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Tumor of the Granulosa of the Ovary About a Case

Zein Ahmed[1, *], Ahmedou Moulaye Idriss[2], Nacer Dine Ould Mohamed Baba[2], Isselmou Sidi[1]

[1]Faculty of Médicine, Cheikh Zayed Hospital of Nouakchott, Nouakchott, Mauritania

[2]Faculty of Médicine, National Hospital Center of Nouakchott, Nouakchott, Mauritania

Email address:

zeineahmed@yahoo.fr (Z. Ahmed)

[*]Corresponding author

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Abstract: Ovarian granulosa tumors are very rare; they belong to the group of sex cord and stromal tumors. Their slow evolution in the adult forms which are more frequent (95%) and less aggressive than the much rarer juvenile forms. The exact etiology of these tumors is unknown, but higher than normal estrogen levels are frequently found in women with ovarian granulosa cell tumors. A woman's menstrual status with excess estrogen is related to the presence of certain symptoms such as: early puberty in young women, increase in the size of the abdomen, menstrual cycle disorders in pre menopause or bleeding abnormal uteri in postmenopausal women. The most frequent ultrasound aspect is the solid-cystic aspect and pathological examination remains the diagnostic key. The treatment is essentially surgical, but sometimes associated with complementary therapies such as: chemotherapy, radiotherapy, hormone therapy. Recurrences occur late, hence the importance of post-therapeutic follow-up. Some aggressive forms relapse and progress more rapidly, which justifies rigorous therapeutic monitoring. The prognostic factors for recurrence identified in the literature are the FIGO stage, the presence of residual tumor and the tumor size. We report a case of observation and we draw attention to the epidemiological, clinical particularities, as well as the various prognostic factors in order to carry out a better therapeutic management.

Keywords: Ovary, Adult, Granulosa, Tumour

1. Introduction

Ovarian granulosa cell tumours (OGCT) were described in 1885 by Rokitansky. OGCT develop from granulomatous and thecal cells (cells of the sex cords) in the ovaries that produce oestrogen (primary female sex hormones). These tumours develop around the menopause with a peak at 50-55 years.

This type of tumors is quite rare - 2-5% of all ovarian cancers, their evolution is slow, recurrences are rare and late, usually appearing after 5 to 6 years [1, 2].

The exact cause of these tumors is unknown, but higher than normal estrogen levels are related to ovarian granulosa cell tumors. A woman's menstrual status depend on excess of estrogen in women and explain the presence of symptoms such as: early puberty in young women, increase in the size of the abdomen, menstrual cycle disorders in pre menopause or bleeding abnormal uteri in postmenopausal women.

These tumors are difficult to diagnose due to their histopathological features which are relatively non-specific, with a recurrence rate of 50% OGCT are often indolent but their evolution is unpredictable.

Careful histological examination of tumor specimens should be performed assessing prognostic factors such as stage, nuclear atypia, and tumor size.

We report a case of OGCT with a review of the literature and emphasis on the clinical, para-clinical, therapeutic and prognostic features.

2. Observation

A 43 year old female patient, 5th gesture, presented with pelvic pain associated with a cycle disorder without signs of compression.

The clinical examination revealed a good general condition, weight 75 kg, height: 1m 68.

The gynaecological examination revealed a normal sized uterus with a hard latero-uterine mass.

Pelvic ultrasound revealed a well-limited heterogeneous cystic tumour measuring 70x50mm.

Surgical exploration revealed a solid cystic mass of the left ovary, mobile without adhesions or associated ascites. The uterus, fallopian tube and contralateral ovary were free and an annexectomy was performed.

The histological study (Figure 1) of the surgical specimen revealed an intra capsular ovarian tumour proliferation, made of trabeculae, cords and masses sometimes hollowed out by small cavities giving micro follicular aspects, in a fibrous stroma with areas of haemorrhagic remodelling. The tumour cells had a characteristic coffee-bean shaped nucleus.

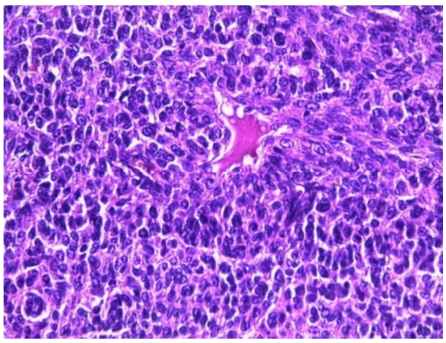

Figure 1. *Ovarian granulosa cell tumour showing intra capsular ovarian tumour proliferation and fibrous stroma with areas of haemorrhagic remodelling.*

There were no mitoses or foci of necrosis. The capsule was sometimes thinned but always intact, not penetrable by the tumour elements.

The postoperative course was simple, the patient refused surgery and is monitored periodically with a 5-year follow-up marked by negative radiological findings.

3. Discussion

These are functional secretory lesions, rare, they represent more than 70% of mesenchymal and sex cord tumours and 5% of all ovarian cancers [2].

The incidence of this tumour is estimated at 1.3 per year per 100,000 women [3]. There are two types: adult granulosa tumours (95%) are most common between the ages of 40 and 70 years and in 70% of cases after the menopause. Juvenile granulosa tumours (5%) are most common before the age of 20 [4].

The juvenile form occurs most often before the age of 20, with a maximum frequency between the ages of 0-10 (44%) [5].

The hormonal status of patients varies in the literature, with 25% of adult forms occurring in postmenopausal women in Norris [6], compared with 67% in Bjorkholm [7]. Some studies show a higher rate of nulliparity compared to the general population [8, 9]. Infertility and use of ovulation inducers have been associated with a higher risk of developing granulosa tumours [10].

The clinical symptomatology of granulosa tumor (GT) is dominated by hormonal manifestations, such as postmenopausal metrorrhagia in 41% of cases, menometroeragia, menstrual irregularities or amenorrhoea [2].

Before puberty, juvenile GTs manifest as precocious pseudo-puberty in up to 80% of cases [2, 4]. In the case of oestrogen secretion, precocious pseudo-puberty is isosexual in the young girl. Hirsutism, clitoral hypertrophy in case of androgen secretion.

Adult granulosa tumours are manifested by a painful abdominal distension syndrome, sometimes monstrous, or by signs of hyperoestrogenism after the menopause with metrorrhagia, endometrial hyperplasia, sometimes atypical, which may precede or be associated with an adenocarcinoma [11].

Generally speaking, asthenia and weight loss are found.

Ultrasound confirms the organic nature of the tumour by showing mixed structures, plurilocular with thick walls, generally without exo- or endocystic vegetations. Their appearance on imaging is not unequivocal, with magnetic resonance imaging (MRI) being superior to CT and Doppler ultrasound.

Adult forms are often unilateral with an average size of 14 cm and extremities of 1 to 30 cm.

For hormone assays, oestradiol is measured in cases of early pseudopuberty; it may be used as a tumour marker.

Serum androgens should be requested in the presence of a masculinising syndrome. Inhibin and anti-mullerian hormone are currently good specific markers for granulosa tumours and are used in diagnosis and monitoring [5].

Microscopically These are often solid cystic tumours [2], grey, white or yellowish in colour, with blood-filled cavities, and are bilateral in 3% of cases, with smooth surfaces, no vegetations and serous content. Haemorrhagic necrotic foci may also be found.

Juvenile granulosa tumours are characterised by dense patches with nuclei without incisure, hyperchromatic and often in mitosis, rare immature mucus-secreting follicles are also seen. Luteinisation is common in juvenile TG. Adult granulosa tumours comprise 5 subtypes of which the most common is micro follicular, which is characterised by the presence of so-called "coffee bean" nuclei and the cellular arrangement in call and exner follicles. Luteinisation in these cases is rare but associated endometrial lesions are seen.

On immunohistochemistry these granulosa tumours express vimentin, CD99, alpha inhibin, cytokeratin and EMA antigen [12]. The vimentin marker is positive in 80% of cases.

The main differential diagnoses of TG are undifferentiated carcinomas, poorly differentiated adenocarcinomas or possibly second-line carcinoid tumours, endometrioid carcinomas, stromal sarcoma, small cell carcinomas, fibrosarcomas and androblastomas [4].

Management is primarily surgical and operative staging is a major prognostic factor.

Treatment is based on total hysterectomy, bilateral amnexectomy and complete staging (omentectomy, peritoneal biopsy and cytological analysis of peritoneal fluid) [2]. Node dissection does not appear to improve survival in early stages [13] due to the rarity of lymph node metastases [2]. According to Shim et all, laparoscopy is possible for this type of tumour [14].

For young patients with a desire for pregnancy in the early stages, conservative treatment can be performed: unilateral adnexectomy, exploration of the abdominal and pelvic cavity and systematic endouterine curettage.

Radiotherapy has not been proven to be effective except in cases of localised recurrence [2]. Platinum-based chemotherapy is proposed for stage Ic or stage II, III and IV. This chemotherapy may be indicated for recurrent disease, large stage I tumours and/or tumours with histological factors indicating a high risk of recurrence [14, 15].

The reference protocol is BVP which combines Cisplatin, Vinblastine and Bleomycin [4] or BEP with Etoposide instead of Vinblastine [16].

Hormone therapy with Megesterol and LHRH agonists has shown some response [17].

Progression is slow, the disease remains confined to the ovaries for a long time and overall survival for stages I and II is 90% at ten years [14].

Recurrences are rare and late, occurring after an interval of 6 to 23 years [2] and especially after conservative treatment their prognosis is poor.

Depending on the stage of the disease, recurrences are 9% in the early stages and 30% in the advanced stages and are often locoregional [2] and are more frequent in the juvenile forms.

Metastases are rare and mainly affect bone, lung and liver.

Monitoring must be prolonged and is based on the dosage of inhibin and anti-millerian hormone, which are more specific than estradiol.

4. Conclusion

Granulosa tumours are rare ovarian tumours of low malignancy, the diagnosis is anatomopathological and the prognosis is related to the initial Figo stage and the treatment is based on surgery.

Conflicts of Interest

The authors declare no conflicts of interest.

Authors' Contributions

All authors contributed to the development and implementation of this work. The authors also declare that they have read and approved the final version of this manuscript.

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