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Original Research Article

Histomorphology of germ cell tumors at various anatomic sites: a 5 years study at a tertiary care centre

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ABSTRACT

Background: Germ cell tumors (GCTs) are a heterogeneous group of neoplasms, which occur in the gonads, and at extra gonadal sites of the body. The aim of the study was to observe the different histopathological patterns of various GCTs in the body at all possible sites and to know their IHC staining patterns.
Methods: The study was conducted for a period of 5 years from 2015 to 2019 and was an observational study. The recorded data was compiled and entered in a spreadsheet and then exported to data editor of SPSS Version 20.0. Continuous variables were expressed as mean SD and categorical variables were summarized as frequencies and percentages. Graphically the data was presented by bar and pie diagrams Chi-square test or Fisher's exact test was applied for comparing categorical values. $P<0.05$ was considered statistically significant. All p values were 2 tailed.
Results: A total of 93 cases were analyzed and the mean age of the patients was 27.8 years. Mature cystic teratoma was the most common histopathological variant and was mostly seen in the ovaries. There was a difference in age predilection of benign and malignant tumors. Most of the malignant GCTs were gonadal while EGCTs were likely to be benign. MGCTs (mixed GCTs) were mostly testicular in origin with only one MGCT being extragonadal.
Conclusions: Mature cystic teratomas were the most frequent GCTs with frequent site being in ovaries. Out 0f 18 EGCTs only 2 were malignant, rest all were mature cystic teratomas.

Keywords: GCTs, Extragonadal GCTs, MGCTs, Teratoma

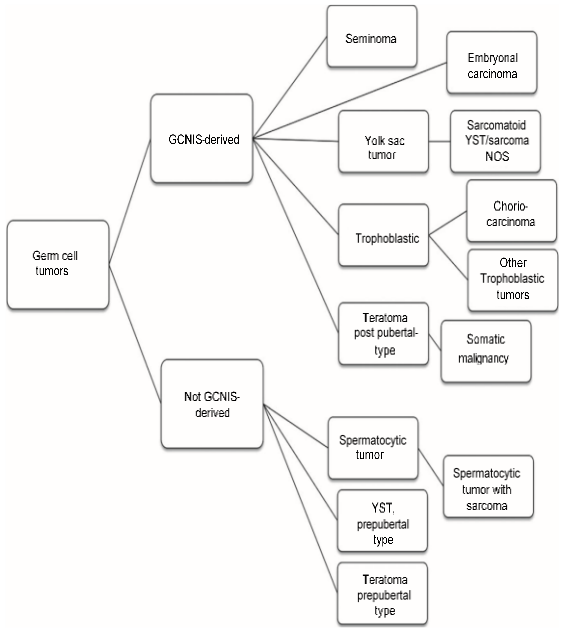
INTRODUCTION

Germ-cell tumors (GCTs) are a heterogeneous group of neoplasms, which occur in the gonads, both the ovaries and the testis, and in different extra gonadal sites along the midline of the body-the retroperitoneal and mediastinal regions, and the midline of the brain (pineal and supra sellar regions. A major change to the structure of the world health organization (WHO) classification system for GCTs is the division into two main groups (Figure 1): (I) tumors predominantly (but not exclusively) occurring in pre pubertal patients, considered not to be derived from germ cell neoplasia *in situ.* (GCNIS); and (ii) tumors derived from GCNIS.[1]

The relative proportion of teratoma among the GCTs is quite different in the two gonads, with about 95% of ovarian GCTs represented by pure teratoma.[2,3] A substantive change to the 2016 WHO classification is the reclassification of spermatocytic seminoma as spermatocytic tumor Embryonal carcinoma is relatively common among testicular GCTs, where 10% are pure embryonal carcinomas and even more have it as a component of a mixed germ cell tumor. Most of the ovarian yolk sac tumors occur as pure neoplasms, whereas pure yolk sac tumors of the testis are rare in adults. EGGCTs (extragonadal GCTs) are similar to those of primary GCTs, but major differences in clinical behavior suggest that gonadal and extragonadal tumors are biologically different.[4] In our study maximum

extragonadal GCTs were reported in the retroperitoneum followed by mediastinum. The usefulness of immune-histologic markers in the differential diagnosis of GCTs has been recognized for decades.[5] The different IHC markers include a) alpha-fetoprotein (AFP), b) the beta subunit of human chorionic gonadotropin (BHCG) d) cytokeratin (CK) and e) PLAP.

Immuno-histochemistry is often performed to assist in accurately assessing the types and extent of germ cell elements present within a tumor.



NOS, not otherwise specified; YST, yolk-sac tumor.

Figure 1: The 2016 edition of the WHO classification, germ cell tumor classification is restructured into tumors derived from GCNIS and those not derived from GCNIS.

Objectives

Objectives of the study was to study frequency and patterns of histopathologically diagnosed GCTs at different anatomic sites and their nature. To study these parameters in various age groups and correlate them.

METHODS

The study was conducted in the department of pathology at Sher-I-Kashmir institute of medical sciences (SKIMS) Srinagar, Kashmir and it included prospective data analysis for one and a half year and retrospective data for three and a half years. The prospective study was carried from 1st June 2018 to 31st Dec. 2019 and the study material included cases of primary GCTs at various sites in different age groups consisting of resected specimens and biopsies received in our department. In the retrospective study the slides and blocks were retrieved from the archives of department and reviewed. Epithelial tumors and recurrent GCTs were excluded. The recorded data was compiled and entered in a spreadsheet (Microsoft excel) and then exported to data editor of SPSS version 20.0 continuous variables were expressed as mean SD and categorical variables were summarized as frequencies and percentages. Graphically the data was presented by bar and pie diagrams. Chi-square test or Fisher's exact test, whichever appropriate, was applied for comparing categorical variables. A $p<0.05$ was considered statistically significant. All p were 2 tailed.

RESULTS

The median age of presentation was 27.8 years. 54 out of the total cases were in the reproductive age group (20-44 years) and comprised of 58.1% in our series (Figure 2).

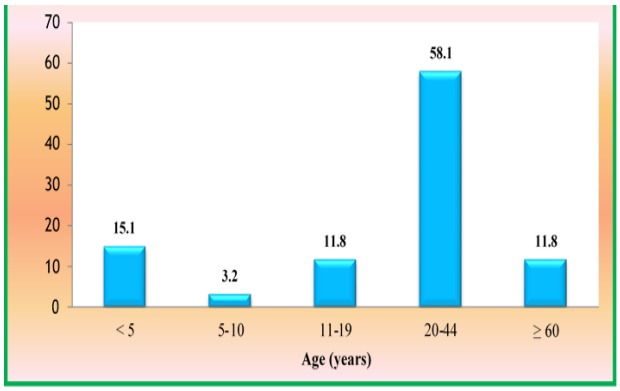


Figure 2: Age distribution of studied patients.

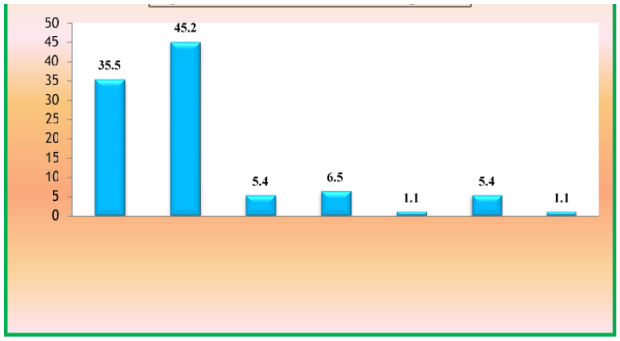


Figure 3: Site of the tumor in studied patients.

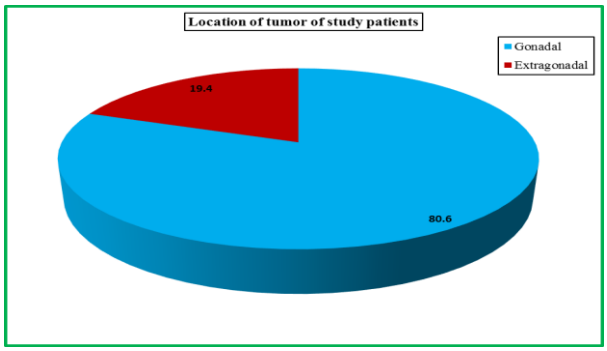


Figure 4: Location of tumor in studied patients.

Out of ninety-three cases, seventy-five (80.6%) were in gonads while only eighteen were seen at the extragonadal sites (19.4%) (Figure 4).

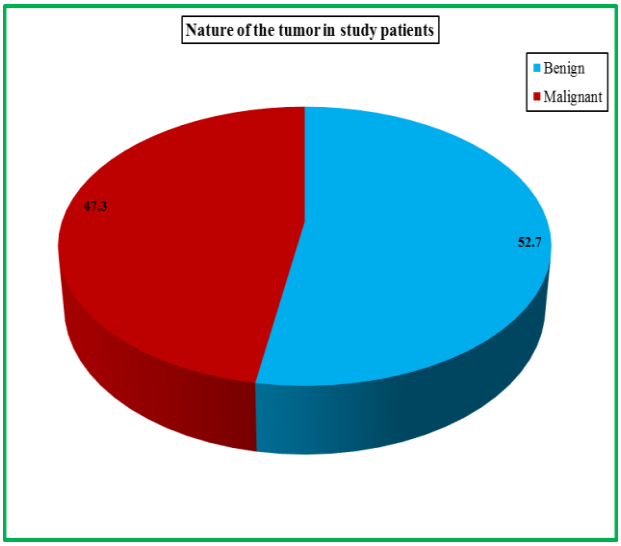


Figure 5: Nature of tumor in patients.

The 52.7% of the cases were benign while 47.3% were malignant (Figure 5).

Table 1: Histopathological diagnosis of tumor.

Tumor	Number	Percentage (%)
Mature cystic teratoma	48	51.6
Classical seminoma	14	15.1
Yolk sac tumor	10	10.8
Dysgerminoma	4	4.3
Yolk sac predominant MGCT	3	3.2
Seminoma predominant MGCT	3	3.2
Embryonal carcinoma predominant MGCT	3	3.2
Teratoma predominant MGCT	2	2.2
YST and teratoma predominant MGCT	2	2.2
Choriocarcinoma	1	1.1
Post pubertal teratoma	1	1.1
Spermatocytic tumor	1	1.1
Monodermal teratoma struma ovary	1	1.1
Total	93	100

The 40 cases of mature cystic teratomas were present in females while only 8 were seen in males. A total of 10 cases of classical seminoma were seen in males 6/10 cases of YST (60%) were seen in males.

Among 13 cases of MGCTs, 10 (76.9%) were present in males (Table 2).

The most frequent tumor that was observed in our series was mature cystic teratoma (51.6%). This was followed by classical seminoma (15.1%) choriocarcinoma, spermatocytic tumor, post pubertal teratoma, struma ovary were rare. The 13 (13.97%) cases in our series were MGCTs (Table 1).

Table 2: Correlation of histopathological diagnosis with gender.

Tumor type	Male	Female	Total
Mature cystic teratoma (%)	8 (16.7)	40 (83.3)	48
Classical seminoma	14	0	14
Yolk sac tumor (%)	6 (60)	4 (40)	10
Dysgerminoma	0	4	4
Choriocarcinoma	0	1	1
Post pubertal teratoma	1	0	1
Spermatocytic tumor	1	0	1
Monodermal teratoma strauma ovary	0	1	1
MGCT (%)	10 (76.9)	3	13

P value<0.001 (Statistically significant).

Table 3: Correlation of nature of tumor with gender in patients.

Gender	Benign		Malignant		P value
	No.	%	No.	%	
Male	8	16.3	32	72.7	<0.001*
Female	41	83.7	12	27.3	
Total	49	100	44	100	

The 72.7% of all malignant GCTs were predominantly seen in males while maximum GCTs in females (83.7%) turned out to be benign (Table 3).

Mature cystic teratomas were mostly seen in ovaries. Most of the malignant GCTs were gonadal while EGCTs were more likely to be benign and included mostly mature cystic teratoma with one case of YST at mediastinum and one case of classical seminoma in adrenal gland. MGCTs were mostly testicular in origin. Only 1 was extra gonadal (Sacro coccyx) (Table 4).

The 24 of the total cases of mature cystic teratoma were seen in the age group (20-44 years). The 12 out of 14 cases of classical seminoma were also seen in the same age group. MGCTs were rare in children and >60-year age group (Table 5).

The 40 cases of mature cystic teratomas were seen in females while only 8 were present in males, 10 cases of MGCT were seen in males while 4 cases out of 10 YSTs were present in females. Most of the cases in males comprised of classical seminomas (14) followed by mixed GCTs (Table 6).

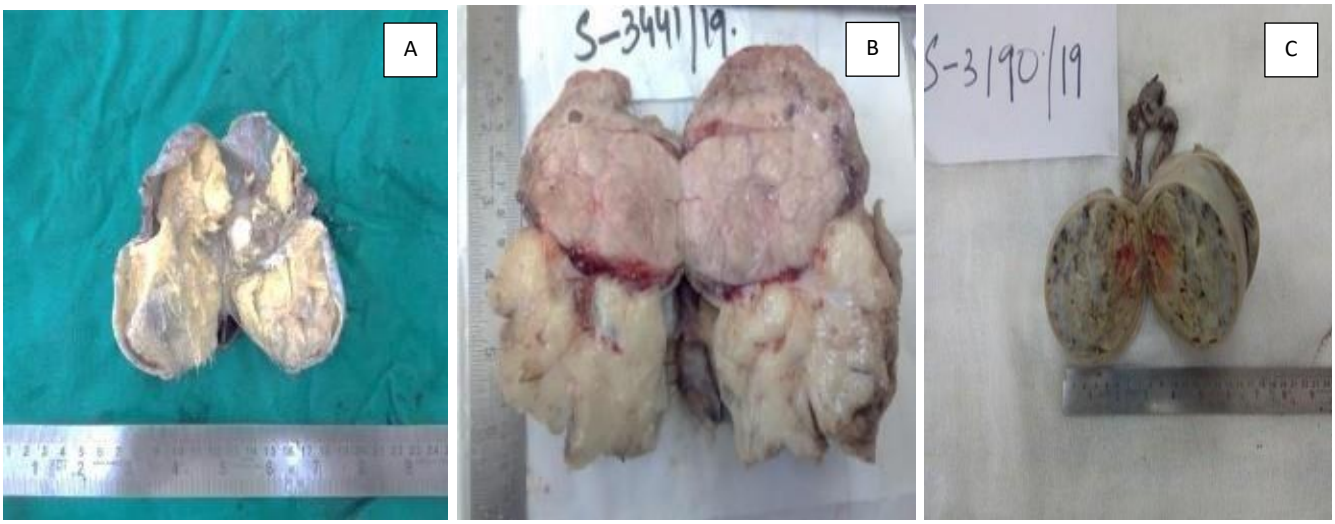


Figure 6 (A, B and C): Gross photograph of an ovarian dermoid showing cheesy material and hair inside, gross photograph of a retroperitoneal teratoma and gross photograph of MGCTs of testis.

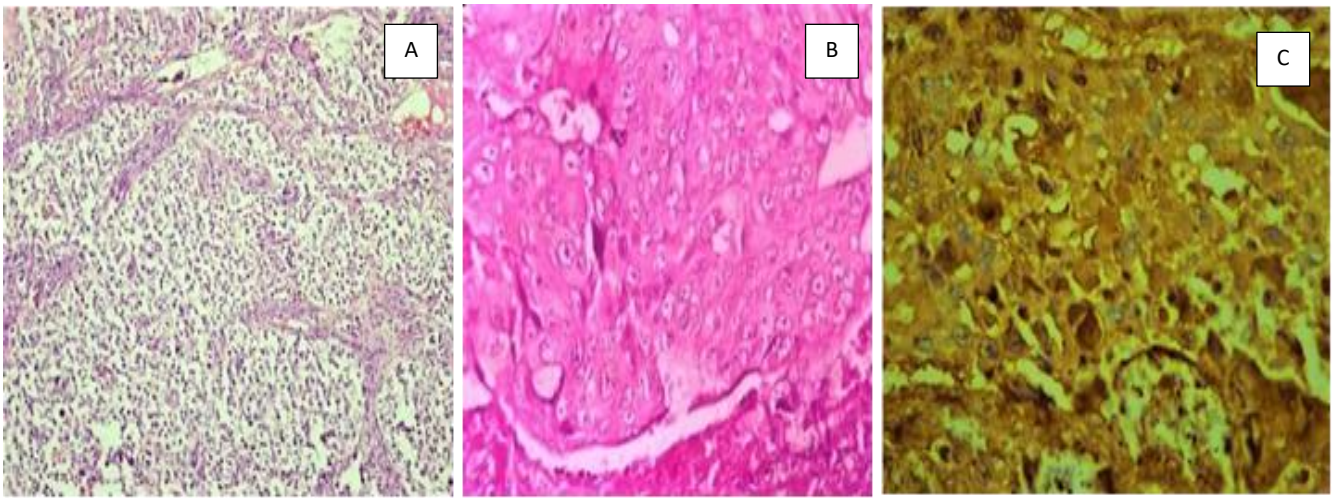


Figure 7 (A, B and C): Classical seminoma with tumor cells present in sheets and intervening fibrous septae. And sheets of malignant cytotrophoblasts and syncytiotroblasts with striking cytological atypia in an ovarian choriocarcinoma and intense βhCG staining in cytoplasm of choriocarcinoma tumor cells.

Table 4: Correlation of tumor diagnosis with primary site of origin.

Tumor type	Total no.	Testis	Ovaries	Mediastinum	RPN	Sacro coccyx	Adrenal	Mesentery
Mature cystic teratoma	48	2	31	4	6	4	0	1
Seminoma	14	13	0	0	0	0	1	0
YST	10	6	3	1	0	0	0	0
Dysgerminoma	4	0	4	0	0	0	0	0
Choriocarcinoma	1	0	1	0	0	0	0	0
Post pubertal teratoma	1	1	0	0	0	0	0	0
Spermatocytic tumor	1	1	0	0	0	0	0	0
Monoderma teratoma Struma ovarii	1	0	1	0	0	0	0	0
MGCT	13	10	2	0	0	1	0	0
Total	93	33	42	5	6	5	1	1

P=0.008 statistically significant.

Table 5: Correlation of histopathological diagnosis with age.

Tumor type	Age (years)					Total
	<5	5-10	11-19	20-44	≥ 60	
Mature cystic teratoma	12	3	2	24	7	48
Classical seminoma	0	0	0	12	2	14
Yolk sac tumor	2	0	3	5	0	10
Dysgerminoma	0	0	2	2	0	4
Choriocarcinoma	0	0	0	1	0	1
Post pubertal teratoma	0	0	0	1	0	1
Spermatocytic tumor	0	0	0	1	0	1
Monodermal teratoma struma ovarii	0	0	0	0	1	1
MGCT	0	0	4	8	1	13

P value 0.007 (statistically significant).

Table 6: Correlation of histopathological diagnosis with gender.

Tumor type	Male	Female	Total
Mature cystic teratoma	8	40	48
Classical seminoma	14	0	14
Yolk sac tumor	6	4	10
Dysgerminoma	0	4	4
Choriocarcinoma	0	1	1
Post pubertal teratoma	1	0	1
Spermatocytic tumor	1	0	1
Monodermal teratoma stauma ovari	0	1	1
MGCT	10	3	13

P<0.001-statistically significant

DISCUSSION

The total cases studied in our series were 93. The study was conducted for a 5-year period between 2015-2019. The occurrence of GCTs in our study was slightly more in females than in males. In the present study maximum patients of GCTs were between 20-44 years of age i.e., in the reproductive age group with the mean age of presentation being 27.8 years±SD of 16 (Figure 2), similar results were found by Norris and Jensen as well as Jha and Karki S in their studies.[6,7]

The most frequent anatomical site for the GCTs was ovaries (42) followed by testis (33). EGCTs although less frequent were reported at mediastinum (5), RPN (6), sacro coccyx (5) adrenal gland (1) and mesentery (1) (Figure 3). Out of 93 cases, in our series, gonadal GCTs (75) outnumbered the extragonadal ones (Figure 4). The most frequent site for EGGCT reported in the study of Arora et al was CNS while in our study RPN was the most frequent extragonadal site for GCTs.8 We reported one case of adrenal gland seminoma in our series (Table 4) Adrenal gland teratoma has been reported in studies like Shrestha et al, Lam et al and Hui et al.[9-11]

Among cases of EGCTs fever and dyspnea was a common complaint particularly in mediastinal tumors. Studies conducted on EGCTs show these symptoms to be frequently present in such patients.[12,13-24]

The 52.7% of the total cases turned out to be benign while 47.3% of the cases were malignant (Figure 5). The commonest histopathological variant was mature cystic teratoma (51.6%) (Table 1). Classical seminoma was next in line comprising of 15.1% of the total cases The latter was the most frequent testicular GCT (Table 4). Our findings were consistent with Hochstetter and Jacobsen et al in this regard who in their study mentioned seminoma as the most common testicular GCT.[25,1] Dysgerminoma was the second most common ovarian GCT (Table 4). Scully et al had reported the same in their study and stated that these represent only about 2% of GCTs in ovaries because of the marked predominance of teratomas in them.[26] YST was less frequent comprising of only 10 cases. MGCTs comprised of 13 cases in series. Beniwal and colleagues also found similar results in their study.[27]

There was a difference in age predilection of benign and malignant tumors. Mature cystic teratoma was seen in all age groups and was the most common tumor overall, while in children <5 years the only malignant tumor found was YST (2 out of 10 cases). The only pure malignant GCT found in elderly was classical seminoma. This age group also saw the presence of struma ovarii, a benign tumor. Benign tumors were more in number (8) than malignant ones (3) in elderly population However no mixed GCT was reported in children <10 years. This data showed a p=0.007 and was statistically significant (Table 5).

Malignant nature of the tumors showed a sex predilection for males. In females benign cystic teratomas were predominant (83.7%) while they were less frequently seen in males This analysis showed p<0.001 and was statistically significant (Table 3). Our results were comparable with the study of Norris and Jensen and Gobel et al and Calaminus et al.[6,28,29] 72.7% of the malignant tumors were seen in males, while only 16.3% of the benign tumors were present in them.

Majority of the mature cystic teratomas were of ovarian origin (31). Testicular benign teratomas reported in our study comprised of only 2 cases out of the total 48. Among extragonadal sites the most frequent site for these tumors was the retroperitoneum (Table 6) which reported 6 cases of mature cystic teratoma followed by mediastinum (4) and sacro coccyx (4).

In our study only one MGCT (mixed germ cell) was seen at the extragonadal site (sacro coccyx), while rest of the MGCTs were predominantly testicular in origin (Table 4).

Knapp et al reported 3 YSTs at this site in 32 patients of NSGCT.[30] Only 2 cases of MGCTs were of ovarian origin. The 10 out of total 13 MGCTs were seen in males (Table 6). The lone GCT reported at the adrenal gland was a classical seminoma and this was the only case of seminoma reported outside the gonads as shown in the Table 4. We also reported a case of benign cystic teratoma at mesentery which was also reported in the study of Al- Arfaj et al.[31]

Limitations

It was a single centre study and the sample size was small

CONCLUSION

We conclude that benign teratomas are the most frequently encountered GCTs seen in all age groups predominantly in females, both at the gonadal and extragonadal sites. Malignant GCTs including MGCTs show a male preponderance. Most of the MGCTs are testicular in origin while extragonadal MGCTs are not frequently encountered. EGCT are likely to be mature cystic teratomas.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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