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CASES REPORT

GRANULOSA TUMORS: ABOUT 10 CASES

Dr. Mettahri Anass, Dr. Tricha Jaber, Pr. Hafsa Taheri, Pr. Saadi Hanane and Pr. Mimouni Ahmed
Department of Obstetrics and Gynecology Mohammed VI Hospital, Faculty of medicine and pharmacy of Oujda Mohammed First University.

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Abstract

Granulosa tumors arise from the mesenchyme and sex cords of the ovary. They are quite rare. Theyrepresent 0.6 to 3% of all ovarian tumors and 5% of ovarian malignancies. They are the mostfrequent tumors of the sexual cords and stroma.

The purpose of our study: To describe the epidemiological, anatomical-clinical and evolutionary characteristics of granulosatumors and to study the different prognostic factors.

Materials and methods: Our retrospective study covers 10 cases of ovarian granulosa tumor diagnosed at the gynecologyobstetrics department of the CHU Mohammed VI of Oujda. Over a period of 5 years, from September2016 to September 2021.

Results:- The average age of onset of the adult form is 58.4 years (35-38-52-57-66-81). And that of theoccurrence of the juvenile form, is 18.6 years (18-19-22-31).Clinical signs were mainly dominated by abdominal distension, chronic abdominal-pelvic pain andmetrorrhagia.All patients had clinically palpable pelvic tumors.Suprapubic pelvic ultrasound was performed in all our patients.It allowed to link the pelvic mass to its adnexal origin, with an average size, 141.5mm, variablebetween 63mm and 220mm.

The CT scan was performed in all our patients. It allowed us to determine the size of the masses andtheir relationship with the surrounding structures.The histological study concluded in a granulosa tumor adult type in 60% of the cases and in agranulosa tumor juvenile type in 40% of the cases.80% of patients received conservative treatment, 20% received radical treatment.60% of our patients have received chemotherapy.No patient had radiotherapy. One patient had a recurrence and all patients are still alive after surgical treatment.

Conclusion: Granulosa tumors are rare, of the group of tumors of the sexual cords and the ovarian stroma. The adult forms are of slow evolution, often diagnosed at an early stage are potentially malignant tumors, the recurrences often very late (10-20 years) their treatment is based essentially on surgery more or less chemotherapy. Juvenile forms, rare (5%) with good prognosis. Prolonged post-therapy follow-up is necessary because of late recurrences for Adult forms, frequent and early for juvenile forms.

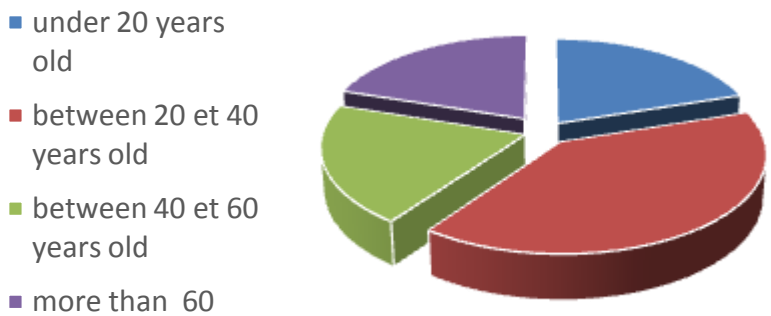
Corresponding Author:- Dr. Mettahri Anass
Address:- Department of Obstetrics And Gynecology Mohammed VI Hospital, Oujda.

Introduction:-

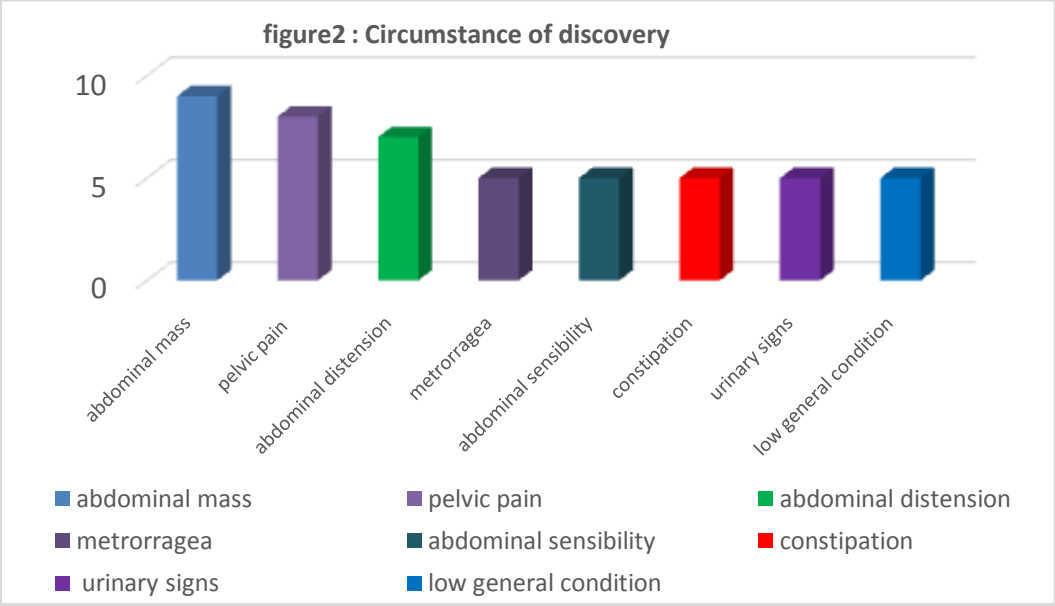
Granulosa tumors of the ovary (TG0) are rare malignant tumors that Represent 2-3% of all ovarian cancers, and occur primarily in the adult population. They originate from the sex cords and stroma and are associated with a good prognosis compared to epithelial ovarian cancers. They exist in two histological forms: an adult form (95%), and a juvenile form (5%). The latter occurs mainly in young women, with more marked signs of malignancy and an increased risk of recurrence (1). These tumors have a specific clinical, histological and evolutionary profile and can recur up to 40 years after the initial diagnosis. The aim of this work is to study the diagnostic, therapeutic and evolutionary particularities of these tumors compared to all ovarian tumors.

Patients and Methods:-

figure 1: age distribution



This is a retrospective study spread over a period of 5 years, from September 2016 to September 2021, conducted in the gynecology-obstetrics department of the Mohammed VI University Hospital of Oujda. Ten cases of GGT were identified; patients were referred to us for varying symptoms. Our study was based on the analysis of the epidemiological profile of the patients: average age, parity, hormonal status, the circumstances of discovery, the particular clinical semiology and paraclinical specificities of these tumors, the treatment instituted, their histology, their staging according to the FIGO classification, their evolution. The medical observations of the patients were collected from the records from the Department archives. The data concerning the follow-up were collected from the medical files



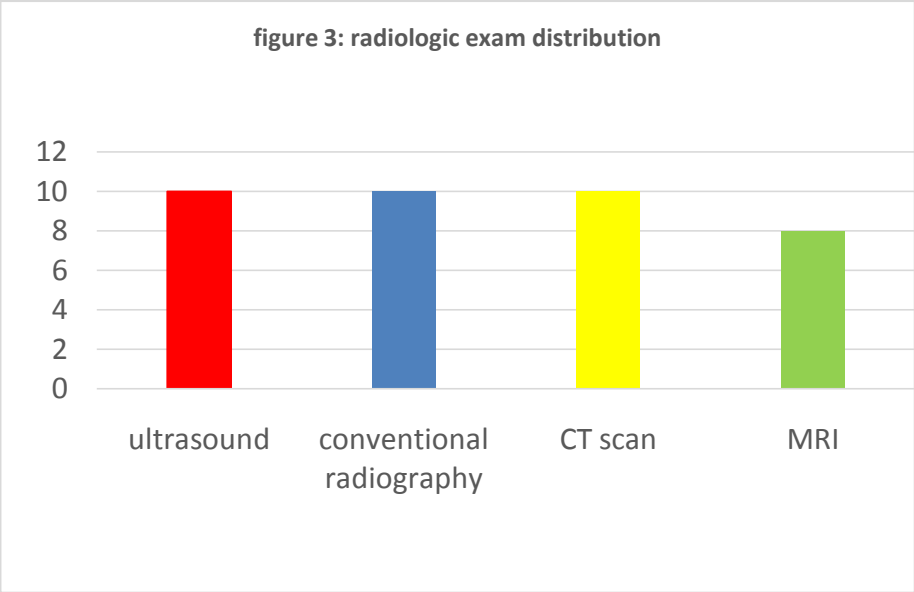
Résultat:-

-The average age of onset of the adult form is 54.8 years (35-38-52-57-66-81). Moreover, that of the occurrence of the juvenile form is 18.6 years (18-19-22-31).

-Clinical signs were mainly dominated by abdominal distension, chronic abdominalpelvic pain and metrorrhagia. - all patients had clinically palpable pelvic tumors

Suprapubic pelvic ultrasound was performed in all our patients.

It allowed the pelvic mass to be related to its adnexal origin, with an average size of 141.5 mm, varying between 63 mm and 220 mm.



-The CT scan was performed in all our patients. It allowed to specify the size of the masses and its relationship with the surrounding structures.

- The histological study concluded in a granulosa tumor adult type in 60% of cases and in a granulosa tumor juvenile type in 40% of cases.

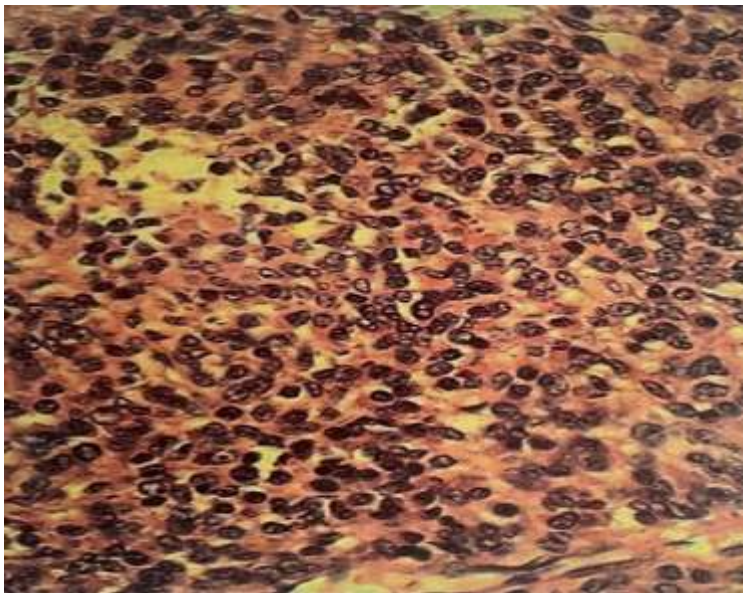


Figure 4:- Microscopic appearance of a juvenile GIST (1).

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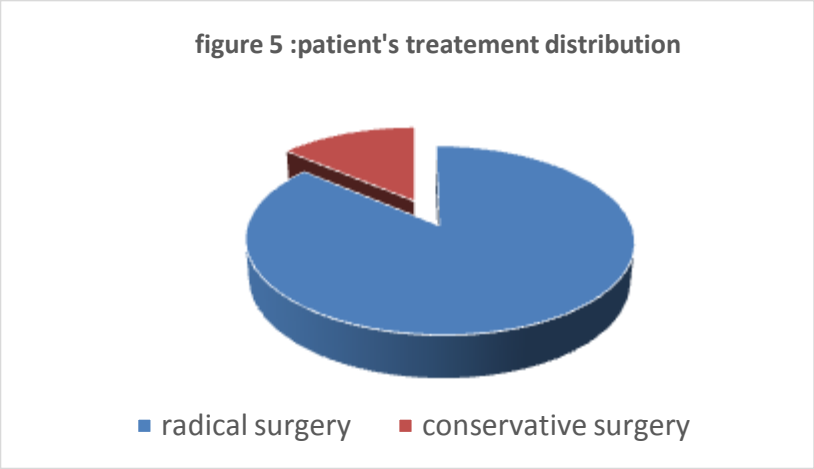

80% of patients received conservative treatment, 20% received radical treatment.
- 60% of our patients received chemotherapy.
- no patient had radiotherapy
-One patient had a recurrence
All patients are still alive after surgical treatment.

Discussion:-

GISTs are rare ovarian neoplasia, but are the most common secretory tumor. They represent 0.6-3% of all ovarian tumors and 5% of ovarian malignancies (2). There are two different anatomic-clinical entities: The "adult" granulosa tumor and the "juvenile" granulosa tumor. The adult type remains the most frequent.
The "juvenile" form occurs most often before the age of 20; with a maximum frequency between 0 and 10 years of age at 44%. The "adult" form usually occurs after the age of 30 and in 70% of cases after the menopause (3).
In our series, 6 patients have adult granulosa tumor and 4 patients have juvenile granulosa tumor.

Table 1:- Comparison of the average age of onset of GTT in the literature.

autor	Period of the study	Case number	Age average
ELLOUZE (2).	1994-2003	16	45(20-70)
BOYCE (4).	1988-2008	72	43(21-58)
FOX1 (5).	1948-1973	92	49,8(8mois-88ans)
TAMURA	2011-2012	2	42,5
Notre série	2016-2021	10	41,8(18-81)

Any situation that decreases ovulation is protective against GERD (6).

In general, multiparity reduces the risk by 15 to 20%, while nulliparity and a late first pregnancy increase the risk of GERD (6).

In our series, 4 out of 10 patients were nulliparous.

Hormonal status is variable in the literature (2). In our series, one patient is peri-menopausal, 4 are menopausal and 6 are genitally active.

Infertility and use of ovulation inducers are associated with a higher risk of developing granulosa tumors (7), (8), (9) none of our patients were on ovulation inducers or oral contraception

Adult granulosa tumors are manifested by signs of hyperoestrogenism in 25 to 75% of cases, depending on the series, with abnormal vaginal bleeding such as metrorrhagia, menorrhagia or menstrual irregularity (10), (11), (12), or by secondary amenorrhea, most often secondary to the secretion of abnormally high levels of inhibin (13), (14).

In our series, the circumstances of discovery were dominated by hormonal manifestations, in fact, there was one case of postmenopausal metrorrhagia, the other cases did not present an endocrine syndrome

The juvenile granulosa tumors are manifested either by a tumor syndrome with painful abdominal distension or by an endocrine syndrome giving a pseudo-puberty, precocious, iso sexual (25) in case of estrogenic secretion and hirsutism and hoarseness of the voice, clitoral hypertrophy and acne in case of androgenic secretion (3) (15). The clinical examination of the patients reveals in the majority of cases a palpable tumor (70-80% of the cases). It is normal in 15% of cases (10). The size of the tumour varies from a few centimetres to sometimes more than 30 cm (24). In our series, this tumor was palpable in 100% of cases with a size of up to 22 cm.

It is important to note the interest of exploring the endometrium, which is thickened in most cases, testifying to oestrogenic impregnation, which may indirectly indicate a tumour of the granulosa or endometrial cancer. In our series, there were two cases of simple hyperplasia diagnosed on surgical specimen and one case of endometrial polyp delivered through the cervix. The other patients had an endometrium in proliferative or secretory phase. Some series report rates of 5.5% to 6.4% of associated breast cancer at the time of diagnosis of the granulosa tumor or in the first few years after diagnosis (16).

The histological study of GIST can be confused with a wide variety of ovarian tumors. Immunohistochemistry study with inhibin and calretinin (17) can be helpful in diagnosis. Inhibin is a sensitive tumor marker but there are false-negative cases both said that Call-Exner bodies are small rounded areas of extracellular fluid and cellular debris, surrounded by well-differentiated granulosa cells, organized in a rosette around these small areas. They are pathognomonic of granulosa tumors, especially the adult form. They are considered a good histological differentiator of granulosa tumors (10) (18).

The main differential diagnoses of granulosa tumors are: poorly differentiated carcinomas of the ovary, carcinoid tumors, endometrioid sarcomas of the ovary, small cell carcinomas, fibrosarcomas, androblastomas.

Treatment is essentially surgical, consisting of total hysterectomy with bilateral adnexectomy and complete staging (12). Conservative surgery is indicated in the early stages and for young patients in order to preserve fertility; on the other hand, radical surgery is indicated for the advanced stages and for women who have reached menopause or who do not wish to become pregnant (19) (20) (11)

Endometrial biopsy must imperatively complete conservative treatment. Dissection of the lymph nodes is still very much debated given the rarity of lymph node involvement. Chemotherapy is indicated in advanced stages following incomplete surgical excision or in palliative situations. Its indication in stage I is unnecessary except for patients with large tumor size with capsular rupture or a high mitotic index (21,22). The overall survival is good, especially since most cases are diagnosed at an early stage, and is more than 90% at 5 years. (21) The evolution was favourable for the 9 patients with a relapse rate corresponding to that of the literature (23). Clinical, ultrasound and biological monitoring must be prolonged because of very late recurrences. In case of recurrence, surgery remains the reference treatment associated with chemotherapy

Conclusion:-

Granulosa tumor is a rare malignant tumor, but one that should be considered in the presence of an ovarian tumor.

It can occur at any age, with a predominance in adulthood (post-menopause).

It is characterized by its clinical particularities with the high frequency of signs of hyperestrogenism making the granulosa tumor the most frequent endocrine tumor of the ovary and by its anatomopathological particularities with the frequency of localized stages and the association with other histological lesions such as glandulocystic hyperplasia of the uterus, which can go as far as degeneration.
Currently, the treatment is based on surgery, both as an initial procedure and for recurrences.

The quality of treatment depends largely on the tumor's evolution. Because of their tendency to recur several years after the initial diagnosis. Prolonged surveillance is essential.

Adjuvant therapy and strategy in the case of recurrent disease remains a controversial issue that is currently being evaluated.

The prognosis remains relatively favorable. It depends more on the stage of the tumor than on the histological type.

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