

## Ovarian Clear Cell Adenofibroma of Borderline Malignancy A Case Report

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### ABSTRACT

A case of ovarian clear cell adenofibroma of borderline malignancy in a 59-year-old woman is presented with histochemical and electron microscopic observation. The tumor was histologically composed of tubular component lined in part with flat or cuboidal clear as well as hobnail cells with mild cytologic atypia and abundant stromal component containing foci of calcification. The epithelial cells had diastase-digestive PAS-positive material in the cytoplasm, and occasionally the luminal surface and intraluminal substance were stained with mucicarmine. Some of the epithelial cells showed positive lipid staining with Sudan III stain. On ultrastructural study, the tumor featured a moderate number of small mitochondria, poorly developed rough endoplasmic reticulum (rER), short microvilli, intercellular tight junction and desmosome and small amount of glycogen granules. The patient is alive and well with no evidence of recurrence six and half years after the operation.

**Key words:** Ovary, Clear cell tumor, Borderline malignancy, Clinicopathological study

### CASE REPORT

The patient was a 59-year-old, married Japanese woman, Gravida 3, Para 2, who presented in June 1982 with lower abdominal pain. Menarche had occurred at age 18, and the menopause at age 46. Her past medical history included gastrectomy for gastric ulcer at age 49. The family history was not contributory. She consulted our clinic in August 1982. Ultrasonogram showed a middle size of the right solid ovarian tumor. In the gynecological examination, a mobile tumor at the right adnexal area was palpated, but laboratory findings were unremarkable. The specimens taken from cervical biopsy and endometrial curettage showed no abnormal findings.

Right salpingo-oophorectomy was performed in September 1982.

She is alive and well with no evidence of recurrence six and half years after the operation.

### MATERIALS AND METHODS

The resected right ovary was fixed in 4% formalin. Paraffin embedded sections were stained with hematoxylin and eosin, periodic acid-Schiff (PAS) with/without diastase digestion, mucicarmine and Sudan III.

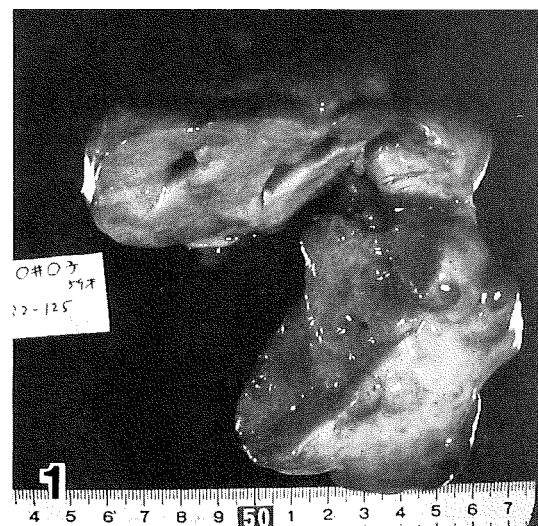
For electron microscopic observation, formalin-fixed tissues were refixed in 2% glutaraldehyde solution after washing in PBS, postfixed in 1% OsO<sub>4</sub>, and then embedded in Epon 812. Ultrathin

sections stained with lead solution were examined with Hitachi H-300 type electron microscope.

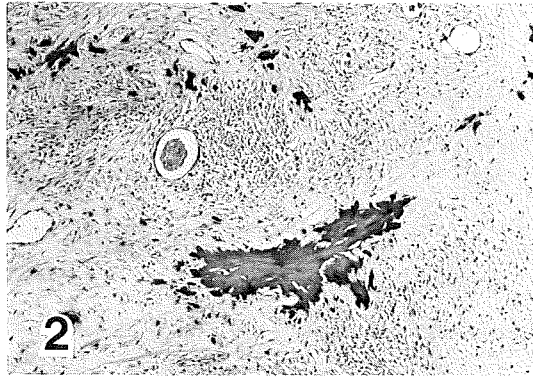
### RESULTS

#### Gross Pathology

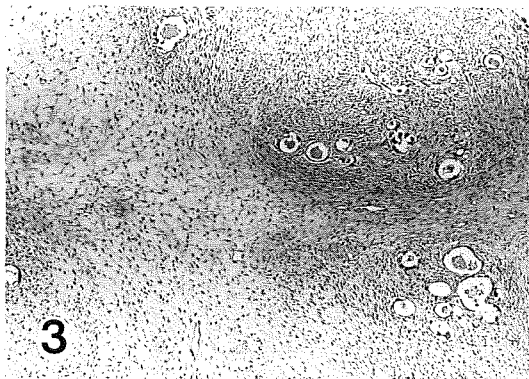
At operation, the right ovary was enlarged with smooth surface, measuring 10×9×7 cm and weighing 300 g. The cut surface of the right ovary was gray to white in color, and was occupied by a



**Fig. 1.** Cut surface of the right ovarian tumor is solid with small cysts.



**Fig. 2.** Right ovarian tumor. Foci of calcification are present in the stroma. (H-E  $\times 40$ )



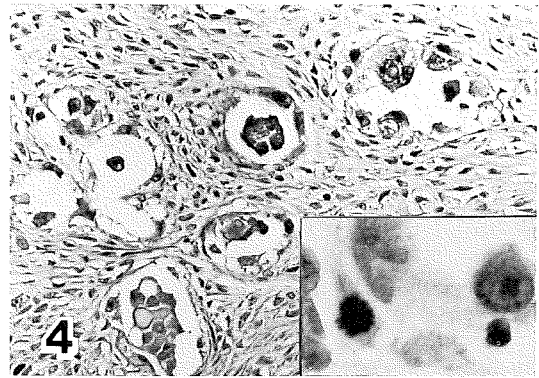
**Fig. 3.** Clear cell adenofibroma of borderline malignancy with pseudobubular pattern in the right ovary. Many tubules are crowded in a cellular fibrous stroma. (H-E  $\times 60$ )

predominantly solid tumor with small cysts across its entirety (Fig. 1). Neither ascitic fluid nor adhesion was noted.

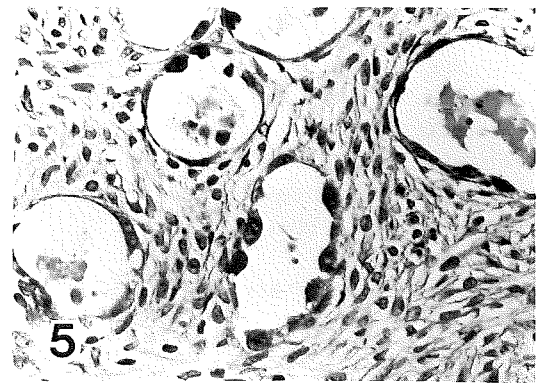
#### Light Microscopic Findings

We found the right ovarian tumor composed of various sized tubules which were surrounded by dense ovarian type stroma, without evidence of stromal invasion, with light microscope. The stroma had a cellular or edematous area with a pseudobubular patterning, and contained foci of calcification (Fig. 2). Many tubules were crowded in the cellular area, but in the edematous area only a small number of tubules could be found (Fig. 3). The tubules were primarily round in shape, although occasionally irregular shaped tubules with some tortuosity were also observed. The tubular epithelium was in part composed of flat or cuboidal cells having clear cytoplasm and in part hobnail type cells and epithelial tufting with irregular protrusion of nuclei into the tubular lumen. Retention of secreted material and necrotic debris could be observed within the tubular lumen (Figs. 4, 5). Papillary structure or cribriform pattern were not present in this case.

The tubular epithelium was lined with cells that



**Fig. 4.** The tubules lined by focally multilayered or enlarged cells, and contain secreted material and necrotic debris in the lumen. (H-E  $\times 150$ ) Occasional mitotic figure is present in the tubular epithelium (Inserted). (H-E  $\times 600$ )



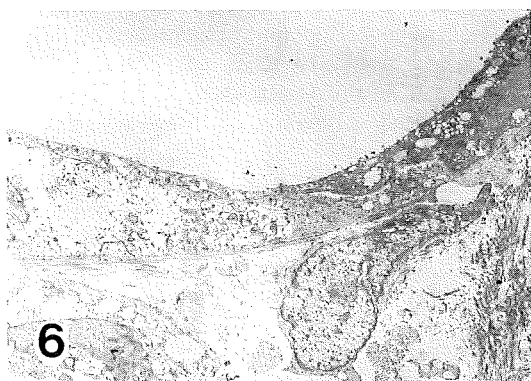
**Fig. 5.** The tubules lined with flat and hobnail-type cells. (H-E  $\times 200$ )

had the mild nuclear atypia (elevated nuclear-cytoplasmic ratio, irregular nuclear contours, irregular clumped chromatin, prominent 1-2 nucleoli) with an occasional mitosis less than one per ten high-power fields (Fig. 4).

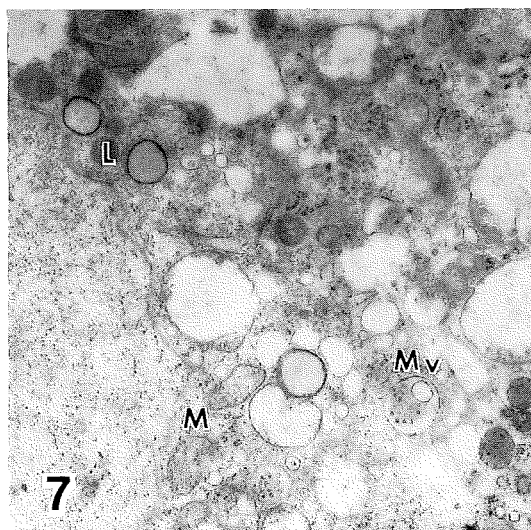
The material positively stained with diastase-digestive PAS was present in the cytoplasm of the epithelial cells and intraluminal substance was stained with diastase-resistant PAS. The material positively stained with mucicarmine was present in both luminal surface of the epithelial cells and intraluminal substance. Some of the epithelial cells showed positive lipid staining with Sudan III stain. Stromal cells were negative with all of the stains used in this study.

#### Electron Microscopic Findings

Ultrastructural study of the right ovarian tumor showed the epithelial cells to be composed of low columnar or hobnail-type projection of cells. There was tight junction and desmosome between adjacent cells, and sparsely distributed short microvilli on the cell surfaces. A basement membrane separated the epithelial cells from the underlying stroma which contained fibroblasts surrounded



**Fig. 6.** Electron micrograph of right ovarian tumor. Tubular epithelium is composed of low columnar cells, and have sparsely distributed short microvilli. (TEM  $\times 2000$ )



**Fig. 7.** Electron micrograph of right ovarian tumor. Mitochondria (M), multivesicular bodies (Mv) and lipid droplets (L) are observed. Small amount of glycogen granules and free ribosomes are distributed. (TEM  $\times 10000$ )

abundant collagen fibers (Fig. 6).

The tumor cells contained round to oval nuclei with fine to coarse chromatin pattern and prominent nucleoli, but irregularly shaped nuclei were also observed in some cells.

The structure of the cytoplasmic organelles was not well preserved due to refixation, but a moderate number of small mitochondria, poorly developed rER, and a small amount of glycogen granules and free ribosomes were observed. A few lipid droplets and multivesicular bodies were also present (Fig. 7).

### DISCUSSION

Clear cell adenofibroma of borderline malignancy is a rare tumor. The first case was reported in the literature in 1943 by Schiller as parvilocular tumor<sup>8</sup>. To date only 18 cases have been reported in English<sup>2,6,7</sup>. The pathological criteria for

separating benign and borderline tumors from invasive clear cell carcinomas was not established until the report of Roth et al<sup>6</sup> in 1984.

According to the literature, the mean age of 8 benign tumors was 49.9 years<sup>2,4,6</sup> and that of 61 malignant tumors was 53.3 years<sup>3,5,7</sup>, while in 18 borderline tumors the mean age, likewise this case, was 59.1 years<sup>2,6,7</sup>, indicating its predilection for the older age group except for one patient prior to menopause. As the number of available cases is small, no definite statement can be made on the incidence of borderline tumor, but according to Russel<sup>7</sup>, it has accounted for 9.1% of all clear cell tumors. Seventeen of the 18 cases with known laterality, including this case, were unilateral in borderline tumors<sup>2,6,7</sup>.

As for gross appearance of borderline tumor, most of the cases were solid with small cysts on the cut surface. The diameter ranged from 6.5 to 23 cm, the mean size of 15 cases was comparatively large, being about 13 cm<sup>2,6</sup>.

The histogenesis of clear cell tumors is considered as being of müllerian origin bases upon ultrastructural study, and in view of the high frequency of coexistence of endometriosis in clear cell tumors<sup>1,3,7,9</sup>.

Bell and Scully<sup>2</sup> described the characteristic histologic features for diagnosis of borderline malignancy: (1) The glands are widely spaced to focally crowded, and sometimes small, smoothly contoured and abundant stromal component, without evidence of stromal invasion; (2) the glands are lined by one to three layers of clear, hobnail, or eosinophilic cells that possess the cytologic characteristics of low-grade malignancy (mild cellular and nuclear pleomorphism, irregular clumped chromatin, prominent irregular nucleoli, and an elevated nuclear-cytoplasmic ratio); (3) evidence of foci of intraglandular epithelial tufting and a rare focal cribriform pattern; (4) the mitotic rate of the epithelial component is less than one per ten high-power fields; (5) the stromal component is predominantly fibrotic and contain foci of hyalinized and calcified area.

Electron microscopic findings of clear cell adenofibroma of borderline malignancy have not been reported in the literature, but according to Silverberg<sup>10</sup>, the characteristic findings of clear cell adenocarcinoma are that the tumor has blunt microvilli, intercellular tight junction and desmosome, interdigitating cytoplasmic process, intracytoplasmic glycogen granules, small mitochondria, numerous free ribosomes, and rER. The difference between malignant and borderline tumor is that borderline tumor has a moderate number of small mitochondria together with poorly developed rER in their periphery, but the amount of glycogen granules is small.

As for prognosis, in the 16 cases including the present case the prognosis is considered to be favorable inasmuch as there has been only one

reported case of lung metastasis four years after surgery<sup>2,6</sup>).

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