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THECA-CELL TUMORS

Clinical features and prognosis

ELISABET BJÖRKHOLM and CLAES SILFVERSWÄRD

Theca-cell tumors, thecomas, were first described by LÖFFLER & PRIESEL (1932). The crude annual incidence among Swedish women in the period 1958 to 1972 was 0.74 per 100000 (BJÖRKHOLM & SILFVERSWÄRD 1980). Thecomas belong to the granulosa-stromal-cell tumor group which consists of neoplasms containing granulosa-cells, theca-cells and stromal cells resembling fibroblasts, singly or in various combinations. Pure theca-cell tumors are almost always benign (SCULLY 1970, NORRIS & CHORLTON 1974) whereas granulosa-cell or mixed granulosa-theca-cell tumors may be malignant (MORRIS & SCULLY 1958). Thus, it is important to identify patients with pure thecomas who should be treated with surgery alone, not including them in the granulosa-cell tumor group in which in certain cases irradiation may be added. Women with thecomas (and granulosa-cell tumors) often have endometrial carcinoma (INGRAM & NOVAK 1951, MANSELL & HERTIG 1955). Sixty-two patients with thecoma have been treated at Radiumhemmet, one fifth of them having concomitant endometrial carcinoma. The clinical features and the treatment of these women are now presented. The survival has been determined by comparison with age- and geographically matched control women.

Material and Methods

During the period 1923 to 1972, 313 women with microscopically confirmed granulosa-stromal-cell tumors were treated at this oncologic department. Material from the ovarian tumor (the original slides or new slides prepared from the original paraffin blocks and stained with haematoxylin-eosin) was still available for 278 cases. A re-evaluation was performed, the clinical data being unknown to the pathologist (C. S.).

The present series ultimately consisted of 62 cases considered to be pure thecomas. Endometrial biopsies dating from time of diagnosis of the ovarian tumor were available for 52 per cent of these cases. The diagnosis thecoma was consistent with the initial diagnosis in 39 cases, 3 cases originally diagnosed as thecoma were now being considered as granulosa-cell tumors as they contained epithelial strands of the granulosa-cell type, and 17 cases previously diagnosed as granulosa-cell tumors were now considered to be thecomas. Six fibromas were at review included in the thecoma group because of typical theca-cell proliferation, some of these also with signs of estrogenic function (the patients having glandular cystic hyperplasia of the endometrium). Clinical data were collected from the hospital records. The system of civil registration in Sweden made it possible to obtain age- and geographically matched control women, limited to the patients residing outside Stockholm City. Forty control women were assigned to 65 per cent (20) of the women with theca-cell tumors living outside Stockholm City at

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the time of diagnosis. The patient and her 2 controls were of the same age when they entered the series at the time of diagnosis of the patient's ovarian tumor. Information on civil status and childbirth for both groups was obtained. A follow-up was performed in 1977 and 1978. A final date for collecting the series was set to 25 November 1977. Causes of death were based on information from death certificates. Survival over time was described with life tables and differences in survival were tested using the log-rank test (PETO et coll. 1977).

Results

The mean age at diagnosis was 59.5 years, range 19 to 81 years (Fig. 1), and 84 per cent of the women had passed the menopause. A history of abdominal pain of varying severity was given by one third of the patients. Abnormal uterine bleeding was reported by 6 of 10 pre-menopausal women and one patient 23 years of age had experienced secondary amenorrhoea during one year before diagnosis. Among post-menopausal women 60 per cent had reported uterine bleeding. All patients belonged to clinical stage I (FIGO), 3 per cent had bilateral tumors and 5 per cent had ascites exceeding 0.5 liter. The mean tumor size was 7 cm, range <1 to 20 cm. Thirteen endometrial carcinomas, 21 per cent of the total series, were confirmed at review, 8 were highly differentiated adenomatous carcinoma, 4 were differentiated adenomatous carcinoma with partly solid areas and 1 was a predominantly solid carcinoma (FIGO). The mean age at diagnosis of the women with a concomitant endometrial carcinoma was 69.8 years, range 47 to 71 years. One case of atypical hyperplasia was diagnosed. Glandular cystic hyperplasia was found in 56 per cent of the reviewed endometrial biopsies. The hormonal changes of the endometrium were impossible to observe in one third of the cases as all endometrial tissue was malignantly transformed. The contralateral ovary was available in 12 cases, one third having ovarian stromal hyperplasia. All patients were operated upon (Table). Additional radiation therapy was given to 60 per cent of the patients, of these 16 per cent had a concomitant endometrial carcinoma. At the follow-up the mean observation time was 15.5 years, range 1 to 34 years. Thirty-two women had died and no patient was lost to the follow-up. No patient with thecoma died from the ovarian neoplasm. Malignant disease caused death in 7 women,

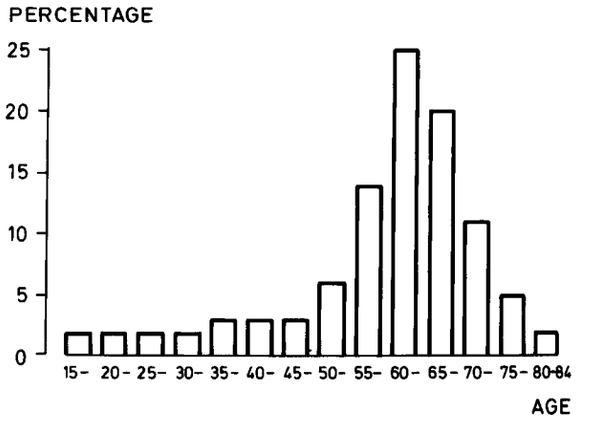

Fig. 1. Distribution of 62 patients with thecoma by age (years).

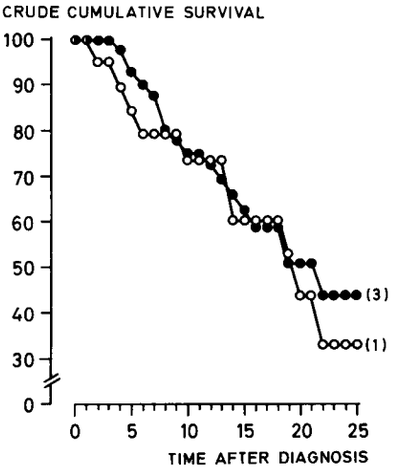

Fig. 2. Crude cumulative survival (per cent) at time after diagnosis (years). The numbers of patients (○) and controls (●) at entry were 20 and 40, respectively, still living and under observation after 25 years were 1 and 3.

3 endometrial carcinomas, one mammary carcinoma and 3 intestinal tumors.

The crude cumulative percentage of survivors (counting deaths from all causes) for the 20 patients with thecoma and their 40 controls is given in Fig. 2, half of the patients had received radiation therapy, 7 of the 20 patients had a concomitant endometrial carcinoma. No statistically significant difference in survival was found between the patient and the control group. The mortality from cerebrovascular and cardiovascular diseases dominated and was equal for both groups. Endometrial carcinoma caused death in 2 women of the patient group, whereas no control woman died of that cause. Of married women in the patient group 71 per cent had given birth

Table

Sixty-two patients who at review were classified as thecoma, by original diagnoses and mode of treatment

Mode of treatment	Original diagnosis			Total No. of cases
	Thecoma	Granulosa-cell tumor	Fibroma	
Unilat. oophorectomy	4	4	0	8
Unilat. oophorectomy and radiation therapy	2	1	0	3
Bilat. oophorectomy	5	1	3	9
Bilat. oophorectomy and radiation therapy	10	6	3	19
Hysterectomy and bilat. oophorectomy	5	2	0	7
Hysterectomy, bilat. oophorectomy and radiation therapy	3	0	0	3
Treatment for concomitant endometrial carcinoma: Hysterectomy and bilat. oophorectomy, with or without radiation therapy	10	3	0	13
Total	39	17	6	62

to at least one child at time of diagnosis; at that time the corresponding figure for the control group was 77 per cent.

Discussion

A thecoma is generally easy to identify at microscopy. It is composed of pale, oval or spindle shaped cells arranged in irregular interlacing bundles, traversed by bands of fibrous tissue with varying degrees of hyalinization. Fat droplets are demonstrable by special stains in and between the cells. It may sometimes be difficult to distinguish thecomas from sarcomatoid granulosa-cell tumors. Granulosa-cell areas, not clearly identifiable on haematoxylin-eosin stained slides, may be present in some thecomas (WAXMAN et coll. 1979). Silver reticulum stains have been used to try to identify granulosa- and theca-cell components. The theca-cells are individually surrounded by this reticulum, whereas granulosa-cells are not at all enclosed, or as groups of cells (TRAUT et coll. 1939). The reticulum stained slides are sometimes confusing and difficult to evaluate (KNIGHT 1948) nor do they always reveal this network (BIGGART & MACAFEE 1955).

No serious differential diagnostic difficulties were encountered when reclassifying this series. In one or two cases a silver-reticulum stain might have added to the diagnostic accuracy, but as only the original slides were accessible and no paraffin blocks, a silver reticulum stain was impossible to perform in those cases.

It is impossible to draw a sharp demarcation line between fibromas and thecomas (MORRIS & SCULLY). They may indeed be variants of a single neoplasm with a common origin from the ovarian stroma (AMIN et coll. 1971). The thecoma is typically estrogenic, the fibroma is non-functioning. In this series fibromas were defined as small tumors with markedly few cells of the spindle-cell type and with an abundance of collagen. Fat is usually not demonstrable in fibromas.

The clinical features of the patients with thecoma in the present series are similar to those previously reported (BANNER & DOCKERTY 1945, STERNBERG & GASKILL 1950). A high proportion of endometrial carcinomas was found in patients with this tumor. Feminizing ovarian tumors (granulosa- and theca-cell tumors) are often complicated by endometrial carcinoma. However, only 0.4 per cent of the patients with endometrial carcinoma treated at Radiumhemmet between 1923 and 1972 had a concomitant feminizing tumor, 0.2 per cent were of the thecoma type (BJÖRKHOLM, unpublished data). Almost all thecomas are benign, but a few malignant cases have been reported. A review of the literature has recently been published by WAXMAN et coll. who proposed that the name malignant thecoma should not be used. Instead they suggested the name stromal sarcoma for those very rare malignant stromal ovarian neoplasms that are composed of primitive mesenchymal cells, fibroblasts and theca-cells.

No woman in the present series died from the

thecoma. No difference in survival was found between the 20 patients and their 40 controls although more than one third of these patients had a concomitant endometrial carcinoma which in the majority of the cases was highly differentiated. Cerebrovascular and cardiovascular disease was the major cause of death in both patients and controls.

WYNDER et coll. (1969) did not find any real differences between patients with ovarian malignancy and controls as regards age at first pregnancy and delivery, last pregnancy and delivery and total number of pregnancies. The number of parous married women was almost the same for the present patients and the controls.

It is noteworthy that half of the patients without endometrial carcinoma received complementary radiation therapy due, no doubt, to a previous uncertainty as to whether these neoplasms were of a malignant nature or not. To-day unilateral oophorectomy in pre-menopausal women with a stage I a (FIGO) disease would be suggested. The possibility of a concomitant endometrial carcinoma has to be ruled out especially for post-menopausal women. No complementary irradiation should be given because of the ovarian tumor.

SUMMARY

During the period 1923 to 1972, 62 women with theca-cell tumors were treated at Radiumhemmet. The mean age at diagnosis was 59.5 years. Concomitant endometrial carcinoma was found in 13 patients. At 1978, after a mean observation time of 15.5 years, 30 patients were alive. No patient died from thecoma. Malignant disease caused death in 7 women. No difference in survival was found between 20 patients and 40 controls matched by age and place of residence.

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