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Case Report

Adenocarcinoma of the Fallopian Tube

An Ultrastructural Study

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Summary. A case of fallopian tube adenocarcinoma was studied by light and transmission electron microscopy. The neoplastic cells contained abundant mitochondria, moderate to large amounts of rough endoplasmic reticulum (RER) arranged in parallel arrays and often containing amorphous material, annulate lamellae, possible secretory vesicles, and glycogen. The presence of stacked RER and annulate lamellae together is unusual in papillary serous cystadenocarcinoma of the ovary, and has not been described in Fallopian tube adenocarcinoma. Golgi complexes were are. Small acini with projecting microvilli as well as junctional complexes were present, but cilia were not found. The electron microscopic findings suggest secretory activity, and are remarkably similar to those found in papillary serous cystadenocarcinomas of the ovary. The findings also support the hypothesis that ovarian serous tumors and adenocarcinomas of the Fallopian tube are derived from coelomic epithelium.

Key words: Fallopian tube – Adenocarcinoma – Annulate lamellae

Adenocarcinoma of the fallopian tube is a rare neoplasm, accounting for 0.2 to 0.5% of primary malignancies of the genital canal (Novak and Woodruff 1974). Electron microscopic studies to date (Rorat and Fenoglio 1976; Ferenczy and Richart 1974; Johnson et al. 1978) have demonstrated features very similar to papillary serous tumors, particularly cystadenocarcinomas, of the ovary (Roberts et al. 1970; Ferenczy 1976; Gondos 1971). Differentiation of the two is frequently not possible by light microscopy due to identical histology and contiguous involvement of the ovary as the lesion grows.

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In order to further define the ultrastructural appearance of fallopian tube adenocarcinoma, and examine the relationship between this tumor and papillary serous cystadenocarcinoma of the ovary, this light and electron microscopic study of a moderately differentiated papillary adenocarcinoma of the fallopian tube was performed.

Case Report

A 61 year old white female was admitted to Divine Providence hospital with a five month history of progressive abdominal swelling with pain, nausea, and vomiting. There were several episodes of vaginal bleeding, without a watery discharge.

Physical examination revealed massive ascites and a movable right pelvic mass. Numerous diagnostic studies including barium enema, intravenous pyelogram, upper gastrointestinal series, and oral cholecystogram were negative.

Exploratory laparotomy revealed a right adnexal mass with numerous omental and peritoneal implants as well as ascites and unresectable nodules of tumor surrounding the gallbladder and pancreas. Endometrial curettage failed to produce sufficient tissue for pathologic examination. Cytologic examination of the ascitic fluid showed clusters of malignant cells. A debulking procedure consisting of a right salpingo-oophorectomy and omentectomy was performed, leaving residual tumor in both the left and right upper quadrants. The uterus and both ovaries were free of tumor grossly, and were not removed due to the extent of the disease. A diagnosis of papillary adenocarcinoma of the fallopian tube was made after pathological examination of the tissue.

The patient made an uneventful recovery, experiencing a decrease in both abdominal pain and ascites. She was referred to Presbyterian-University Hospital for chemotherapy, and received 14 courses of Adriamycin, Cytoxan, and 5 Fluorouracil at monthly intervals. A second laparotomy performed just before the completion of chemotherapy revealed two small unresectable nodules of residual tumor in the right upper quadrant surrounding the common duct. A total abdominal hysterectomy and left salpingo-oophorectomy were performed. Pathologic examination of the tissues showed no evidence of tumor.

Ten months later, a third laparotomy was performed to debulk a recurrent tumor mass. Biopsy of a right supraclavicular lymph node as well as examination of the resected tissue revealed metastatic adenocarcinoma consistent with her original neoplasm. At present, she is responding well to Melphalan therapy, and is alive with residual disease in the right upper quadrant two and one-half years after diagnosis.

Materials and Methods

Paraffin embedded and wet formalin fixed tissue from the omentum and right fallopian tube were obtained from Divine Providence hospital. Light microscopic examination included hematoxylin and eosin stain on all blocks and PAS, Mucicarmine, Alcian Blue, and Colloidal Iron stains on selected blocks.

Portions of tumor were washed in tap water, refixed in 2% glutaraldehyde for two hours, post-fixed in osmium tetroxide, dehydrated, infiltrated and embedded in epon araldite. One micron thick sections were cut and stained with Toluidine blue. Light silver sections were then cut from selected areas with a Sorvall MT2 ultramicrotome, stained with uranyl acetate and lead citrate, and examined with a Philips 200 electron microscope.

Pathology

A 4.0×2.0 cm portion of the right fallopian tube was dilated and had intraluminal projections of hard, white, gritty tumor with both solid and cystic patterns of growth. There was deep infiltration of the wall. Grossly, the portions of omentum contained several large tumor implants with focal cystic degeneration.

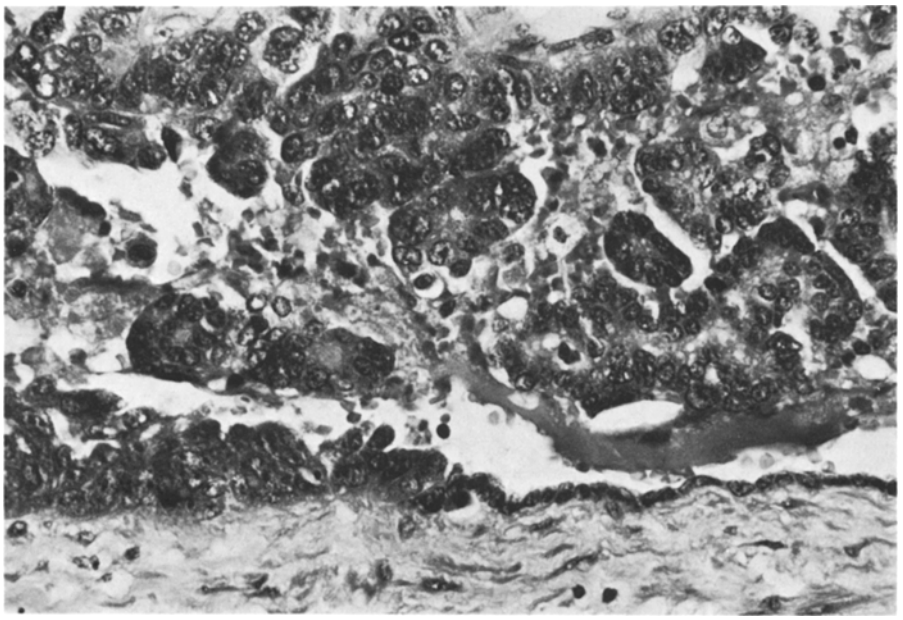


Fig. 1. Light photomicrograph of papillary adenocarcinoma arising from the epithelium of the right Fallopian tube. Note transition from flattened, low columnar epithelium to fronds of malignant cells. (× 500)

By light microscopy there was a gradual transition from normal columnar epithelium to severe dysplasia and fronds of frankly malignant cells (Fig. 1). The malignant cells were slightly pleomorphic with abundant cytoplasm which was focally vacuolated. Mitotic activity was abundant. Numerous psammoma bodies were seen, and a cellular fibrous stroma was present between nodules of tumor. Omental sections had fat infiltrated by papillary adenocarcinoma identical to that in the fallopian tube. Intracellular PAS positive diastase resistant material was found within the malignant cells, and cells in the cyst fluid had a similar reaction with the PAS stain. Weak, focal positivity was seen within cells and stroma with the Alcian Blue and Colloidal Iron stains, but the Mucicarmine stain was negative.

Ultrastructurally, there were islands of homogeneous polygonal cells surrounded by small amounts of connective tissue. The nuclei were round to oval with moderate indentation of the nuclear membrane, a single nucleolus, and peripheral condensation of chromatin. There were moderate amounts of cytoplasm and moderate to large amounts of rough endoplasmic reticulum frequently arranged in parallel arrays and occasionally in whorls (Fig. 2). Numerous mitochondria, rare lipid vacuoles, and glycogen were present. Portions of the rough endoplasmic reticulum were dilated and contained amorphous material (Fig. 3). Golgi complexes were rare. Occasional structures resembling secretory vesicles were present within the cytoplasm, but membrane bound dense granules were not seen. Well formed junctional complexes bordered acini into which microvilli projected (Fig. 2). Annulate lamellae were present (Fig. 4), but cilia were absent. Duplication of mito-

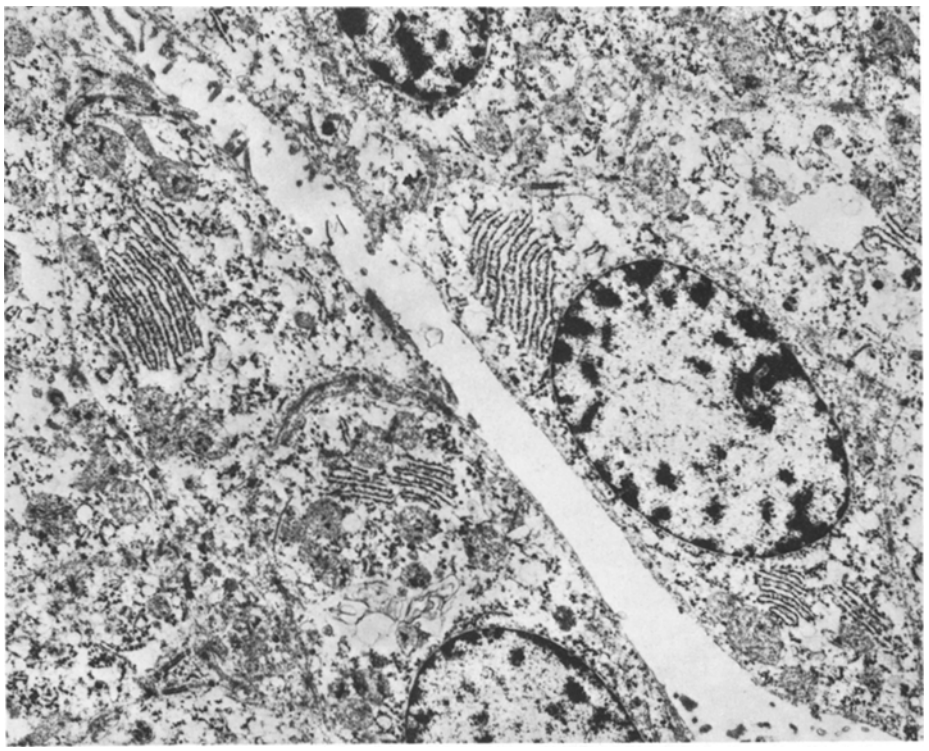
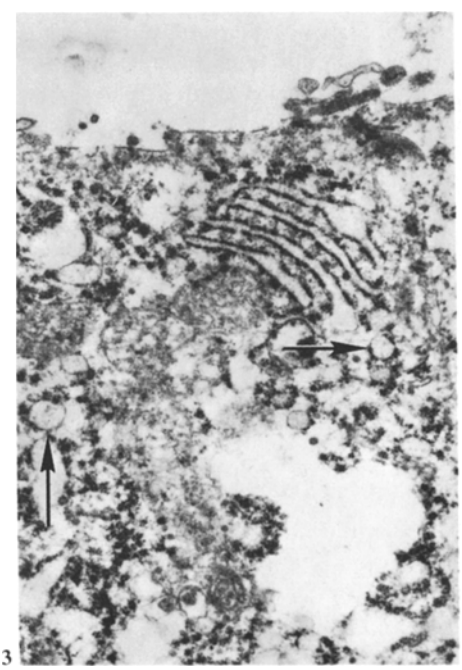


Fig. 2. Electron micrograph of tumor cells showing moderate amounts of stacked RER, frequent desmosomes, an acinus, and microvillous projections. Mitochondria and free ribosomes are also present. (× 8,800)



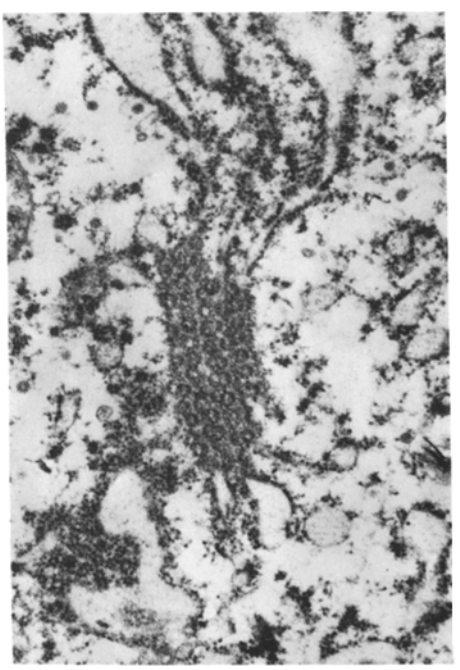


Fig. 3. Electron micrograph showing dilated vesicles of rough endoplasmic reticulum (*arrows*). Cell surface microvilli are present. (× 28,200)

Fig. 4. Electron micrograph illustrating annulate lamellae intimately related to RER within tumor cells. (21,500)

chondrial membranes, terminal webs, and nuclear inclusions were not identified. There was little interdigitation of neighboring cells. Multivesicular bodies were not found, and basement membrane-like material was not prominent. Nuclear pores were only occasionally seen.

Discussion

Papillary adenocarcinoma of the fallopian tube is similar to ovarian carcinoma in its clinical presentation and histologic appearance, and is rarely diagnosed preoperatively (Chalmers and Marshall 1976; Hu et al. 1950; Sedlis 1978). Our patient's clinical presentation was that of an ovarian carcinoma, except for the presence of vaginal bleeding unrelated to endometrial disease.

By light microscopy, differentiation of fallopian tube adenocarcinoma from secondary ovarian carcinoma involving the tube may be impossible. The following criteria must be met to establish the presence of a primary lesion: 1) The main tumor must lie in the tube, 2) microscopically it should show a papillary pattern, and 3) if the tubal wall is involved to a great extent the transition between benign and malignant tissue should be demonstrable (Hu et al. 1950; Southwood 1956). All of these criteria were fulfilled in this case, making the diagnosis unequivocal. In addition, the histochemical reactions within the tumor cells and cystic areas were identical to those found in the cells of normal fallopian tube mucosa. Previous ultrastructural studies of fallopian tube adenocarcinoma have stressed the similarity of these lesions to serous adenocarcinomas of the ovary (Rorat and Fenoglio 1976; Ferenczy and Richart 1974). The fallopian tube mucosa as well as the endometrium is of Mullerian origin, derived from secondary infoldings of coelomic epithelium, and normally contains ciliated, secretory, and intercalated cells. Therefore, tubal mucosa is embryologically related to ovarian surface epithelium, which has a direct coelomic origin. Well differentiated adenocarcinomas of both ovarian and tubal origin may show large numbers of ciliated cells, although non-ciliated tubal-type secretory cells and even small numbers of endocervical or endometrial-type cells can be seen (Ferenczy and Richart 1974; Roberts et al. 1970). Membrane bound dense granules, microvillous processes, and secretory vesicles may also be found in both tumors (Gondos 1971). However, a well-differentiated fallopian tube adenocarcinoma devoid of cilia and secretory granules has been described by Johnson et al. (1978) with a postulated origin from the intercalary cell of the tubal mucosa. Rorat et al. (1976) also recognized the similarity between serous ovarian and tubal carcinoma, and described prominent Golgi complexes, haphazard arrangement of RER, and dense granules within the cells.

Our case did not demonstrate a multiplicity of cell types, nor were there cilia or promient Golgi complexes. Instead, there was abundant stacked RER in association with annulate lamellae and secretory vesicles, suggesting active protein synthesis and the production of secretory material. Stacked RER is also reminiscent of endometrial carcinoma. Annulate lamellae have previously been described in ovarian serous tumors (Ferenczy and Richart (1974), but not in fallopian tube adenocarcinoma. Their origin and signifi-

cance are still obscure, but they are thought to arise from the nuclear membrane (Swift 1956) or endoplasmic reticulum and may function in the transport of information between nucleus and cytoplasm. They have also been described in other gynecologic (Ferenczy 1976) and non-gynecologic neoplasms (Bhawan et al. 1978). Therefore, the association of annulate lamellae with stacked RER and secretory vesicles is not surprising, although the relative lack of Golgi activity in this case remains unexplained.

In view of the heterogeneity of subcellular organelles and multiple cell types seen in previous ultrastructural studies of fallopian tube carcinoma, it seems reasonable to assume that the degree of cellular differentiation is responsible for the variable appearance of the neoplastic cells. The presumed origin of both serous ovarian and fallopian tube adenocarcinomas is from coelomic epithelium or its Mullerian derivatives, which theoretically have the capacity for differentiation along any line which recapitulates the cells of normal tubal mucosa. As such, the variability of cell types reported in these lesions would still be consistent with origin from Mullerian epithelium, and the findings in our case support this hypothesis. In our case, and those previously reported, it has been impossible to differentiate ovarian from tubal serous adenocarcinoma on the basis of ultrastructural study, supporting the hypothesis that these tumors share a common origin. Because of the small number of reported cases, further study of these tubal neoplasms is necessary to determine whether or not any significant ultrastructural differences exist between ovarian and tubal serous adenocarcinomas.

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