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Endosalpingioma of the ovary : a review of the literature and a study of thirteen cases diagnosed at Nebraska Methodist Hospital

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ENDOSALPINGIOMAS OF THE OVARY: A REVIEW OF THE LITERATURE AND A STUDY OF THIRTEEN CASES DIAGNOSED AT NEBRASKA METHODIST HOSPITAL

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INTRODUCTION

In the past there has been much confusion in the classification of ovarian tumors. There is one class, the epithelial cystomas which include serous and psuedomucinous cystadenomas, cystadenocarcinoma, and endosalpingiomas of which this has been particularly true. The confusion has not been so marked with the psuedomucinous cystadenomas and the cystadenocarcinomas but is for the most part concerned with serous cystadenomas and endosalpingiomas. It is the belief of Schenken (1) that these are two distinct entities and should be differentiated, recognized, and separated by pathologists because of the more benign qualities of the endosalpingioma.

a) Definition. Endosalpingioma is a benign epithelial ovarian umor which can be seen to duplicate, functionally and morphologically, those characteristics commonly noted in the normal human fallopian tube. Patterns seen in this tumor correspond to those occurring in the human tube during the various phases of the menstrual cycle, during pregnancy, and the menopause. The active proliferative and functional character of the "Mullerian" epithelium retained in this tumor gives rise to varied microscopic pictures and peculiar gross pathological and clinical conditions, Barzilai (2).

b) History and Terminology. The fact that this group of tumors goes by no less than fifty different names in the literature only goes to demonstrate the confusion which has arisen in the minds of clinicians and pathologists concerning this group of tumors.

c) Purpose of this paper. The purpose of this paper of to discuss epithelial cystomas of the ovary and to suggest reasons why another type of tumor, the endosalpingioma, because of its benign character, should be added to the classification. I shall also present a survey of the cases diagnosed as endosalpingioma at the Nebraska Methodist Hospital.

FREQUENCY AND AGE INCIDENCE

The frequency and age incidence of this tumor cannot be determined from statistical studies because the literature only speaks of serous cystadenomas. Barzilai (2) in her experience sets the peak age incidence at the third and fourth decades, the height of the woman's reproductive life, and claims them to comprise about 20% of all ovarian tumors. Schenken (1) finds the frequency to be about 17% of all ovarian tumors, Table I, 23% of epithelial ovarian cystomas, and the age to range from 18 to 75 years with an average age of 36 years. Allan (3) in a series of 922 epithelial cystomas found 36.5% to be benign serous cystadenomas without any further breakdown in classification.

OVARIAN TUMORS	
Serous and Pseudomucinous cystadenomas	49
Endosalpingioma	25
Cystadenocarcinoma	19
Dermoid	13
Seroanaplastic carcinoma	12
Fibroma	11
Teratoma (2 Struma ovarii)	5
Thecoma	4
Metastatic carcinoma	3
Dysgerminoma	3
Giant cell tumor	1

Table 1. Showing the relative frequency of various ovarian tumors seen at Nebraska Methodist Hospital since 1951.

Dockerty (4) states that benign serous cystadenomas make up about 15% of ovarian neoplasms in his series and lists the highest incidence between 20 and 50 years of age. Bell (5) lists the incidence of cystadenomata as 48% in a series of 2603 cases with an age range of 17 to 73 years and an average age of 44 years.

SIGNS AND SYMPTOMS

The signs and symptoms of this tumor are many, varied, and non-specific. In Schenken's series one presented because she had been unable to eat a full meal for some time. Others may present in shock, or with an acute abdomen because of one of the complications, which may include ascites, emaciation, pressure effects, adhesions with bowel obstruction, torsion of the pedicle, hemorrhage, rupture, and peritonitis, Ewing (6). The most common presenting complaints are shown below:

Signs and Symptoms	Bell	Dockerty	Schenken
Abdominal Swelling	63.2%		28.6%
Abdominal Pain	44.8		78.6
Backache	11.5		14.3
Ascites	5.1		0.0
Dysmenorrhea	21.6		0.0
Menstrual Irregularities and Metro-Stasis	30.7		35.7
Post-menopausal	35.0		21.4
Sterility		25.0%	

Table II. Showing frequency of occurrence of presenting complaints.

Date	Patient	Age	Color	Marital Status	SYMPTOMS: Abdominal Pain	Back Pain	Menorrhagia	Menometrohagia	Amenorrhea	Mass	Fatigue	Nausea and Vomiting	Abdominal Signs: Mass	Tenderness	Distention	Pelvic Signs: Mass	Cervix	Uterus	Adnexa	Other
10-18-50	MS	43	W	M	/	/	-	-	-	-	/	-	-	/ /	-	-	-	-	-	/*
12-28-50	VC	30	W	M	/	-	-	-	/	-	-	/	-	/ /	-	/	-	-	/	-
	JS	23	W	M																-
	AC	40	W	M	/	-	-	/	-	-	-	-	-	-	-	-	/	E	-	-
8-5-51	HS	23	W	S	/	-	-	-	-	/	-	-	/	/	-	/	-	-	-	-
11-4-52	LE	18	W	S	/	-	-	-	/	-	-	/	-	/	-	-	-	-	-	/*
3-30-53	HP	25	W	S	/	-	-	-	-	/	-	-	/	/	-					-
5-8-53	VJ	29	W	M	/	/	-	-	-	-	-	-	?	/	-					-
6-8-53	BW	41	W	M	/	-	-	-	-	/	-	-	/	/	-					
7-25-53	WD	28	W	M	/	-	-	-	/	-	-	-								/**
1-23-54	KB	61	W	M	/	-	-	-	-	-	-	/	-	/	/	-	-	-	-	/*
3-11-54	NO	61	W	M	-	-	/	-	-	-	-	-	-	-	-					
10-5-54	MB	71	W	M	/	-	-	-	-	/	-	-	/	/	-	/	-	-	/	-

* Leukocytosis

** Leukocytosis
Rbc 2.93 Hb 81%

E Enlarged

Clinical Diagnosis	Operative Findings	Pathology	Course	Follow-up
Ovarian Cyst Endometriosis	Ovarian Cyst	Endosalpingioma Endometrial Hyperplasia Endometrosis Leiomyoma	Uneventful	Unable to locate
Ectopic Pregnancy	Uterine Pregnancy Cystic Ovary	Endo salp ingioma	2 u of Blood	Febr., 1955 O. K.
	Ovarian Cyst Conization done	Chronic ulcerative endocervicitis with Epidermization of glands Endosalpingioma	1 u of Blood	Unable to locate
Metrohagia Cervicitis	Bilateral cystic ovaries	Endosalpingioma Endometriosis Chronic cervicitis	Uneventful	Oct., 1954 O. K.
Ovarian Cyst or Pregnancy	Ovarian cyst with 2 L. Fluid	Endosalpingioma	Uneventful	March, 1955 O. K.
Acute Appendix or Ectopic Pregnancy	Acute appendix, Cyst growing from fimbriated end of tube	Endosalpingioma Acuteappendicitis	Uneventful	Jan., 1955 O. K.
Ovarian Cyst	Lf. ovarian cyst with 2L fluid. Papillary tumor of right ovary	Bilateral endosalpingioma with invasion of capsule	Uneventful	Jan., 1955 No. Evidence of recurrence
	Bilateral cystic ovaries	Endosalpingioma Follicular cysts	Uneventful	Nov., 1954 O. K.
Ovarian Cyst	Ovarian Cyst size of six month pregnancy	Endosalpingioma	Uneventful	Aug., 1953 O. K.
Ectopic Pregnancy	Ruptured ectopic with tube and ovary massed in clot	Endosalpingioma Ectopic pregnancy	3 u of Blood	June, 1954 O. K.
Ca of Bowel Ovarian Cyst Diverticulitis	Volvulus 10x of pedicle of right ovarian cyst	Endosalpingioma	Paralytic ileus, severe	Jan., 1955 O. K.
Post menopausal bleeding of undetermined origin	Ovaries atrophic Uterus normal	Endosalpingioma Atrophic ovaries	Uneventful	July., 1954 O. K.
Ovarian Cyst	Bilateral Ovarian cyst	Bilateral endosalpingioma	Uneventful	Nov., 1954 O. K.

PATHOLOGY

a) Gross. Grossly the tumor shows great variation; hence the diversity of terminology. Though these tumors are one and the same cytologically, grossly they may appear as:

> "1) A uni-or parvi-locular cystopapillary type with
> a) intracystic papillary outgrowths and a smooth outer surface.
> b) intracystic and extracystic papillary outgrowths.
> 2) A solid form with superficial papillary outgrowths;
> 3) A mulberry or grape-like form." Barzilai (2)

The cystic form is the most common and important.

The type with the intra-cystic papillary outgrowths and smooth outer surface, whether uni- or parvi-locular, are usually unilateral and may become quite large. The surface may often be lobulated indicating the presence of daughter cysts. The cut surface of the tumor may reveal numerous daughter cysts of various sizes, Barzilai (2). In the smaller cavities a serous, transparent fluid is seen while in the larger cavities the fluid may be dark and opaque due to intracystic hemorrhage, Ewing (6).

> "The cyst wall is usually made up of 3 layers: an outside fibrous layer somewhat recalling the ovarian albuginea, a central layer of loose connective tissue, and an inner layer facing the cyst cavity." Barzilai (2)

The cyst wall may bulge irregularly due to intra-mural

cystic and papillary formations. The cyst wall may bulge irregularly due to intra-mural cystic and papillary formations. The cyst lining epithelium may be smooth and shiny but is more often velvety and may have numerous papillary excresences. The smooth wall cyst without papillary projections has been called by some authors simple serous ovarian cysts.

The smooth-walled cyst is always well pedunculated, usually grows free in the peritoneal cavity but may on occasions be intraligamentous. Twisting of the pedicle, adhesions to surrounding viscera, secondary infection, rupture with peritoneal seeding, ascites, and pleural effusion may occur. The last complex being quite uncommon.

"The cysto-papillary form with intra-cystic and extra-cystic papillary masses show a cystic cavity", Barzilai (2) similar to the one above. The tumor is usually smaller and more frequently bilateral than the above described type. It has luxuriant intracystic and extracystic papillary projections which are identical in appearance. Peritoneal seeding and ascites with pleural effusion are very common in this type.

> b) Microscopic. "The solid form with superficial papillary outgrowths appears as a fibrotic new growth and reveals a few small papillary projections that are most frequently of the low, warty, sessile type." Barzilai (2)

The mulberry- or grape-like type consists of a central core surrounded by small solid or cystic masses attached to a branching connective tissue stalk, Barzilai (2). It resembles a bunch of grapes. Barzilai (2) believes this type represent "a degenerative form of one of the tumors characterized by extra-cystic papillary types." Barzilai (2)

c) Cytology. Structurally the tumor is papillary. The neoplastic epithelium resembles the epithelium seen in the normal adult salpinx. The ciliated, secretory, intercalary, and vesicular cells of the neoplasm resemble similar cells of the salpinx and can be seen to undergo functional changes closely resembling changes undergone by the tubal epithelium during menstruation, pregnancy, lactation, and post-menopause.

> "The cells seen in the epithelial portion of the tumor may appear as: 1) secretory cells; 2) ciliated cells; 3) intercalary cells; 4) intra-epithelial cells.
>
> "I. The secretory cells are non-ciliated. They have a scant finely granular, darkly staining protoplasm and a large nucleous with its axis parallel to the long axis of the cell body . . . These cells show morphological changes according to their functional stage.
>
> They may appear as:
>
> a) Tall columnar cells with homogenous, darkly staining, prismatic or slightly ovoid nuclei, and a moderate amount of

granular protoplasm massed at the base and free border of the cells: PROLIFERATIVE STAGE.

b) Club- or pear-shaped cells, with widened upper portions and convex, free borders, through which the protoplasm seems to herniate: SECRETORY STAGE.

c) Prismatic or pear-shaped cells with protruding nuclei, extrusion of protoplasmic clumps, or even extrusion of the nucleus itself into the interpapillary space: EXCRETORY STAGE.

d) Low cylindric and almost cuboidal cells, with more or less convex free borders, homogenous darkly staining ovoid nuclei and granular, darkly stained protoplasm: RESTING STAGE.

"II. The ciliated cells have a clear, almost refractile, abundant protoplasm. The roundish or, more often, ovoid nucleous is usually placed near the free border of the cell, at right angles to its long axis. These cells show ciliary projections that are more or less evident and appear neatly individualized or clumped together . . . These cells may be a) Tall, prismatic cells about 40 microns high and 12 microns wide; b) Low cylindric cells; c) Low cuboidal or almost flat cells,"

depending on the functional state and correspond to the intermenstrual, premenstrual, menstrual, or post-menstrual period of the monthly cycle as is seen in the ciliated epithelium of the salpinx.

"III. The intercalary or peg cells are tall, slender, and almost bare of protoplasm, with rod- or wedge-shaped, very darkly staining,

homogenous nuclei. They are very similar to the secretory cells in the early proliferative phase of which they may be a modification.

"IV. The interpapillary vesicular cells are large and round, with transparent protoplasm and round very dark central nuclei."

The types of cell often occur in patches of which secretory cells are most commonly seen. There is often an unevenness of the free border due to the difference in height of the two types of cells. Multistratification may occur due to tangential sectioning of papillae and lead to the erroneous interpretation of malignancy, Barzilai (2).

HISTOGENESIS

The origin of these tumors has been the subject of much controversy in the past and still has not been settled to the satisfaction of all authors. The various theories postulated are as follows in the order of their inception:

1) That they arise from the Graffian follicle,
2) That they arise from some type of connective tissue overgrowth,
3) That they arise from Pflueger's ducts,
4) That they arise from the para-ovarial elements particularly from granulosa cells,
5) That they arise from Mullerian body remnants,
6) That they arise from toti-potential cells from the germinal epithlium of the Wolffian body,
7) That they are of tubal origin.

Schenken (1) is convinced of the theory of their origin from the tube because he has found two growing from the fimbriated end of the tube without any attachments to ovary or any other surrounding structures.

MALIGNANCY

Malignancy is a question of prime importance with endosalpingioma as it is with any neoplasm. The question of whether these are malignant or can be potentially malignant often arises. Barzilai (2) believes that all endosalpingiomas are benign, in spite of frequent areas of multi-layering, because of their origin from tubal epithelium. Schenken (1) states that he has never seen a malignant one in spite of invasiveness, but does not believe that malignancy within these tumors is beyond the realm of possibility. Meyer (8) believes that all cystomas have a malignant potential. This view is held by many other pathologists. Therefore the beliefs concerning the malignancy of this tumor will be influenced by the belief of the pathologist concerning the origin of the tumor, i.e., tubal origin, or ovarian origin.

Few believe that malignancy can be told grossly, but usually the finely villous extremely papillomatous type tends to exhibit the more malignant characteristics, while the hard fibrous type rarely exhibit such qualities. Microscopic criteria for malignancy should be as follows: 1) Proliferation and multi-layering of epithelium,

2) Adenomatous patterns, 3) Anaplasia and neoplasia,

4) Stromal invasion, and 5) Extension to adjacent organs.

TREATMENT

Surgery is the treatment of choice but the question rests at how far to go. The tendency at present seems to be in favor of unilateral ovariectomy if the other ovary is explored and found to be without abnormality, Barzilai (2), Schenken (1), Bell (5), and Dockerty (4). This is especially true in the child-bearing age where the woman may want to have children, and since it is felt that these are benign, it is not deemed necessary to subject a young lady to an artificial menopause.

CONCLUSIONS

From the above it can be noted that the most common presenting complaint in the Nebraska Methodist Hospital Series is abdominal pain 78.6% although in two of the cases endosalpingiomas were incidental findings at laprotomy for acute abdomens, one being an ectopic pregnancy and the other an acute appendicitis. Other presenting complaints include menstrual irregularities 35.7%, mass 28.6%, and backache 14.3%. In this series there was one four year cure, one three year cure, two two year cures, six one year cures, one less that one year cure, and unable to locate two of the patients.

Also noted is the case of H. P. who had bilateral ovarian tumors invading the capsules and surrounding organs. A panhysterectomy was done and after two years there is no evidence of recurrence.

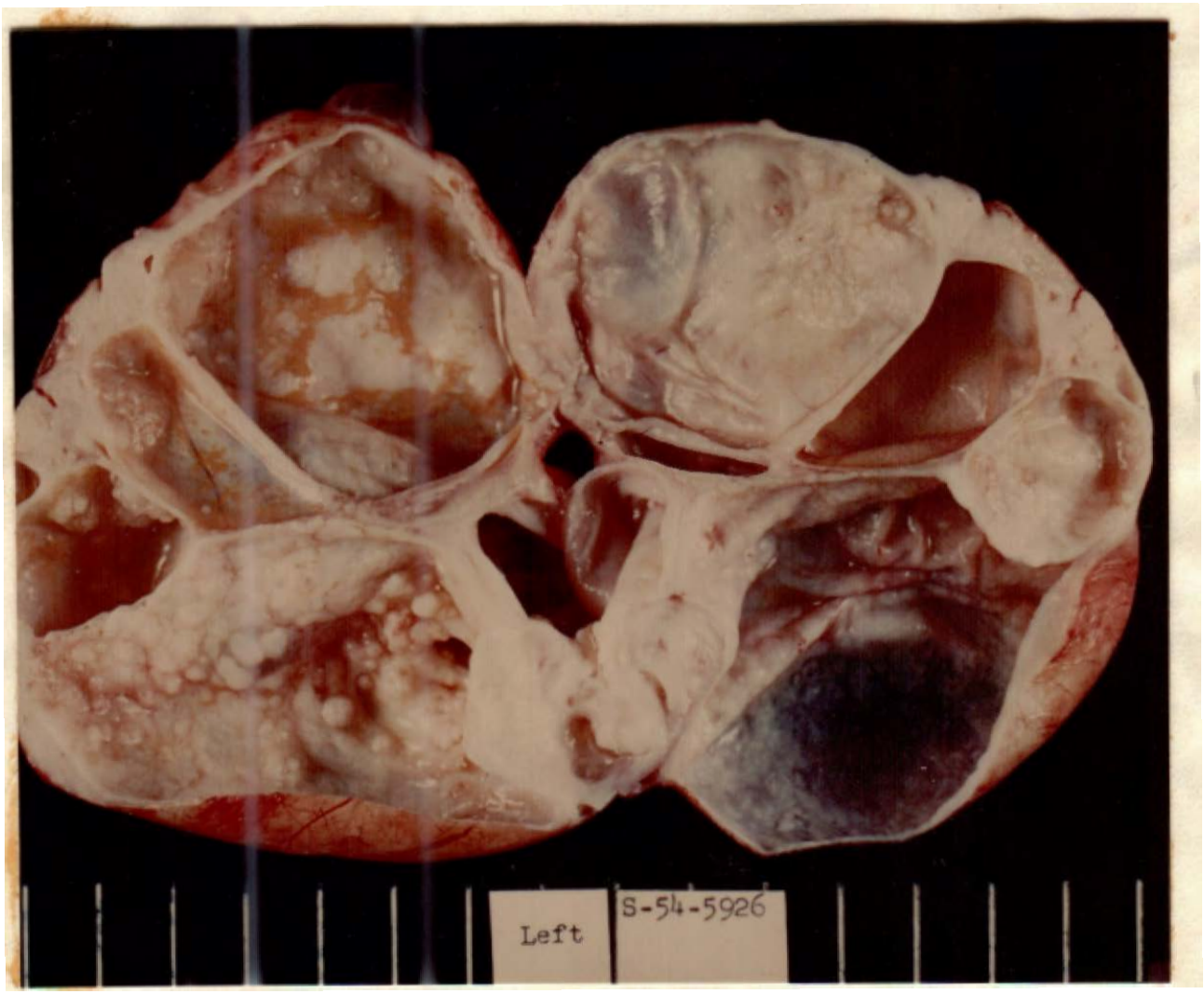
The fact that Schenken has found two such tumors growing from the fimbriated end of the salpinx tends to substantiate the fact that these tumors can be or are of tubal origin. It is too early and too little appears in the literature for one to completely evaluate this tumor.

SUMMARY

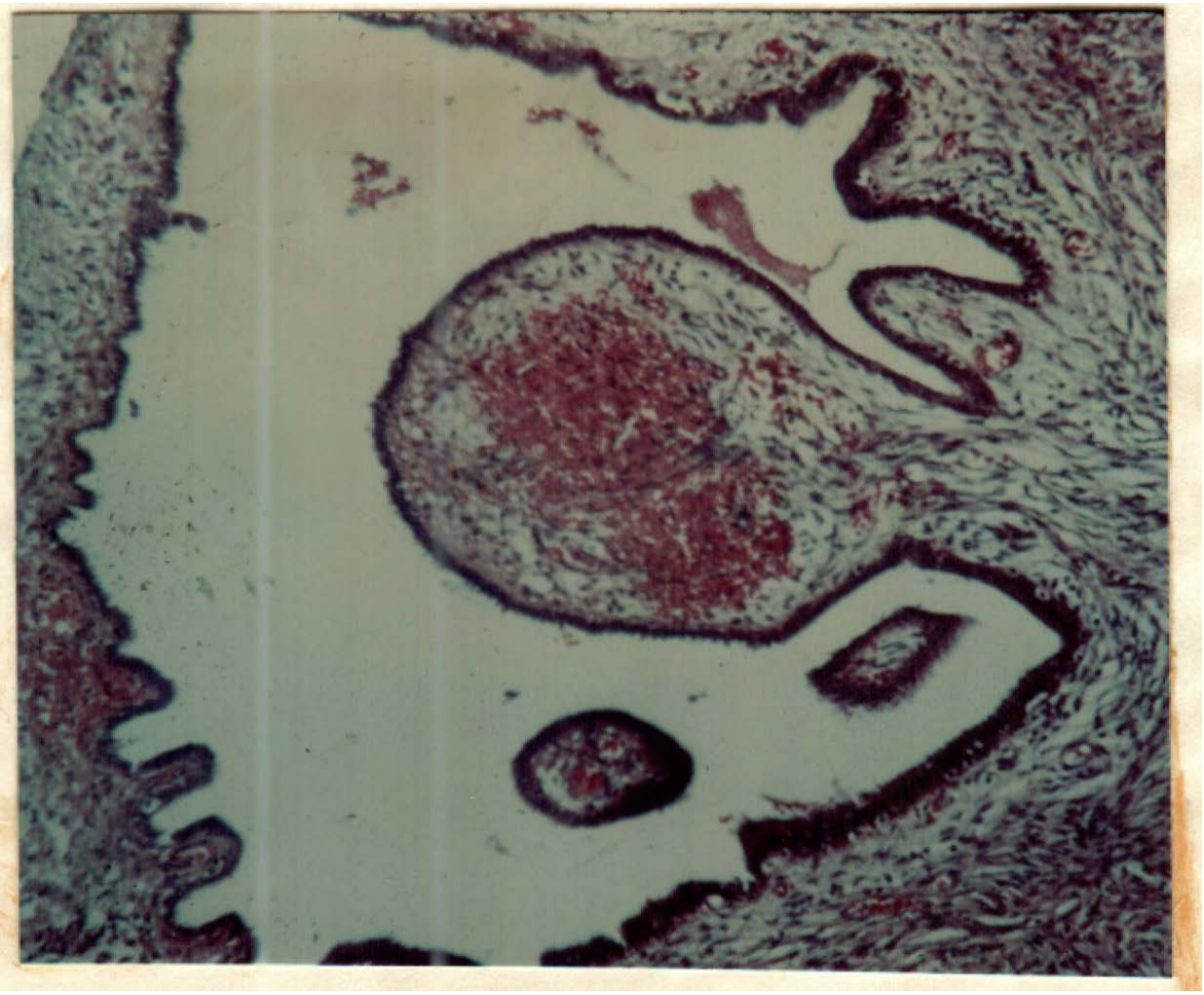
There is still much confusion in the classification of ovarian tumors. There are those authors who believe another group, the endosalpingiomas, should be added because of the resemblance of their morphologic and histopathologic appearance to epithelial and stromal elements of the normal fallopian tube.

1) These tumors comprise about 17-20% of all ovarian tumors and peak incidence is in the third and fourth decade.
2) Signs and symptoms in order of frequency are abdominal pain, abdominal mass, menstrual irregularites, and backache.
3) Many theories as to origin of these tumors have evolved. The latest theory is that they are of tubal origin which is in part substantiated by the finding of two growing from the fimbriated end of the tube without attachment to other organs.
4) These tumors are not believed to be malignant in spite of their tendency to invade their capsule and surrounding organs.
5) Dr. Barzilai gives a very comprehensive pathological description of these tumors.
6) An analysis is made of thirteen cases diagnosed and treated at Nebraska Methodist Hospital between the years of 1950 and 1955.
7) Surgery is the treatment of choice.

Finally, it seems evident that this tumor, in spite of capsule invasion and spread to adjacent organs, does not carry the malignant potential of the rest of the group of cystadenomas and should therefore be classified separately. In this manner some women could be spared the grim prognosis which is attached when the diagnosis of invasive cystadenoma is made.



Photograph showing tumor mass with numerous cystic cavities lined with numerous papillary outgrowths.



Photograph showing microscopic
appearance of tumor.

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