

A Case of Ovarian Strumal Carcinoid A Histochemical, Immunohistochemical and Ultrastructural Study

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ABSTRACT

A histochemical, immunohistochemical and electron microscopic study was made on a case of ovarian strumal carcinoid arising from a mature cystic teratoma. This tumor formed a solid nodule and was histologically composed of both thyroid tissue and carcinoid tumor. In this nodule, the carcinoid component was predominant and a trabecular pattern was observed with ribbons of identical cells. Carcinoid cells had argyrophilic granules with Grimelius stain, but argyrophilic granules could not be detected in the thyroid tissue. Both components were negative to Masson-Fontana reaction. By immunoperoxidase technique, immunoreactive thyroglobulin was demonstrated within the thyroid follicles and their epithelial cells. Serotonin was positive in some of the carcinoid cells, but negative in the thyroid components. Carcinoembryonic antigen (CEA), calcitonin, α -fetoprotein and adrenocorticotrophic hormone (ACTH) were all negative in these components. Microfollicles or acinar structures in the intermediate zone from the thyroid tissue to the carcinoid component showed a mixed characteristic, being positive for thyroglobulin and Grimelius stain. Electron microscopically, round and dense-cored neurosecretory granules could be seen in the cytoplasm of the trabecular part. These findings suggest that strumal carcinoid developed in close association with the teratomatous thyroid tissue in the mature cystic teratoma of the ovary.

Ovarian strumal carcinoid is a rare ovarian neoplasm and is composed of thyroid tissue of teratomatous origin intimately admixed with the carcinoid having predominantly a trabecular pattern. Since the first description of this tumor by Scully in 1970, more than 50 cases have been reported in the literature⁷⁾, but the characteristics of this tumor have not yet been elucidated.

A case of strumal carcinoid of the ovary in a female in the fifth decade is presented together with a discussion of our detailed histochemical, immunohistochemical and electron microscopic studies of this ovarian tumor.

CASE REPORT

The case is a 44-year-old married Japanese woman, gravida 5, para 5, who visited our clinic on July 10, 1981 with the left ovarian tumor detected in an earlier cancer screening program. Ultrasonogram showed a small left ovarian tumor measuring 4.3 × 4.1 × 4.7 cm in size with a mixed pattern (mainly cystic and partly solid) (Fig. 1). A diagnosis of dermoid cyst of the ovary was made and periodic examination was undertaken every three months.

On January 20, 1985, pelvic examination revealed a myoma nodule of under hen's egg in size

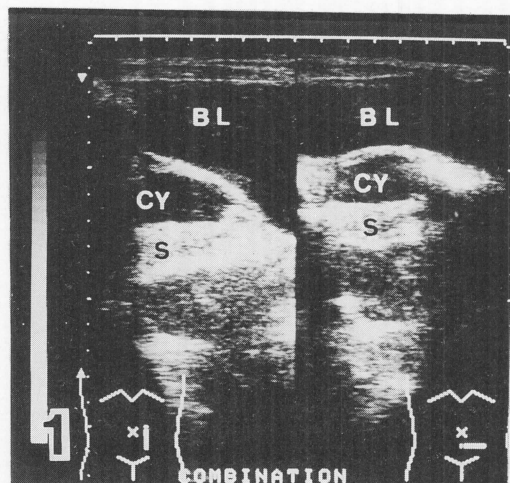


Fig. 1. Ultrasonogram. Longitudinal (left) and transverse (right) scans of the left ovarian tumor show a mixed pattern. (S: solid part, Cy: cystic part, BL: bladder)

on the anterior uterine wall and ultrasonogram indicated that the left ovarian tumor had increased to $7.1 \times 6.5 \times 5.6$ cm in size.

She also complained of hypermenorrhea and lower abdominal pain. She was admitted to our ward for a surgical procedure. General examination and laboratory data did not demonstrate any abnormal findings.

Total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed on July 18, 1985. Her postoperative course was uneventful and she was discharged on August 1, 1985. She did not receive postoperative chemotherapy and is doing well 18 months following surgery. She did not experience any symptoms of carcinoid syndrome before or after surgery.

MATERIALS AND METHODS

The resected left ovary was fixed in 4% formalin and paraffin embedded sections were stained with hematoxylin and eosin, periodic acid Schiff (PAS), Alcian blue, mucicarmine, Grimelius stain (for argyrophilic granules) and Masson-Fontana stain (for argentaffin granules). These sections were also used for immunoperoxidase stain with peroxidase anti-peroxidase (PAP) method for thyroglobulin, calcitonin, α -fetoprotein and ACTH, and avidin-biotin peroxidase complex (ABC) method for CEA and serotonin. The antibodies used in this study were as follows: Thyroglobulin, calcitonin, α -

fetoprotein and ACTH: DAKO PAP KIT, CEA: Mochida, Japan. (1:600)

Serotonin: Sera Lab., England. (1:800)

Control incubations were performed by replacing primary antibodies with non-immune swine serum.

For electron microscopic observation, formalin-fixed tissues were refixed in 2.5% glutaraldehyde solution, postfixed in 1% OsO₄, and then embedded in Poly/Bed 812. Ultrathin sections which were stained with uranyl acetate and lead solution were examined with a Hitachi H-300 type electron microscope.

RESULTS

Gross Findings

At operation, the left ovary was found to be enlarged, measuring $7.5 \times 5.5 \times 4.5$ cm, and had a smooth surface. On cut surface, the left ovary was replaced by a polycystic and partly solid tumor. The larger cyst contained a greasy material, teeth and hairs. The mandibular-like bone was identified and a solid nodule measuring 2 cm in diameter and yellow to tan in color was found beneath it. No papillary projection could be observed within the cysts (Fig. 2). The right ovary was of normal size. The uterus had a myoma nodule on the anterior wall and the thickness of endometrium was within normal limits.

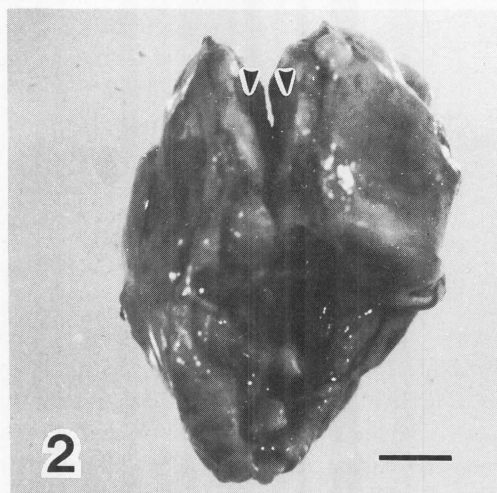


Fig. 2. Gross appearance of cut surface of the left ovary. Arrowheads indicate the solid nodule beneath the mandibular-like bone. Two teeth are also seen (lower). Bar=1 cm.



Fig. 3. Skin and its appendages line the cyst. (S: squamous epithelium, AD: adipose tissue) Hematoxylin-eosin $\times 100$

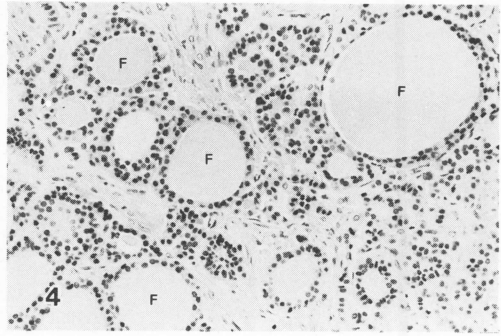


Fig. 4. Thyroid follicles are lined by flattened epithelium. Some follicles contain colloid-like material (F). Hematoxylin-eosin $\times 100$

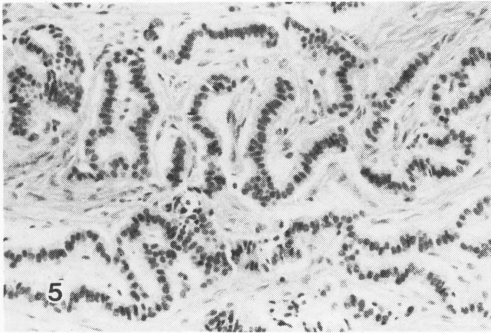


Fig. 5. Carcinoid cells show a trabecular arrangement with ribbons of identical cells. Hematoxylin-eosin $\times 100$

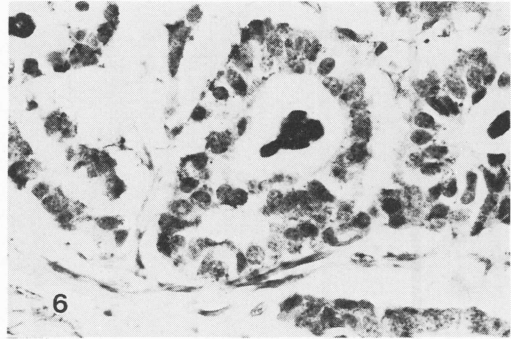


Fig. 6. Microfollicles show argyrophilic granules in the cytoplasm. Grimelius stain $\times 400$

Histopathology

The cystic part of the left ovary was composed of skin and its appendages, which are the findings typical of a dermoid cyst (Fig. 3). The solid part contained thyroid tissue and carcinoid component and intimately admixed area was also present (Fig. 4). The carcinoid component showed a trabecular pattern with ribbons of identical cells. These cells had eosinophilic cytoplasm and round to oval nuclei (Fig. 5). The thyroid component showed the appearance of normal thyroid tissue. Colloid-like material was stained strongly with PAS. Most of the carcinoid part and microfollicles or acinar structures in the intermediate zone from the thyroid tissue to the carcinoid component had argyrophilic granules with Grimelius stain (Fig. 6). Argentaffin granules could not be detected with Masson-Fontana stain. A very small part of the

thyroid component was positive to Alcian blue but negative to mucicarmine.

Immunohistochemical Findings

Sections of the solid part of the left ovary examined with PAP and ABC methods were positive for thyroglobulin and serotonin, but negative for calcitonin, α -fetoprotein, CEA and ACTH. Thyroglobulin was demonstrated within the thyroid follicles and their epithelial cells and also microfollicles in the intermediate zone from the thyroid area to the carcinoid component. Some carcinoid cells were also positive for thyroglobulin in trabecular part (Figs. 7A and 7B). Serotonin was immunostained only in some carcinoid cells (Fig. 8).

This specificity was demonstrated by comparison with negative controls.

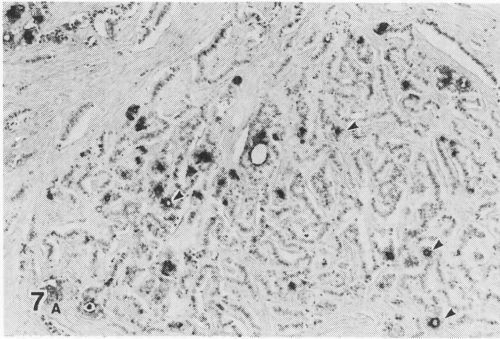


Fig. 7A. Immunoreactive thyroglobulin is positive in the acinar structure in the intermediate zone (arrowheads). Immunoperoxidase and Mayer's hematoxylin counterstain $\times 40$

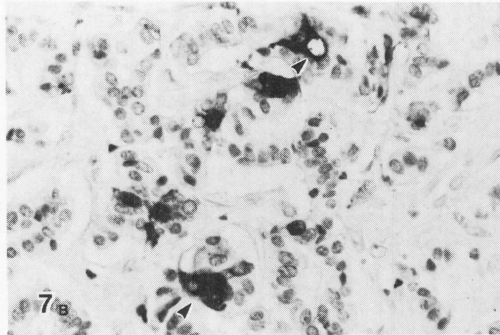


Fig. 7B. Higher magnification of the acinar structure. Immunoperoxidase and Mayer's hematoxylin counterstain $\times 400$

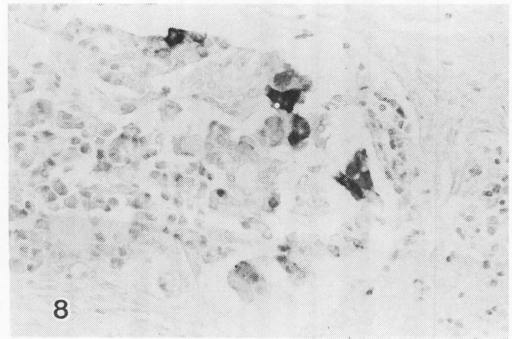


Fig. 8. Immunoreactive serotonin is positive in carcinoid cells. Immunoperoxidase with methylene blue counterstain $\times 400$.

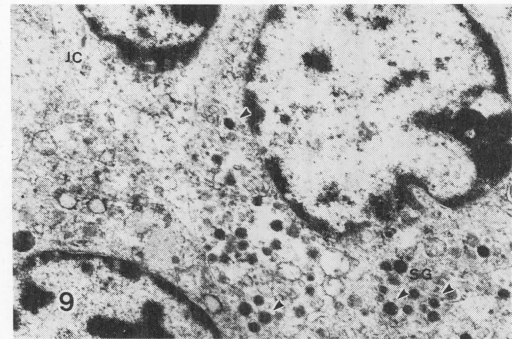


Fig. 9. Carcinoid cells contain electron dense-cored neurosecretory granules (SG) in the cytoplasm. Some granules have limiting membrane (arrowheads). (JC: desmosome) $\times 13,000$.

Electron Microscopic Findings

In the ultrastructural study of this ovarian tumor, the carcinoid cells contained usually round to oval nuclei with prominent nucleoli, but irregularly shaped nuclei were also appeared in some tumor cells. The cytoplasm had mitochondria and electron dense-cored neurosecretory granules, measuring 150–350 nm in diameter, with the halo being separated by limiting membrane. Cytoplasmic microfillaments, which were intermingled with neurosecretory granules, and desmosome were also seen (Fig. 9).

DISCUSSION

Primary ovarian carcinoid tumors are divided into insular, trabecular, strumal and mucinous types. Insular type is most common and more than 70 cases have been reported⁵. Strumal

type is the second common one, and since the first description of this carcinoid by Scully in 1970, more than 50 cases have been reported in the literature⁵. Other types are very rare, only a few case reports have been described⁷.

The age incidence of patients with primary ovarian carcinoids ranges widely but most patients are postmenopausal⁹.

Strumal carcinoid, including our case, is composed of thyroid tissue intimately admixed with carcinoid component, having predominantly a trabecular pattern^{5,6,8}. This type is not associated with carcinoid syndrome such as insular one. Our case also had no signs of carcinoid syndrome. Although primary carcinoids should be treated as low malignant potential ovarian tumors, strumal carcinoid, except for one rare

case, tends to behave in a clinically benign manner^{5,8}.

Attempts have been made by several investigators^{2,5,6,8,10,11} to ascertain the cell origin of strumal carcinoid by histochemistry, immunohistochemistry and electron microscopy. In 1974, Arhelger and Kelly¹ discovered dense-cored neurosecretory granules and amyloid fibrils in the strumal carcinoid, and suggested that strumal carcinoid was analogous to medullary carcinoma of the thyroid gland (C-cell concept). This concept was supported by the positive stain of calcitonin. On the other hand, Ranchoid et al⁴ and Livnat et al³ reported that cells of both thyroid tissue and carcinoid component had dense-cored neurosecretory granules by electron microscopy, and concluded that strumal carcinoid was a pure one from the thyroid tissue. Other investigators⁸ have suggested that strumal carcinoid developed from the teratomatous gastrointestinal or respiratory epithelium lining the mucinous cysts. They also reported that serotonin was not specific for medullary carcinoma of the thyroid gland and CEA was often positive in medullary carcinoma.

In our case, an intimately admixed area was present between thyroid component and carcinoid area. Thyroid follicles and their epithelial cells had positive immunoreactivity for thyroglobulin and negative one for CEA. The cells of the carcinoid part had argyrophilic granules with Grimelius stain and electron dense-cored neurosecretory granules were also observed in the cytoplasm. The carcinoid cells were also positive for serotonin. These finding suggested that strumal carcinoid arose from the thyroid component in the mature cystic teratoma of the ovary.

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