STUDY OF TUMOUR MARKERS IN OVARIAN NEOPLASMS—II—SEX CORD STROMAL TUMOURS

By

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SUMMARY

We could demonstrate presence of oestradiol in 67% of 12 cases of sex cord stromal tumours of the ovary by immunohistochemical technique, consisting of 7 granulosa cell tumours and 1 case of sex cord tumour with annular tubules. Five granulosa cell tumours showed presence of alpha foetoprotein (AFP) and 1 case showed presence of human chorionic gonadotropin (HCG) with or without coexisting oestradiol secretion. Keratin was absent in tumours of this group.

Introduction

Immunohistochemistry has proved itself to be an invaluable tool in demonstrating the various tumour markers known to be associated with ovarian tumours (Gaffney *et al* 1983; Eoin *et al* 1984) and, at present, there is a great need for screening procedures and carefully evaluated research to conclude the significance of these markers in the biology of these tumours. Despite apparently clear cut oestrogenic activity of granulosa cell tumours, there has been a remarkable pausity of endocrinological studies in women with such tumours (Fox, 1985) and, it is not clear whether the feminising effect of these tumours is due to hypersecretion or to prolonged uninterrupted normal oestrogen level (Gerbei and Gerbei, 1975). Jansen and Shearman (1981) is of view that the Granulosa cells produce oestrogen only by aromatisation of androgenic precursors synthesised by theca cells and oestrogen has been demonstrated by immunohistochemistry in the granulosa cells of these tumours (Kurman, 1984) or in both granulosa cells and in luteinised theca cells (Taylor and Warner, 1983). It has been our intention to demonstrate oestradiol in sex cord stromal tumours of the ovary and to probe as to how many of these secrete other tumour markers as alpha foetoprotein (AFP) and/or human chorionic gonadotropin (HCG).

Materials and Methods

Formalin fixed paraffin embedded tissue blocks from sources detailed in Part-I of the same paper were used for this study and consisted of 10 granulosa cell tumours, 1 sex cord tumour with annular tubules (SCTAT) and 1 malignant lipid cell tumour. After routine H & E stain and diagnosis, immunohistochemistry was resorted to, to demonstrate presence or absence of oestradiol, AFP, HCG, and keratin in these tumours. The markers and other reagents were imported from

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sources detailed in Part-I of this paper and the technique described by Sternberger (1970) was used for this study.

Results

90% of patients came for pain and mass in the abdomen with 42% showing clinical evidence of hormonal imbalance. One case of granulosa cell tumour had hirsutism and clitoromegaly. Histologically the granulosa cell tumours showed the whole spectrum of patterns, viz. microfollicular (30%), trabecular (20%), diffuse (20%), watered silk (10%), insular (10%) and macro-follicular (10). SCTAT and malignant lipid cell tumour presented classical histologiacl features. Alcian blue-PAS material was consistently lacking in granulosa cell tumour and lipid tumour, whereas, diastase resistant PAS positivity was seen in the hyaline bodies in the centre of tubules in SCTAT.

Immunohistochemistry

Oestradiol could be demonstrated in 7 cases (70%) of granulosa cell tumours and in the single case of SCTAT. In the former, isolated tumour cells and plump stromal cells exhibited the positivity (3 cases) whereas larger numbers of both tumour cells and stromal cells secreted oestrogen in 4 cases. AFP could be demonstrated in 5 cases of granulosa cell tumours, few individual cells exhibiting the positivity in 3 and larger number of cells showing the positivity in 2 cases. HCG was seen in small groups of cells in 3 cases. The spectrum of functional pattern was AFP + HCG + (1), HCG + Oestrodiol + (1), AFP + HCG + Oestradiol + (1), Oestradiol + (2) and AFP + Oestradiol + (3). Two cases of granulosa cell tumour did not show presence of any marker.

The SCTAT demonstrated oestradiol secretion in few cells lining the tubules and was negative for other markers. The malignant lipid cell tumour did not show presence of any marker under study. Thus 42% of sex cord stromal tumours (5 granulosa cell tumours) showed presence of AFP by immunohistochemistry, the positive cells being few and isolated and seen in the undifferentiated areas of the tumour. 3 granulosa cell tumours (25%) showed positivity for HCG, the positive cells being scattered in the highly cellular areas of the tumour. Keratin was negative in this series of tumours. Table I gives details of clinical correlation and the presence of the markers under study.

Discussion

The histochemical studies by Fox and Langley (1976) and Scully (1979) have established the close association between the basement membrane and hyaline bodies in SCTAT. The functional nature of this tumour as suggested by Crissman and Hart (1981) could be confirmed by us by immunohistochemistry in the case studied by us. Donaldson (1980) detected high serum AFP level in one case of granulosa cell tumour and we have been able to demonstrate that AFP secretion can occur in these tumour cells. Similarly presence of HCG in stromal tumours as suggested by Morris and Scully (1958) with positive pregnancy test and elevated serum HCG has been confirmed by our study of demonstrating HCG in granulosa cell tumours. Oestradiol was found to be secreted by either the tumour cell or the stromal cell thereby emphasising their common histogenesis. We found that out of the 5 cases with clinical manifestations

TABLE I

Study of Tumour Markers in Ovarian Neoplasms—II—Sex and Stromal Tumours

Case No.	Name and Age (Yrs.)	Clinical Features	Gross	H & E Provisional Diagnosis
1	2	3	4	5
1.	Mrs. N. 57	Mass in the abdomen — 2 months	Solid ovarian tumour with small cystic spaces	Malignant granulosa cell tumour Microfollicular pattern
2.	Mrs. S. 48	Pain in the abdomen — 2 months Irregular bleeding PV 2-months	Solid ovarian tumour 6 x 4 x 4 cm size	Malignant granulosa cell tumour watered silk pattern
3.	Mrs. B. 45	Mass in the abdomen — 4 months Irregular bleeding PV-2-months	Solid soft to firm ovarian tumour	Malignant granulosa cell tumour. Diffuse pattern
4.	Mrs. K. 36	Irregular bleeding PV 2 years Mass per abdomen 1 year	Soft to firm solid ovarian tumour	Malignant granulosa cell tumour. Diffuse pattern
5	Mrs. K. 46	Pain and mass in the abdomen	Solid tumour 6 x 5 x 5 cm size with foci of haemorrhage	Malignant granulosa cell tumour
6.	Mrs. P. 65	Bleeding PV 6 months pain abdomen 4 months	Solid tumour 8 x 4 x 4 cm size with small cystic areas	Malignant granulosa cell tumour Trabecular pattern
7.	Miss K. 13	Hirsutism 3 months Clitoromegaly 2 months	Cystic ovarian tumour with thick wall capsule infiltrated	Malignant granulosa cell tumour Macrofollicular pattern
8.	Mrs. R. 48	Mass per abdomen 4 months	Solid grayish white firm ovarian tumour	Malignant granulosa cell tumour trabecular pattern
9.	Mrs. K. 49	Pain abdomen 4 months	Solid ovarian tumour 8 x 6 x 6 cm size	Malignant granulosa cell tumour Microfollicular pattern

TABLE I

Histochemistry PAS	Alcian blue	AFP	HCG	Estra-diol.	Kera-tin	Final diagnosis
6		7	8	9		10
—	—	—	—	Few tumour cells & occasional stromal cells +ve.	—	Malignant granulosa cell tumuour
—	—	Large number of cells show intense cytoplasmic positivity	—	Many tumour cells and plump stromal cells show cytoplasmic + vity	—	Malignant granulosa cell tumour
—	—	—	Few isolated tumour cells show cytoplasmic + vity	Occasional tumuour cells and plump stromal cells show cytoplasmic + vity	—	Malignant granulosa cell tumour
—	—	Few tumour cells show intense cytoplasmc + vity	—	Few plump stromal cells and many tumour cells + ve		Malignant granulosa cell tumour
—	—	Many cells show cytoplasmic + vity	—	Tumour cells and isolated stromal cells + ve	—	Malignant granulosa cell tumour
—	—	Individual tumour cells show + ve cytoplasma	Isolated individual cells show cytoplasmic + vity	Many tumour cells and plump stromal cells + ve	—	Malignant granulosa cell tumour
—	—	—	—	—	—	Malignant granulosa cell tumour
—	—	Infrequent cells + ve	Small groups of cells + ve	—	—	Malignant granulosa cell tumour
—	—	—	—	—	—	Malignant granulosa cell tumour

TABLE I (Contd.)

Case No.	Name and Age (Yrs.)	Clinical Featurues	Gross	H & E Provisional Diagnosis
1	2	3	4	5
10.	Mrs. N. 54	Pain abdomen 5 months	Solid soft to firm ovarian tumour	Malignant granulosa cell tumour Microfollicular pattern
11.	Mrs. M. 40	Pain in the abdomen 5 months	Solid soft to firm tumour. A small area of capsule infiltrated	Sexcord stromal with annular tubules
12.	Mrs. F. 44	Pain abdomen 4 months	Solid ovarian tumour capsule infiltrated omentum adherent	Malignant lipid cell tumour

of hormonal imbalance the secretion pattern was oestradiol + (1), oestradiol + HCG + (1), oestradiol + AFP + (1) and oestradiol + HCG + AFP + (1) with the single case of hirsutism demonstrating no marker under study. Amongst 5 cases of granulosa cell tumour with no clinically manifest hormonal imbalance, the secretory pattern as shown by immunohistochemistry was oestradiol + (2), AFP + (1), AFP + HCG + (1) with no tumour marker under study in one case. It appears that the quantity of hormone secreted by the tumour is not the only factor deciding on clinical manifestations of hormonal imbalance. We could confirm by this study that immunohistochemistry is indeed a very important adjunct in the study of functioning tumours, especially those of the ovary.

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TABLE I (Contd.)

Histochemistry PAS	Alcian blue	AFP	HCG	Estradiol	Keratin	Final diagnosis
6		7	8	9		10
—	—	—	—	Many tumour cells and plump stromal cells + ve	—	Malignant granulosa cell tumour
± ve hyline bodies continuous with the basement membrane	—	—	—	Few cells lining the tubules + ve	—	Sexcord stromal tumour with annular tubules
—	—	—	—	—	—	Malignant lipid cell tumour

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