

Mucinous tumors of the ovary: Analysis of 38 cases

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Summary

Ovarian mucinous tumors stem from ovarian surface epithelium and are divided into benign, borderline and malignant. It is difficult to differentiate borderline and malignant mucinous tumors. Thirty-eight cases of ovarian mucinous tumors which were diagnosed at the Pathology Department of Dicle University Medical Faculty were reviewed. Of these, 18 (47.3%), six (15.7%) and 14 (36.8%) were benign, borderline and malignant, respectively. The patients' ages ranged from 18 to 67 (average 44.5) years. Bilaterality was detected in 1/18 (5.5%), 0/6 and 4/14 (28.5%) of benign, borderline and malignant mucinous tumors, respectively. Mean tumor size was 26.4 cm. Microscopically, there was no stratification in the benign tumors. The borderline tumors had papillary infoldings and 2-3 layers of atypical epithelial cells but no invasion of the stroma. Malignant tumors had four or more layers of atypical epithelial cells and stromal invasion.

Key words: Ovary; Mucinous tumors; Histopathology.

Introduction

The histogenesis of ovarian mucinous tumors is controversial. It has been thought that these tumors may be considered as teratomas which have only endodermal features since some of these tumors contain endocervical-type cells, goblet cells of intestinal mucosa, paneth cells, neuroendocrine cells, and that 5% of these tumors appear with cystic teratomas [1-5]. On the contrary, the fact that mucinous tumors are present together with serous, endometrioid and brenner tumors supports the view that these tumors are of müllerian origin [1, 6]. Recently, it has however been explained through müllerian and non-müllerian metaplasia, which can be seen on ovarian surface epithelium arising from celomic epithelium [7]. When the surface epithelium transforms to müllerian metaplasia, various types of tumors which mimic normal müllerian tissues may exist: i.e. tuba (serous tumors), endocervical (endocervical-type mucinous tumors) and endometrium (endometrioid tumors). In case surface epithelium transforms into non-müllerian metaplasia, this may result in intestinal (intestinal-type mucinous tumors), transitional (brenner and transitional cell carcinoma) or clear cell (clear cell carcinoma) [4, 7]. Mucinous tumors have been classified as benign, borderline and malignant [4]. It is much more difficult to distinguish borderline tumors from malignant mucinous tumors as compared with serous tumors. It is not always possible to demonstrate stromal invasion in mucinous tumors as compared with serous tumors [6, 13].

The aim of this study was to investigate the pathological and clinical features of ovarian mucinous tumors.

Materials and Methods

The histologic sections from surgical specimens of ovarian mucinous tumors of 38 cases treated at the Medical Faculty, Dicle University, between 1992-2000 were reviewed. According to the histologic criteria of Bostwick *et al.* [9], mucinous tumors were classified as benign, borderline malignancy and carcinoma (Table 1). In addition, patient age, menopausal status, and the diameter, localization and bilaterality of the tumor were investigated.

Table 1. — *Diagnostic criteria for ovarian mucinous tumors.*

<i>Benign mucinous tumor</i>
– absence of complex glandular structure
– nucleus with basal localization in a typical single cell line
– rare mitosis
<i>Borderline mucinous tumors</i>
– complex villoglandular model
– mitotic figure and/or cytologic atypia
– cell stratification (3 or less)
<i>Malignant mucinous tumors</i>
– ovarian stromal invasion
– epithelial cell stratification (4 or more)
– abnormal mitosis and/or cytologic atypia

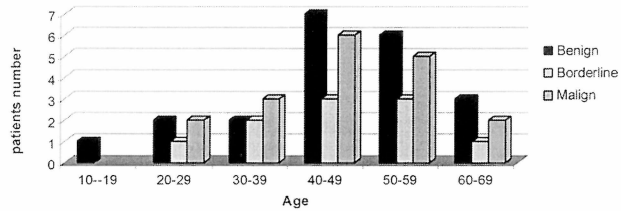
Results

Pathologic sections of 38 cases were evaluated; of these 18 (47.3%), six (15.7%) and 14 (36.8%) were benign, borderline and malignant, respectively. The patients' ages ranged from 18 to 67 (average 44.5) years. Additionally, the mean age for patients with benign, borderline and malignant mucinous tumors was 38 years (range: 18-44 years), 50 years (range: 22-60 years) and 54 years (range: 20-67 years), respectively. Seventeen (35.4%) patients were in postmenopause. As for this

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finding, statistical analysis of different histological types demonstrated that there was no difference between ages of patients presenting different histological types. The relationship between age and histologic types is shown in Table 2.

Table 2. — The relationship between age and histologic types in mucinous tumors.



The diameter of mucinous tumors ranged from 2 to 40 cm in size (mean diameter 26.4 cm). Bilaterality was detected in 1/18 (5.5%), 0/6 and 4/14 (28.5%) of benign, borderline and malignant mucinous tumors, respectively. Multilocularity was present in 35/38 (89.5%). Presence of solid areas was respectively demonstrated in 4/18 (22.2%), 5/6 (83.3%), 14/14 (100%) of cases with benign, borderline and malignant mucinous tumors (Table 3).

Benign mucinous tumors had a smooth capsule containing thick, tenacious mucinous material. The epithelium of benign mucinous tumors showed a single layer of uniformly tall columnar cells with clear, homogeneous cytoplasm, and small and basal nuclei. There was no epithelial stratification in benign tumors (Figure 1). Additionally, goblet cells of intestinal mucosa were determined in 5/18 (23.8%) of benign mucinous tumors. Borderline mucinous tumors had smooth capsules with swollen veins. Microscopically, they revealed a papillary area with 2-3 cell rows. Mild to moderate nuclear atypia was encountered in borderline tumors. There was no stromal invasion (Figure 2). Malignant mucinous tumors had irregular surfaces and thick vessels. The cut surface of mucinous tumors had solid areas, luminal nodules, hemorrhage and necrosis. Microscopically, mucinous tumors were characterised by isolated foci of disordered growth of small irregular glandular acini or single cells in desmoplastic stroma. All malignant mucinous tumors presented four or more layers of atypical cells and stromal invasion. Inflammatory cells, necrosis and hemorrhage were respectively detected in 7/14 (50%), 5/14 (35.7%) of cases with malignant mucinous tumors. Epithelial cells showed large, hyperchromatic nuclei and prominent nucleoli, and severe atypia (Figure 3). Goblet cells were seen in 4/14 (28.5%) of malignant mucinous tumors.

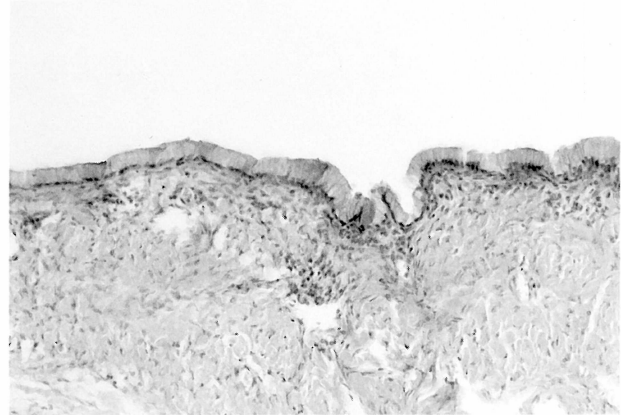


Figure 1. — Benign mucinous tumor. Note the single layer of uniformly tall columnar cells lining the cyst wall (H&E, original magnification x82).



Figure 2. — Borderline mucinous tumor. Note the hyperplasia with papillary projections and slight to moderate cellular atypia. The cellular stratifications show 2-3 layers (H&E, original magnification x41).

Discussion

Benign mucinous tumors comprise 20% [10] of benign tumors of the ovary, and 80% [11] of all mucinous tumors. It has been reported that they can be mostly seen in 3-5 decades, and 5% of them may be bilateral [1, 4, 11]. They present a cystic nature, mostly multilocular, with a diameter from 1-50 cm. The inner surface of the cyst may be smooth or papillary and the lumen of the tumor contain mucinous material [4, 11]. In our study, median age of patients with benign mucinous tumors was 38 years. The mean diameter of tumors was 16.8 cm with 77.7% and 5.5% being multilocular and bilateral, respectively. One

Table 3. — Age, localization and macroscopical features of mucinous tumors.

	Case		Median age	Right ovary		Left ovary		Bilaterality		Median diameter (cm)	Multilocularity		Unilocularity		Solid area	
	(n)	%		(n)	%	(n)	%	(n)	%		(n)	%	(n)	%		
Benign	18	47.3	38	7	38.8	10	55.5	1	5.5	16.8 (2-32)	14	77.7	4	22.3	4	22.2
Borderline	6	15.7	50	2	33.3	4	66.6	—	—	18.6 (6-28)	6	100	—	—	5	83.3
Malignant	14	37	54	7	50	7	50	4	28.5	24.4 (8-40)	14	100	—	—	14	100
Total	38	100	44.5	16	42.1	21	57.9	5	13.1	26.4 (2-40)	34	89.5	4	10.5	27	71

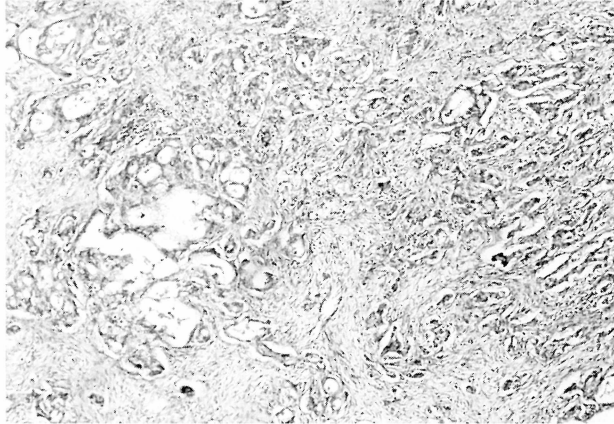


Figure 3. — Malignant mucinous tumor. The tumor epithelia show severe atypia with stromal invasion (H&E, original magnification x82).

case with benign mucinous tumor presented appendix mucosel. Siedman *et al.* [12] reported that when mucinous tumors were present in both ovaries and appendix, the rate of pseudomyxoma peritonei was 72%. In contrast we did not detect pseudomyxoma peritonei in our case.

It has been reported that borderline mucinous tumors constitute 17-52% of mucinous carcinoma [4, 13], 10-15% of all mucinous tumors [10, 13]. The mean age was reported as 35 years and the rate of bilaterality was 5-10% [9, 10, 12, 13]. Macroscopically the outer surface of the cyst is smooth. It is mostly multilocular with a median diameter of 17 cm. The inner surface of the capsule is thickened and a papillary area can be seen [4, 9, 11]. All of our cases with borderline mucinous tumors were multilocular, an average age of 50 years and a median diameter of 18.6 cm. Microscopically borderline mucinous tumors revealed papillary and glandular configurations showing 2-3 cell rows. Epithelial cells had a large nucleus with irregular contour and a prominent nucleolus. While none of the borderline tumors displayed stromal invasion, mild to moderate atypia and papillary areas with 2-3 cell layers of stratification were encountered.

Since the treatment and prognosis of borderline tumors are different from malignant mucinous tumors, it is thought that borderline tumors need to be distinguished from malignant mucinous tumors [9]. The distinction between the two is based on histologic criteria [4]. Hart and Norris [13] suggested that the tumors displaying 2-3 cell stratification layers without stromal invasion should be classified as borderline, while those showing 4 or more cell stratification layers without stromal invasion and those forming a solid mass, cribriform pattern without connective tissue space and stromal invasion should be considered as malignant mucinous tumors.

Fifteen percent of all borderline mucinous tumors, contain pure endocervical epithelium and the prognosis of these tumors is reported to be better compared to borderline tumors constituting pure intestinal epithelium [14, 15]. We observed goblet cells in only one case (1/6, 16.6%). However, these cells were found to be scattered among the endocervical cells.

Malignant mucinous tumors comprise 3-10% of all ovarian tumors. Median age has been reported as 35 years and the rate of bilaterality as 9-23% [1, 13, 14]. Macroscopically malignant mucinous ovarian tumors show cystic and multilocular patterns with a median diameter of 5-50 cm. They present more papillary structures and solid areas than other types [4, 14]. Of these tumors, 28% presented bilaterality, while all tumors were multilocular with a median diameter of 24.4 cm. All of them showed solid areas of various sizes. Thus, apart from the median age of our patients, other features were compatible with the literature findings. Microscopically the diagnosis of malignant mucinous tumors depends on indications of destructive stromal invasion. However, if there is no stromal invasion the other parameters such as the presence of prominent nuclear atypia, more stratification than 3 cell rows of atypia and widespread cribriform structures should be investigated [7]. All of our cases displayed evident stromal invasion.

In summary, our results suggest that mucinous tumors of the ovary should be classified according to the worst differentiated area, since these tumors may present different differentiated fields. To establish the correct diagnosis, one block for each 1-2 cm of tumor should be prepared and particularly, solid areas should be investigated with utmost care.

References

- [1] Coriker M., Dockerty M. M.: "Mucinous cystadenomas and mucinous cystadenocarcinomas of the ovary. A clinical pathologic study of 355 cases". *Cancer*, 1954, 7, 302.
- [2] Fox H., Kazzaz B., Langley F. A.: "Argyrophil and argentaffin cells in the female genital tract and ovarian mucinous cysts". *J. Pathol. Bacteriol.*, 1964, 8, 479.
- [3] Scully R. E.: "Germ cell tumors of the ovary". In: Sturgis S. H., Taymor M. L. (eds) "Progress in Gynecology". Vol. V, New York, Grune and Stratton, 1970, 343.
- [4] Kurman R. J.: "Blaustein's Pathology of the Female Genital Tract". 4th ed. Mucinous Tumors. Springer-Verlag, New York, 1994, 724.
- [5] Sternberg S. S.: "Diagnostic Surgical Pathology". 3rd ed. Lippincott Williams and Wilkins, Philadelphia, 1999, 2307.
- [6] Scully R. E.: "Recent progress in ovarian cancer". *Hum. Pathol.*, 1970, 1, 73.
- [7] Tornos C., Silva E. G.: "Pathology of the epithelial ovarian cancer". *Obstet. Gynecol. Clin. North Am.*, 1994, 21(1), 63.
- [8] Scully R. E.: "Ovarian tumors". *Am. J. Pathol.*, 1977, 87, 686.
- [9] Bostwick D. G., Tazelaar H. D., Schwarts P. E.: "Ovarian epithelial tumors of borderline malignancy. A clinical and pathologic study of 109 cases". *Cancer*, 1986, 58, 2052.
- [10] Kent S. W., Mckay D. G.: "Primary cancer of the ovary". *Am. J. Obstet. Gynecol.*, 1960, 80, 430.
- [11] Cotran R. S., Kumar V., Robbins S. L.: "Robbins Pathologic Basis of Disease". 6th ed. WB Saunder Company, Philadelphia, 1999, 1070.
- [12] Seidman J. D., Elsayed A., Sabin L. H. *et al.*: "Association of mucinous tumors of the ovary and appendix". *Am. J. Surg. Pathol.*, 1993, 17(1), 22.
- [13] Hart W. R., Norris H. J.: "Borderline and malignant mucinous tumors of the ovary. Histologic criteria and clinical behavior". *Cancer*, 1973, 31, 1031.
- [14] Tornos C., Silva E. G.: "Borderline tumors of the ovary". *Obstet. Gynecol. Clin. North Am.*, 1994, 21(1), 93.
- [15] Rutgers J. L., Scully R. E.: "Ovarian müllerian mucinous papillary cystadenomas of borderline malignancy. A clinicopathologic analysis". *Cancer*, 1988, 61, 340.

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