in abdominal volume revealed the diagnosis in patients of both groups equally in 33.3% of cases. The amenorrhea and cycle disorders were found in one case (8.3% of cases). Digestive disorders like constipation were also found in a patient. One patient had a chronic inflammatory disease. 3 patients

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Table 1: Morphological classification of FIGO granulosa cell tumors in our series.

Stratification	Number of cases	Percentage
I	6	50
Ia	3	25
Ib	1	8,33
Ic	2	16,66
II	4	33,33
IIa	1	8,33
IIb	2	16,66
IIc	1	8,33
III	1	8,33
IV	1	8,33

had Dyspnea associated with pleural effusion.

Clinically, the majority of women had pelvic or abdominal-pelvic tumor (75%). The size was not specified in all cases. Ascites was present in 7 patients 58.3% of cases. The uterus was increased in size in 3 cases 25% of cases. An adnexal mass was found in the pelvic touches in 2 cases 17% of cases.

The addition pubic pelvic ultrasound was performed in all our patients and objectified: a mass at the expense of the ovary in 9 cases (75% of cases) and a uterus increased in size in 4 cases (33.33% of cases). Transvaginal ultrasound was performed in a single woman and she showed adnexal mass and thickened endometrium.

CT was performed in all patients; she could not specify the origin of the tumor in one case. In 3 of our patients, she suspected malignancy of the ovarian tumor.

IVU was performed in any of our patients.

The AC 125 was performed in 8 of our patients and it was revealed increased in 3 cases. Beta HCG was performed in 4 patients and was abnormal in 2 cases. Alpha FP also performed in 4 patients returned elevated in 2 cases. ACE practiced in one case, it is normal income.

The inhibin was performed in 2 cases and was elevated in one of the two. The Estradiol has been practiced in one case and high income. No patient received the determination of anti-Müllerian hormone.

The exploratory laparotomy was performed in all our patients, for staging are macroscopically the tumor and perform the surgery (Table 1). The mid cystic solid appearance is the most frequent macroscopic appearance.

Surgical treatment was the initial treatment for all our patients. It was conservative in 2 of our patients (16.66% of cases), in one case it was a young person with a stage IA either case, the patient was lost from sight before realization of radical surgery. Radical treatment consisted of a total hysterectomy with bilateral oophorectomy with or without omentectomy. This radical treatment was performed in 10 patients. (83.33% of cases). The radical surgical treatment associated with small bowel resection was performed in one patient. The principle appendectomy was performed in one patient (8.33% of cases). The Omentectomy was performed in 7 patients (58.33% of cases). No surgical complications were chosen.

6 of our patients (50% of cases) received chemotherapy. The protocols used are: Bleomycin / Etoposide / Cysplatin in 1 patient, CDDP vinblastine in 1 patient, CDDP Etoposide in 1 patient, CAP (cyclophosphamide/doxorubicin/cysplatin) in 2 patients, PC (Cysplatin/Cyclophosphamide) in 1 patient with an average 3 cures. Paresthesias related to cysplatin and disturbance of liver function tests are the only notes complications.

A pathological examination, all tumors in our series is tumors of the adult granulosa proliferation with a dominant sheet (33.33%). The cell nuclei have a central groove in coffee bean in 72.5% of cases. The bodies Call-Exper are present in 70% of cases. Immunohistochemistry was done in two cases and showed positive staining of tumor cells by anti α inhibin. Search for estrogen receptor and progestin was not made.

The decline of our patients is 1 to 122 months with a mean of 20 months. 2 patients 12 relapsed (pelvic): The first stage IIb, relapsed 25 months after radical treatment and a CAP type of chemotherapy made of 6 treatments followed by a second natural look; the second stage III, has relapsed after radical treatment and a PC type of chemotherapy made of 6 treatments, requiring cyto-reduction. Analysis of these recurrences showed that these tumors exhibited poor prognostic factors: Stage> IIb (locally advanced), incomplete surgery with significant residual tumor post -operatories.

Discussion

The granulosa cell tumors can occur at any age, but most often during periods peri and post-menopausal early. The average age of diagnosis is between 50 and 55 years in most series [2-4]. The average age of patients was 53 years with extremes ranging from 40 to 76 years and a peak incidence between 40 and 53 years.

Hormonal status and gender do not seem to be related to the incidence of granulosa cell tumors [2-5]. Other factors such as infertility treatments and oral contraceptives are associated with a greater risk [2-7]; and unlike epithelial ovarian tumors, there would be no particular genetic susceptibility mutations BRCA1 and BRCA2 [2-9].

The postmenopausal bleeding is a symptom master [2-12] resulting from prolonged exposure endometrial tumor secretes estrogen, which causes endometrial hyperplasia and even an endometrial adenocarcinoma. In our series 67% of menopausal women looked for bleeding, none of our patients showed adenocarcinoma of the endometrium. In women of childbearing age, menstrual disorders may be the type of menstrual irregularities, menorrhagia or secondary amenorrhea, which can be confused with early menopause [13]. In our series, 8.3% of women of childbearing presented amenorrhea. Pelvic pain is a sign often reported by patients (30 to 50% of cases) [10-13], they are due to the fact that granulosa cell tumors are usually large (> 10-15cm) and hemorrhagic. In our series, pelvic pain is found in 83.3% of cases. The increased volume of the abdomen is due to the tumor development (large tumors) or ascites. In our series, 33.33% of our patients looked for an increase in abdominal volume. Rarely, the clinical picture is associated with granulosa cell tumors to androgen secretion making signs of masculinization with hirsute.

The clinical examination allows finding a pelvic mass or abdominopelvic which must note the size, usually> 10cm with or without ascites was found in 12.4% of cases [13]. The pelvic touches found an adnexal mass with a uterus increased in size. In our series, the abdominal-pelvic mass is found in 75% of cases, ascites is present in 58.3% of cases, the uterus is increased in size in 25% of cases and

the adnexal mass was found in 17% of cases.

Ultrasound can reveal a great mass echoic or a cystic mass with partitions, making a multilocular appearance but unilocular aspect is also found, or it may appear homogeneous or heterogeneous pure solid nature. And unlike epithelial tumors, calcifications and peritoneal metastases are rare. The intra cystic vegetations are not found [1,2]. Ultrasound will also mount a thickened endometrium, reflecting the hyperestrogenism related tumor granulosa. In a study of Sharony et al. [14], five women with a tumor on 7 granulosa have abnormally thickened endometrium. In our series, pelvic ultrasound confirmed adnexal mass in 75% of cases, and showed a uterus increased in size in 33.3% of cases. Ultrasound has a neighbor detection rate and sometimes higher than that of CT in the presumptive diagnosis of ovarian tumors and is to be preferred to the scanner. CT may be justified before a large pelvic tumor that poses the problem of its former headquarters and its relationship with adjacent anatomical structures (gastrointestinal tract, bladder and urethra) [15,16]. In our study, CT was performed in all patients. The information provided by MRI does not seem higher than a pelvic ultrasound performed in excellent technical conditions by an experienced sonographic [15,17]. T1, tumor granulosa presents hyper signal due to the presence of intra-cystic haemorrhage, characteristic of this type of tumor. T2, it will appear like a sponge with areas is also recognized [1]. L'UIV is not carried out systematically, and it could be replaced by a TDM coupled to an injection urinary contrast medium. No patient in our series has benefited from IVU or MRI.

Estradiol has been identified among the first substances secreted by the granulosa cell tumors, and is responsible for the clinical manifestations described above. What did suggest its use as a tumor marker? However, it has been shown that it cannot serve as a marker in all patients. Lappôhn et al. [18] found a correlation between estradiol and tumor activity exists only in three patients in six. Rey et al. [19] also found that the absence of estradiol secretion was observed in 30% of women with a tumor of the granulosa. However, estradiol may be useful for monitoring some patients. Several studies consider that inhibin is a better marker than oestradiol activity of granulosa cell tumors. [17] Anti-Müllerian hormone is considered a specific marker, reliable and sensitive granulosa cell tumors. In our series, 2 patients were given a dose of inhibin and estradiol dosing in 1 patient by cons no patients received the dose of anti-Müllerian hormone.

Laparotomy is the rule whenever it is deemed suspicious ovarian tumor or organic ultrasound because surgery is the main initial treatment and uses the same principles of treatment of epithelial ovarian cancer [20]. This surgery can be radical (basic intervention, it has a total hysterectomy with bilateral oophorectomy with or without an Omentectomy sometimes visceral resection for optimal tumor reduction) or conservative (unilateral Adnexectomy).

The stages must have a total hysterectomy [2-21]. The quality of surgery depends on fate of the patient and the higher or lower risk of recurrence [10-21]. Surgical Post residue is a very important parameter and is involved in the quality of response to chemotherapy.

Regarding localized stages, the therapeutic approach is not unique. Some authors [21], radical surgery should be adopted even for IA stages unless the woman is willing to pregnancy. Other teams favor a unilateral salpingo-oophorectomy provided that initial surgical staging confirms localized nature through the practice of peritoneal cytology, biopsy of the peritoneum and the contra lateral ovary and a biopsy endometrial curettage to remove an associated neoplastic. For these authors, four reasons why this behavior:

The young age of the patients with the aim of conservative treatment, the lateness of recurrence [22,23], scarcity of bilateralism of the tumor, the 5-year survival of 92% for stage I. In our series, all patients underwent an initial surgery, and radical treatment was the most accomplished, the omentectomy was also practiced in the majority of cases, and the dissection was performed in 2 cases.

Chemotherapy is indicated in advanced stages when surgical excision cannot be complete or palliative setting. The indication for (stage I) is useless except for patients with a large tumor size with a capsular rupture or a high mitotic index [24]. In our series, the chemotherapy regimens followed the evolution of protocols over time, since the combination cysplatin / vinblastine / or Bleomycin Cysplatin / Etoposide / Bleomycin

Immuno-histochemical searching for estrogen receptor and progestin receptors is a good indicator of response to hormonal therapy. In our series, no patient has been benefited from hormone therapy.

Typically, the disease progression occurs over several years. Periods of remission obtained the waning of treatment, are interrupted by relapses. Recurrences are poor prognoses, responsible for a high mortality rate, 72 and 86% depending on the series [10], decreased overall survival. The median survival of patients with a recurrence is around 62 months.

A prolonged post-operative monitoring, careful and regular must rule before all TG especially after conservative treatment, this is the risk of sometimes very late recurrence is so special for this type of tumor. The monitoring is based on: Clinical, pelvic and abdominal ultrasound, tumor markers (inhibin, anti-Müllerian hormone and estradiol).

Conclusion

The aim of our study was to try to identify clinical, radiological, biological or pathological to guide, preoperatively, in a patient with an ovarian mass to a tumor granulosa.

The best policy factors are the clinical signs of hyperestrogenism, specific to each stage of life (before puberty, in childbearing and menopause).

At ultrasound, endometrial hypertrophy associated with an ovarian tumor often solid-cystic may be a sign of direction.

The search for a partner endometrial cancer is a major step, especially if it provides conservative treatment.

Estradiol, inhibin and Anti-Müllerian hormone tumor markers are used for the detection of late relapses and to detect residual tumor post-operatively.

Histologically have conventionally associated tumors in a ring with a longitudinal groove which gives them a characteristic appearance in coffee bean. The cells also show characteristics cavities bodies Call-Exper.

On the immuno-histochemical level, have tumors that express high proportion of valentine, inhibin, anti-Müllerian and so much less hormone keratins, they are negative for epithelial markers EMA, CEA.

Treatment typically involves radical surgery for some advanced forms, except when to become pregnant, while for advanced forms combines adjuvant therapy.

These tumors require a long-term surveillance given the frequency of late recurrence.

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