DOI: 10.7860/JCDR/2017/24892.9781

Case Report

Pathology Section

Pure Primary Extragonadal Retroperitoneal Yolk Sac Tumour in a Young Child: A Case Report

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ABSTRACT

Germ Cell Tumours (GCTs) in children are uncommon, constituting approximately only 3% of all malignancies in children younger than 15 years of age. Primary extragonadal GCTs constitute only 1-5% of all GCTs and a retroperitoneal site is seen only in 4% of all extragonadal GCTs. Extragonadal GCTs arise from local transformation of primordial germ cells which have been misplaced during the migration of these cells through the midline dorsal mesentery in the fourth-sixth week of embryogenesis. GCTs in children show remarkable variability in age, site, presentation and histology. This is the case of a three-year-old male child who presented with a history of an abdominal swelling which was rapidly progressive in nature. Radiology showed a large retroperitoneal mass and lesions in the liver. Histopathology, immunohistochemistry and serum Alpha-fetoprotein (AFP) values confirmed a diagnosis of pure primary extragonadal yolk sac tumour.

Keywords: Alpha- fetoprotein, Germ cell tumours, Schiller–Duval bodies

CASE REPORT

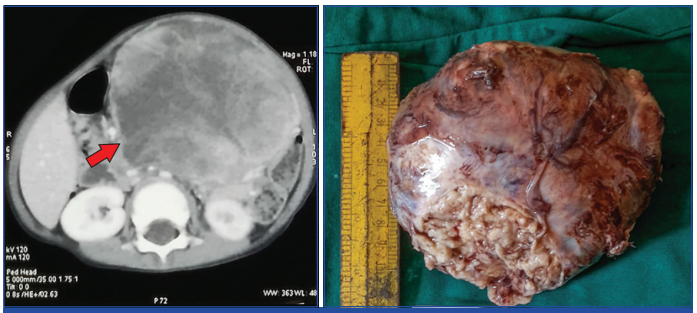
A three-year-old male child presented with an abdominal swelling which the parents reported as being insidious in onset and rapidly progressive in nature. The child had a normal developmental history and was fully immunized.

Clinical examination yielded no significant findings apart from a single, smooth, hard, 12x10 cm mass in the umbilical region extending from the epigastric region to left lumbar region and right hypochondrium. All routine investigations were within normal limits. Liver Function Test (LFT) revealed elevated liver enzymes. C-Reactive Protein (CRP) was elevated and PT, aPTT values were prolonged. An ultrasound scan of the abdomen showed a large mixed echoic mass in the epigastrium (9.4 x 9.3 cm) behind the stomach, abutting the body and tail of the pancreas, the radiological diagnosis for which was suggested to be “pancreatic mass” or “adrenal cyst”. A CT scan of the abdomen revealed a large well defined lesion (10 x 8.8 x 10 cm) in the epigastric region extending from subhepatic region to level of umbilicus. Multiple hypodense lesions were noted in both lobes of the liver, the largest being in the right lobe (1 x 1 cm) [Table/Fig-1]. A radiological diagnosis of mesentric tumour or primitive neuroectodermal tumour with liver metastasis was posited. Serum AFP levels (5799.9 IU/ml) and serum Lactate Dehydrogenase (LDH) levels (1777 IU/ml) were found to be markedly raised and serum beta Human Chorionic Gonadotropin (HCG) was also found to be mildly raised (2.0 IU/ml).

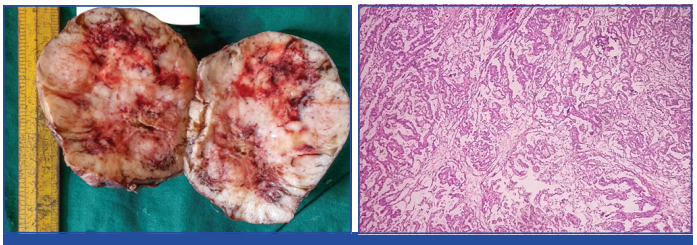
CT guided trucut biopsy of the mass was performed, which on histopathological examination suggested the possibilities of yolk sac tumour or hepatoblastoma. Following this, an exploratory laparotomy was performed and the retroperitoneal mass was excised. The specimen received was a large nodular, capsulated grey brown mass which showed a breach in the capsule on one aspect. The mass measured 14.5 x 12 x 7 cm and weighed 636 gm. Cut surface of the mass was soft, grey-white, with a few cystic spaces filled with brown mucoid fluid, and small areas of haemorrhage noted [Table/Fig-2,3].

On microscopy, sections showed tumour cells arranged in a variety of patterns including glandular-alveolar, microcystic/reticular, macrocystic solid nests and singles [Table/Fig-4]. These tumour cells had large, pleomorphic, vesicular nuclei with prominent nucleoli. The cytoplasm was scant, vacuolated and eosinophilic. Tumour cells also showed marked nuclear atypia with many atypical mitotic figures. At many places, the tumour cells were arranged in glomeruloid structures, surrounding a blood vessel (Schiller-Duval bodies) [Table/Fig-5]. The fibrocollagenous stroma was loose and oedematous with mixed inflammatory cell infiltrate. Areas of haemorrhage were seen. On staining with PAS, many PAS positive hyaline globules were noted [Table/Fig-6]. Immunohistochemistry was done with cytokeratin AE 1/3 and the tumour cells showed diffuse cytoplasmic positivity [Table/Fig-7]. With the above histopathological features, a diagnosis of a pure primary retroperitoneal yolk sac tumour was made.

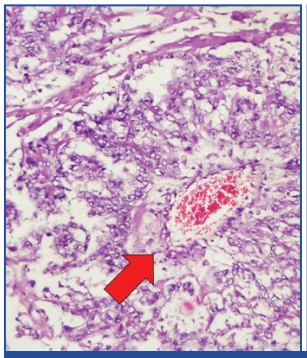
Post-surgery, the patient was started on chemotherapy with cisplatin, etoposide and bleomycin. Following six cycles of chemotherapy, the AFP levels were back to normal (2 IU/ml) and the child is doing well with no signs of disease on six month follow up. The lesions in the liver were determined to be fibrosis and not metastasis as initially thought.

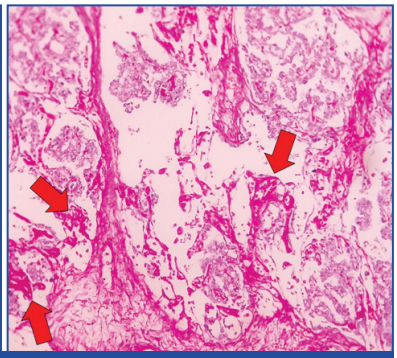


[Table/Fig-1]: CT: Axial section showing the large retroperitoneal mass (Arrow). **[Table/Fig-2]:** Gross picture showing the outer surface of the mass.

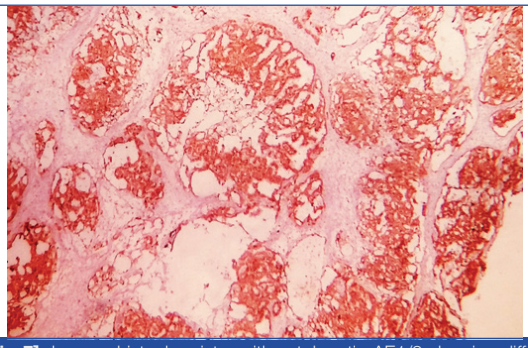


[Table/Fig-3]: Gross picture showing the cut surface of the mass which was grey-white, with a few cystic spaces filled with brown mucoid fluid, and small areas of haemorrhage. **[Table/Fig-4]:** Microphotograph showing the microcystic/reticular arrangement of tumour cells (H&E; 4X).





[Table/Fig-5]: Schiller-Duval body (Arrow) (H&E; 40X). **[Table/Fig-6]:** PAS positive hyaline globules seen (Arrows) (H&E; 40X).



[Table/Fig-7]: Immunohistochemistry with cytokeratin AE1/3 showing diffuse cytoplasmic positivity (IHC; 10X).

DISCUSSION

GCTs account for approximately 3% of all malignancies in children younger than 15 years of age [1,2]. Histologically, GCTs can occur in pure or mixed form (tumour is composed of two or more histological types), with mixed forms accounting for 32-54% of all GCTs [3].

GCTs in children show remarkable variability in age, site, presentation and histology [4]. They can be gonadal or extragonadal in site. GCTs in extragonadal sites arise from remnants of progenitor germ cells during its migration to the developing gonadal ridge [5]. These extragonadal tumours usually occur in midline locations (mediastinal, retroperitoneal, sacrococcygeal or cranial) [4]. Klinefelter's is the only known predisposing factor [6]. Primary extragonadal GCTs constitute only 1-5% of all GCTs and a retroperitoneal site is seen only in 4% of all extragonadal GCTs [5].

Patients with retroperitoneal GCTs usually present late, after their tumours have reached large dimensions. The presenting symptoms are usually an abdominal mass which may or may not be associated with pain, backache and weight loss. The international consensus classification makes no distinction between a primary GCT arising in the testis and one arising retroperitoneally. So, all diagnostic, therapeutic and prognostic criteria for a primary GCT from the testis apply to a retroperitoneal GCT as well [7].

Yolk Sac Tumour (YST) also known as "endodermal sinus tumour" or "orchioblastoma" is a type of GCT. YSTs show a bimodal distribution with an increased incidence in the first four years of life and then during the 2nd to 4th decade of life. YSTs constitute about 20% of all malignant GCTs [8]. Pure or mixed YSTs have been seen to occur in extragonadal sites such as mediastinum, the sacrococcygeal region, the pineal gland, and the female reproductive tract such as vagina, vulva, and uterine corpus [6]. Compared to these sites, the abdomen, pelvis and retroperitoneum are relatively uncommon sites [6].

A YST is characterised by numerous patterns that recapitulate the yolk sac, allantoin and extra embryonic mesenchyme [3]. Grossly, YSTs are white-grey or grey-yellow tumours with areas of necrosis and haemorrhage [8].

Microscopically, the appearance of YST is the same regardless of patient age and primary site [3]. Several different patterns are usually present in varying proportions, though one pattern may predominate. YSTs that present with only one histological pattern are exceedingly rare [3]. Some of these patterns include microcystic/reticular pattern, macrocystic pattern, solid pattern, glandular-alveolar pattern, endodermal sinus pattern, papillary pattern, myxomatous pattern, polyvesicular vitelline pattern, hepatoid pattern and enteric pattern [3]. Schiller–Duval bodies are a hallmark of YST [3]. YSTs contain intra- and extracellular PAS positive hyaline globules [8]. Serum AFP levels are elevated in patients with YSTs and serial monitoring of serum AFP levels is useful for diagnosing YSTs and also in monitoring the response to therapy and prognosis [8]. Immunohistochemically, YSTs are positive for AFP, CK AE1/AE3, Glypican-3, SALL4 and are negative for EMA and CK7 [8,9]. A negative CD30 and beta-HCG on immunohistochemistry can help rule out the mixed components of embryonal carcinoma and choriocarcinoma respectively [9].

Pure primary extragonadal retroperitoneal YSTs of children less than 15 years of age are extremely rare. Mixed GCTs are more common and are usually secondary to a primary testicular tumour. However, ours is a pure primary YST in a retroperitoneal location in a very young child and as such is only the 8th such case in literature. There was one seen in a 15 month child reported in 1976 [10] and another case was reported in 1981 [11]. Two cases of paediatric pure primary retroperitoneal YSTs were reported in 1985 [12] and one case in 1993 [13]. Recently in 2013, one case was reported in a 28-month-old child [14] and another in 2014 in an eight-month-old child [15].

The treatment for YST includes surgery and cisplatin based neoadjuvant chemotherapy (3-6 cycles of cisplatin, bleomycin and etoposide) which has been found to be quite effective and gives a good prognosis [4,5,15].

CONCLUSION

Pure primary extragonadal retroperitoneal YST are extremely rare and usually seek attention only when they reach a considerable size. A high AFP value with a large retroperitoneal mass should always raise the suspicion of such a tumour. Morphology of these tumours is characteristic and the role of immunohistochemistry is limited to cases with a suspected mixed component.

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Oct 18, 2016**
Date of Peer Review: **Nov 03, 2016**
Date of Acceptance: **Dec 11, 2016**
Date of Publishing: **May 01, 2017**