TESTICULAR TUMOURS IN INFANTS - A SEVEN-YEAR PROSPECTIVE STUDY

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ABSTRACT

BACKGROUND

Paediatric testicular tumours are rare and it accounts for 2% of solid malignant neoplasm in boys. Below 2 years of age, it is very rare and difficult to diagnose.

Since retrospective study may not provide information due to non-availability of records as required, a prospective study was planned at SMS Medical College and attached SPMCH Institute, Jaipur, from Jan 2009 till April 2012 and continued at National Institute of Medical Sciences, Jaipur, from May 2012 to December 2015, a 7-year period.

MATERIALS AND METHODS

A proforma was made and kept in OPD and ward and a qualified paediatric surgeon were appointed to fill the form regarding age, provisional diagnosis, symptomatology, investigations, routine and special like USG, CT, MRI, tumour marker study, treatment plan, result and followup. Undescended testis and torsion testis were excluded, whereas infants with scrotal swelling below 2 years of age were included.

RESULTS

Out of 17 patients, one died after 6 months due to relapse in mixed germ cell tumour group, rest all sixteen survived and have 6 to 1 years' followup. Surgery was done in all cases, whereas 5 cases needed chemotherapy in addition to surgery. Radiotherapy was not given in any case. Tumour markers like α-fetoprotein and β-hCG markedly reduced after orchidectomy.

CONCLUSION

Yolk sac tumour and teratoma all cases responded well to high inguinal orchiectomy, chemotherapy required only in 5 cases. One case of mixed germ cell tumour have relapse after surgery and chemotherapy and died after 6 months postoperatively.

KEYWORDS

Yolk Sac Tumour, Testicular Tumour in Infants, Teratoma Testis in Infants, Malignant Testicular Tumour.

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BACKGROUND

Paediatric testicular tumours are rare, accounting for 2% of solid malignant neoplasm in boys.[1] In case of infants it is very difficult to diagnose, because such cases presented as scrotal swelling and most of the paediatricians diagnose as hydrocele and advice parents that there is fluid inside scrotum that will subside by the age of 1 year. In such cases, early referral to paediatric surgeon in early stage saves life. The objective of this study is to get awareness in paediatricians and general practitioners to refer such cases at an early stage. Although, 20% may be associated with reactive hydrocele.[2]

MATERIALS AND METHODS

Plan for prospective study was there; hence, a protocol was laid down. Case selection - infants below the age of 2 were included, undescended testis, torsion testis and other cystic lesions of cord, testis and epididymis were excluded.

Proforma included history, clinical exam. Investigations USG, CT, MRI; radiological investigations of chest, tumour marker and surgical procedure.

Age (In months) At the time of Presentation	No. of Cases			
	Total	**Yolk Sac**	**Teratoma**	**Mixed Cell**
6 - 12	11	7	4	0
12 - 18	4	3	1	0
18 - 24	2	1	0	1
Total	**17**	**11**	**5**	**1**

Table 1

Total No. of Patients = 17

Ultrasonography - Done in all cases, which suspected testicular mass.

Computed Tomographic Scan - Confirmed the diagnosis. No enlargement of retroperitoneal lymph nodes.

Magnetic Resonance Imaging - Done in one case.

X-Ray Chest - No metastasis.

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Type of Tumour	No. of Cases	α - fetoprotein	β-hCG
Yolk Sac Tumour	11	1200 - 1600 ng/mL	80 I.U.
Teratoma	5	1100 - 1500 ng/mL	200 I.U.
Mixed Cell	1	1754 ng/mL	250 I.U.

Table 2. Tumour Marker Study

β-hCG was also done in all cases and found elevated, which dropped down to normal level except in one after 48 hours postoperatively; α-fetoprotein also significantly dropped after 1 week postoperatively.

RESULTS

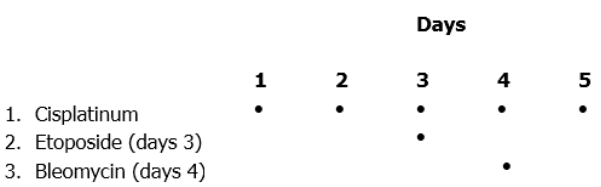
Out of 17 cases who underwent surgery 16 survived and followup done from 6 to 1 year. Only one infant who had testicular tumour with mixed germ cell origin died 6 months postoperatively due to distant metastasis in retroperitoneum and lungs. Following table will show the treatment plan with results.

Sl. No.	Mode of Treatment	No. of Cases
1.	High Inguinal Orchiectomy	17
2.	High Inguinal Orchiectomy with Retroperitoneal Lymph Node Dissection	2
3.	High Inguinal Orchiectomy + Chemotherapy	5

Table 3

Chemotherapy Protocol

These infants received chemotherapy consisting of cisplatin, vinblastine and bleomycin (PVB, modified Einhorn regimen) for 12 weeks (in two cases) 3 patients received a combination of cisplatin, etoposide and bleomycin (PEB), (Plantinol : Day 1 to 5). This regimen works well and has been followed by others also.[3]



These patients repeat the course for 3 weeks and last for 3 - 5 weeks on average.

Followup

Patients continued chemotherapy and were followed up in OPD every month for six months, then 3 monthly intervals for 2 years, 6 monthly intervals for 48 months. At each visit, they were investigated for blood count, USG scrotum and abdomen, x-ray chest and tumour markers like α fetoprotein.

DISCUSSION

Clinical examination is an important part of the study, which raise a suspicion and differentiate from hydrocele and inguinal hernia. Transillumination test of scrotum, again an important clinical test which clinches the diagnosis of testicular tumour. After clinical examination, these patients were subjected to ultrasonography inguinoscrotal region, pelvis and abdomen to rule out enlargement of retroperitoneal lymph nodes which is further confirmed by CT, MRI abdomen, pelvis and scrotum. Blood samples taken for study of tumour markers like α-fetoprotein and β-hCG.

After confirmation of diagnosis, all infants were subjected for high inguinal orchidectomy in which testis along with cord structures removed en-bloc with ligation of hernial sac and cord structure in a single ligature. In two cases, retroperitoneal node dissection and a few small lymph nodes were taken for histopathologic examination. Entire excised tissue, i.e. testis cord structure, hernial sac, retroperitoneal lymph node were subjected for histopathologic examinations.

Major risk factors for development of testicular tumour during childhood is the presence of undescended testicle. Typically, the histologic tumour types related to the cryptorchid testicle are seminoma and embryonal carcinoma and presentation, more typically in the fourth decade of life.[4,5]

History taking and clinical examination is equally important as the diagnostic modalities. Since the patients of this study group are nonverbal infants, hence mother has noticed the swelling on either side of scrotum and took advice of a family physician or a paediatrician who referred to a paediatric surgeon; delay sometimes happen due to unawareness and lack of physical examination by a paediatrician, who thinks it to be a hydrocele which will subside by the age of two years. Paediatrician have been found to have a wrong notion. On arrival to paediatric surgeon, he must concentrate on painless swelling in the scrotum noticed by either of parents and physical examination. Clinical approach - important is physical examination, i.e. palpation of testis - during examination of scrotal contents the thumb and forefinger should be placed between the anterior testis and the posterior and superior epididymal and cord structures. The testis then can be palpated, as it slides between the examiner's fingers and masses in the testis can be felt and separated from the abnormalities of the epididymis or cord. By such examination, one can find associated hydrocele or inguinal hernia. In present study I noticed 3 cases each of hydrocele and inguinal hernia (18% each), whereas others have noticed reactive hydrocele in 20% cases[2] and inguinal hernia in 27 cases.[6]

Transillumination test should also be done because all testicular tumours are translucent in contradiction to hydrocele or hernia.

If a testicular mass is suspected also on history and physical examination, the diagnosis should be confirmed by imaging techniques and tumour markers.

Preoperative assessment of serum markers (Alpha fetoprotein, β-hCG) is essential, because it serves as the basis for staging and patient monitoring; α-fetoprotein (AFP) is a single chain glycoprotein produced by the foetal yolk sac, liver and gastrointestinal tract. Its half-life is 5 days; hence, if tumour is completely resected its serum level will drop down after one week. If it does not happen, then complete resection of tumour is probably not done. Normal α-fetoprotein level is given in the following table.[7]

New Born	41687 ng/mL
3 months	398 ng/mL
6 months	108 ng/mL
1 year	18 ng/mL
2 years	4 ng/mL
Adult	0.6 ng/mL
Normal α-Fetoprotein Level	

Beta human chorionic gonadotropin (β-hCG) is a glycoprotein that is produced by embryonal carcinoma and mixed teratoma. The normal serum value for β-hCG is less than 5 IU/L. The half-life of β-hCG is 24 hours. Thus, preoperative elevated β-hCG levels should return to normal within 5 to 8 days after surgery, if all the tumour tissue has been removed.

Ultrasonography is instrumental in localising the scrotal mass with respect to the testicle and for distinguishing a simple hydrocele from a reactive hydrocele associated with testicular tumour. Ultrasonography identified the yolk sac tumours as solid masses; focal masses were evident when the tumour replaced the entire testicle. The masses were described as hyperechoic and isoechoic. Colour Doppler study will show flow of blood in tumour,[8] but not done in this series.

Metastatic evaluation should include CT of the abdomen and pelvis to evaluate retroperitoneal lymph node, in addition to chest radiography and CT and bone scintigraphy with 99m Tc-pertechnetate. In this series bone scintigraphy was not done, because of in infancy these tumours rarely metastasize to bone. CT scan of chest before surgery is recommended, but in x-ray chest of all infants no suspicion of tumour metastasis was there.

Tumour Histology

All the testicular masses were subjected for pathological examination. All tumours were solid masses; in some cases, there were areas of necrosis and haemorrhage. Testicular enlargement was evident when the tumour replaced the entire testicle. Histological micrographs demonstrated pathologies typical of yolk sac tumours, which showed a microcapsule and reticular structure in 11 cases; 5 cases showed gland tube and gland bubble and variegated appearance; 1 case showed mixed germinal cells.

Previously, the only staging system used consistently for prepubertal patient with testicular tumours was that proposed by Evan et al,[9] which defined disease according to whether it was confined to scrotum, metastatic to regional lymph nodes (within the abdomen) or metastatic to distant sites. Recently, investigations from POG and CCG developed staging criteria that also account for tumour marker status and trans-scrotal surgical violation, children's oncology group staging of testicular tumours.

Stage	
I	Limited to testis, completely resected to high inguinal orchiectomy or trans-scrotal orchiectomy with no spill. No clinical, radiographic or histologic evidence of disease beyond the testis. Tumour markers normal after appropriate post-surgical half-life decline; patients with normal or unknown markers at diagnosis must have a negative ipsilateral retroperitoneal node dissection to confirm stage I
II	Trans-scrotal orchiectomy with gross spill of tumour. Microscopic disease in scrotum or high in spermatic cord (< 5 cm from proximal end) Retroperitoneal lymph node involvement (≤ 2 cm). Increased tumour marker after appropriate half-life
III	Retroperitoneal lymph node involvement (> 2 cm), no visceral or extra-abdominal involvement
IV	Distant metastasis including liver
Tumour Histology	

In present series, 16 patients were classified in Stage I, whereas one patient was in Stage IV.

The various types of testicular tumours in pre-pubertal age is classified by Kay R.[10]

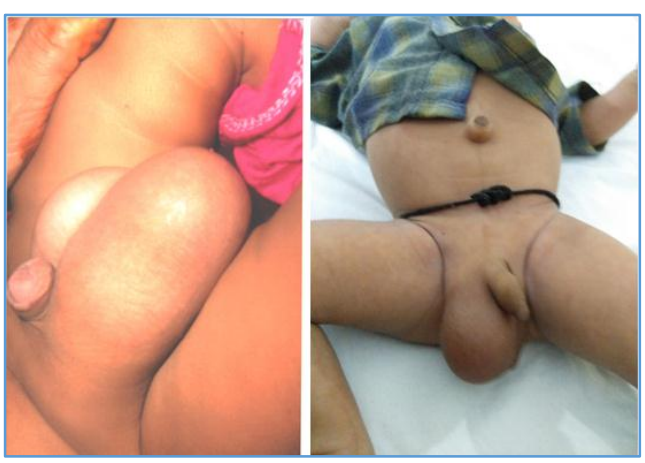
			Age of Presentation
I.	Germ Cell Tumour		
	(i)	Yolk Sac (Endodermal sinus tumour)	Less than 2 years
	(ii)	Teratoma	2 - 4 years
	(iii)	Mixed Germ Cell	Not available
	(iv)	Seminoma	4th decade
II.	Gonadal Stromal Tumours		4th decade
	Leydig Cell		
	Sertoli cell		
	Juvenile granuloma cell		
	Mixed		
III.	Gonadoblastoma		5 - 10 years

IV.	Tumours of supporting tissues		3rd to 4th decade
	Fibroma		
	Leiomyoma		
	Haemangioma		
V.	Lymphomas and leukaemias		
VI.	Tumour-like lesions		
	(i)	Epidermoid cyst	
	(ii)	Hyperplastic nodule	
	(iii)	Secondary to congenital adrenal hyperplasia	
VII.	Secondary tumours		
VIII.	Tumours of the adnexa		

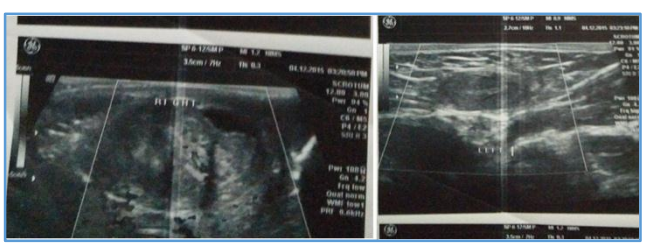
CONCLUSION

- A solid scrotal mass should be considered malignant until proved otherwise.
- Any suspicion of testicular tumour should be operated by inguinal approach.
- The most common mode of presentation was painless scrotal mass.
- Yolk sac tumour is most frequent Germ Cell Tumour (GCT) of testis in children. Early presentation have good prognosis. Chemotherapy is not recommended below the age of 6 months. Radiotherapy is not at all required.

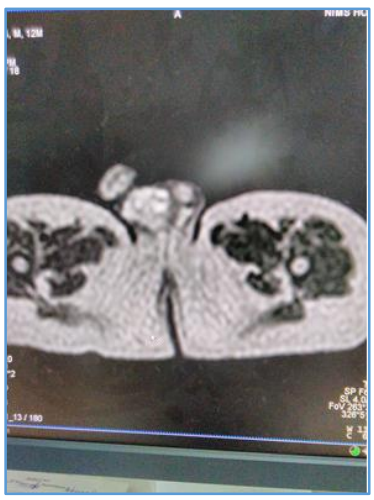
Photographs



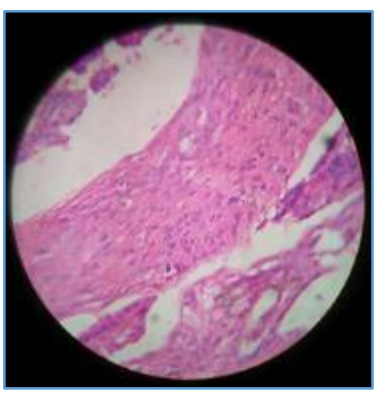
Marked Enlargement of the Testis (Facing Page 3)



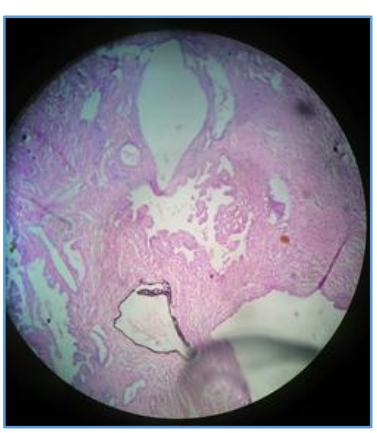
Ultrasonography showing Testicular Mass, No Fluid Seen (Facing Page 3)



MRI showing Testicular Tumour



Malignant Germinal Cells in Yolk Sac Tumour (H.P.)



Yolk Sac Tumour (L.P.)

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