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CLINICOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL ANALYSIS OF 72 CASES OF EXTRAGONADAL GERM CELL TUMOURS – SINGLE INSTITUTIONAL EXPERIENCE

Pathology

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ABSTRACT

Introduction: Germ cell neoplasm is relatively uncommon at extragonadal locations. They are primarily located in midline such as brain, mediastinum, retroperitoneum and coccyx. Present study was aimed to study the clinical and histopathological characteristics of extragonadal germ cell tumours (EGGCTs) along with the expression of immunohistochemical markers.

Methods: Retrospective data of EGGCTs were collected from the hospital software and relevant clinical, histopathological and immunohistochemical data were noted.

Results: Total 72 cases were found between year 2016 to 2020. Mean age was 15.8 years with slight male prepordance. Yolk sac tumour (YST) was the most common histomorphology found in prepubertal/child age group while mature teratoma in postpubertal/adult age group. Placental like alkaline phosphatase (PLAP) was positive in most of the cases of seminoma, choriocarcinoma and mixed germ cell tumour, while in 43.9% cases of YST. CD117 (c-Kit) and OCT3/4 were positive in all cases of the seminoma, AFP was positive in all the cases of YST while beta human chorionic gonadotropin(ß-hCG) in all choriocarcinoma cases.

Conclusion: Extragonadal germ cell tumours caries the poor prognosis compared to gonadal counterpart. Accurate diagnosis along with an exclusion of the differentials is very critical for the management of EGGCTs. Histomorphology along with immunohistochemistry plays a very important role in the early diagnosis as well as for subtyping of the tumour.

KEYWORDS

Extragonadal germ cell tumours, Immunohistochemistry of extragonadal germ cell tumours, Germ cell neoplasm

INTRODUCTION

Extragonadal germ cell neoplasms are relatively uncommon and arises from the extragonadal anatomical locations in absence of primary tumours in the gonads.[1] Extragonadal germ cell tumours (EGGCT) are primarily located in every structure along the midline of the body, starting from the brain to the coccyx. However, the most common anatomical locations are mediastinum, retroperitoneum and brain, followed by fewer cases in pineal gland and sacrococcygeal. Isolated cases have also been reported in rare sites such as bladder, prostate, paratesticular, adnexa, vulva, pelvis, uterus, kidney and other.[1]

Histopathological characteristics of EGGCTs are similar to that of gonadal counterparts, but fewer studies confirmed that their clinical and biological characteristics are quite different.[2] Treatment and prognosis of gonadal and extragonadal germ cell tumours (GCTs) as well as between seminomatous and nonseminomatous tumours are different. For these reasons it is necessary to make accurate diagnosis.[2] In present study we evaluated the clinicopathological parameters of EGGCTs along with usefulness of various immunohistochemical markers.

MATERIAL AND METHODS

The present study is retrospective descriptive, conducted in the department of oncopathology in Western India from year 2016 to 2020. Seventy-two cases of EGGCTs were included in study. The EGGCTs with primary in the gonads were excluded. All the relevant clinicopathological parameters were collected from data base. All the specimens were fixed using 10% formalin and then embedded in paraffin. H and E staining was done of 4 µm cut sections. Another set of 4 µm sections were used for immunohistochemical (IHC) study. Various antibodies used are Placental-like alkaline phosphatase (PLAP), OCT3/4, CD117 (cKit), Beta-human chorionic gonadotrophin (ß-hCG), and AE1. A semiquantitative scoring system was used for grading of immunohistochemical expression.

Statistical Analysis

All the obtained data was arranged in a tabulated form and analyzed using SPSS software.

RESULTS

Total of 72 cases of EGGCT between year of 2016 to 2020 were included in study. Clinical and histopathological characteristic of cases were presented in table 1. Mean age of patients were 15.8 (±17.2) years with age range from 4 months to 71 years and M: F ratio is 2.1: 1. For prognostic purpose we divided the cases in three age group neonatal/congenital (<7 months), prepubertal/ child (7 months to 12 years) and postpubertal/ adult (>12 years). In prepubertal/child sacrococcygeal location was the most common site while mediastinum in postpubertal/adult. Two cases of EGGCTs were found in CNS, one in the suprasellar region and other in pineal regions. Rare sites involved in our study were suprarenal gland (3), renal (2), lung (2), peritoneal (1), cervix (1), liver (1), paraaortic region (1) and cheek (1). In prepubertal/child age group of malignant yolk sac tumour (YST) (48.6%) was the most common while in postpubertal /adult age group mature teratoma (39.4%), followed by germinoma (21.2%). YST with mature teratoma (60%) was the most common mixed type GCTs found. Others were YST and immature teratoma, YST and seminoma, YST and mature teratoma with embryonal carcinoma.

Table 1: Clinical And Histopathological Characteristics.

Parameters	Neonatal/ congenital (<7months) n=2	Prepubertal/child (7 months to 12 years) n=37	Postpubertal/adult (> 12 years) n=33
Male: Female ratio	1:1	1.4:1	3.1 :1
Site	Retroperitoneum-2	Mediastinum-2 Sacrococcygeal-26 Retroperitoneal-2 CNS-1 Others-6	Mediastinum-21 Sacrococcygeal-1 Retroperitoneal-4 CNS-1 Others-6
Histological diagnosis	Mature teratoma-2	Yolk sac tumour-18 Mature teratoma-9 Immature teratoma-3 Seminoma-1 Choriocarcinoma-0 Mixed GCT-6	Yolk sac tumour-6 Mature teratoma-13 Immature teratoma-0 Seminoma-7 Choriocarcinoma-3 Mixed GCT-4
Treatment	Surgery-2	CT-13 CT+RT-1 CT+RT+Surgery-2 CT+surgery-5 Surgery-5 Lost follow up-10	CT-13 CT+RT-4 CT+Surgery-6 Surgery-5 Lost follow up-6

CT- Chemotherapy, RT-Radiotherapy.

In most of the cases diagnosis was made on histomorphology. IHC, however, is mandatory in few cases for confirmation and for exclusion of other differentials. Total 90.9% of YST were positive for AFP and out of this 63.7% cases had strong immunostain. CD30 were negative in all the tumours except one case with mixed germ cell tumour which had one component of embryonal carcinoma. Immunohistochemical

marker analysis results were discussed in table 2.

Table 2: Immunohistochemical Markers Study.

Parameters	Yolk sac tumour	Seminoma	choriocarcinoma	Mixed GCT
PLAP	6/14	8/8	3/3	2/2
CD117(c-Kit)	0/2	8/8	0/2	1/1
OCT3/4	1/14	8/8	0/3	-
AFP	20/22	1/2	0/2	2/2
EMA	0/4	0/4	1/3	-
CD30	1/6	0/3	0/2	1/1
AE1/ CK	17/19	0/2	3/3	2/2
ß- hCG	-	-	3/3	-

PLAP- Placental-like alkaline phosphatase, AFP- Alfa fetoprotein, ß-hCG - *Beta human chorionic gonadotropin.*

DISCUSSION

Malignant germ cell tumours are the most common malignancy in men aged 15–35 years and 5% of the them are of extragonadal origin.[3] An EGGCTs showed same histologies of that of gonadal origin, but located outside of the gonads. This clinical entity was first described in the 19th century. [4,5] Behavior of EGGCT is different in pediatric and adult age group. Within the pediatric age range, prognosis is worse with increasing age.[6-10] In one study[11] they found that age 12 years or older is a significantly adverse prognostic factor, especially for thoracic tumors.

Most common EGGCTs in congenital/neonatal age group is mature or immature teratomas.[12] In our study there were two case which presented in neonatal age group showed histomorphology of mature teratoma.

In prepubertal/child the incidence of teratoma will fall where is the incidence of pure YSTs will rise.[13] In our study 48.6% cases had pure YST histology while 24.3% cases had mature teratoma histology.

In Postpubertal/Adult age group the mediastinum is the most common anatomic location for EGGCTs and most frequently affecting the males.[14,15] which was concordant with our study. In study of Moran CA et al[16] approximately 43% of all mediastinal GCTs showed teratoma histology. In our study 39.4% cases of mediastinal GCTs showed histology of mature teratoma followed by seminoma 21.1%.

Most of cases of CNS extragonadal germ cell tumors occur in children and adolescents especially during 10-20 years of age.[17] In our study two cases of mature CNS teratoma was found one in prepubertal and other in postpubertal age group.

Immunohistochemical markers of EGGCTs shows similar immunoreactivity of their gonadal counterparts.[18] PLAP is lack sensitivity but was traditionally used to verify germ cell origin (mostly seminoma) of tumour in the case of an "undifferentiated" neoplasm,[19] Our study PLAP were positive in all cases of seminoma, choriocarcinoma and mixed germ cell tumour, while YST showed <50% immunoreactivity. Strong and diffuse CD117 immunoreactivity was reported in 75% to 100% of seminomas,[20] which was concordant with our study. Oct3/4 is the newer marker that has better specificity for germ cells tumors specifically for seminomas and embryonal carcinomas[22]. These findings were correlate with our study.

CONCLUSION

EGGCTs are rare tumour and normally arise in midline structures. Clinicoradiological and histopathological correlation along with immunohistochemistry will aids in early diagnosis of EGGCTs.

Conflict Of Interest
None.

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