Germ Cell Tumours- A Histopathological Evaluation of Eighty Cases in a Tertiary Care Institution of Eastern India

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ABSTRACT

BACKGROUND

Germ cell tumours (GCTs) are a heterogenous group of neoplasms, that arises due to variation from normal differentiation of germ cells with remarkable variability in histology and site of presentation. Though GCTs most commonly affect the gonads, variety of extragonadal sites are also involved in small numbers. We wanted to analyse the GCTs with respect to their age, sex, and site with special references to their histopathological subtyping.

METHODS

This is a combined prospective and retrospective study of 80 cases of GCTs in a tertiary health care institute of eastern zone of India with clinicopathological details, histopathological subtyping.

RESULTS

Eighty cases of GCTs were diagnosed during the time period of four years among 3055 tumourous specimens received, which accounted for 2.61% of all tumours. Of these GCTs, testicular GCTs accounted for 27.5% (22/80) cases, ovarian for 61.25% (49/80) cases, and 11.25% (9/80) were in extragonadal sites. Most of the ovarian GCT patients were in their 3rd decade, while in testis most patients were in 3rd and 4th decade. Extragonadal tumours were common below 1 yr. (3/9). Mature cystic teratoma was the common histological variant of ovarian GCTs, while seminoma was common in testicular site and mature teratoma at extragonadal sites. Most common extragonadal site was retroperitoneum. Mixed GCTs accounted for 31.83%, 6.14% of the morphological subtypes for testis and ovary respectively, while in extragonadal site no mixed component was noted.

CONCLUSIONS

Tumour location, extension, stage, level of tumour markers and histopathological subtypes play an important role in clinical management and prognostication of GCTs. Extensive study with proper clinicopathological evaluation, management and follow up status are needed for selection of treatment and to know the biological behaviour of these tumours.

KEYWORDS

Testis, Ovary, Extragonadal Germ Cell Tumour, Pathology

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BACKGROUND

Germ Cell Tumours (GCTs) are a heterogenous group of neoplasms, that arises due to variation from normal differentiation of germ cells with remarkable variability in histology and site of presentation.[1] Though GCTs most commonly affect the gonads, variety of extragonadal sites are also involved in small numbers. The mediastinum is the most common extragonadal site while other sites are sacrococcygeal region, retroperitoneum and cranial cavity.[2] Approximately 95% of all testicular tumours are GCTs, while it accounts for 15-20% of ovarian tumours (Robbins).[3] Testicular GCTs (TGCTs) accounts 1-1.5% of male neoplasms and the common age group is between 20-40 years.[4-7] 95% of ovarian GCTs (OGCTs) are benign and only 3-4% are malignant.[8] Mature cystic teratoma is the most common GCT of ovary also the most common tumour of patients under 20 years of age.[9]

In this study, we analysed the GCTs with respect to their age, sex, site having special references to their histopathological subtyping according to the WHO classification.

METHODS

Both prospective and retrospective study, was carried out in the department of pathology for a duration of four years in a tertiary health care institute of eastern zone of India. During this period 80 cases of GCTs were encountered. Patient having other gonadal tumours were excluded from the study. Clinicopathological details such as age, sex, site. Serum tumour marker levels (alpha-fetoprotein (AFP), beta-human chorionic gonadotrophin (β-hCG), and lactate dehydrogenase (LDH), radiological and surgical details were obtained. Histopathological evaluation of all (gonadal and extragonadal) germ cell tumours were undertaken. In retrospective cases the pathological materials were retrieved from departmental archival section. The detail clinical history, relevant investigation, gross feature were obtained and the tumours were classified according to the diagnostic criteria put forth by WHO classification. Routine hematoxylin and eosin stained sections were made with 10% neutral buffered formalin as fixative. The specimens were grossed as per CAP protocol. Special stains like PAS and PAS-D were done whenever necessary. Immunohistochemistry was performed using panel of antibodies (DAKO) which included Oct4, SALL4, CD45, Pancytokeratin, CD30, AFP, wherever indicated.

RESULTS

Total eighty cases of GCTs were diagnosed during the time period of four years among 3055 tumourous specimens received, which accounted for 2.61% of all tumours. Among which TGCTs were 27.5% (22/80), OGCTs 61.25% (49/80) and in extragonadal sites 11.25% (9/80) cases. Patient age group of TGCTs ranged from 11 month to 55 years with a mean age of 30.68 years. Maximum cases were in the age group of 3rd to 4th decade i.e. 72.72%. For OGCTs the age group ranged from 4 yrs. to 40 yrs. with a mean age of 25.48 yrs. and maximum cases in their 3rd decade, accounting for 46.93% of GCTs. For extragonadal sites the age group ranged from 7 months to 37 yrs. with maximum patients below one yr (3/9). Age distribution of cases highlighted in figure 1. Different histological subtypes with their age distribution highlighted in table 2, figure 1.

Gross Features of TGCTs

Bilateral involvement noted in one case (4.54%), while right testis in 12/22 (54.54%) and left in 9/22 (40.90%) cases. Size of the tumour ranged from 3 to 15 cms. Tumour was mostly solid (90.9%) cases being solid and cystic in rest cases (9.09%).

Gross Features of OGCTs

Bilateral ovaries were involved in 3/49 cases, while left and right side involvement noted in equal number of cases i.e. 23 each. The tumour size ranged from 3 to 30 cms in maximum dimension. Tumour was predominantly cystic in 29/49, solid 13/49 and both solid and cystic in 7/49 cases.

Gross Features of Extragonadal GCTs (EGGCTs)

Out of 9 cases 5 cases were from retroperitoneal location, while 3 cases located in sacrococcygeal location, and one near pineal region of brain. Size of the tumour ranged from 2 to 20 cm. The tumours were solid (4/9) and cystic (4/9) while one case was both solid and cystic (1/9).

Site	Histological Subtypes	No. of Cases	%
Testis	Seminoma	10	45.45
	Embryonal carcinoma	02	9.09%
	Mature teratoma	01	4.54%
	Yolk sac tumour	02	9.09%
	Mixed GCTs	07	31.83%
Ovary	Dysgerminoma	12	24.485
	Mature cystic teratoma	29	59.18%
	Yolk sac tumour	05	10.20%
	Mixed GCTs	03	6.14%
Extra gonadal sites	Immature teratoma(RP)	02	22.22%
	Choriocarcinoma(RP)	01	11.11%
	Mature teratoma(RP-2,SC-3)	05	33.33%
	Germinoma(pineal body)	01	11.11%

Table 1. Histological Subtypes of Different Types of GCTs

RP: Retroperitoneum, SC: sacro coccygeal region

In testis, Mixed GCTs accounted for 31.83% (7/22) cases with different components were embryonal carcinoma with mature teratoma (2/7), embryonal carcinoma with yolk sac tumour (1/7), seminoma with embryonal carcinoma (1/7), seminoma with yolk sac tumour (1/7), seminoma with embryonal carcinoma and mature teratoma (1/7), immature teratoma with choriocarcinoma (1/7).

Site	Type of Tumour	0-1 Yr.	1-10 Yrs.	11-20 Yrs.	21-30 Yrs.	31-40 Yrs.	41-50 Yrs.	51-60 Yrs.	Total No. of Cases
Testis	Seminoma	-	-	-	5	5	-	-	10
	Embryonal carcinoma	-	-	1	-	-	1	-	02
	Mature teratoma	1	-	-	-	-	-	-	01
	Yolk sac tumour	-	1	-	1	-	-	-	02
	Mixed GCT	-	-	-	4	1	1	1	07
Ovary	Dysgerminoma	-	2	6	1	3	-	-	12
	Yolk sac tumour	-	1	2	2	-	-	-	5
	Mature cystic teratoma	-	1	1	19	8	-	-	29
	Mixed GCTs	-	-	1	1	1	-	-	03
Extra gonadal GCTs	Immature teratoma	1	-	1	-	-	-	-	02
	Choriocarcinoma				1		-	-	01
	Mature teratoma	2	1			2	-	-	05
	Germinoma			1					01

Table 2. Age Distribution of Germ Cell Tumours

In ovary Mixed GCTs accounted for 6.14% cases (3/49) and the combinations were Dysgerminoma with choriocarcinoma and yolk sac tumour (1/3), and two cases dysgerminoma with yolk sac tumour (2/3). For extra gonadal sites, no mixed component identified.

DISCUSSION

Germ cell tumours originate from germ cell at varying stages of development. Though it commonly arises from gonads but extragonadal sites i.e., pineal gland, retroperitoneum, mediastinum and sacral region are also involved in primary EGGCTs. It is hypothesized that EGGCTs may have been originated due to abnormal migration and differentiation of primordial germ cells during early embryogenesis. Another hypothesis suggests metastatic dissemination of primary gonadal tumour to extragonadal location, where the primary disease has subsided and hence remains undetected. In our study eighty cases of GCTs were diagnosed during the time period of four years among 3055 tumourous specimens received, which accounted for 2.61% of all tumours. Of these GCTs testicular GCTs accounted for 27.5% cases, ovarian for 61.25% cases and 11.25% were in extragonadal sites. Santaram chavan et al, also in their study found ovary as the most common site accounting for 64.79% of all GCTs.[10] Prevalence of ovarian GCTs in our study is 19.44% (49/252) out of all ovarian tumours. Of which the percentage of different subtypes were; dysgerminoma-4.76%, yolk sac tumour-1.98%, mature cystic teratoma-11.6%, mixed GCTs-1.19%. While different studies have different prevalence rate of GCTs that vary from 23.15 -42.2%.[11,12,13] In India the prevalence rate is low in compared other studies while significant higher percentage noted in South Africa.[14] We observed most of our patients of OGCTs in the 3rd decade, which is in accordance to several studies.[8,15,16] The common presentation was abdominal mass and distension while second common presentation was associated pain in our study. Abdominal pain and lower abdominal mass are the most common symptoms of OGCTs.[1] Bilateralism of tumour are noted in three cases (6.12%), while different studies showed difference in their incidence.[1,15,17] In our study the common histological variant was mature cystic teratoma (59.18%) and is also consistent with other studies.[11,15] Histologically TGCTs are classified as seminomatous and non seminomatous GCTs. TGCTs develop from premalignant intratubular germ cell neoplasia (ITGCN) that is believed to arise from the failure of normal maturation of gonocytes during fetal or postnatal development. Progression toward invasive TGCTs (seminoma and nonseminoma) then occurs after puberty. However, exception to this rule are Yolk sac tumours, teratomas and spermatocytic seminoma. For this reason, commonest age range of TGCTs are between 20-45 yrs.[18] In our study also 72.72% cases are of the age range of 21-40 yrs. Among the children, one case of mature teratoma was noted in an eleven month baby and one case each of yolk sac tumour and embryonal carcinoma. Testicular mass was the common presentation and in 3 cases associated with pain was observed. Predominant histologic subtype was seminoma (45%), which was in concordance with other studies.[19] The relative frequency of seminoma and nonseminoma, respectively, is thought to be around 50% each in different studies, is almost noted in our study.[20,21]

EGGCTs are GCTs at sites other than gonads like primary mediastinal EGGCTs and tumours originating in the sacrococcygeal or pineal region. In retroperineal location, are more often associated with premalignant lesions in one of the testes and behave clinically in a manner very similar to that of the primary testis counterpart. (Schmoll).[22] Like their counterparts of gonadal origin, EGGCTs occur in several characteristic histological patterns that reflect the stages of normal embryonic and fetal development with seminomatous (germinoma/dysgerminoma) and non seminomatous germ cell tumours including endodermal sinus tumour, yolk sac tumour, embryonal carcinoma, choriocarcinoma and mature or immature teratoma. Seminomatous histology is seen 20-24% cases in contrast to Gonadal GCTs where seminomatous and non seminomatous histology are almost of same proportion.[23] In our series seminomatous morphology are observed in 11.11% case. Most common locations of EGGCTs are mediastinum and retroperitoneum. In our study retroperitoneum was the common location, while we didn't get a case from mediastinum. The major limitations of our study were: lack of follow up data, unavailability of serum markers in all patients also proper pathological staging was not done in all cases, as some cases tissue was received in pieces.

Tumour location, extension, stage, level of tumour markers and histopathological subtypes play an important role for clinical management and prognostication of GCTs. Extensive study with proper clinicopathological evaluation, management and follow up status are needed for selection of treatment and to know the biological behaviour of these tumours.

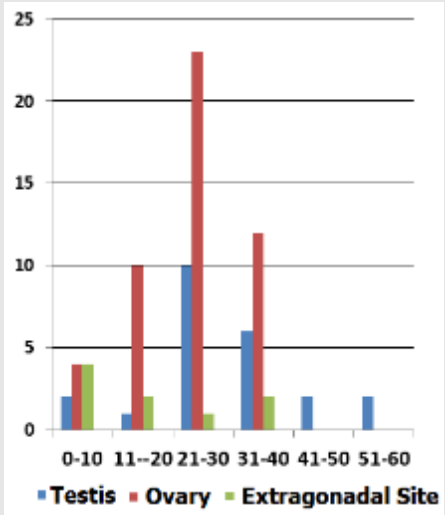

Figure 1. Displaying the Age Group of Patients of GCTs at Different Sites

Figure 2. (A) Mature Cystic Teratoma with Hair Tufts (Arrow), (B) Dysgerminoma-Lobulated, Solid, Gray White and Soft Tumor, (C) Mixed GCT with Areas of Haemorrhage and Necrosis of an Orchidectomy Specimens

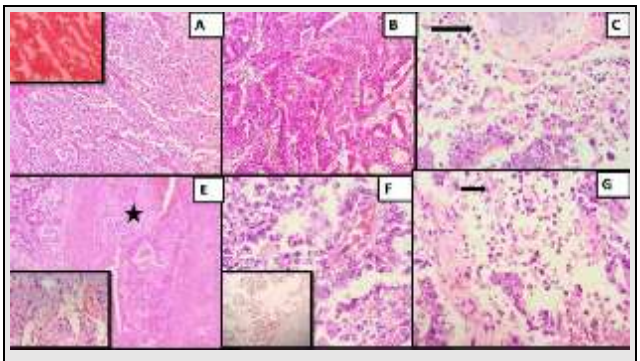

Figure 3. Histology Pictures of Various Types of GCTs

A: Dysgerminoma -with sheets of large polyhedral tumor cells and intervening scant fibrous stroma infiltrated by lymphocytes, the tumor cells immunopositive for CD117 (Inset) (H&E 100X)

B: Embryonal carcinoma- Undifferentiated large cells arranged in tubule-papillary pattern (H&E 100X)

C: Mixed GCT displaying component of embrynal carcinoma and mature teratoma(arrow highlighting mature cartilage) (H&E 100X)

D: Mixed GCTs displaying yolk sac tumor component and choriocarcinoma component (marked with asterix). Inset highlights the cytotrophoblasts and syncytiotrophoblasts. (H&E 400X)

E: Schiller Duval body of Yolk sac tumor (Inset: tumor cells positive for SALL4) (H&E 400X)

F: Hyaline globules of Yolk sac tumor (Arrow) (H&E 400X)

CONCLUSIONS

Tumour location, extension, stage, level of tumour markers, and histopathological subtypes, play an important role in clinical management and prognostication of GCTs. Extensive study with proper clinicopathological evaluation, management and follow up status are needed for selection of treatment and to know the biological behavior of these tumours.

REFERENCES

[1] Ceccheto G. Gonadal germ cell tumours in children and adolescents. J Indian Assoc Pediatr Surg 2014;19(4):189-194.

[2] Zynger DL, Everton MJ, Dimov ND, et al. Expression of glypican 3 in ovarian and extragonadal germ cell tumours. Am J Clin Pathol 2008;130(2):224-230.

[3] Ellenson LH, Pirog E. Female genital tract. In: Kumar V, Abbas A, Aster J, eds. Robbins and Cotran pathologic basis of disease. South Asia edition. Vol. 2. 9th edn. Elsevier 2015: p. 1029.

[4] Oosterhuis JW, Looijenga LH. Testicular germ-cell tumours in a broader perspective. Nat Rev Cancer 2005;5(3):210-222.

[5] Chieffi P, Franco R, Portella G. Molecular and cell biology of testicular germ cell tumours. Int Rev Cell Mol Biol 2009;278:277-308.

[6] La Vecchia C, Bosetti C, Lucchini F, et al. Cancer mortality in Europe, 2000-2004, and an overview of trends since 1975. Ann Oncol 2010;21(6):1323-1360.

[7] Engholm G, Ferlay J, Christensen N, et al. NORDCAN-a Nordic tool for cancer information, planning, quality control and research. Acta Oncol 2010;49(5):725-736.

[8] Sah SP, Uprety D, Rani S. Germ cell tumours of the ovary: a clinicopathologic study of 121 cases from Nepal. J Obstet Gynaecol 2004;30(4):303-308.

[9] Pepe F, Panella M, Pepe G, et al. Dermoid cyst of the ovary. Eur J Gynaecol Oncol 1986;7(3):186-191.

[10] Chavan SS, Toppo SM. Study of 92 cases of ovarian germ cell tumour at tertiary health care centre. Indian J Pathol Oncol 2019;6(3):464-470.

[11] Ayhan A, Bukulmez O, Genc C, et al. Mature cystic teratomas of ovary: case series from one institution over 34 years. Eur J Obstet Gynecol Reprod Biol 2000;88(2):153-157.

[12] Jha R, Karki S. Histological pattern of ovarian tumours and their age distribution. Nepal Med Coll J 2008;10(2):81-85.

[13] Gupta N, Bisht D, Agarwal AK, et al. Retrospective and prospective study of ovarian tumours and tumour-like lesions. Indian J Pathol Microbiol 2007;50(3):525-527.

[14] Lancaster EJ, Muthuphei MN. Ovarian tumours in Africans: a study of 512 cases. Cent Afr J Med 1995;41(8):245-248.

[15] Mondal SK, Banyopadhyay R, Nag DR, et al. Histologic pattern, bilaterality and clinical evaluation of 957

ovarian neoplasms: a 10-year study in a tertiary hospital of eastern India. J Cancer Res Ther 2011;7(4):433-437.
[16] Benjapibal M, Boriboonhirunsarn D, Suphanit I, et al. Benign cystic teratoma of the ovary: a review of 608 patients. J Med Assoc Thai 2000;83(9):1016-1020.
[17] Trama A, Berrino F. The epidemiology of malignant germ cell tumours: The EUROCARE Study. In: Nogales FF, Jimenez RE, eds. Pathology and biology of human germ cell tumours. Berlin Heidelberg: Springer-Verlag 2017:11-21.
[18] Vasdev N, Moon A, Thorpe AC. Classification, epidemiology and therapies for testicular germ cell tumours. Int J Dev Biol 2013;57(2-4):133-139.
[19] Zhang T, Ji L, Liu B, et al. Testicular germ cell tumours: a clinicopathological and immunohistochemical analysis of 145 cases. Int J Clin Exp Pathol 2018;11(9):4622-4629.
[20] Kennedy BJ, Schmidt JD, Winchester DP, et al. National survey of patterns of care for testis cancer. Cancer 1987;60(8):1921-1930.
[21] Mead GM. Testicular cancer and related neoplasms. BMJ 1992;304(6839):1426-1429.
[22] Schmoll HJ. Extragonadal germ cell tumours. Ann Oncol 2002;13 Suppl 4:265-272.
[23] Bokemeyer C, Nichols CR, Droz JP, et al. Extragonadal germ cell tumours of the mediastinum and retroperitoneum: results from an international analysis. J Clin Oncol 2002;20(7):1864-1873.