

OVARIAN SEX CORD TUMOR WITH ANNULAR TUBULES: IN THE VIEWPOINT OF HISTO-PATHOLOGICAL ANALYSIS

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Introduction

Scully described additional 3 cases of "sex cord tumor with annular tubules" (SCTAT) with such 13 tumors in literature in 1970¹¹⁾, and it has been assumed that SCTAT might develop from granulosa cells¹¹⁾. We experienced one case of SCTAT, and light microscopic and immuno-histochemical analysis was done. The present study was designed to identify the steroid behavior of SCTAT and to disclose the character of its tumor cells.

A Case Report

Case N.K.

A 14 year old woman with irregular menses for last year was admitted because of hypogastric mass. Patient received right salpingo-oophorectomy and partial resection of left ovary on October 13, 1983. The entire pelvis was filled with right ovarian tumor reaching to 12.2×7.5×6.8cm in size with smooth glitter surface and rubber consistency without adhesion. The peritoneal cavity was smooth and glittering. Ascites reached to 100ml in volume and possessed serous and yellow-coloured

property.

Post-operative gastro-intestinal tract examination could not reveal any polyp.

Endocrinological analysis showed high serum estrogen and progesterone with low serum gonadotropins, and a finding that suggested hormone-producing tumor (Table 1).

There was a marked enlargement of tumor reached to 12.2cm in the greatest diameter and a rubber consistency. The cut surface showed a complete replacement of all the structures including the right ovary by solid yellowish tumor tissue, which had many lobulations, that the demarcation could be identified.

The cytologic specimens were obtained from cystic fluid. Serous yellow-coloured fluid contained uniformly oval or round tumor cells arranged in a follicular or tubular fashion. Nuclear size was almost uniform, and smoothly distinctive nuclear rim was disclosed. Nuclear chromatin pattern was fine granular. Moderate sized single nucleolus was confirmed in each tumor cell. Nuclear-cytoplasmic ratio was moderate. Findings of these tumor cells were suggestive of those of granulosa cell tumor (Fig. 1).

Table 1. Endocrine findings

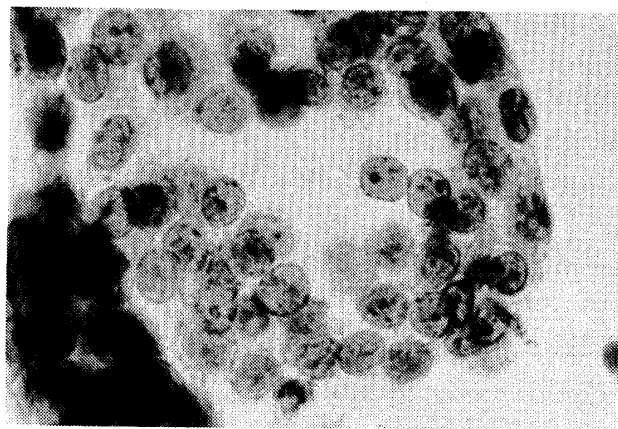
Hormone	HCG	PRL	LH	FSH	E2	Prog	Test	17-OHCS	17-KS	Serotonin	5-HIAA	Androsterone	Aldosterone
Specimen	serum	serum	serum	serum	serum	serum	serum	urine	urine	serum	urine	serum	serum
Standard		2-20	12.2± 3.7	11.0± 3.7	68.0± 42.4	2.13± 2.5	0.29± 0.07	4.5± 7.10	3.6± 1.91	≤230	2-8	0.1-1.2	2-12
Units	ng/ml	ng/ml	mIU/ml	mIU/ml	pg/ml	ng/ml	ng/ml	mg/day	mg/day	ng/ml	mg/l	ng/ml	ng/dl
Pre-	0.26	22.5	2.7	≤2	96.6	3.6	0.4	2.5	1.9	102	2.5	0.124	6.6
Post-(1)		19.1	6.5	12.8	≤6.7	≤0.4	0.7						
Post-(2)		7.4	13.1	6.7	28.1	≤0.2							

Pre- : pre-operative state, Post-(1) : 2 weeks after operation, Post-(2) : 4 weeks after operation

PRL : Prolactin, E2 : Estradiol, Prog : Progesterone, 5-HIAA : 5-hydroxy-indol-acetate

These standard values are evaluated from normal female aged from 13 to 15.

Fig. 1. Nuclear chromatin pattern is fine granular. Moderate sized single nucleolus is confirmed in each tumor cell. (PAP, $\times 1000$)



There was thickening of the walls and septa surrounding the tumor cells islands. The tumor cells islands were composed of simple and complex annular tubules. The tubules had the shape of a ring, with nuclei located along and almost attached to the peripheral border of island and a central round body of amorphous material. The annular tubules were made up of inter-communicating rings in places, and continued to the peripherally lined cells. Sometimes the same amorphous material as that in annular tubules could be found on periphery of island. Tumor cells composed of island had almost round nucleus and foamy cytoplasm. Nuclei contained irregular and notched borders (coffee-bean mimetic) and single enlarged nucleolus in places (Fig. 2). Tumor cells composing islands were positive in Sudan III staining, but amorphous material in annular tubules negative. Intra-

Fig. 2. Multiple islands are characterized by simple and complex ring-shaped solid tubules and by the presence of hyaline bodies. (H & E, $\times 200$)

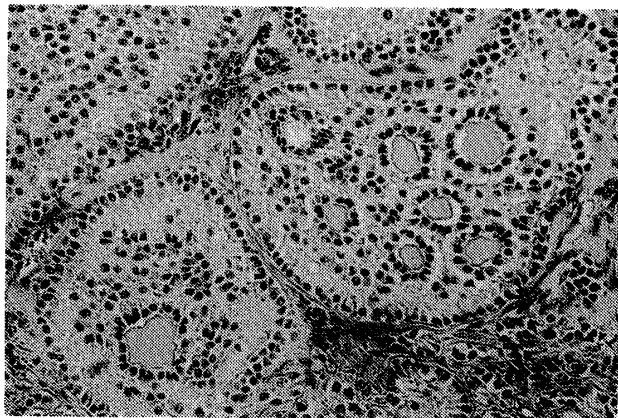


Fig. 3. Progesterone is found in tumor cells composing of islands with rabbit anti-progesterone-11a-BSA serum (Miles-Yedd Ltd.), but reaction of each tumor cell is different. (FITC, $\times 1000$)

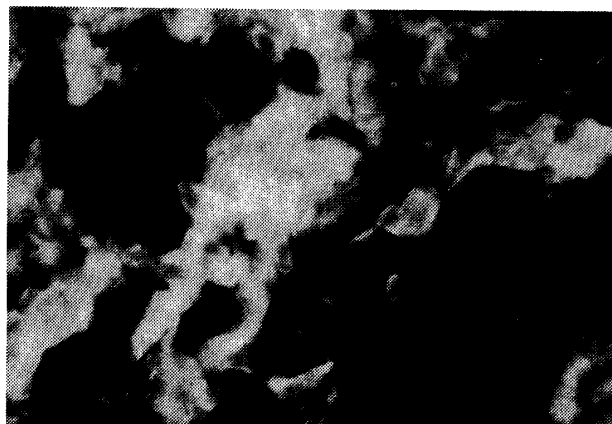


Fig. 4. Estradiol is especially disclosed in annular tubules with rabbit anti- 17β -estradiol-6-BSA serum (Miles-Yedd Ltd.) (FITC, $\times 400$)

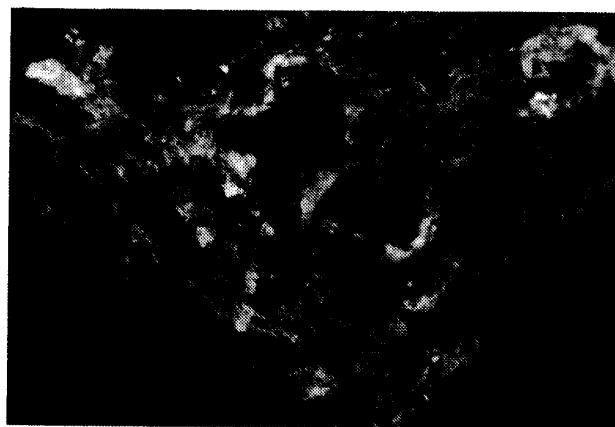
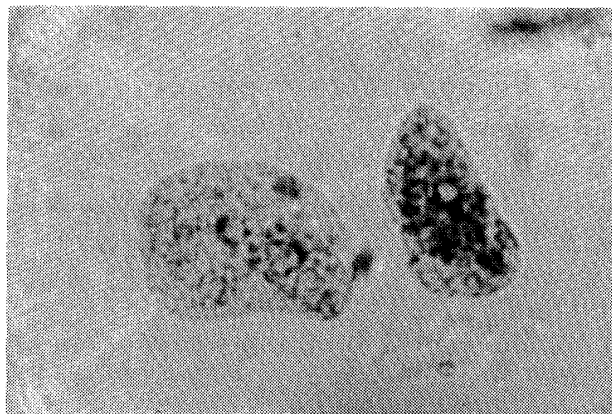


Fig. 5. X-chromatin is positive in smear. Large single sex chromatin is observed on the inside of nuclear rim. (Orcein, $\times 1000$)



tubular amorphous material was positive for PAS staining after diastase digestion. And amorphous material also invaded into reticulin framework. Left ovary not-affected by the tumor revealed primordial follicles.

In immuno-histochemical analysis, estradiol and progesterone were positive in the peripheral part of island and peri-tubular cells for further particulars. Behavior of progesterone staining was similar to those of estradiol staining, either (Fig. 3,4).

In detection of X- and Y-chromatin, X-chromatin was positive and Y-chromatin was negative in smear (Fig. 5).

Discussion

Macroscopically, this case disclosed large unilateral tumor reaching to 12.2cm in greatest diameter. In Scully's paper, he supposed that the size of SCTAT with Peutz-Jeghers syndrome (PJS) might develop as other types of ovarian tumor than SCTAT, such as mucinous cystadenoma, adenofibroma, Sertoli-Leydig cell tumor, and dysgerminoma¹¹⁾. Conversely the tumors without PJS were larger, reaching to 17cm in the greatest diameter, unilateral, and less frequently complicated, multilobular, and with rubber consistency similar to other hormone-producing tumor. Janowski and Paramanandhan showed a case that small foci of SCTAT were presented in dysgenetic gonad. Our case revealed right large ovarian SCTAT and left developing gonad with primordial follicles.

In cyto-pathologic findings, smear obtained from tumor cyst showed uniformly oval or round tumor cells arranged in a follicular or tubular arrangement. Nucleus had smooth rim, uniform fine chromatin distribution, and single nucleolus. These findings seemed to correspond to those of granulosa stromal cell tumors.

Histopathologic finding of SCTAT was very popular in annular tubules. Generally it was thought to be easy to distinguish gonadoblastoma from SCTAT by the presence of primitive large germ cells in islands. In Scully's paper about SCTAT, he reported two cases of dysgerminoma combined with contra-lateral ovarian SCTAT. One of these cases revealed dysgenetic gonads and he postulated that microscopic foci of SCTAT with originally have been gonadoblastoma in which primitive germ cell had been disappeared.

Controversy continued to whether SCTAT was classified, as classification of sex cord stromal cell tumors were in confusion. In Scully's study of SCTAT and other ovarian tumors, he postulated that SCTAT was thought to arise from granulosa cells, but to grow in a pattern more characteristic of Sertoli cells especially in SCTAT without PJS because of similar annular tubules found in cryptorchid²⁾⁴⁾¹¹⁾¹⁵⁾. He could not find true tubules with narrow lumina and definite proof of Sertoli cell differentiation. Crissman et al.¹⁾, Hart et al.³⁾, and Young et al.¹⁵⁾ failed to identify Charcot-Bottcher crystalloids found in Sertoli cells¹⁾³⁾¹⁵⁾. Many reports revealed coffee-bean nuclear grooves, perpendicularly placed nuclear arrangement against basement membrane, and hyaline-bodies mimetic to Call-Exner bodies in SCTAT. Furthermore, ultrastructural studies suggested granulosa cell differentiation of SCTAT¹⁾³⁾¹⁵⁾. They demonstrated numerous desmosomes attached adjacent cells, hyaline bodies consisting of accumulating concentric lamellae of basement membrane, and resembled those of follicles. Deep nuclear indentations, which appeared as nuclear grooves or folds on light microscopy, were seen. Abundant microfilaments were commonly aggregated and often were associated with and attached to desmosomes. In view of the histologic and ultrastructural similarities with granulosa cell tumors, last authors proposed that SCTAT might be the variant of granulosa cell tumor (A distinctive annular and membranous variant of granulosa cell tumor).

In past reports, light microscopic and ultrastructural analyses showed that SCTAT might be resembled to granulosa cell in morphology, but could not distinctly disclose the histochemical characteristics. Signs and histopathologic findings of imbalance of sex steroid hormone, sometimes hyperestrinism, were reported in about half cases with SCTAT¹¹⁾¹⁵⁾. Abnormal vaginal bleeding and anovulation were usually observed. In this report we will schedule to characterize the clinicopathologic features of SCTAT especially in immunohistochemistry of sex steroids. Functioning ovarian tumors had been discussed from the standpoint of steroid biosynthesis and immunohistochemistry. In hormone-producing granulosa-theca cell tumor nest of granulosa elements generally behave

estrogenic, and surrounding stroma regarded as the theca elements were non-functional⁶⁾¹⁰⁾. Lomax et al. showed that progesterone might also be elaborated by "pure" granulosa cell tumors⁹⁾. Kurman disclosed that granulosa cells showed positive staining for estradiol in 11 cases, testosterone in seven, and progesterone in seven⁸⁾. Controversely Sertoli-Leydig tumor was generally androgenic, and Sertoli-Leydig tumor cells produced estrogen and progesterone as well as testosterone in some cases⁵⁾⁷⁾. The observation that serum estrogen levels decreased following removal of tumor in this case corroborated the ability of this tumor to synthesize estrogen. Immunohistochemical staining for estradiol and progesterone were diffusely distributed in islands of SCTAT, especially in margins of annular configurations. And tumor cells around the tubules revealed positive in parts. All tumor cell composed of islands of SCTAT could not be positive for sex steroid survey by FITC method, but it might be by reason that islands were composed of different tumor cells in steroid production. Testosterone staining was failed in SCTAT. As based on these findings, we suppose that SCTAT produces estradiol and progesterone, and it might be simmilar to granulosa-stromal cell rather than Sertoli-Leydig cell in steroid biosynthesis. In chromatin staining tumor cells were positive for sex chromatin. Recent analysis revealed different positivity in chromatin staining for cancer patients, and the finding was interpreted as variation responsible for stage, degree of malignancy and clinical stage¹⁰⁾¹²⁾¹⁴⁾.

The practical conclusion drawn from these examination with histological analyses in literature is that SCTAT may be corresponded to granulosa stromal cell tumor.

Addendum

In this case the diagnosis of sex cord tumor with annular tubules was agreed by R.E. Scully, M.D., Professor of Pathology, Massachusetts General Hospital, on November 16, 1983.

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