SHORT REPORT

Clinical profile, treatment and survival outcomes of peadiatric germ cell tumours: A Pakistani perspective

Irfan Ul Islam Nasir,[1] Muhammad Ijaz Ashraf,[2] Nouman Ahmed,[3] Muhammad Fahd Shah,[4] Muhammad Taqi Pirzada,[5] Aamir Ali Syed,[6] Abid Quddus Qazi[7]

Abstract

Germ Cell Tumours (GCTs) are rare tumours. Generally 80% are benign and 20% malignant with a bimodal age distribution. The retrospective study was conducted at Shaukat Khanum Cancer Hospital, Lahore, Pakistan, and comprised all paediatric patients below 18 years of age who received treatment for histology-proven GCT from 2006 to 2014. Of the 207 patients, 98(42.3%) were males and 109(52.7%) were females. The most common GCT was yolk sac tumour in 90(43.5%) children followed by mixed GCT in 40(19.3%) and dysgerminoma in 34(16.4%). Gonads were most commonly involved in 165(79.7%) patients with metastasis in 24(11.6%) at presentation and recurrence in 26(12.5%) patients. Overall, 133(64.3%) patients are well and followed up at regular intervals and 55(26.5%) have been lost to follow-up with an expected overall 5-year median survival of 45%. Despite the distinct clinical profile of paediatric GCT, survival can be improved by early diagnosis, regimented treatment according to set guidelines, protocols and by improving follow-up.

Keywords: Germ cell tumours, Yolk sac tumour, Dysgerminoma.

Introduction

Germ Cell Tumours (GCTs) are rare tumours. Generally 80% of the GCTs are benign compared to 20% malignant (constituting 2-3% of heterogeneous rare malignant paediatric tumours).[1,2] During the teen years, girls are slightly more frequently affected compared to boys with a ratio of 1:0.8.[3,4]

The GCT may present clinically with a testicular or ovarian mass.[5] Common sites of GCT in children are gonadal, presacral and retroperitoneal. Prognosis is mainly dependent on the site, stage and age at diagnosis.[6] The ovarian GCT are mostly diagnosed in the fifth decade of lifewith 12% patients below age 30,[6] whereas testicular tumours have a bimodal age distribution, with a first peak in infants and a second peak in older age group (30-60 years).[7,8] Testicular tumours in paediatric age group constitutes 1-2% of neoplasms with yolk sac tumours being the most common malignant tumour.[9]

In past limited data with lack of focus on adjuvant treatment on paediatric GCT led to non-uniform treatment. Various guidelines are now available in literature regarding management.[10] With this perspective of ethnic variation and gradual increase in incidence of GCT, we are unable to standardise the available guidelines. As the true incidence of paediatric GCT in this part of the world is not known, mainly due to paucity of published local data. The current study was planned to fill that gap.

Methods and Results

The retrospective study was conducted at Shaukat

[1,4-6]Surgical Oncology, [2,3]General Surgery, 7 Pediatric Surgeon, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan.
Correspondence: Irfan Ul Islam Nasir. Email: kmcite905@hotmail.com

Table-1: Patient Characteristics at Presentation.

Demographics		No. of Patients	Percent (%)
Area	Punjab	144	69.5
	KPK	51	24.6
	Sindh	3	1.4
	Balochistan	5	2.4
	Afghanistan	6	2.9
Tumour Location	Gonadal	165	79.7
	Extragonadal	42	20.2
Age	<1 year	24	11.6
	1-5 years	72	34.8
	>5 year	111	53.6
Histopathology	Yolk sac tumour	90	43.5
	Mixed GCT	40	19.3
	Dysgerminoma	34	16.4
	Teratoma	31	15
	Choriocarcinoma	1	0.5
	EmbryonalCa	4	2
	Other	7	3.4
Secretory Tumour	Yes	41	19.8
	No	166	80.2

KPK: Khyber Pakhtunkhwa
GCT: Germ cell tumour.

Table-2: Management.

Type of Surgery	No. of cases	Percent %
Orchidecomy	72	34.8
Salphingoophrectomy	78	37.7
Laparatomy	8	3.8
Excision of mass	24	11.6
Irresectable	5	2.4
No Surgery	20	9.6
Chemotherapy		
Yes	166	80.1
No	41	19.8
Mets at presentation		
Yes	24	11.6
No	183	88.4
Site of Metastasis		
Pulmonary	11	45.8
Mediastinal	4	16.6
Abdominal masses	2	8.3
Liver	6	25
Bone	1	4.1
Recurrence		
Yes	26	12.6
No	181	87.4

Khanum Cancer Hospital, Lahore, Pakistan, and comprised all paediatric patients below 18 years of age who received treatment for histology-proven GCT from 2006 to 2014. Patients above the age of 18 years were excluded. Parameters identified to record initial clinical presentation, clinical findings, imaging and laboratory investigations included tumour marker levels. Decisions of multidisciplinary team meetings (MDTs) retrieved with patients stratified on the basis of age, clinical stage and type of tumour. Kaplan Meier curve was used to determine estimated overall survival. All analysis was performed using SPSS 20.

Of the 207 patients, 98(47.35%) were males and 109(52.7%) females. Most of the patients were from Punjab 144(70%) followed by Khyber Pakhtunkhwa 51(25%). Yolk sac tumour 90(43.5%) was the most common tumour, followed by mixed GCT in 40(19.3%) children (Table-1). Gonads were the most frequently involved site 165(79.7%). Majority of the patients 111 (53.6%) were above the age of 5 years. Besides, 195(94.7%) patients had upfront excisional surgery outside hospital and were referred to our hospital. Each individual patient, the treatment decision was taken after discussion in the multidisciplinary team meeting as per hospital policy. Of them, 166(85%) received chemotherapy according to internationally accepted guideline at the time individual patient was treated (Table-2). Metastasis occurred in 24(11.6%) patients, and 18(75%) of them underwent debulking surgery, 4(16.6%) were found to be unresectable and in 2(8.8%) patients metastatectomy was performed. On long-term follow-up, 133(64.3%) patients were on regular follow-up and in good health, 19(9.2%) had diedduring the course of treatment, and 55(26.5%) were lost to follow-up with an overall expected 5-year survival of 45% with median survival 36 months (IQR 12-60 months).

Discussion

GCTs are rare tumours with diverse heterogeneous histology, including both benign and malignant tumours. Since these are rare tumours, a retrospective analysis was conducted to evaluate the outcomes of paediatric GCTs in our hospital. All the patients received chemotherapy according to internationally accepted guidelines.[11] Girls were more frequently affected in our study compared to boys which is consistent with literature.[5]

In our study, 80% of the cases had gonadal involvement and 20% extra-gonadal involvement with yolk sac tumour being the most common, whereas in anotherstudy extra-gonadal was more prevalent (72.7%) with teratoma being the most common.[4] In our study 5-year survival rate was around 45% which is quite less compared to different studies.[3,12] It was owing to late presentation after initial surgery, delay in chemotherapy initiation, long travel distances and limited financial resources.

There are limitations of our study as majority of the patients had been operated upfront outside our hospital and were referred here for further treatment with limited clinical and tumour marker information. Yet, to our knowledge, this is the first study reporting considerable data from any centre in Pakistan. Based on this data we intend to prospectively include parameters of assessment which will enable us to improve our results on the basis of stronger data set.

References

1. Rescorla FJ. Pediatric germ cell tumors. Semin Pediatr Surg 2012; 21: 51-60.
2. Schneider DT, Calaminus G, Koch S, Teske C, Schmidt P, Haas RJ, et al. Epidemiologic analysis of 1,442 children and adolescents registered in the German germ cell tumor protocols. Pediatr Blood Cancer 2004; 42: 169-75.
3. Poynter JN, Amatruda JF, Ross JA. Trends in incidence and survival of pediatric and adolescent patients with germ cell tumors in the United States, 1975 to 2006. Cancer 2010; 116: 4882-91.
4. Zachary H, Schlatter M, Schultz S. Pediatric germ cell tumors. Surg Oncol 2007; 16: 205-13.
5. Fresneau B, Orbach D, Faure-Conter C, Verité C, Castex MP, Kalfa N,

et al. Sex-Cord Stromal Tumors in Children and Teenagers: Results of the TGM-95 Study. Pediatr Blood Cancer 2015; 62: 2114-9

6. Quirk JT Natarajan N. Ovarian cancer incidence in the United States, 1992-1999. Gynecol Oncol 2005; 97: 519-23.
7. Hofmann M, Schlegel PG, Hippert F, Schmidt P, von-Schweinitz D, Leuschner I, G€obel U, Calaminus G, Schneider DT, MAKEI study group. Testicular sex cord stromal tumors: Analysis of patients from the MAKEI study. Pediatr Blood Cancer 2013; 60: 1651-5.
8. Bujons A, Sfulcini JC, Pascual M, Feu OA, Garat JM, Villavicencio H. Prepubertal testicular tumours and efficacy of testicular preserving surgery. BJU Int 2011; 107: 1812-6.
9. Nerli RB, Ajay G, Shivangouda P, Pravin P, Reddy M, Pujar VC. Prepubertal testicular tumors: our 10 years experience. Indian J Cancer 2010; 47: 292-5.
10. Schmoll HJ, Souchon R, Krege S, Albers P, Beyer J, Kollmannsberger C, Fossa SD, Skakkebaek NE, De Wit R, Fizazi K, Droz JP. European consensus on diagnosis and treatment of germ cell cancer: a report of the European Germ Cell Cancer Consensus Group (EGCCCG). Annals of Oncology. 2004; 15: 1377-99.
11. Goldman S, Bouffet E, Fisher PG, Allen JC, Robertson PL, Chuba PJ, Donahue B, Kretschmar CS, Zhou T, Buxton AB, Pollack IF. Phase II trial assessing the ability of neoadjuvant chemotherapy with or without second-look surgery to eliminate measurable disease for nongerminomatous germ cell tumors: A Children's Oncology Group Study. Journal of Clinical Oncology. 2015 Jun 22: JCO-2014.
12. Silberstein JL, Bazzi WM, Vertosick E, Carver BS, Bosl GJ, Feldman DR, et al. Clinical outcomes for local and metastatic testicular sex cord-stromal tumors. J Urol 2014; 192: 415-9.