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Abstract

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ADENOMATOID TUMOR OF THE UTERUS: REPORT OF A CASE AND REVIEW OF THE LITERATURE

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Abstract. A case of uterine adenomatoid tumor in a 47-year-old female was studied with both light and electron microscopes. The tumor was circumscribed, 2.5cm in diameter, and located in the posterior wall of the uterus. In light microscopy, tumor cells showing "signet-ring" appearance arranged in cords or tubules. Hyaluronidase-sensitive acid mucopolysaccharide was present in the cells and luminal surfaces. Mucicarmine stain was negative and periodic acid-Schiff reaction was faintly positive. In electron microscopy, the tumor showed basal laminae, well-developed desmosomes and numerous microvilli. Intercellular spaces were present between adjacent cells. Small intercellular spaces were separated from the large lumens by desmosomes and tight junctions, while large spaces communicated with the tubular lumens. Forty-four reported cases of adenomatoid tumor in females were briefly reviewed.

The adenomatoid tumor is a rare neoplasm confined to the genital tract. Most reported cases have occurred in males at the epididymis and tunica vaginalis. In females, they are found in the Fallopian tube and uterus, and rarely in the ovary and paraovarian connective tissue. The histogenesis of these tumors is obscure. Possibilities of mesonephric, Müllerian, endothelial and mesothelial origins have been suggested over the years. Recent histochemical and ultrastructural studies have revealed that adenomatoid tumors show striking similarities to mesotheliomas and also to normal mesothelium. The resemblances have strongly supported the possibility that the adenomatoid tumor is of mesothelial origin. The authors report histochemical and ultrastructural findings of a uterine adenomatoid tumor and compare them with those of previous studies.

CASE REPORT

A 47-year-old woman, gravida IV, para III, abortus I, was admitted to the hospital with a 6-month history of heavy, irregular vaginal bleeding. Pelvic examination revealed an enlargement of the uterus. A vaginal cytologic smear was negative for malignant cells. A total hysterectomy was performed. The patient's postoperative course was uneventful.

Weight of the uterus was 300 g. The cut surface showed a diffuse thickening of the uterine wall and two round masses in the posterior wall of the uterus. Both tumorous masses were well-circumscribed and located in the myometrium (Fig. 1). On microscopic examination, one was leiomyoma, the other was adenomatoid tumor. The thickening of the uterine wall was produced by adenomyosis.

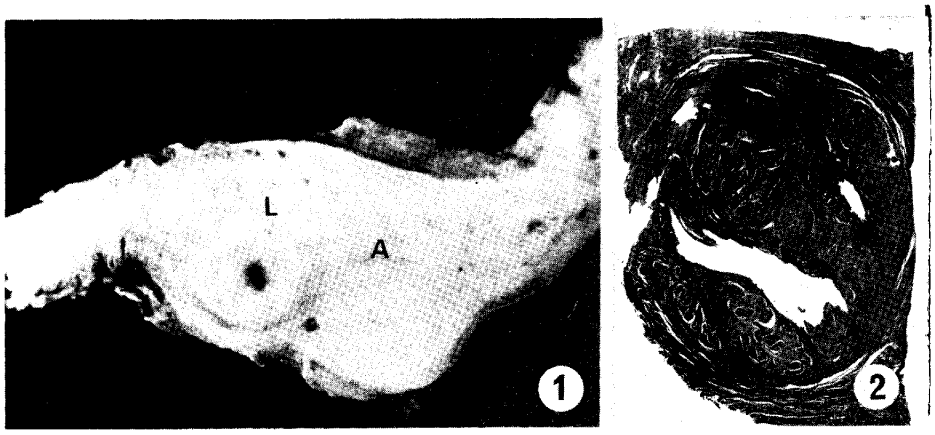


Fig. 1. Cut surface of the posterior wall of the uterus showing two nodules; leiomyoma (L) and adenomatoid tumor (A).

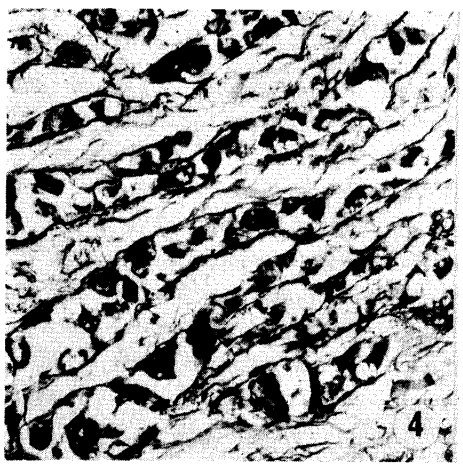
Fig. 2. Low power view of the adenomatoid tumor. Note the resemblance to leiomyoma. Hematoxylin-eosin stain. ×2.

The adenomatoid tumor was approximately 2.5 cm in greatest diameter, greyish-white in color and whorled in appearance.

For light microscopy, tissues were fixed in 10% formalin and embedded in paraffin. Sections were stained with hematoxylin-eosin and various special stains. The tumor was separated from the serosa by a thin band of muscle. Groups of tumor cells surrounded by fibrous stroma were found between the bundles of smooth muscle which were arranged in a whorl-like pattern. Histological features suggested that the tumor arose in a nodule of leiomyoma (Figs. 2, 3). In most areas, tumor cells were cuboidal and arranged in solid cords (Fig. 4). Lumens lined by tumor cells were separated from each other by fibrous stroma (Fig. 5). Where the lumens were not dilated, cuboidal cells with abundant cytoplasm were arranged in tubules (Fig. 6). Many of the cells contained intracytoplasmic vacuoles producing a "signet-ring" appearance (Fig. 7). Each of vacuolated cells had a round, eccentrically placed nucleus. Mitotic figures were not present. Luminal surfaces and intracytoplasmic vacuoles were strongly positive to Alcian blue. The fibrous stroma reacted weakly. This material was partially digested by pretreatment with hyaluronidase. Mucicarmine stain was negative, and periodic acid-Schiff reaction was faintly positive. The stroma consisted of

collagenous tissue surrounding the cords and tubules of tumor cells. Elastic fibers were not found in the stroma. Reticulin stain demonstrated an abundant network of fibers surronding each of the tumor cell groups (Fig. 4). Lymphocytes were dispersed in the stroma and in the lumens lined by tumor cells (Fig. 5).

Fig. 3. Adenomatoid tumor infiltrating between muscle bundles. Left region is the peripheral musculature surrounding the tumor. Hematoxylin-eosin stain. ×70.



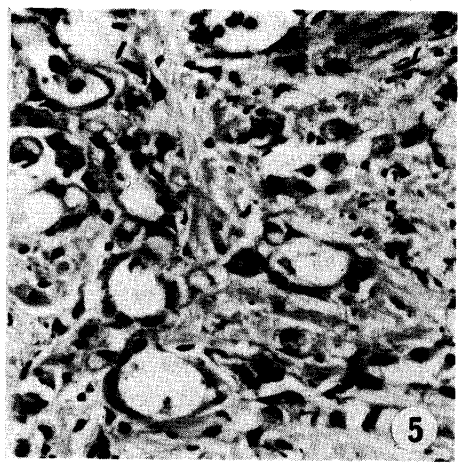


Fig. 4. Plexiform pattern of the tumor. Strands of tumor cells are surrounded by reticulin fibers. Pap's silver stain. ×270.

Fig. 5. Gland-like arrangement of tumor cells. Lymphocytes are scattered mainly in the stroma. Hematoxylin-eosin stain. ×160.

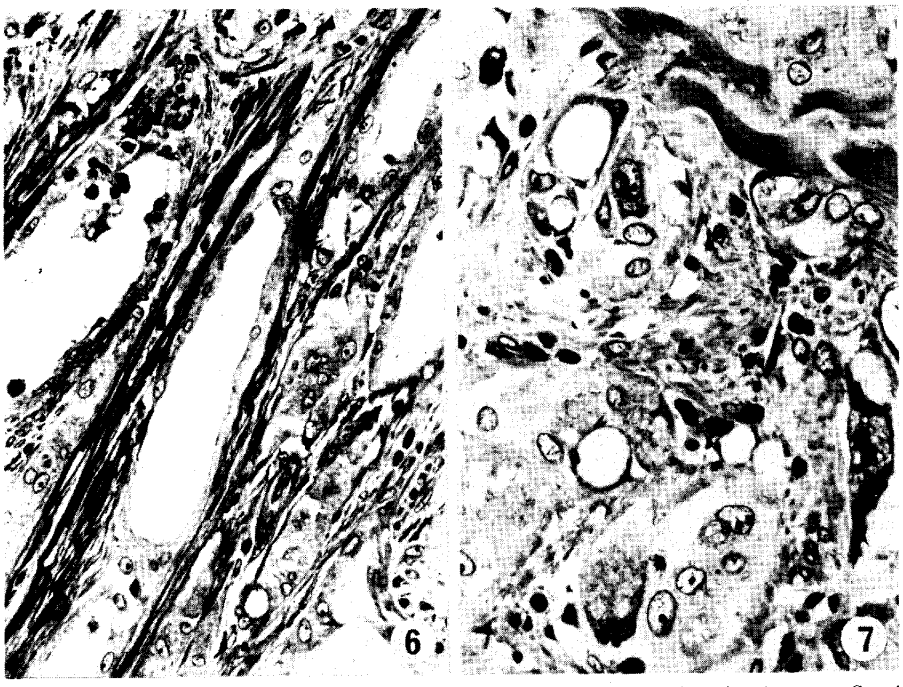


Fig. 6. Cords of tumor cells are separated by fibrous stroma and forming lumens. Semi-thin section. Toluidine blue stain. ×260.

Fig. 7. Large cell vacuoles producing a signet-ring appearance. Semi-thin section. Toluidine blue stain. ×520.

For electron microscopy, small blocks of the formalin-fixed tissue were washed in phosphate buffer for 24 hr, fixed in 1% osmium tetroxide, and embedded in Epon-812. Thin sections were stained with uranyl acetate and lead solutions, and examined with a JEM 7-A electron microscope. The tumor cells were separated from the collagenous stroma by well-defined basal laminae (Fig. 8). Adjacent cells were united by many well-developed desmosomes (Figs. 8, 10). Tight junctions and interdigitations of the cell membranes were also found. The distended intercellular spaces with or without microvilli were present and communicated with the large lumen. When the intercellular spaces were small in size, they were closed from the large lumen by desmosomes and tight junctions. Numerous microvilli were present at the luminal cell surfaces (Fig. 9). The nuclear outlines varied from oval to invaginated. The nucleolus was small and therefore found in only a few nuclear sections. The cytoplasm contained the usual organelles such as small mitochondria, vacuoles and a Golgi complex. Lysosomes were present in a few cells. Pinocytotic vesicles were not found. All cells displayed cytoplasmic filaments; these usually arranged in bundles and

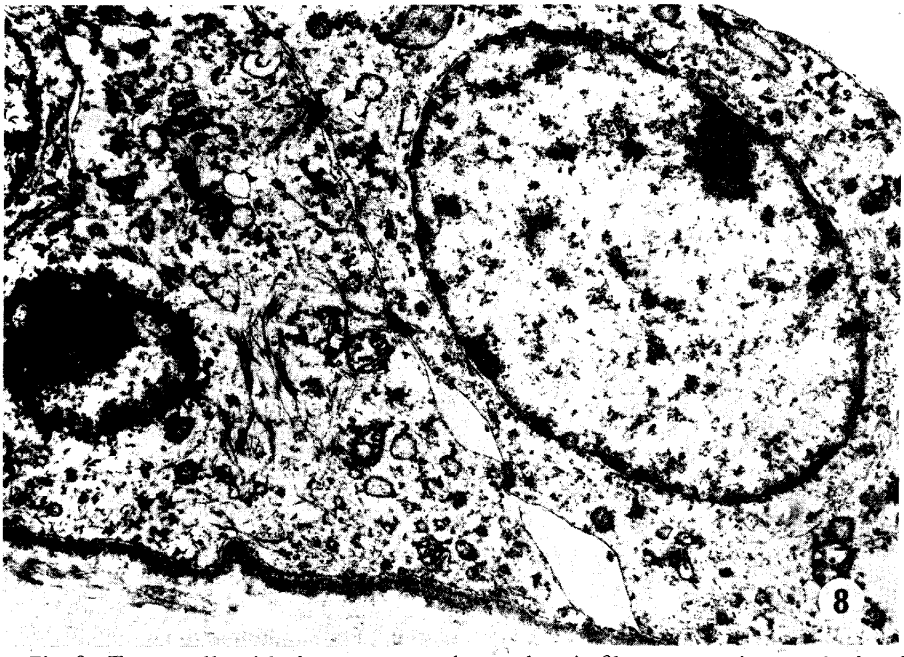


Fig. 8. Tumor cells with desmosomes and cytoplasmic filaments resting on the basal lamina. ×6000.

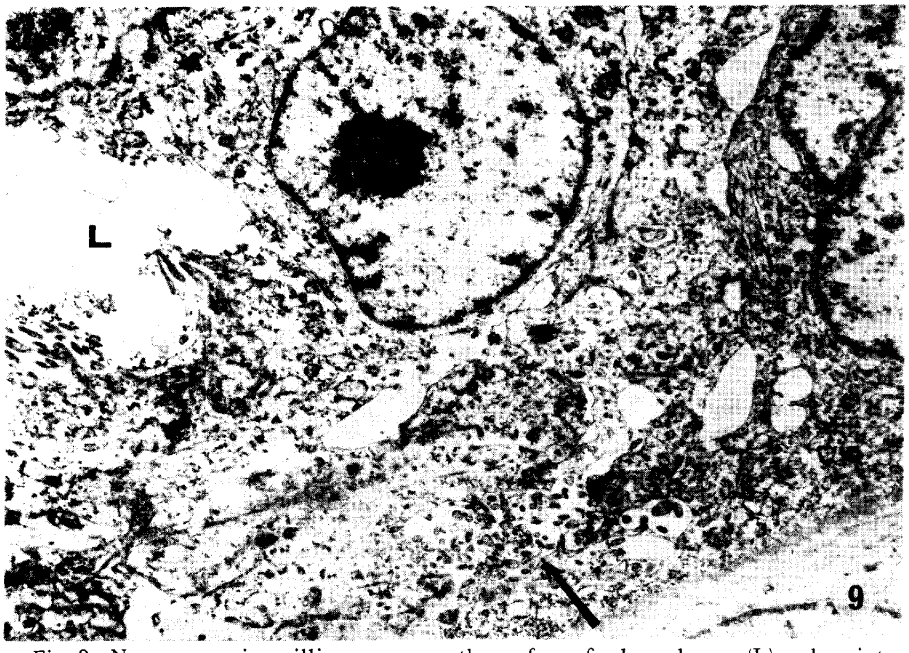


Fig. 9. Numerous microvilli are seen on the surface of a large lumen (L) and an intercellular canaliculus (arrow). ×3600.

distributed irregularly. Some of them were associated with desmosomes (Fig. 10).

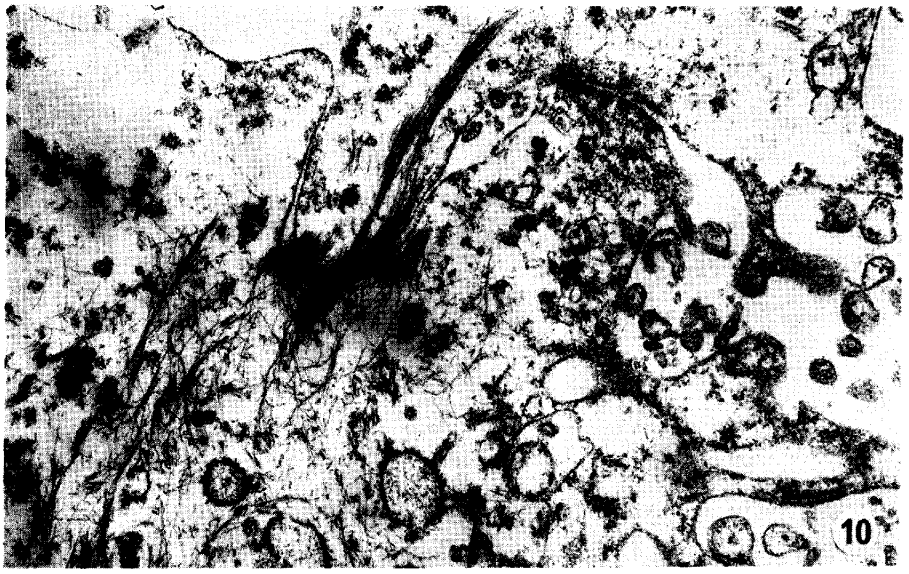


Fig. 10. Intracytoplasmic filaments associated with well-developed desmosomes. ×22000.

DISCUSSION

In 1907, Kermauner reported the first adenomatoid tumor which developed in the Fallopian tube under the diagnosis of lymphangioma (1). The earliest report of the male adenomatoid tumor was that of Sakaguchi, in which he termed it adenomyoma (2). Thereafter, the neoplasm was described under a variety of terms such as lymphangioma (3), adenoma (4), adenomyofibroma (5), mesothelioma (6), adenomatoid tumor (7), and angiomatoid formation (8). Because of the uncertain histogenesis of this neoplasm, the term "adenomatoid tumor" proposed by Golden and Ash (7) has been wiedely used.

Tables 1, 2 and 3 show 16 previous reports on the adenomatoid tumor in females. Although the age of the patients ranged from 28 to 74 years, most patients were between the ages of 30 to 55. The size of the tumors, except in 2 cases, ranged from 0.5 to 3.5 cm in diameter. The uterine tumors were somewhat larger than the Fallopian cases. The tumors were usually located beneath the serosa. However, continuity between the serosal cells and the tumor cells lining the lumens was demonstrated in only a few cases (6, 9, 10, 11). The majority of the tumors were single, and multiple lesions were very rare. Youngs and Taylor reported a case of multiple adenomatoid tumor of the uterus and of the Fallopian tube (11).

TABLE 1. ADENOMATOID TUMORS OF THE UTERUS

Author and reference no.	Patient's age	Location of the tumor	Size (cm)	Symptom	Associated finding
Taxy *et al.* (14)	53	Subserosa		Enlarging abdomen Vaginal bleeding	Leiomyoma. Cervical polyp
Evans (6)	52	Intramural, extending to the serosa	7	Pelvic symptom	
Teel (28)	55	Surface of uterus			Descensus of uterus Leiomyomas
	63	Left lateral wall	1		Descensus of uterus
	27	Right uterine cornu	3.3	Sterility	Leiomyomas
	39	Myometrium	0.6		Relaxed vaginal outlet
	53	Pedunculated mass, beneath serosa near right uterine cornu	3.5		Leiomyomas
Salazar *et al.* (10)	45	A subserosal mass of the left cornual region	2	Menorrhagia	Leiomyomas. Adenomyosis
Horn *et al.* (15)	33	Beneath the serosa of the uterus		Dysmenorrhea	
	35	Posterior wall	2	Sterility	Leiomyoma
	38	Right cornual region, beneath the serosa	3	Meno-metrorrhagia	Leiomyomas Endocervical polyp
	41	Right cornual region, beneath the serosa	2		Cervical cancer Leiomyomas
	48	Right cornual region, beneath the serosa	3	Menorrhagia and polymenorrhea	Endometrial hyperplasia
Lee *et al.* (9)	28–59	10 cases were located on the posterior aspect of the uterus and 2 on the anterior surface	0.5–3	Dysmenorrhea Meno-metrorrhagia Lower abdominal discomfort, etc	6 cases of leiomyomas A case of adenocarcinoma Endometriosis. Retroversion Subinvolution

TABLE 2. ADENOMATOID TUMORS OF THE FALLOPIAN TUBE

Author and reference no.	Patient's age	Location of the tumor	Size (cm)	Symptom	Associated finding
Taxy *et al.* (14)	28	Left Fallopian tube		Menorrhagia Cramping	Leiomyoma Tubo-ovarian abscess
Evans (6)	45		0.8	Profuse menstruation	Leiomyoma Endometrial polyp
Teel (28)	37		1	Menorrhagia	Leiomyomas
Salazar *et al.* (10)	29	Ampullar portion	0.8		
Lee *et al.* (9)	51	Posterior aspect of the right tubal wall	1	"Bearing down" sensation and irregular menses	Endometritis
	52	Subserosa of the left tube	1	Pain in the left lower abdomen	Leiomyoma Endometrial polyp
Sanes *et al.* (3)	55	Left Fallopian tube	1.1	"A tumor in the abdomen"	Leiomyoma
Kermauner (1)	50	Isthmus of the right tube	A bean-sized	Hypermenorrhea	Leiomyomas
Scott *et al.* (26)	55	Left ampullar portion	1		Cervical cancer
	38	Midportion of the left tube	0.5	Metrorrhagia	Cervical cancer Endometrial cancer Leiomyomas
Burke *et al.* (24)	42	Right tube, proximal to the fimbriated opening	2	Menorrhagia and metrorrhagia	Cervical polyp
Laufe (25)	36	Middle third of the oviduct	1.5	Incidental finding at the time of surgery	

TABLE 3. ADENOMATOID TUMORS OF THE OVARY AND PARAOVARIAN CONNECTIVE TISSUE

Author and reference no.	Patient's age	Location of the tumor	Size (cm)	Symptom	Associated finding
Ferenczy *et al.* (13)	44	Hilar region of the right ovary	0.7	Found at palliative ovariectomy (Breast cancer)	
Williamson *et al.* (16)		Right ovary	3	Found at laparotomy for the purpose of sterilization	
Lee *et al.* (9)	39	Right ovary	1.4	Irregular menses and inconstant pain	Leiomyomas Hydrosalpinx
Morehead (8)	26	Right ovary	1.5		
Siddall *et al.* (27)	40	Left ovary	8	A mass in the abdomen and dull pain	Leiomyomas
Williamson *et al.* (16)		Adjacent to the right ovary	1		Endometrial carcinoma
Teel (28)	46	Paraovarian connective tissue at one pole of left ovary	0.5	Abdominal pain	Leiomyomas Relaxed vaginal outlet
Akhtar *et al.* (12)	43	Posterior leaf of broad ligament, attached to right tube & ovary	7.5	Right abdominal mass Menorrhagia	
	50	Uterine round ligament	1.5	Found at herniorrhaphy	

Lee *et al.* classified histological features of the tumors into three patterns: canalicular, tubular, and plexiform (9). These patterns were usually mixed in a single tumor. In our case, plexiform pattern was predominant. Previous histochemical studies demonstrated the presence of hyaluronidase-sensitive acid mucopolysaccharide in the tumor cells, lumina and stromal areas of all cases (11–14). Mucin was found in a few cases by mucicarmine stain (9, 14, 15). Because of unsuitable fixation with formaldehyde solution, tests for presence of glycogen were inconclusive (7, 16). We found only one report that described the presence of diastase-sensitive PAS-positive material (13). Lee *et al.* reported a negative result of glycogen stain in one case of fresh tissue fixed in absolute alcohol (9).

The stroma was formed mainly by bands of collagen fibers and a meshwork of reticulin. Although Weigert's elastic tissue stain was negative in our case, elastic fibers have been demonstrated in some reports (2, 6, 9). Youngs and Taylor reported bone formation in the stroma of a tubal adenomatoid tumor (11). Infiltration of lymphocytes with or without follicle formation was not uncommon. Germinal centers were not produced in the lymph follicles (6, 7, 10, 11). In our case, a striking feature was the presence of abundant smooth muscle fibers in the nodular mass. It might be explained by the infiltration of tumor cells into the preexisting leiomyoma. However, leiomyomas frequently show massive hyaline and/or cystic degenerations, calcification and necrosis. Such secondary degenerative changes have not been reported in the uterine adenomatoid tumors. Therefore, we are convinced that the smooth muscles surrounding the tumor have proliferated to inhibit the growth of tumor cells by forming a nodular mass.

The histogenesis of the tumor was controversial. The ultrastructural features of the tumor such as abundant desmosomes and microvilli militated against the endothelial origin (17–19). Dilated intercellular spaces were not present in the endometrial gland derived from Müllerian duct (20). Moreover, hyaluronidase-sensitive acid mucopolysaccharide was not found either in endothelium or in Müllerian or mesonephric epithelium. Histochemical reactions and ultrastructural features of the adenomatoid tumor were quite similar to those of normal mesothelium and mesotheliomas, and a mesothelial origin of the adenomatoid tumor was strongly supported (10, 13, 17, 18, 21). However, the adenomatoid tumor is benigh, while many cases of the mesothelioma are malignant. Although a few malignant adenomatoid tumors have been reported, such cases were found in males but not in females (22). Moreover, a papillary configuration, present in mesotheliomas, is very rare in adenomatoid tumors (6), whereas vacuolated cells resembling signet-ring cells, found in adenomatoid tumors, were not seen in mesotheliomas. Evans suggested that the histogenetic factors concerned might be related to the difference in potentialities of the mesothelium

between the genital tract and the remainder of the peritoneum (6). However, neither histochemical nor structural differences have been hitherto demonstrated. Hanrahan's report was the only case that demonstrated the presence of a benign mesothelioma, which developed in a part remote from the genital tract and showed the histological resemblance to the adenomatoid tumor by light microscopic examination (23).

The ultrastructure and histochemical reactions of the adenomatoid tumor cells are sufficient to support a mesothelial origin. However, there seems to be little evidence, at this point, to explain structural differences in the light microscopic level between the adenomatoid tumor and the mesothelioma. With increasing reports of adenomatoid tumors and benign mesotheliomas, their relationship will be more clearly elucidated.

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