Granulosa And Theca Cell Tumors Of The Ovary

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Credit for the first description of granulosa cell tumor is given to von Werdt and to Loeffler and Piesel for thecoma. Collectively these tumors are known as feminizing mesenchymomas. More than 1100 granulosa cell and 300 theca cell tumors have been reported in the world literature. Age incidence is wide. A thecoma was removed from a woman aged 92 years and bilateral granulosa cell tumors from an infant aged 14 weeks. About 50% of granulosa cell tumors and 40% of thecomas occur before the menopause. Approximately 5% of granulosa cell tumors are seen in the pre-pubertal age group; however, thecomas are rare before the age of 30. Only 3 thecomas have been reported before the age of 10 and one of these in a patient under one year.

Classifications of ovarian tumors often list both granulosa cell and theca cell tumors as “functioning tumors”, and some authors have reported between 60% and 95% as functional. However, in many instances, no “functioning” influence is present. In most cases the clinical parameter of function was estrinism; but rare cases have shown virilism. Depending on the age group, the earliest symptom may be precocious pseudo-puberty, menorrhagia, or postmenopausal bleeding. On physical examination an adnexal mass may be felt, but no statistics are available which show the percentage of these tumors to be palpable. Abnormal uterine bleeding incidental to the tumor is often associated with hyperplastic endometrium. Some authors report an increased incidence of endometrial carcinoma in patients with granulosa cell tumor of the ovary. If in a patient with postmenopausal bleeding the first and second dilatation and curettage yields endometrium which is hyperplastic, a repeated episode of bleeding would suggest the need of laparotomy even in the absence of positive pelvic findings.

Recent publications list the incidence of malignancy of granulosa cell tumor as 10% or more. The degree of malignancy of the tumor is difficult to predict even by histologic appearance. Each granulosa cell tumor should be considered potentially malignant and a thorough microscopic examination done. Only 10 cases of malignant thecomas are reported in the literature.

The granulosa cell tumor is usually unilateral and solid and varies in size from a few millimeters to 34 pounds. It may be cystic, hemorrhagic and variable in color. Microscopically the pattern is cylindromatous, microfollicular with Call-Exner bodies (Fig. 1) sarcomatous or undifferentiated. Grossly, thecomas appear similar to fibromas or leiomyomas. Microscopically they show fibrous and thecal elements and may require fat stains to differentiate them from the fibromas. Luteomas may be included here since Novak and others consider them lutinized granulosa-theca cell tumors and not a separate class.

Treatment depends upon the age of the patient. If in the prepubertal patient the tumor is bilateral, or unilateral and locally invasive, removal of both adnexae and uterus is indicated. If the tumor is unilateral and non-invasive a unilateral...
Oophorectomy is acceptable provided the patient is carefully and frequently followed.

The patient in the menstrual age group presents a greater problem. Formerly, it was suggested that if the tumor was unilateral and non-invasive it was permissible to save the uterus and opposite ovary, depending upon the patient's desire for more children. Because of recurrence even when the tumor is non-invasive, confined to one ovary, and apparently benign conservatism based on age or child-bearing potential should not be considered, and patients in this group should have bilateral oophorectomy and hysterectomy.

In the postmenopausal patient, regardless of one or both ovary involvement, bilateral oophorectomy and hysterectomy are indicated. Radiation is best reserved for patients in whom invasion or recurrence is proved. Granulosa cell tumors
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have been known to recur 22 years following surgery and may respond well to radiation. Treatment of thecomas is the same as for any benign unilateral ovarian lesion unless malignancy upon microscopic examination is shown. Patients with either type of tumor should be closely followed for the rest of their lives.

CASE DISCUSSION

This report is of 17 patients, three of whom present unusual features. The earliest symptoms included some form of abnormal uterine bleeding in six of the ten patients with granulosa cell tumors and four of the seven with thecomas. A definite pelvic mass was present preoperatively in only seven of the 17. Total hysterectomy and bilateral salpingo-oophorectomy was performed on 11 patients and unilateral oophorectomy with or without hysterectomy on the remaining 6. Two patients received radiation, one of whom is still living.

In our granulosa cell tumor group the mortality was 30%. This figure is deceptive just as are the figures in many large series which show five-year cure rates but fail to allow for late recurrence of the tumor. A summary of granulosa and theca cell tumor cases seen at this clinic for the past 30 years is shown in Table I.

Case No. 13 represents one of the youngest patients with thecoma yet reported. In 1950 no case of thecoma in a patient under age 16 had been reported, but by 1959 there were 5, one of whom was less than one year old. Our patient was 13 years of age, and onset of menses was at age 10. The menses were regular until age 11½ when the patient because of excessive bleeding was examined by a physician. The patient was given “shots and pills” to control the menses but with only partial success. The patient was first seen at this hospital because of excessive bleeding, and the significant findings were development of secondary sex characteristics beyond that expected for her age and an adnexal mass considered to be a granulosa cell tumor preoperatively. At operation a thecoma was found, and fat stains were done to differentiate it from a “cellular fibroma”. The patient is reported without recurrence 7½ years after unilateral oophorectomy.

Case No. 2 is unusual because the patient had a recurrence of tumor in her remaining ovary 18 years after the original tumor was removed and one year later died of widespread metastases.

Case No. 9 represents a patient who had had a unilateral oophorectomy for a granulosa cell tumor, and eight years later developed recurrence in the other ovary. This ovary, and a granulosa cell tumor mass on the serosa of the colon were excised, and a biopsy of an infiltrating lesion of the pelvic wall which also proved to be granulosa cell was done. The patient received 2,400 r of deep x-ray therapy and is living without further evidence of recurrence after five years.

DISCUSSION

The experience at this clinic with granulosa and theca cell tumors of the ovary is similar to that reported in the literature. The number of “functional” tumors found and the percentage of tumors clinically palpable are less than other authors
<table>
<thead>
<tr>
<th>CASE</th>
<th>PRESENTING SIGNS AND SYMPTOMS</th>
<th>HORMONE ACTIVITY</th>
<th>TREATMENT</th>
<th>PATHOLOGY</th>
<th>FOLLOW-UP</th>
<th>YEARS SURVIVED</th>
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<tbody>
<tr>
<td>2. C. H.</td>
<td>Unknown.</td>
<td>Unknown</td>
<td>Hyst. Bilat. S&amp;O.</td>
<td>Granulosa cell tumor</td>
<td>Died 18 years after primary due to wide metastases.</td>
<td>18</td>
</tr>
<tr>
<td>16. V. A.</td>
<td>Stress incontinence, no vag. bleeding. R. Ovarian cyst.</td>
<td>? Estrin</td>
<td>Total hyst. R. oophorectomy, Left previously.</td>
<td>Combination of thecal &amp; granulosa cell without definity,</td>
<td>No recurrence.</td>
<td>3 plus alive</td>
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report. The mortality rate compares with similar series and is high enough to consider all granulosa-cell tumors as potentially malignant.

The results of unilateral versus bilateral oophorectomy with or without hysterectomy, as related to prognosis, is not as clear-cut in this series as it is in others. However, bilateral surgery does appear to offer the best chance for survival. Several cases reported elsewhere show unilateral, non-invasive and well-differentiated granulosa cell tumors to have been found in patients 18-30 years of age. These patients were treated by conservation of one ovary and later developed fatal recurrences.

The gynecologist who finds a granulosa cell tumor in a patient in the menstrual age group must carefully consider further treatment indicated on the basis of all available information. There is no clear-cut basis for the management of these patients, and each must be given individual consideration. Some gynecologists consider the patient’s desire for future child-bearing as a basis for conservative management while others feel that malignant or potentially malignant tumors should be treated the same in all patients regardless of age.

SUMMARY

This report is a survey of 17 cases of granulosa cell and theca cell tumors and represents a 30-year experience at this clinic. Three cases show unusual features. Age is the chief factor considered in treatment. The mortality rate, number of functional tumors found and surgical treatment are compared with similar series appearing in the literature.

REFERENCES


ADDITIONAL REFERENCES

Tumors of the Ovary


Wilkins, L.: The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence, Springfield, Thomas, 1950, p.156.