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Pathology

GRANULOSA CELL TUMOR OVARY ASSOCIATED WITH ENDOMETRIAL ADENOCARCINOMA- A CASE REPORT

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ABSTRACT Ovarian granulosa cell tumors represent uncommon neoplasms (2-5% of all ovarian neoplams) with estrogen-secreting capacity. Due to their association with persistently increased levels of estrogen, modifications of the endometrial tissue ranging from hyperplasia to malignant transformation may be encountered. The incidence of associated endometrial carcinomas is under 5%. In patients with granulosa cell tumors, most of these endometrial cancers are well-differentiated endometrioid adenocarcinomas that carry a good prognosis when detected early.

We present the case of a 45-year-old patient who presented with excessive vaginal bleeding. The endometrial biopsy raised the suspicion of an atypical endometrial hyperplasia and the patient was submitted to surgery. Histopathological studies of the specimen of total hysterectomy with bilateral salpingo-oophorectomy revealed the presence of a well-differentiated endometrial carcinoma associated with a granulosa cell tumor of the ovary. In conclusion, a high index of suspicion as well as good imaging and histopathologic analyses are important in making this diagnosis as the association between adult granulosa cell tumors of the ovary and endometrial carcinomas is rare

KEYWORDS : Granulosa cell, adenocarcinoma, estrogen

INTRODUCTION

Ovarian granulosa cell tumors represent uncommon neoplasms arising from the ovarian sex-cord stromal cells, and account for 2-5% of all ovarian cancer [1-3]. They occur more often in post-menopausal than pre-menopausal women, with a peak incidence between 50 and 55 years of age. They are the most common estrogenic ovarian tumors diagnosed clinically, but the precise proportion of adult granulosa cell tumors that secrete hormones is difficult to establish because an endometrial tissue specimen used to evaluate the effects of estrogenic stimulation is often unavailable. The typical endometrial reaction associated with functional tumors in this category is simple hyperplasia that usually exhibits some degree of pre-cancerous atypicality. Reports of the incidence of an associated endometrial carcinoma, which almost always is well differentiated, have ranged from slightly less than 5% to slightly more than 25% of cases [4,5]. The wide variation in these figures is attributable at least in part to differing views of the dividing line between complex atypical hyperplasia and grade 1 adenocarcinoma. If strict criteria for the diagnosis of carcinoma are used and all patients with granulosa cell tumors, not only those who have undergone endometrial curettage or hysterectomy, are considered, the best estimate of the incidence of an associated endometrial carcinoma is under 5% [4].

Most tumors are large, solid or cystic, with slow growth and tendency for late recurrence [1, 6, 7]. When it comes to their hormonal activity, the estradiol concentration is not a reliable marker of disease activity, no significant correlation has been established between it and the presence of bulky disease [8, 9]. Most often, malignant endometrial transformation comprises well-differentiated endometrioid adenocarcinoma; in rare cases, another pathological pathway might be incriminated, unrelated to estrogen stimulation, leading to development of serous carcinoma. [10].

CASE REPORT

A 45-year-old patient presented for lower abdominal pain and excessive vaginal bleeding since two months. The local examination showed no modifications of the uterine cervix; Papanicolau test excluded any microscopic modification of the uterine cervix, while ultrasonography revealed the presence of fibroid. The patient was submitted to endometrial biopsy, which confirmed the presence of an endometrial hyperplasia with rare atypia; the patient was submitted to surgery radical hysterectomy with bilateral adnexectomy and pelvic lymph node dissection.

Grossly, uterus with cervix measured 10.5x8x4.5 cm and left ovary measured 3x3x1.8 cm. The surface of ovary was smooth and cut surface was solid. The histopathological studies revealed the presence of an adult ovarian granulosa cell tumor (Figure 1) in the left ovary associated with a well-differentiated endometrioid adenocarcinoma (Figure 2). Microscopical evaluation revealed a diffuse growth pattern of adult granulosa cell tumor, with low mitotic activity of 1-2 mitoses per 10 high-power fields, with no surface involvement. The uterine body presented lesions of complex hyperplasia with cellular atypia associated with the presence of a locally well-differentiated invasive glandular process involving less than 50% of the myometrial depth.

The postoperative course was uneventful, the patient was discharged on the tenth postoperative day.

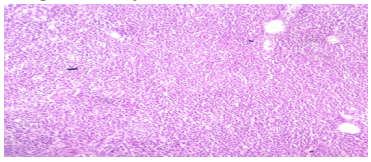

Figure 1. Photomicrograph showing Granulosa cell tumor ovary

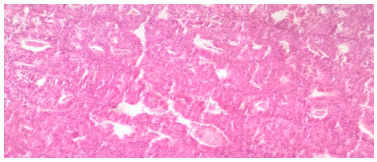

Figure 2: Photomicrograph showing Endometrioid adenocarcinoma endometrium FIGO Grade I

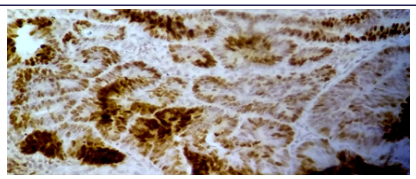

Fig. 3 Photomicrograph showing ER positive endometrioid Adenocarcinoma

DISCUSSION

Adult granulosa cell tumors account for approximately 2-5% of all ovarian tumors [1-3]. Adult granulosa cell tumors occur more often in post-menopausal than pre-menopausal women [4]. This was not the case with our patient, who was pre-menopausal. If strict criteria for the diagnosis of carcinoma are used and all patients with a granulosa cell tumor, not only those who have undergone endometrial curettage or hysterectomy, are considered, the best estimate of the incidence of associated endometrial carcinomas is under 5% [4]. In order to reach the right diagnosis, an endometrial biopsy is required; most commonly, endometrial hyperplasia exists; however, it seems that up to one-third of the specimens are associated with the presence of endometrial atypia. The natural progression of the disease is through low-grade endometrial endometrioid adenocarcinoma, which is reported in 5% up to 20% of cases. Less commonly, a serous adenocarcinoma will develop; however, it seems that is more likely to be related to the presence of *p53* mutation than to an excess of estrogen [7, 10, 11, 12]. In patients with ovarian granulosa cell tumor, a four-fold increased incidence of breast cancer has also been reported [13].

In order to determine the most important prognostic factors which might predict the association with endometrial cancer, Ottolina *et al.* conducted a retrospective study involving 150 patients with adult granulosa cell tumors of the ovary. They demonstrated that endometrial carcinoma was most often present in symptomatic patients (p=0.001) over 40 years of age or post-menopausal (p<0.001) [14].

However, it seems that not only estrogen synthesis is responsible for the endometrial cancer in these patients. Another associated factor is the presence of steroid hormones [15, 16], while the presence of progesterone has an antagonistic action by down-regulating estrogen receptors and enhancing the conversion of estradiol to the less active estrone by increasing the activity of 17 β-hydroxysteroid dehydrogenase [14].

When it comes to the most important prognostic factors of women diagnosed with ovarian granulosa cell tumors, one of the most important factors predicting the recurrence rate and overall survival remains the presence of nuclear atypia. A significant association between the presence of nuclear atypia and time to recurrence also exists: tumors which develop early recurrence usually have a higher rate of nuclear atypia, of up to 77%, while those with late recurrence present nuclear atypia in up to 33% of cases [4, 6, 17,18]

CONCLUSION

As association between adult ovarian granulosa cell tumor and endometrial cancer is an uncommon situation, a high index of suspicion as well as good imaging and endometrial biopsy are important in making this diagnosis; whenever a modified aspect of the endometrium is found, the standard therapeutic protocol consists of total radical hysterectomy with bilateral adnexectomy.

REFERENCES

1. Evans AT III., Gaffey TA, MalkaSIAN GD Jr., Annegers JF. Clinicopathological review of 118 granulosa and 82 theca cell tumors. Obstet Gynecol. 1980;55: 231-238.
2. Fox H, Agrawal K, Langley FA. A clinicopathological study of 92 cases of granulose cell tumor of ovary with special reference to the factors influencing prognosis. Cancer. 1975; 35: 231-241.
3. Unkila-Kallio L, Tiitinen A, Wahlstrom T, Lehtovirta P, Laminen A. Reproductive features in women developing ovarian granulose cell tumorat a fertile age. Hum Reprod. 2000; 15: 589-593.
4. Young RH, Scully RE. Blaustein's Pathology of the Female Genital Tract. 5. New Delhi: Springer-Verlag; 2002. Sex cord-stromal, steroid cell, and other ovarian tumours, and paraneoplastic manifestations; pp. 907–917.
5. Deligdisch L, Holinka CF. Endometrial carcinoma: two diseases? Cancer Detect Prev. 1987;10:237–246
6. Pectasides D, Pectasides E, Psyrri A. Granulosa cell tumor of the ovary. Cancer Treat Rev. 2008; 34: 1-12.
7. Bjorkholm E, Silfversward C. Prognostic factors in granulose cell tumors. GynecolOncol. 1981; 11: 261-274.
8. Lappojn RE, Burger HG, Bouma J, Bangah M, Krans M, de Bruijn HW: Inhibin as a marker for granulose cell tumors. N Engl J Med. 1989; 321: 790-793.
9. Rey RA, Lhomme C, Marcillac I, Lahlou N, Duvillard P, Josso N, Bidart JM. Antimullerian hormone as a serum marker of granulose cell tumors of the ovary. Comperative study with serum alpha-inhibin and estradiol. Am J Obstet Gynecol. 1996; 174: 958-965.
10. Lax SF. Molecular genetic pathways in various types of endometrial carcinoma: from a phenotypical to a molecular based classification. VirchowsArch. 2004; 444: 213-223.
11. Aboud E, Crow J, Gordon H. Sex cord- stromal tumors of the ovary- a 25-year review. J ObstetGynaecol. 1997; 17: 554-556.
12. Rabban JT, Gupta D, Zaloudek CJ, Chen LM. Synchronous ovarian granulose cell tumor and uterine serous carcinoma. a rare association of a high risk endometrial cancer with anestrogenic ovarian tumor. GynecolOncol. 2006; 103: 1164-1168.
13. Ohel G, Kaneti H, Schenker JG. Granulosa cell tumors in Israel: a study of 172 cases. GynecolOncol. 1983; 15: 278-286.
14. Ottolina J, Ferrandina G, Gadducci A, Scollo P, Lorusso D, Giorda G, Breda E, Savarese A et al. Is the endometrial evaluation routinely required in patients with adult granulose cell tumors of the ovary? GynecolOncol. 2015. 136: 230-234.
15. Sachdev D, Yee D. Disrupting insulin like growth factor signalling as a potentialcancer therapy. Mol Cancer Ther. 2007; 6: 1-12.
16. Gadducci A, Genazzani AR. Steroid hormones in endometrial and breast cancer. Review.Eur J GynecolOncol. 1997; 18:371-378.
17. Miller BE, Barron BA, Wan JY, Delmore JE, Silva EG, Gershenson DM. Prognostic factors in adult granulose cell tumor of the ovary. Cancer. 1997; 79: 1951-1955.
18. Kietlinska Z, Pietrzak K, Drabik M. The management of granulose-cell tumors of the ovary based on long term follow up. Eur J GynaecolOncol. 1993; 14:118-127.