



Morphological Spectrum of Ovarian Teratomas: A 6 Years Experience at a Specialized Diagnostic Institute

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ABSTRACT

Introduction: Ovarian teratomas include mature cystic teratoma (MCT), immature teratoma (IT) and monodermal teratoma (MoT). Malignant transformation (MT) can occur in MCT and MoT, which remains a diagnostic challenge.

Aims & Objectives: To discuss the morphological spectrum of ovarian teratomas reported during the last six years at our specialized diagnostic institute and determine the frequency of MT in MCT and MoT.

Place and duration of study: The study was carried out at Chughtai Institute of Pathology from January 2015 to December 2020.

Material & Methods: A retrospective study was performed by retrieving 1018 cases of ovarian teratomas reported in last 6 years. SPSS version 20 was used for data analysis.

Results: MCT was most frequent ovarian teratoma with frequency of 95.6% (n=973), 2.26% (n=23) being IT and 2.16% (n=22) being MoT. IT were mostly seen in pediatric age group. MT in benign MCT was seen in 0.72% of MCT (n=7). Squamous cell carcinoma was most frequent malignancy 71.4% (n=5). One case of MoT also showed MT into papillary thyroid carcinoma, classic type, with frequency of MT in MoT being 4.76% (n=1). All MT in MCT had age >30 years which was a significant finding (p <0.001).

Conclusion: Ovarian masses in postmenopausal patients with suspicious radiological features, irrespective of lesion size warrant a thorough gross examination, extensive sampling and a careful microscopic evaluation.

Key words: Ovary, Teratoma, Malignant

INTRODUCTION

Ovarian teratomas are germ cell tumors (GCT) that arise from ectopic pluripotent stem cells that fail to migrate from yolk sac endoderm to the urogenital ridge during embryogenesis. They comprise elements from all three embryological germ layers i.e. endoderm, mesoderm and ectoderm.¹

Teratomas include mature cystic teratomas (MCT), immature teratomas (IT) and monodermal teratomas (MoT). MCT are well differentiated relative to the germ cell layers while immature teratomas are incompletely differentiated and contain embryonic tissue along with neuroepithelium.^{2,3,4,5} The IT are graded from I to III on the basis of quantity of neuroepithelium.^{6,7} MoT are composed of a single tissue type and usually contain thyroid tissue, in which case they are referred to as struma ovarii.⁸ Malignancy can also arise in struma ovarii. The age of presentation of malignancy in struma ovarii is usually in the 5th decade of life, with thyroid type malignancies being the most common.^{9,10,11}

Presence of a concomitant malignancy arising in a teratoma is a diagnostic challenge not only for clinicians but also for pathologists. The preoperative risk assessment of teratomas with malignant transformations (MT) are challenging and it is of great importance that optimal management options be selected carefully.¹²

We hereby discuss the morphological spectrum of ovarian teratomas reported in the last six years (January 2015-December 2020) at the Chughtai Institute of Pathology.

MATERIAL AND METHODS

After approval from Institutional Review Board, a retrospective study was performed in all histologically diagnosed cases of ovarian teratomas in females of all ages, from January 2015 to December 2020 at the Department of Histopathology, Chughtai Institute of Pathology. All diagnosed cases of MCT, IT of all grades, MoT and malignancies arising in MCT were included in the study. Specimens received unfixed or received from an outside laboratory were excluded from the study. Non-probability consecutive sampling was used.

The data was retrieved using institutional software Nexus Pro. A total of 1018 cases of teratomas were retrieved. Clinico-pathological parameters including age, tumor size, histological type and laterality were obtained from Pathology reports.

Statistical analysis:

Data was analyzed using SPSS version 20. The mean and standard deviation were calculated for quantitative variables including age and tumor size. MT was noted in both MCT and MoT. Qualitative variables including histologic type and laterality has been presented in the form of frequencies and percentages. Effect modifiers like age and tumor size have been controlled through stratification (for MT). Post stratification Chi-Square test was applied by taking P value of 0.05 as significant.

RESULTS

A total of 1018 cases were included in the study. Mean age was 30.7+/- 10.2 years. 46.6% (n=474) of the cases were right sided, 37.2% (n=379) were left sided while 7.0% (n=71) were bilateral (Table-1). 39.7% (n=404) of the cases were between age group of 20-29 years (Table-3). Mean size of the tumor was 8.1 +/-3.6 cm, with 60.5% (n=616) cases being between 5 to 10cm. A total of 95.6% (n=973) were MCT with 94.9% (n=966) diagnosed as benign MCT (Table-2). 0.72% (n=7) of the cases showed a malignancy arising in MCT. 5 cases were of squamous cell carcinoma (71.4%), 1 was mucinous adenocarcinoma, 1 was high grade B-cell Non-Hodgkin Lymphoma (NHL). Mean age of cases with malignancy arising in MCT was 45.1 years and mean size was 9.73cm (Table-4). All malignancies arising in MCT had age >30 years with 3.05% chance of malignancy over the age of 40 years compared to overall chance of malignancy of 0.72% for all age groups. This finding was significant with a P value of <0.001 (Table-5). No correlation with size and malignancy was noted (Table-6). 2.10% (n=21) cases were diagnosed as MoT. 1 case of MoT showed papillary thyroid carcinoma arising in it, while one case was of strumal carcinoid. 2.26% (n=23) were IT (n=2 for grade I, n=9 for grade II and n=12 for grade III). 73.9% (n=17) of IT were diagnosed in patients under 30 years of age.

AGE	
Age (years)	30.7 +/-10.2 years
SIZE	
Size (cm)	8.1 +/-3.6cm
Frequency and percentage of laterality	
Right	474 (46.6%)
Left	379 (37.2%)
Bilateral	71 (7.0%)
Not specified	94 (9.2%)
Different histologic subtypes	
MCT	973 (95.6%)
G1, IT	2 (0.20%)
G2, IT	9 (0.88%)
G3, IT	12 (1.18%)
MoT	22 (2.16%)

Table-1: Break down of results (n=1018)

Tumor Size	Histologic Type						
	MCT	Malignancy in MCT	G1, IT	G2, IT	G3, IT	MoT	Malignancy in MoT
<5.0cm	166	0	0	0	1	5	0
5-10.0cm	585	5	2	6	7	10	1
>10.0cm	215	2	0	3	4	6	0

Table-2: Frequency of different histologic subtypes and tumor size stratification

Age Group	Histologic Type						
	MCT	Malignancy in MCT	G1, IT	G2, IT	G3, IT	MoT	Malignancy in MoT
<10 years	4	0	1	2	4	0	0
10-19 years	83	0	1	1	2	1	0
20-29 years	391	0	0	4	2	7	0
30-39 years	309	1	0	2	2	4	0
40-49 years	133	3	0	0	2	4	0
>50 years	46	3	0	0	0	5	1

Table-3: Frequency of different histologic subtypes and age group stratification

Sr. No.	Diagnosis	Laterality	Age	Size
1	Moderately differentiated Squamous cell carcinoma	Right	42	5.0cm
2	High Grade B-cell NHL	Right	40	8.2cm
3	Moderately Differentiated Squamous cell carcinoma	Left	53	6.9cm
4	Poorly Differentiated Squamous cell carcinoma	Right	55	18.0cm
5	Moderately differentiated squamous cell carcinoma	Left	40	8.0cm
6	Well Differentiated Squamous Cell Carcinoma	Right	51	12.0cm
7	Mucinous Adenocarcinoma	Left	35	10.0
8	Papillary Thyroid Carcinoma in Struma Ovarii	Left	55	6.5cm

Table-4: Malignancies Arising in Teratomas

Age group	Benign MCT	Malignancies in MCT	
< 40 years	787	1	788
≥ 40 years	179	6	185
	966	7	973 (Grand total)

P=<0.00001 (Significant=<0.05)

Table-5: Age Group and Malignancies

Size	Benign MCT	Malignancies in MCT	TOTAL
<5.0cm	166	0	166
5-10.0cm	585	5	590
>10.0cm	215	2	217
TOTAL	966	7	973 (Grand total)

P=0.16 (Significant=<0.05)

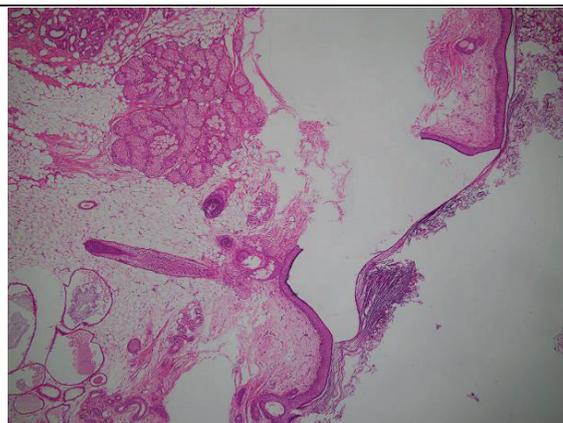
Table-6: Size correlation and Malignancies in MCT

DISCUSSION

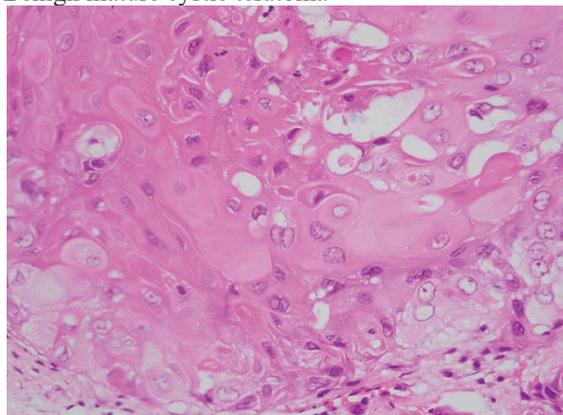
Teratomas are one of the most common germ cell tumors with mature or immature histological features. MCT are composed of well differentiated derivations from at least two of the three germ layers (ectoderm, endoderm and mesoderm) and are benign in nature whereas IT, are rare tumors comprising incompletely differentiated tissue found either in pure form or as a component of a mixed germ cell tumor and occurs essentially during the first two decades of life.^{1,2,3,4,5} They clinically have a malignant behavior and are characterized by the presence of immature (neuroectodermal) tissue. Immature teratomas are typically larger than mature cystic teratomas and are graded as I to III according to the percentage of neuro epithelium. The higher the grade of the mass, the more aggressive behavior is expected.^{5,6} Monodermal teratomas, as the name indicates, are composed predominantly or solely of one tissue type. There are three main types of ovarian monodermal tumors: Struma ovarii, ovarian carcinoid tumors and neural tumors. Struma ovarii is the commonest monodermal teratoma⁸ and has an excellent prognosis until malignant transformation occurs. Malignant transformation most commonly occurs in the form of papillary thyroid carcinoma (PTC), however rarely follicular carcinoma, poorly differentiated carcinoma and anaplastic carcinoma can also arise in this tumor type.^{9,10,11}

In this study we determined the morphological spectrum of more than a thousand ovarian teratomas (n=1018) diagnosed in a span of six years at Chughtais Institute of Pathology, Lahore. Benign MCT (Fig-1A) were most frequent, comprising 94.9% (n=966) of total cases. Mean age of the patients was 30.7 years with most of the cases (37.4%) presenting within the age group of 20-29

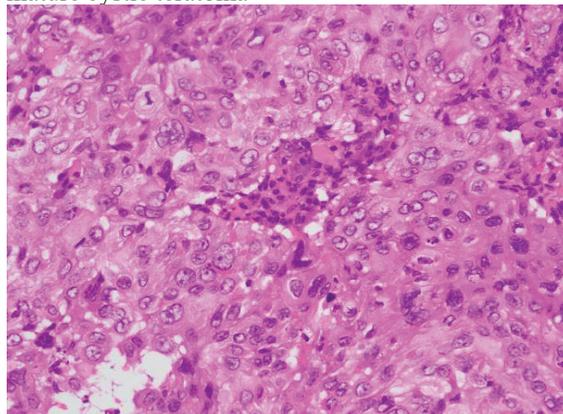
years. These findings are consistent with a study conducted by Trabzonlu et al. in which mean age of the patients 34.5 years.¹³ Average size of the teratomas was 8.01cm with 59.8% of the cases being in between 5-10cm. These findings are partially consistent with a study performed by Rathore et al¹⁴ and Trabzonlu et al. with an average size of 7.60cm and 8.37cm respectively. In our study majority of the teratomas were right sided (46.6%) with 7% being bilateral. Right side predominance has also been reported by Ismail et al. and Chun et al.^{15,16} However, a study conducted by Khan et al from Peshawar showed left sided predominance.¹⁷



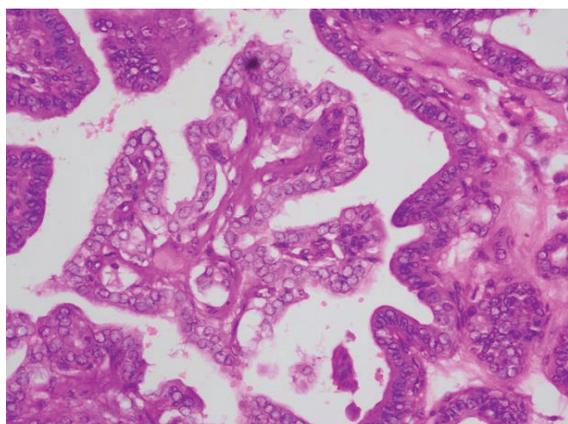
A. Benign mature cystic teratoma



B. Well differentiated squamous cell carcinoma arising in mature cystic teratoma



C. Moderately differentiated squamous cell carcinoma



D. Papillary thyroid carcinoma arising in Monodermal Teratoma

Fig-1: Different Morphological Spectrum in Teratomas.

Malignant transformation (MT) in a MCT is a known phenomenon but is a rare occurrence. Numerous studies have demonstrated a frequency of MT in MCT to be not more than 2% and usually effecting patients in the post-menopausal age group.^{8,9,12} A variety of malignant transformations are documented till date, the commonest being squamous cell carcinomas (88.3%), followed by adenocarcinoma, fibrosarcoma, rhabdomyosarcoma, malignant melanoma, urothelial carcinoma, adenosquamous carcinoma, endometrioid carcinoma, carcinosarcoma and papillary thyroid carcinoma.¹⁸⁻²⁵ In our study, malignancy arising in MCT, was seen in 7 cases, which comprises 0.72% of all included cases. A study conducted by Ud Din N et al. showed frequency of epithelial malignancies arising in MCT as 1.9%.¹² Another study conducted by Ulker et al. also showed malignant transformation in 1.9% of the total cases.²⁰ MT was mostly seen in patients of peri-menopausal and post-menopausal age group with 6 cases out of a total of 7 being ≥ 40 years of age (85.8%). The mean age in our study for these MT cases was 45.1 years compared with 30.7 years for all cases of MCT. This difference in age between benign MCT and MT in MCT was statistically significant with a p value of <0.001 . Our findings are consistent with these national and international studies. The average size of the teratomas with MT in MCT was 9.73cm. There was no significant correlation between sizes of MT in MCT and benign MCT. Previous studies have identified some risk factors for malignant transformations in MCTs; these factors broadly include older age at presentation, post-menopausal status, and raised serum tumor markers; especially serum CA-125 levels. Other findings consistently seen in patients with MT in MCT include larger tumor masses with grossly visible areas of

hemorrhage and necrosis.¹² Our findings are consistent with the general notion of a larger lesional size in case of MT in MCT as compared to benign MCT.^{12,13,21}

Most common malignancy reported to arise within the MCT is squamous cell carcinoma and it usually comprises more than 70% of the malignancies.^{12,13,20-23,26} In our study, squamous cell carcinoma was the most frequent MT in MCT comprising 71.4% (n=5) of all cases showing malignant transformation (Fig-1B and 1C). One case was of mucinous adenocarcinoma while another case was of a high grade B-cell non-hodgkin lymphoma (NHL). Our case with a mucinous adenocarcinoma arising in MCT of the ovary was confirmed to have a germ cell origin confirmed by its reactivity for CK-20 immunohistochemical (IHC) stain and negativity for CK-7 IHC stain.^{27,28} Ovarian B cell lymphomas are very rare and usually are of primary ovarian origin, without any associated teratoma. The high grade B-cell NHL included in our study was associated with an ovarian MCT.²⁹

Overall frequency of immature teratomas was 2.26% (n=23) with mean age of 20.8 years, mean size of 8.62cm and were right sided predominantly (n=12, 52.2%). Most of immature teratomas were of grade 3 (n=12, 52.2%). A study conducted by Gallion et al. also showed majority of cases of immature teratomas being diagnosed in patients under 25 years of age.³⁰ A study conducted in India showed a median age of 19 years. In this study, Grade II (IT) were most frequent, comprising 46% of the cases while grade III (IT) comprised 25% of the cases.⁵ These results were in contrast to our findings in which grade III (ITs) were the most frequent.

22 MoT were included in the study with an average age of 36.3 years and a mean size of 7.29cm. 1 case (4.55%) showed papillary thyroid carcinoma (PTC) arising in the background of MoT (Fig-1D). The age of that patient was 55 years with tumor size being 6.50cm. One case was of strumal carcinoid (4.55%). The frequency of PTC and strumal carcinoid arising in MoT is reported to be in between 5% to 10%.^{31,32,33}

CONCLUSION

Ovarian teratomas have a diverse morphological spectrum including the mature cystic, immature and monodermal subtypes. Malignancies arising in each one of these subtypes is a rare phenomenon. However, ovarian masses in postmenopausal patients with suspicious radiological features,

irrespective of lesional size warrant a thorough gross examination with extensive sampling of the specimen and a careful microscopic evaluation. Correlation with serum tumor markers and intra-operative consultation in such cases should be sought to determine the best modality of treatment for these patients.

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