GRANULOSA CELL TUMOUR OF OVARY

(A Report of Six Cases)

by

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Sex cord stromal tumours of ovary have been broadly classified (Serov *et al,* 1973) under the following groups depending entirely on the morphological terms without reference to hormone production.

(a) Granulosa stromal cell tumours

(b) Androblastoma (Sertoli-Leydig cell tumours)

(c) Gynandroblastoma

(d) Unclassified.

Granulosa cell tumour (GCT) is the most frequently encountered ovarian tumour associated with endocrine anomalies. While reviewing the literature Hughesdon (1958) has reported that the name of the tumour was given by Von Werdt (1914). The incidence of GCT varies from 2 to 4% of all the ovarian tumours (Gault *et al,* 1954; Mehta and Purandare, 1964; Tyagi *et al,* 1967; Ramachandran *et al,* 1972).

Generally these tumours have been discussed along with other ovarian tumours or as case reports in Indian literature. Very few reports are available where a big series of granulosa cell tumours have been reported (Talib *et al,* 1975).

The authors take this opportunity to report a series of 6 cases of granulosa cell tumour as they presented some interesting and unusual morphological pictures.

Material and Methods

During the histopathological study of 145 ovarian tumours examined in the Department of Pathology, Jawaharlal Nehru Medical College, A.M.U., Aligarh, 6 cases were diagnosed as granulosa cell tumours.

In each case, after taking brief history, a detailed gross examination was done and at least 4 blocks from each tumour were taken from the representative areas for histopathological examination. Sections were cut at 4 to 5 microns thickness. Besides routine haemotoxylin and

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eosin stain special stains were done wherever necessary.

Observation

In the present series GCT constituted 4.1% of total ovarian tumours and 14.2% of all the malignant growths of the ovary. The age of the cases ranged from 22 to 65 years, average age being 45 years. The most common presenting symptoms in these cases were irregular uterine bleeding and a gradually increasing lump in the lower abdomen. The duration of the symptoms ranged from 3 months to 3 years. Parity of the cases ranged from 2 to 10. Physical examination revealed more or less the similar findings in all cases. Ascitis was present in 2 cases.

Gross Pathology

Bilateral ovarian tumour was seen in 1 case (Fig. 1), in 3 the left ovary was involved and in 2 the right ovary. The tumours varied in size from 12 to 25 cms. in diameter weighing from 800 gms to 3200 gms. There was no apparent correlation between the age of the patient, size of the tumour and duration of the symptoms. The surface of the tumour was smooth in 2 and lobulated in 4. No surface adhesions were present. The consistency was firm in 5 cases while partly cystic and partly solid in 1.

Cut surface of all the tumours presented a varigated picture. The colour varied from greyish-white to yellowish-brown or bluish or blackish in different areas. Multiple small cystic spaces were seen in 5 tumours filled with coagulated material. There were areas of necrosis and haemorrhage.

The heaviest tumour (3200 Gms) was nodular in shape, nodules varying from 5 to 10 cm. in diameter. On cutting, the tumour was multilocular, some loculi were filled with dark brown coagulated material while others with yellowish necrotic material.

Panhysterectomy was done in 4 cases. In 3 cases endometrial polyp was seen which was filling more or less the entire cavity of an atrophied uterus in 1 case (Fig. 1).

Microscopic Pathology

The tumours presented a variety of morphological pictures. The varied pattern was not only present in different tumours but also in different portions of the same tumour and even in the same section. The tumour cells were characterised by the presence of illdefined scanty cytoplasm and prominent vesicular nuclei of variable size.

The arrangement of granulosa cells was very much complex not only in different tumours but also in the same tumour. In 1 case (bilateral tumours) the cells were arranged diffusely or in large masses or papillary cord like structures separated by edematous stroma. At one or two places foreign body type of giant cells were seen. Cells forming the boundary of the tumour masses were arranged in palisading manner.

In most of the tumours the cells were arranged diffusely or in trabecular form or in groups. Characteristic follicular pattern was rarely seen. In 1 tumour besides above morphological picture the tumour cells were arranged in a perithelial manner (Fig. 2). The centre of the mass was occupied by a blood vessel sorrounding which there was some loose connective tissue and then a palisading row of one to two cells imparting the picture of endodermal sinus tumour but other features of the tumour were missing.

In another case, besides cells being arranged as cords, diffuse sheets, islands

and trabeculae the cells were showing extreme degree of pleomorphism, bizarre nuclei and fair number of division figures, more or less giving the appearance of sarcoma (Fig. 3).

The Call-Exner bodies, one of the main distinguishing feature of the tumour, were present in 2 tumours. In 1 case innumerable microcysts were present of varying size and filled with light stained eosinophilic fluid (Fig. 4). Thus more or less every tumour had some peculiar morphology. Mitoses ranging from 1 to 4 per high power field were present in 4 cases.

Connective tissue stroma was scanty in 4 while abundant in 2. Reticulin stain revealed the presence of reticulin fibres surrounding groups of cells. Marked edema was noticed in 1.

Endometrial Changes in GCT

In 4 cases hysterectomy was done, whereas in 2 endometrial biopsy tissue was obtained. Histologically the endometrial reaction was proliferative in all the cases with cystic hyperplasia in 4. The glands were filled with dark brown fluid or blood and in 1 case the glands were seen penetrating deep into the musculature. In remaining 2 cases the endometrium showed occasional dilatation of glands. The stroma was compact and cellular.

Ascitis was present in 2 cases. The fluid was clear in 1 case while haemorrhagic in the other. Cytological examination of fluid was negative for malignant cells.

Discussion

In the present series the incidence of GCT was 4.1% of total ovarian tumours and 14.2% of all the malignant growths of the ovary. This was in total agreement with the observations of the other workers (Falls *et al*, 1949; Mehta and Purandare, 1964; Tyagi *et al*, 1967; Vora and Bhargava, 1969 and Talib *et al*, 1975). In 1 case the tumour was bilateral (16.7%). Herbut (1953) has also reported the incidence of bilateral tumours as 17.5%.

These tumours were seen in the age group of 20 to 70 years with an average age of 45 years and manifested mainly as irregular uterine bleeding. Einsel *et al* (1953) have also reported that 60% of GCT occur after menopause, whereas Talib *et al* (1975) have reported average age as 30 years. However, these tumours can be seen at any age with varying symptomatology according to age involved.

Generally these tumours are solid as was observed in the present study though cystic granulosa cell tumours have been reported occasionally (Baveja *et al*, 1972). The size of the tumour may vary from 0.4 to 40 cm. (Hertig and Gore, 1961). However, in the present study in 4 cases the tumour was above 15 cm in diameter.

The most interesting feature was the variable morphological picture seen not only in different tumours but also in the same tumour or even in the same section. The characteristic follicular arrangement was rather sparse. Diffuse lay out of the tumour cells separated by thin fibrous septa was the commonest pattern. In 1 case the morphological pattern was that of pseudosarcoma where biarre nuclei and atypical division figures were seen.

Perithelial arrangement of the cells may be confused with that of endodermal sinus tumour but other features like tubules and cysts formation were missing and moreover the presence of endometrial polyp further ruled out the possibility of a teratomatous growth. Other unusual finding was the presence of mitotic figures

ranging from 1 to 4 per high power field in 4 cases and these cases were labelled as malignant granulosa cell tumours. GCT are mostly benign looking on morphology but with a malignant course. Hence, for all practical purpose GCT is considered as malignant. Kottmeier (1953) has reported that no connection seems to exist between clinical and histological malignancy as far as granulosa cell tumours are concerned.

The symptomatology of GCT is usually due to its endocrine activity and its size. Metastases are generally local. Distant metastases are very rare. The papillary arrangement in the tumour may be confused with epithelial tumour having a 'tubal type' differentiation of the mesothelium.

GCT is the commonest functioning tumour of the ovary as was evident in the cases under review. The characteristic cystic hyperplasia of the glands was seen in 4 cases whereas in 2 occasional dilatation of the glands was observed. Sometimes these tumours are associated with carcinoma uterus or cancer breast (Hertig and Gore, 1961). When there is partial or complete leutinization of the tumour evidence of progesterone effect upon the endometrium may be seen in the form of typical secretory phase of endometrium (Novak and Woodruff, 1974). A high incidence of adenomyosis has been reported (Hertig and Gore, 1961). It was seen in 1 case out of 6 in the present series.

Histogenetically GCT along with thecoma has been considered to arise from the ovarian stromal cells (Novak and Woodruff, 1974) and the old concept of Meyer (1931) that GCT arises from the redundant granulosa cells or 'granulosa-ballen' is generally discarded.

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Summary

Six cases of Granulosa cell tumour occurring in the age group of 20 to 70 years have been reported. All of them presented with an increasing lump in the lower abdomen and irregular vaginal bleeding. The incidence of this tumour was 4.1% of all the ovarian tumours or 14.2% of all the malignant growths of the ovary. Bilateral tumours were seen in one case (16.7%).

Five tumours were solid and one partly solid and partly cystic. Histologically varied morphological picture was seen not only in different tumours but also in the same tumour. In four tumours diagnosis of malignant granulosa cell tumour was made depending on the microanatomic picture. Three cases had endometrial polyp in the uterine cavity.

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See Figs. on Art Paper VII