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A MALIGNANT PAROVARIAN TUMOR ACCOMPANIED BY OVARIAN SEROUS CYSTADENOMA OF LOW POTENTIAL MALIGNANCY

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Synopsis A rare case of malignant parovarian tumor accompanied by ovarian serous cystadenoma of low potential malignancy is reported in a 23-year-old nulligravidous unmarried woman.

The parovarian tumor 10×10×9 cm in size was located in the left broad ligament, unilocular and cystic, with small papillary growths projecting into the lumen. Histologically, it was a papillary serous cystadenocarcinoma of low grade. Tumor cells were predominantly cuboidal to columnar with occasional cilia and stratified to 3 to 4 layers in places. They showed nuclear atypism with prominent nucleoli and suspect vascular invasion, but rare mitotic activity. Two types of tumor cells, ciliated and nonciliated, were also identified by electron microscopy. Their nuclei were irregular and deeply indented with occasional prominent nucleoli. The tumor cells were connected to each other with desmosomes, but interdigitations were not prominent. They were separated by a smooth basement membrane from the underlying stroma.

The right ovary was enlarged to 8×7×6 cm in size and the left to 6×4×4 cm in size, both being multilocular and cystic. Histological diagnosis of the right ovarian mass was a papillary serous cystadenoma of low potential malignancy, and that of the left a serous cystadenoma.

The incidental findings of argyrophil cells in both parovarian and ovarian tumor are interesting and to be further investigated in association with a theory of dual histogenetic origin of ovarian mucinous tumors. The patient was treated by surgery followed by chemotherapy and is now under follow-up studies.

Key words: Malignant parovarian tumor

A majority of the parovarian tumors are now considered to be of paramesonephric or mesothelial origin, only 2 per cent arising from the mesonephric duct[6]. Malignant variants, paramesonephric or mesonephric, are extremely rare. In this paper, we describe a rare parovarian adenocarcinoma of Mullerian origin accompanied by ovarian serous cystadenoma, low potential malignancy.

Case Report

A 23-year-old nulligravidous unmarried woman was admitted to Osaka University Hospital on February 23, 1978 with lower abdominal pain and vomiting lasting for 2 days. Her past history disclosed appendectomy in 1958. Her father died of rectal cancer 2 years ago at age 50. Her menarche was at age 13. Since then, she has had regular menstruation every 30 days. Her last menses began on January 29, 1978 lasting for 5 days.

Physical examination revealed a cystic tumor, the size of a child's head, in the pelvic cavity. Her stature was 160 cm, and her body weight 52 kg. Anomalies were not found in any other parts of the body. Her blood pressure at admission was 128/76 mmHg. Pulse was regular, of normal tension, and 70 per minute. Laboratory examination revealed normal values in the peripheral blood analysis, the serum electrolytes and liver functions.

Laparotomy was performed on February 28, 1978. No ascites was found in the abdominal cavity. The uterus was anteflexed and normal in size and consistency. The right ovary was enlarged to 8×7×6 cm and the left to 6×4×4 cm, both being polycystic. In addition, a cystic parovarian tumor 10×10×9 cm with an elongated fallopian tube was found in the left broad ligament. No pathology was found in

other organs in the pelvic cavity. The parovarian tumor was removed with the left tube, but perforated during manipulation, resulting in the spillage of cystic contents. Also, most of the right ovarian mass and more than half of the left were removed.

One week later, the patient received the 2nd surgical treatment, because the pathological diagnosis of the parovarian tumor was a papillary serous cystadenocarcinoma of low grade, that of the right ovary a papillary serous cystadenoma, low potential malignancy, and that of the left a serous cystadenoma. The uterus, the right tube and the remaining masses of both ovaries were removed. A dose of 20 mg of mitomycin C was administered intraperitoneally at operation. After surgery, she was treated with a course of chemotherapy (5-fluorouracil, cyclophosphamide, mitomycin C, and toyomycin), and discharged on April 24, 1978.

Pathological Findings

Gross. The specimens removed by the first operation were a parovarian tumor with the left tube and the tumorous masses of both ovaries. The parovarian tumor was cystic and 10×10×9 cm in size. On cut section, it was unilocular and proliferated with some small papillary growths (Photo. 1). Cystic fluid was yellowish but translucent. The left tube was elongated around the tumor. The masses of both ovaries were also cystic. On cut section, they were multilocular and contained serous fluid in most cysts, but slightly mucinous in some. Small papillary growths were seen in one cyst of the right ovarian mass.

The specimens submitted after the second operation were the uterus with a hematoma in the adjacent right broad ligament, the edematous right tube, and the remaining tissues of both ovaries (Photo. 2).

Microscopic. The lining cells of the left parovarian cystic tumor were predominantly cuboidal with occasional cilia and stratified up to 3 to 4 layers in places, especially in the papillary growths and showed suspect vascular in-

Photo. 1. Macroscopic appearance of the left parovarian tumor with Fallopian tube.

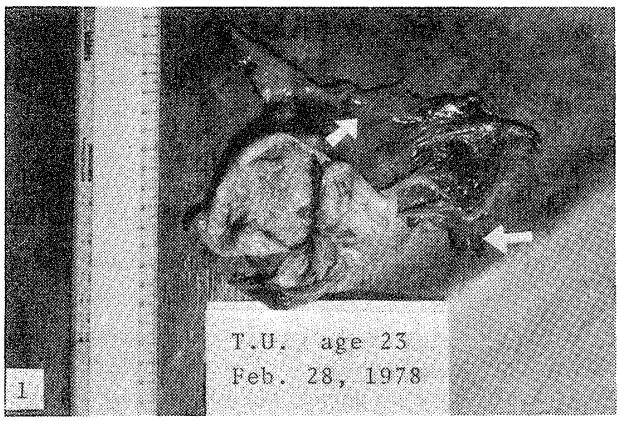


Photo. 2. Macroscopic appearance of the uterus and both adnexes, which are reconstructed with the left parovarian tumor and the resected masses of both ovaries.

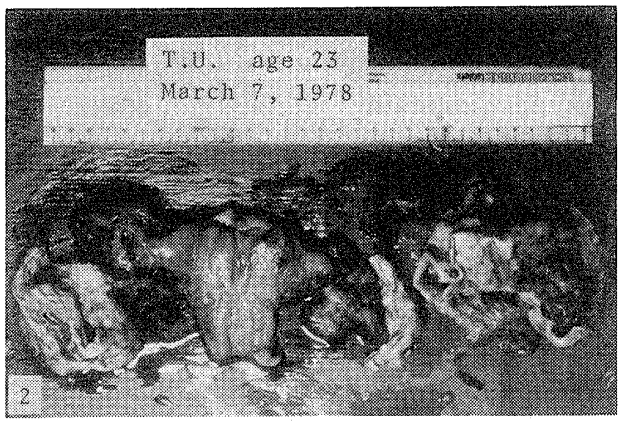


Photo. 3. Low-grade papillary serous cystadenocarcinoma in the left parovarium. Hematoxylin-Eosin, ×40

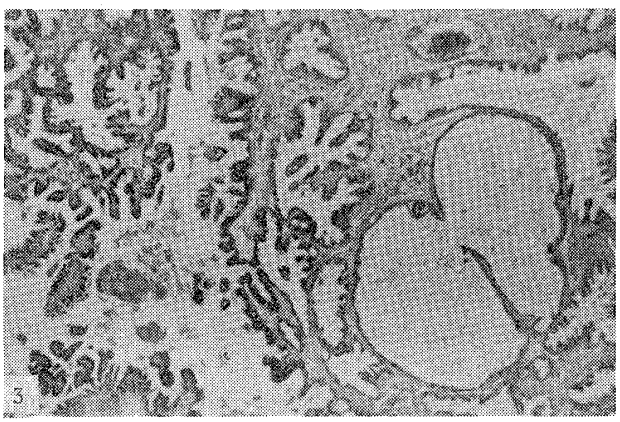


Photo. 4. Stratified lining cells, ciliated and nonciliated, in a higher magnification of Photo. 3. Hematoxylin-Eosin, ×100

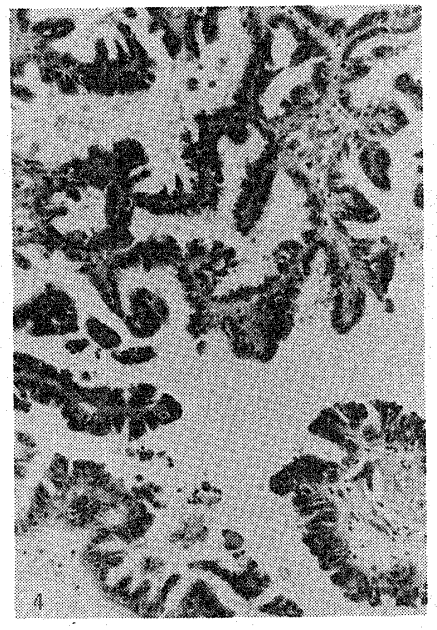
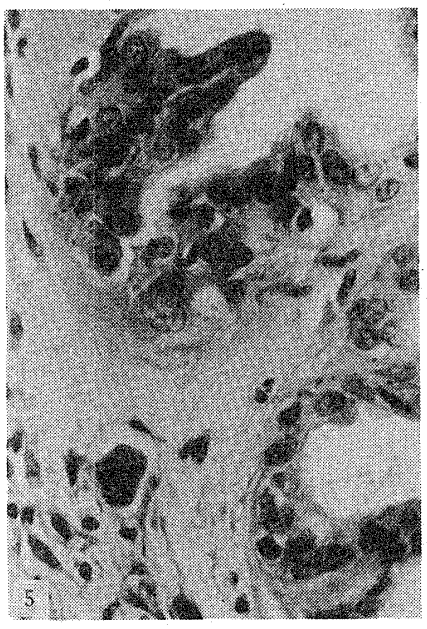


Photo. 5. Stratification, nuclear atypism and suspect vascular invasion of the tumor cells shown in Photo. 3. Hematoxylin-Eosin, ×400



vasion in a few areas (Photos. 3 to 5). The nuclei of tumor cells showed atypism with prominent nucleoli, but rare mitotic activity. Some of the lumens and tumor cells contained the materials stained positively by PAS and alcian-blue staining. Some tumor cells were also shown to be argyrophil (Photo. 6) by Grimelius staining[8]. The pathological diagnosis was a papillary serous cystadenocarcinoma of low grade in the left parovarium.

The right ovarian mass was predominantly composed of multiple cysts lined with a layer of cuboidal cells, but partly of papillary growths, in which the lining cells were multilayered up to 3 showing nuclear atypism with prominent nucleoli (Photos. 7 and 8). Psammoma bodies were also identified. Some tumor cells and lumens contained the materials stained by PAS and alcian-blue method. Also, argyrophil granules were stained in some tumor cells. The diagnosis was a papillary serous cystadenoma, low potential malignancy, of the right ovary.

The left ovarian mass was also composed of multiple cysts lined with a sheet of cuboidal epithelium and rarely with slight focal papillary structures. Psammoma bodies were seen, but no premalignant changes were observed. The diagnosis was a serous cystadenoma of the left ovary.

Photo. 6. Argyrophil cells in some areas of papillary serous cystadenocarcinoma shown in Photo. 3. Grimelius, ×400

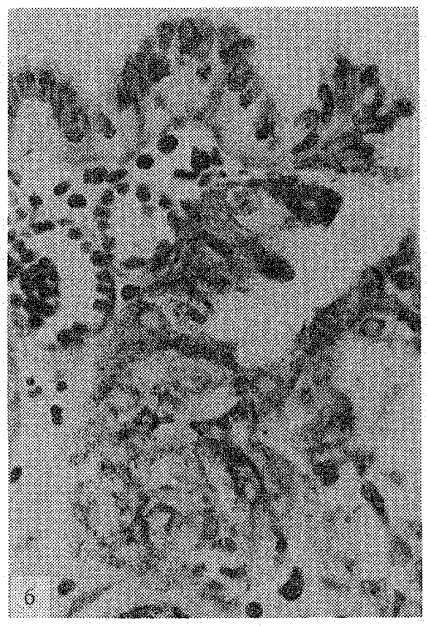


Photo. 7. Papillary serous cystadenoma of low potential malignancy with psammoma bodies in the right ovary. Hematoxylin-Eosin, ×40

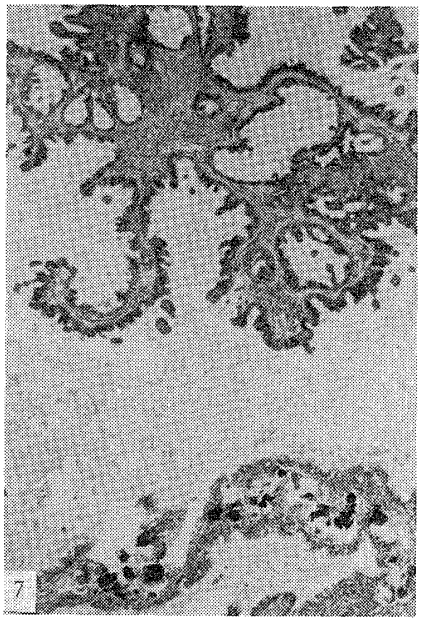
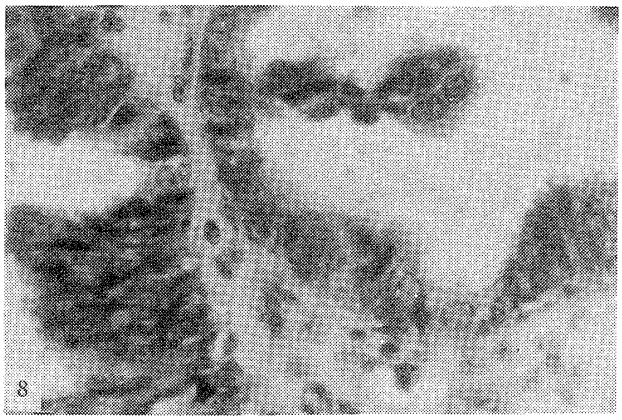


Photo. 8. A higher magnification of the same tumor as in Photo. 7, showing stratification of the lining tumor cells. Hematoxylin-Eosin, ×400



Electron Microscopy

The parovarian tumor was cut into tiny pieces and fixed in 2.5% cold buffered glutaraldehyde. After postfixation in 2% buffered osmium tetroxide followed by dehydration in graded alcohols, the tumor tissues were embedded in Epon. Ultrathin sections were stained with uranyl acetate and lead citrate for electron microscopy.

Photo. 9. Two types of parovarian tumor cells, ciliated and nonciliated, and a smooth basement membrane. Electronmicrograph, ×3,300

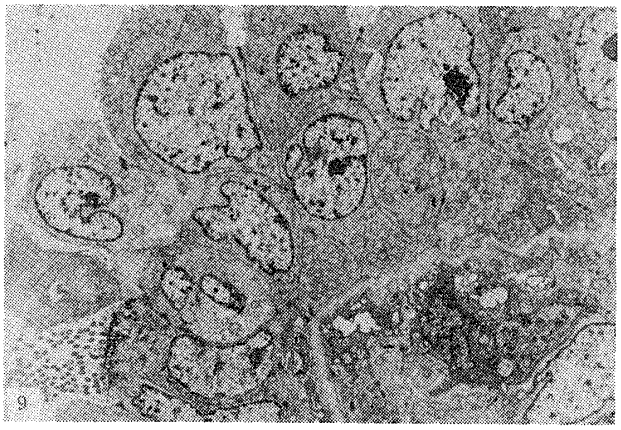
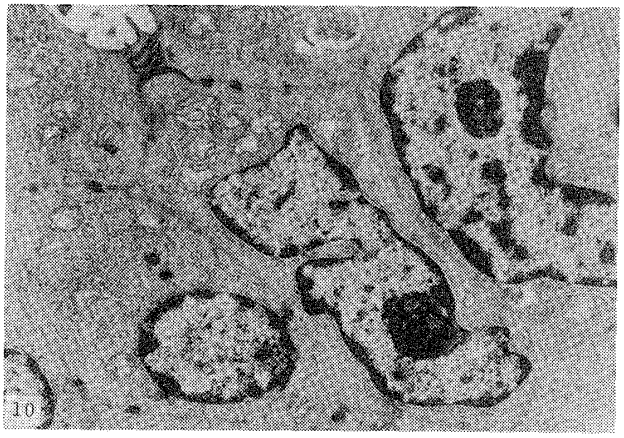


Photo. 10. Stratification of parovarian tumor cells which connect each other with desmosomes without interdigitation and have deeply indented nuclei with prominent nucleoli. Electronmicrograph, ×11,000



The tumor was composed of 2 types of cells, ciliated and nonciliated. The cells were multilayered up to 2 to 4 in places. Their nuclei were irregular and deeply indented with occasional prominent nucleoli. Many mitochondria were seen in the cytoplasm of some tumor cells, but the development of endoplasmic reticulum was generally poor. The tumor cells were connected to each other with desmosomes, but the interdigitations were not prominent. They were separated by a smooth basement membrane from the stroma (Photos. 9 and 10).

Discussion

Non-neoplastic cysts of the parovarium are frequently encountered accounting for about 10% of specimens of so-called ovarian tumors[12]. Parovarian neoplasms, however, are extremely rare. Some tumors of probable mesonephric origin were documented, usually benign but rarely malignant[13)15]. Benign tumors of paramesonephric origin were reported by Gardner et al.[4], Janovski and Bozzetti[11], Honoré and Nickerson[10], and Genadry et al.[6]. Malignant tumors were reported by Hertig and Gore[9], Czernobilsky and Lancet[1], and Genadry et al.[6]. The histogenetic origin of parovarian carcinomas documented by Gardner et al.[5] and Lennox and Meagher[14] was not determined.

The histologic differences between paramesonephric and mesonephric elements were studied in detail by Gardner et al.[4)5]. Mesonephric tumors have a well developed muscular layer, a low cuboidal epithelium without cilia, no secretion, and a distinct basement membrane. In contrast, the tumors of Müllerian origin have a columnar epithelium with occasional cilia, luminal secretion, and an indistinct basement membrane. The histological features of the present tumor are consistent with those of paramesonephric tumors. The electron microscopic studies revealed that the tumor was somewhat similar to the borderline serous tumor of the ovary[7], thus suggesting the low-grade malignant nature of the present tumor. Although the histological criteria are easily applicable to malignant tumors of low grade, it would be difficult to establish the histogenetic origin of more undifferentiated carcinomas. The true primary site would not be identified when the tumors involved the adjacent organs. This may explain why malignant tumors in the parovarian area have been generally of low grade nature.

In the present case, the neoplasms in the parovarium and both ovaries are considered to have been developed independently by the same etiologic factors, judging from the gross and histological findings. A similar case was documented by Czernobilsky and Lancet[1], in which the ovarian borderline lesion was found in the same side as the parovarian, whereas in the present case the lesion was found in the opposite ovary.

The incidental findings of argyrophil cells in both parovarian and ovarian tumors are very interesting in association with their histogenesis. Argyrophil cells are well known to be in the mucinous cystadenoma of the ovary, especially when accompanied by the teratomatous tissues[3]. However, the present tumors are basically of a serous type. This suggests that the presence of argyrophil cells may not necessarily support a teratomatous origin of mucinous tumors, but the idea of metaplastic transformation of celomic epithelium[2)3].

Because cystic fluid containing malignant cells entered the abdominal cavity during surgery, the patient was further treated by chemotherapy. She is now under follow-up studies.

Acknowledgements

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概要 23歳，未婚婦人における卵巣漿液性嚢胞腺腫（低悪性度）に合併した悪性旁卵巣腫瘍の極めて稀な1症例を報告した．

旁卵巣腫瘍は10×10×9cm 大で，左広間膜に位置し，単胞性嚢胞状で，内腔に面して小乳頭状の増殖を示していた．組織学的には分化型の乳頭状漿液性嚢胞腺癌で，腫瘍細胞は比較的背が低く，3～4層までの増殖を示し，時に絨毛を有するものも混じている．異型性も可成り認められるところもあり，リンパ管内浸潤を疑わせる部分もあるが，核分裂像は稀である．電顕的にもこれら細胞形態像は確かめられている．

右卵巣腫瘍は8×7×6cm 大，左は6×4×4cm 大で，何れも多胞性嚢胞状で組織学的に右は乳頭状漿液性嚢胞腺腫（低悪性度）で，左は良性の漿液性嚢胞腺腫である．

旁卵巣腫瘍および右卵巣腫瘍の一部に，銀好性細胞が認められたことは全く新しい発見であり，その意義に関しては今後の研究に残されている．患者は術後化学療法が行われ，経過観察中であるが，現在（術後1年6カ月）までのところ再発の徴候はない．