Teratomas in children:an institutional retrospective study

K.V.Sathyanarayana[1*], P. Sarweswar Reddy[2]

[1]Assistant Professor, Niloufer Hospital,Osmania Medical College, Hyderabad, India
[2]Associate Professor, Kurnool Medical College, Kurnool , India

ABSTRACT

Aim and Objectives: The aim is to study the clinical presentation, malignant potential of teratomas and their management in pediatric age group. **Materials and Methods:** This is a retrospective study done in 52 cases of teratomas in children . All the cases were evaluated clinically, investigated , treated and were on regular follow up. **Results:** In our series 52 cases of teratomas were studied retrospectively. 43% of teratomas are sacrococcygeal teratomas and by far the commonest. There is a relatively high incidence of retroperitoneal tumors occupying second place ,constituting 25% (13 cases) of teratomas as against the other series which range between 5-10%. The ovarian teratomas has an unusually lower incidence at 15.3%. There are 12 cases of malignant tumors out of 52 cases (23%), Immature teratomas being 9.6% and mature teratomas 67.4%. Though retroperitoneal teratomas constitute 25% of paediatric teratomas , the malignant potential is equivalent to that of sacrococcygeal teratomas. Malignant teratomas in the extragonadal site is seen in children below 5 years whereas in the gonadal site they are seen in children above 5 years. In sacrococcygeal teratoma there is no evidence of malignancy below one month of age whereas in three cases reported in infancy, malignant changes were seen. Incidence of malignancy related to the sex of pt F = 8 M = 4 (RP-3,Testicular-1). More cases of malignant variety were present in Altman type III & IV. Of 12 malignant teratomas, 9 cases were endodermal sinus tumours (Yolk sac tumour). There were 4 deaths recorded in this series representing a mortality rate of 7.76%, one death occurred due to postoperative bleeding, whereas in other 3 cases it was due to malignancy related complications. The 5year survival rate for benign tumours is 97.5% and of malignant teratomas is 75% . **Conclusion:** There is a high malignant potential in the retroperitoneal tumours and it increases with the age. The female incidence of sacrococcygeal teratomas is more than 90%. The levels of AFP correlates with the progress of the tumours. All the malignant changes seen in sacrococcygeal teratomas and retroperitoneal teratomas are between infancy and 5 yrs age.

Key words: teratomas,yolk sac tumours, Altman type, Mortality.

Introduction

A teratoma is a tumor with tissue or organ components resembling normal derivatives of more than one germ layer. Although the teratoma may be monodermal or polydermal (originating from one or more germ layers), its cells may differentiate in ways suggesting other germ layers [1]. The tissues of a teratoma, although normal in themselves, may be quite different from surrounding tissues and may be highly disparate; teratomas have been reported to contain hair, teeth, bone and, very rarely, more complex organs or processes such as eyes, torso, and hands, feet, or other limbs. The term 'teratos' is derived from Greek meaning monster. The modern therapy of origin of teratoma evolved from work of 'Telium[2]in that they are totipotential cells from primitive germ cells which have gone astray during their migration from the endoderm of yolk-sac to the genital ridge in the retroperitoneum. The aberrant germ cells can differentiate either into embryonal structures giving rise to teratoma or into extra embryonic structures i.e., trophoblast or yolksac. Since they the totipotential cells, they are capable of generating the derivatives of ectoderm, endoderm and mesoderm in a single tumor. Based on the histological grade of differentiation of the cells they are classified as 1. Mature, 2. Immature & 3. Malignant tumours. The commonest component of a malignant teratoma is yolk sac tumour[3] Sacrococcygeal teratoma[4] is the commonest type among all the other sites of origin including retroperitoneum, gonads(ovary and testis), pelvis , mediastinum, cervicofacial and intracranial. In 1841, Stanley [5] described the gross appearance of a sacrococcygeal teratoma and reported the first successful

**Correspondence*
Dr. K.V.Sathyanarayana
Assistant Professor, Niloufer Hospital, Osmania Medical College, Hyderabad, India

excision. The mainstay of therapy is the complete surgical removal and postoperative chemotherapy if the histopathology report suggests malignant variety or a high grade immature teratoma associated with high levels of AFP(alphafetoprotein). The main aim of the study is to analyze clinical presentation, the malignant potential of teratomas in pediatric age group and their management.

Materials and methods

This is a retrospective study done between December 2004 to December 2014 over a period of 10 years. In this study, 52 cases of teratomas were studied. All the cases were evaluated clinically, investigated, treated and were on regular follow up . The commonest presentation is the swelling at various sites except the mediastinum where the patients presented with respiratory symptoms of recurrent upper respiratory tract infection and tachypnea. The investigations included imaging, ultrasound of the abdomen and swelling, CT scan, and blood examination for tumour markers. Postoperative follow up period ranged between 6months to 3years, evaluated with regular clinical follow-up and appropriate investigations to know the recurrence of the tumour.

Results

Table 1: Demographic distribution of tumours in study

Sites of Tumour	Male	Female	Total	Percentage
Sacrococcygeal	2	20	22	43.3%
Retroperitoneal	7	6	13	25%
Mediastinal	1	3	4	7.7%
Ovarian	---	8	8	15.3%
Testicular	4	---	4	7.7%
Other (Back)	1	---	1	1.9%
Total	15	37	52	

Table 2: Distribution of tumour in age groups and presenting symptoms

Type of tumour	Age	Symptoms
Sacrococcygeal	New born to 3 years	Swelling over the buttocks, constipation
Retroperitoneal	4-6 months	Lump on abdomen, pain, fever
Ovarian	8-10 years	Lump on abdomen, pain
Mediastinal	2-4 months	Respiratory distress, fever
Testicular	2-3 years	Scrotal enlargement

In our series of 52 cases of teratomas were studied retrospectively, 43.3% are sacrococcygeal teratomas . There is a relatively high incidence of retroperitoneal tumors constituting 25% (13 cases) as against the other series(Amit Chaudhary *et al*) which range between 5-10%. The ovarian teratomas has an incidence of 15.3%, similar to that of other series (Ahmed H Al Salem *et al*).

Table 3: Age specific incidence of malignancy

Age	SCT	RPT	OT	TT
<1 m	0	0	0	0
1m -1year	3	2	0	0
1 yr- 5 yrs	2	3	0	0
>5 yrs	0	0	1	1

Table 4: Histological types of teratomas

Histological Type	Number	Percentage
Mature	35	67.4%
Immature	5	9.6
Malignant	12	23

Table 5: Site specific incidence of malignancy

Site of tumours	% of tumour	% of malignancy
Sacrococcygeal	43.3	41.6
Retroperitoneal	25	41.6
Ovarian	15.3	8.3
Testicular	7.7	8.3
Mediastinal	7.7	---

Table 6: Type of tumour and site

Type of tumours	Number of cases	Site
Yolk Sac tumours	9	RPT+SCT
Embryonal Cell	1	SCT
Undifferentiated	1	RPT
Not Known	1	RPT

There are 12 cases of malignant tumors out of 52 cases(23% of all teratomas), Immature teratomas being 9.6% and mature teratomas 67.4%. Though the retroperitoneal teratomas constitute 25% of paediatric teratomas, their malignant potential is same as that of sacrococcygeal teratomas. The incidence of malignancy in gonadal tumors is also less in children. Malignant teratomas in the extragonadal site is seen in children of less than 5 yrs age, where as in the gonadal site they present in children above 5 yrs . In sacrococcygeal teratoma there is no malignant elements below 1 month of age. Three cases that are reported in infancy had changes of malignancy. The incidence of malignancy related to the sex of pt F = 8 M = 4 (RPT-3,Testicular-1).

Table 7: Malignancy based on Altman type

Altman type	Number of cases	Malignancy cases
I	4	0
II	8	1
III	6	2
IV	4	2

Table 8: Treatment followed in the study

Type of tumour	Surgical treatment		Adjuvant therapy	
	Complete Excision	**Debulking/ Biopsy**	**Cisplatin/ Etoposide**	**VAC regime**
Sacrococcygeal	21	1	3	2
Retroperitoneal	12	1	2	2
Mediastinal	4	---	---	---
Ovarian	1	---	1	---
Testicular	1	---	1	---

Table 9: Site of tumour and causes of death in study

Site of tumours	No. of deaths	Cause of death
Sacrococcygeal	2	1-PO bleeding, 1-Inadequate excision with intolerance to chemotherapy
Retroperitoneal	2	1-Inadequate Excision, 1-Tumour recurrence
Ovarian	---	---
Mediastinal	---	---

Malignant changes were present mostly in cases of Altman type III & IV. Of 12 malignant teratomas, 9 cases were endodermal sinus tumours (Yolk sac tumour). In one case of pelvic tumours, embryonal carcinoma was seen. In one case of retroperitoneal tumours undifferentiated teratocarcinoma was recorded. There were 4 deaths recorded in this series representing a mortality rate of 7.76%. One death occurred due to postoperative bleeding. In other 3 cases it was because of malignancy related complications with gradual deterioration. In one case of retroperitoneal tumors though the histopathology report suggested a benign tumour, the patient died of rapid recurrence of the tumour inspite of total resection. In the other two cases where debulking of the tumour done, both children succumbed to disease. This suggest that the total surgical removal has a definitive role in controlling the disease and the survival rate. The 5 year survival rate with the benign tumours is 97.5% and that of malignant teratomas was 75%.

Discussion

Many have done studies related to malignant potential of teratomas in paedriatic age group. Monica Terenziani *et al*[6] , demonstrated that teratomas showed a benign clinical behaviour, however they may recur if malignant components are present. In our study, patients with teratoma were collected from 2004 to 2014. Teratomas were classified as mature and immature based on WHO classifications[7-10] Patients with pathological aFP and/or bHCG and those with a malignant germ cell component were not included in the study. The study by Monica Terenziani enrolled 219 patients (150 mature, 69 immature) with a median age at diagnosis of 42 months. The primary sites involved were 118 gonadal and 101 extragonadal teratomas. 2 females with ovarian teratomas had a positive family history. Complete and incomplete surgeries were performed in 85% and 9% of cases. 17 events occurred in which 6 females had a second metachronous tumour (5 contralateral ovarian teratoma, 1 adrenal neuroblastoma) and 11 teratomas relapsed/progressed (3 mature, 8 immature teratomas). 2 patients died, one of progressive immature teratoma and one of surgical complications. At a median follow up of 68 months, the event free, relapse free, and overall survival rates were 90.6%, 94.3%, 98.6% respectively. This study concluded that teratomas show a good prognosis especially the mature ones. Claire L Templeman *et al*[11] , in their study showed that Mature cystic teratomas (MCT) are the most common ovarian tumours seen in children and adolescents. This is a retrospective study. Fifty-two patients of less than 21 years of age had surgical removal of an MCT, 14 of whom were approached laparoscopically. Compared with laparotomy, those patients managed laparoscopically had a significantly shorter hospital stay[12,13] . Intra-operative tumour spillage occurred in 27 (52%) patients; there were no cases of chemical peritonitis[14]. Available follow-up data on 34 (65%) patients revealed seven pregnancies [15,16] occurring at a median of 70 months (46–123) postoperatively, including four in patients with intraoperative MCT spill. There were no cases of tumour recurrence during the follow-up period among the 27 (52%) patients managed with ovarian cystectomy. These results demonstrate that some of the conclusions regarding the contemporary management of MCT in adults are applicable to children and adolescents.

U Gobel *et al*[17].showed that Since 1982, mature and immature teratomas have been recruited into the MAHO and MAKEI protocols of the German Society for Pediatric Oncology and Hematology (GPOH) for testicular and non-testicular germ cell tumors in order to study the epidemiology and clinical behaviour of teratomas. Patients were registered in the epidemiologic German Childrens Cancer Registry and the GPOH Childrens Tumor Registry for pathological review. Patients with immaturity grade 2 and 3 according to Gonzales-Crussi[18]were eligible for adjuvant chemotherapy[19,20] The consecutive protocols MAKEI 83/86/89 have been published previously in detail (and will be compared to the data of MAKEI 96. For this comparison, 274 patients from MAKEI 83/86/89 and 261 patients from MAKEI 96 are evaluated. The results after complete tumor resection have been estimated to be 0.96 +/- 0.01 in both observation periods. Incomplete tumor resection remains the main risk factor for relapse (EFS 0.55 +/- 0.09). The relapse rate declined from 13.9 % in MAKEI 83/86/89 to 9.5 % in MAKEI 96. 4) In MAKEI 83/86/89 four newborns with teratoma died due to perioperative complications and nine children as a result of tumor progression, whereas in MAKEI 96 no newborn died, only one child died from tumor progression, and another

child died during long time observation for another reason (meningitis). In accordance to the experience of the MAKEI 83/86/89 studies, no child of the MAKEI 96 study presented with yolk sac tumor at recurrence if adjuvant chemotherapy was administered during first-line treatment because of immaturity. In contrast, more than half of the children with tumor recurrence after watch and wait strategy had yolk sac tumor in addition to teratoma.

Amit Chaudhary *et al*[21] aims to highlight the clinical features, investigations and treatment of retroperitoneal teratomas condition. The methods are as follows 12 patients (8 females and 4 males, age range-2 months to 14 yrs) of retroperitoneal teratoma were admitted to the department of Pediatric Surgery, King George Medical University, Lucknow between 1980 and 2004 were studied. Investigations included hematology, plain X-ray of the abdomen, intravenous urography, ultrasound, computerised tomography (CT) of the abdomen (after 1990, 8 patients), and serum alpha-fetoprotein assay (after 1991, 6 patients, preoperatively). All patients underwent surgery. Serum alpha-fetoprotein assay was used during follow-up to detect recurrence. The results were majority of the tumors were left pararenal in location. In two patients there was bilateral involvement. In all except one, the tumor could be excised easily preserving the kidneys. In one child with a massive cystic tumor with bilateral involvement, the tumor was marsupialised in the first stage and excised subsequently. One child died postoperatively, the other 11 children are well and there has been no tumor recurrence on follow-up. It concluded that retroperitoneal teratomas are uncommon lesions in children mostly arising in close relation to the kidneys. The majorities are benign but complete excision is necessary for cure. Even large tumors with bilateral involvement of the retroperitoneum can be excised while preserving adjacent organs. Serum alpha-fetoprotein assay is a reliable method of detecting recurrence.

Ahmed H Al Salem *et al*[22] showed that teratomas are a unique group of tumors with variable behavior depending on the site, size, histology and age at diagnosis. The medical records of all infants and children with the diagnosis of teratoma treated between 1989 and 2007 were retrospectively reviewed for: age at diagnosis, sex, presenting symptoms, site of tumor, treatment, histology and outcome. The results were over a period of 18 years, we treated 29 infants and children with teratomas at various sites of the body. These included sacrococcygeal (14), ovarian (4), cervical (5), retroperitoneal (4), gastric (1) and buttock (1). There were 14 sacroccocygeal teratomas, all were females except two. The age at presentation ranged from birth to 18 months, but the majority (78.6%) presented within the first week of life. According to Altman's classification, 10 were type 1, 2 type 2, and 1 type 3. In one patient, it was difficult to classify. The majority (77%) were benign. Two of the three with malignant sacrococcygeal teratoma presented late. Five had cervical teratoma. All were left sided. In all, the swelling was large to the extent that 3 presented with acute respiratory distress necessitating emergency intubation and one developed brain hypoxia. All were benign except one who had immature grade I teratoma. Four had ovarian teratoma, one of them presented as an emergency. Two were malignant. Four had retroperitoneal teratoma, one of them was malignant. A 4-days old male with a very large abdominal mass and calcifications was found to have a large gastric teratoma which was immature grade I. A 6-months old female was found to have a benign teratoma of the buttock. It concluded that teratomas are an interesting group of tumors with similar histological picture but variable behavior.

Sacrococcygeal teratoma is the commonest and the majorities are benign but the risk of malignant transformation increases with age[23-25] The majority of cervical teratomas are benign, but they can cause significant morbidity and mortality as a result of respiratory compromise. Surgical excision of these large tumors needs to be planned. We found staged excision in some of these patients beneficial. Retroperitoneal teratomas[28] are rare and the majority present with an abdominal mass which can attain a large size. Careful attention to adjacent major blood vessels in the vicinity of the tumor at the time of resection is very important as these tumors tend to distort major blood vessels including the renal vessels. Ovarian teratomas are the second most common teratoma in infants and children. The majorities are easily resectable but they can attain a large size and present as an emergency because of a twist. Gastric teratoma[25] is very rare and resection is curative.

Conclusion

There is a high incidence of retroperitoneal tumours in our series. There is a high malignant potential in the retroperitoneal tumours and it increases with the age. Females have more incidence of malignancy than males. The female incidence of SCT is more than 90%. The levels of AFP correlates with the progress of the tumours. All the malignancies in SCT and RPT are between infancy and 5 yrs age. Very low incidence of ovarian teratomas was recorded. Mortality relatively increases where there is inadequate surgical removal.

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