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CLINICOPATHOLOGICAL PROFILE OF WILMS' TUMOR: STUDY FROM A TERTIARY CARE HOSPITAL

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ABSTRACT

Introduction: Nephroblastoma or Wilms' tumour is the most common primary renal malignancy of childhood. Most often they are found in children 2 to 4 years old (median age for males and females respectively are 37 and 43 months).[1] The most important prognostic indicators for Wilms' tumour are the histologic subtype and the stage at presentation. Despite being a malignant tumour, a survival rate of over 90% seen today due to the use of multimodal therapy.[2,3] The purpose of this study is to look at the morphological patterns of Wilms' tumour **Material and Methods:** This is a prospective study of the cases of Wilms' tumour in our institution over a 2- year period (from july 2016 to july 2018). The nephrectomy samples were received and grossing was given protocol. It was processed and stained with routine H and E stain. All cases were subjected to WT1 and Ki67 immunohistochemistry. **Result:** In this study, 28 patients had Wilms tumour with males 16(57.1%) and females accounting 12(42.9%). 15(53.6%) of the tumours were located on the right side while 13(46.4%) were seen on left side. Most of the tumours weighed between 501-1000 grams representing 11(39.2%). Necrosis was observed in 92.8% cases. 89.2% cases in histology exhibited triphasic morphology. **Conclusion:** The predominant histological pattern of Wilms' tumour in our study is the triphasic pattern. It is most common in children between the age 2 to 4 years with average tumour weight of between 501 to 1000 grams.

KEYWORDS: Wilms' tumour, Favourable histology, WT1 IHC.

INTRODUCTION

Wilms' tumours comprise more than 80% of renal tumours of childhood.[4] It affects approximately 1 in 8000 children. [5] Most often they are found in children 2 to 4 years old (median age for males and females respectively are 37 and 43 months), they are relatively uncommon in the first six months of life and in children older than 6 years. Wilms' tumours are rare in the neonatal period. There is a slight preponderance of females. It is associated with a number of recognized syndromes including WAGR, Beckwith-Wiedemann syndrome, Denys-Drash syndrome, associations with congenital anomalies, specifically cryptorchidism, hypospadias, other genital anomalies, hemihypertrophy, and aniridia are well recognized.[4] It is rare in adults and the stage at presentation and frequency of anaplasia are higher than in children and response to therapy is poor. The most important prognostic indicator for Wilms' tumour in histology is anaplasia basing on this it is further categorized into favourable or unfavourable histologies. Anaplasia is rare during the first 2 years of life, and increases in prevalence to approximately 13% by 5 years of patient age.[5] Wilms' tumour generally have a restricted pattern of metastasis, most commonly to the regional lymph nodes,lungs and liver. Other metastatic sites such as bone or brain are unusual. Approximately 10-15% of sporadic Wilms' tumours harbour mutations in the Wilms' tumour-1 protein (WT1) gene. Overexpression of both wild type and mutant WT1 has been reported.[6,7] WT-1 protein is encoded by WT1 gene located on chromosome 11p13. It is a 4 zinc finger DNA binding transcription factor that plays a critical role in kidney development and differentiation. The WT1 gene was originally considered as a tumour suppressor gene, but later studies have shown the overexpression of WT1 mRNA in various solid tumours highlighting its oncogenic potential as well.[8] In normal adult tissue, it is expressed in mesothelium, glomerular podocytes, CD34 positive haematopoietic stem cells, sertoli cells of testis, stromal cell, surface epithelium and granulosa cells of the ovary, myometrium.[9] The WT1 protein has been demonstrated in myeloid leukaemias, malignant mesothelioma, malignant melanoma, glioblastoma, ovarian serous adenocarcinoma and osteosarcoma. Despite a malignant tumour, a survival rate of over 90% is now seen today

(compared to 30% in thirties) and this resulted from success of collaborative trials & use of multimodal therapy.[3]

MATERIALS AND METHODS

This study was conducted from July 2016 to July 2018 in Department of pathology SCB Medical college.

This is a prospective study. Clinical data including history, investigations like USG or CT scan of abdomen were taken.

Sampling technique: After surgical removal all intact nephrectomy specimens were received in our department. The surface of the specimens were photographed and inked to facilitate the recognition of displacement artifacts from the smearing of tumour cells over the specimen surface during sectioning, as well as to evaluate margins. It was fixed in 10% neutral buffered formalin 18-24 hrs. During grossing of the samples adequate attention was paid to any obvious degenerative changes like haemorrhage, necrosis. The tumour size in largest diameter, site, weights were recorded. Renal vein inspected for tumour thrombus, as this is a common route by which Wilms' tumour exits the kidney. One microscopic section per centimeter of maximal tumour diameter were taken. Random tumour sections taken from the periphery of the tumour, as this is where the invasive pattern of the tumour can be identified and interface with the capsule and native kidney can be evaluated. The most important sections were those taken from regions of sinus adjacent to the tumour to demonstrate involvement of sinus vessels. It was then fixed & embedded in paraffin wax according to standard protocol. Sections cut at 3-4 microns & stained with routine H & E stain.

Histopathology: depending on presence of blastema, epithelium and stromal components histologic type whether monophasic, biphasic or triphasic were reported and degree of anaplasia noted.

All the cases were subjected to mouse monoclonal WT1 antibody. The fraction of positively stained tumour cells was scored semi-quantitatively after examining under 10 high power fields(x400) for each case. Nuclear/cytoplasmic staining in >10 percent of tumour cells was required to define WT1 positivity. Immunohistochemical results for WT1 were scored as weak (11-25%-1+), moderate (26-50%-2+) and strong(>50%-3+).[10]

These were all recorded in a pre-designed data form. Statistical analysis was done by using SPSS software.

OBSERVATION

Table no 1: Age and sex distribution.

Age group(n=28)	Male (16)	Female (12)
<2 yrs	01(3.5%)	00
2-4yrs	13(46.4%)	05(17.8%)
5-7yrs	01(3.5%)	06(21.8)
8-10yrs	00	01(3.5%)
>10yrs	01(3.5%)	00

In the present study 16 cases were males and 12 cases were females. Majority of patients 16 lied in the 2-4 years of age group.

Table no 2: Frequencies.

		Sex		
		Male	Female	Total
Position of tumour	Left	07	06	13(46.4%)
	Right	09	06	15(53.6%)
Weight in grams	<500	00	02	02(7.1%)
	501-1000	04	07	11(39.2%)
	1001-1500	06	03	09(32.1%)
	1501-2000	02	00	02(7.1%)
	>2000	04	00	04(14.5%)

The above table showed 15(53.6%) cases were detected on right side. 11(39.2%) cases measured 501-1000 grams.

Table no 3: Clinical features.

Clinical features	No of patients	Percentage
Pain, lump, hematuria	03	10.7%
Pain in abdomen	02	7.1%
Lump in abdomen	24	85.7%
Hematuria	05	17.8%
Others (fever, weight loss)	03	10.7%

Majority of patients presented with lump in abdomen (85.7%) followed by haematuria.

Table no 4: Gross findings.

Total no of cases(28)	Present	Absent
Necrosis	26(92.8%)	02(7.2%)
Haemorrhage	27(96.4%)	01(3.6%)
Cystic degeneration	18(64.2%)	10(35.8%)

On gross inspection necrosis was present in 92.8% of cases and haemorrhage was noted in 96.4% of cases.

Table no 5:- Histopathology type.

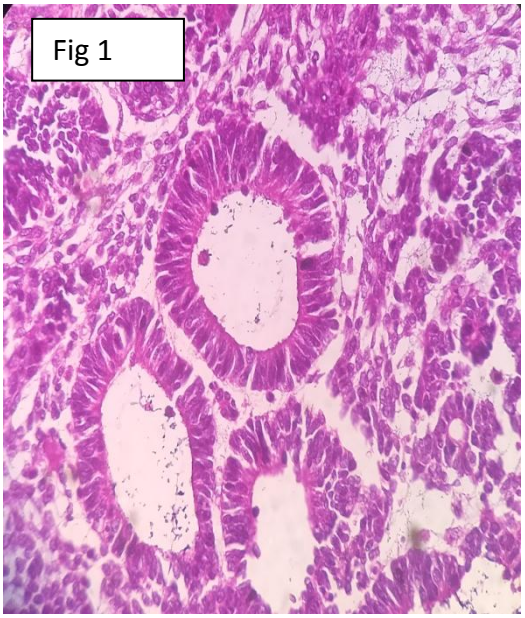
No.of cases studied (28)		
Triphasic	25	89.2%
Biphasic	02	7.1%
Monophasic	01	3.7%
With favourable histology	27	96.4%
Without favourable histology	01	3.6%

In the present study triphasic histological pattern was present in 89.2% cases, biphasic pattern in 7.1% cases and monophasic pattern in 3.7%. only one case showed without favourable histology.

Table no 6: WT1 immunostaining.

n =28	No of cases	Cases positive for WT1	%positivity	Intensity of immunostaining
Stromal component	26	12	42.8	1+(nuclear)
Epithelial component	27	20	71.4	2-3+(nuclear)
Blastemal component	27	22	78.5	2-3+(nuclear)

WT1 expression was higher in blastemal component (78.5%) showed 2-3+ immunoreactivity followed by in epithelial component(71.4%). In stromal component WT1 expression was found in 42.8% cases with 1+ immunoreactivity.



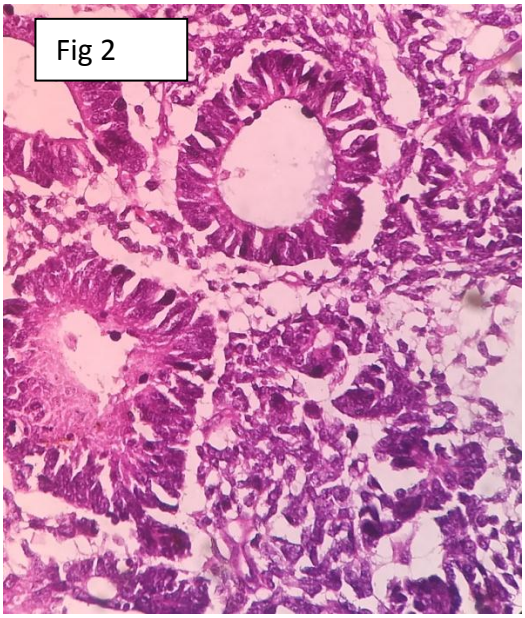


Fig no. 1 Triphasic Wilms tumour comprising of blastemal, epithelial,stromal elements (H&Ex 100).
Fig no. 2 Biphasic Wilms tumour comprising of blastemal and epithelial elements (H&Ex 100).

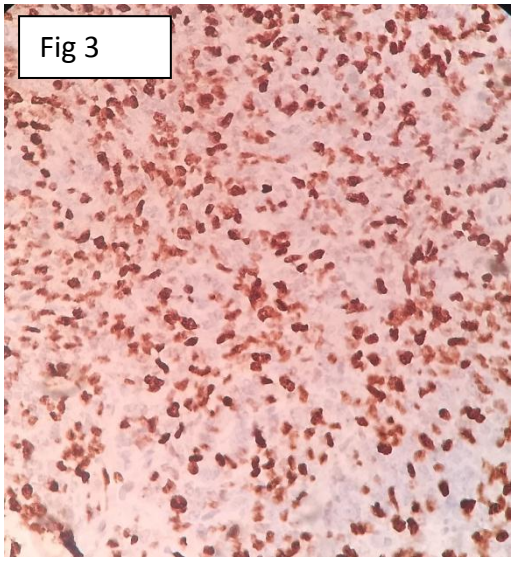


Fig no. 3 Blastemal component showing strong nuclear WT1 staining X100.

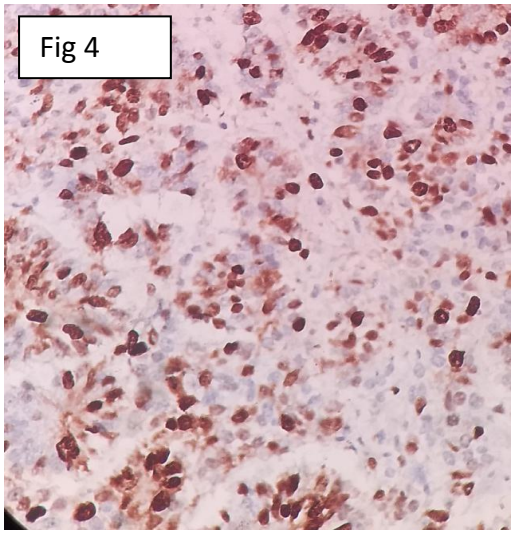


Fig no. 4 Epithelial component showing strong nuclear WT1 staining.

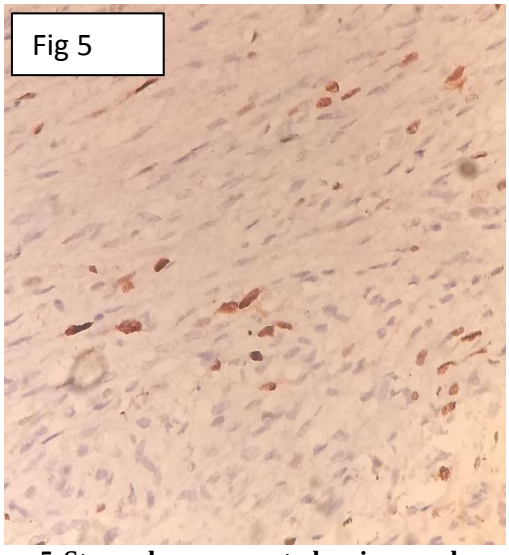


Fig no. 5 Stromal component showing weak nuclear WT1 staining.

DISCUSSION

Wilms' tumours are typically composed of variable mixtures of blastema, epithelium and stroma, although in some tumours only two and occasionally only one, component is present. Blastema consists of sheets or randomly arranged densely packed small cells with darkly staining nuclei, frequent mitotic figures, and inconspicuous cytoplasm, resembling to some extent, other small blue cell tumours of childhood. Blastema is commonly arranged in three patterns serpentine, nodular and diffuse. Serpentine and nodular are most common and diagnostically helpful. They consist of anastomosing serepiginous or spheroidal aggregates of blastema sharply circumscribed from the surrounding stromal elements. The epithelial component usually consists of small tubules or cysts lined by primitive columnar or cuboidal cells. The nuclei of the epithelium are often elongate and wedge shaped. The epithelium of Wilms tumour may also form structures resembling glomeruli or may differentiate in extrarenal directions being mucinous, squamous, neural or endocrine in type. Wilms' tumour's stroma may differentiate along the lines of almost any type of soft tissue. While loose myxoid and fibroblastic spindle cell stroma are most common, smooth muscle, skeletal muscle, fat, cartilage, bone, and neural components also occur.[1]

Wilms' tumours are divided into two categories :favourable and unfavourable histologies, based on the absence or presence of anaplasia. Anaplasia is found in approximately 6% of Wilms' tumours; it is rare in patients younger than 1 year and more than 80% of affected patients are older than two. Anaplasia has been defined by the NWTS as the combination of cells with very large hyperchromatic nuclei and multipolar mitotic figures. For correct recognition of anaplasia recquires proper fixation, sectioning, and staining. The enlarged nuclei must be at least three times as large as typical blastemal nuclei in both axes and their hyperchromasia must be obvious. In addition to the enlarged nuclei, hyperdiploid mitotic figures must be present.

Wilms' tumours are generally found in children between the ages of 2 and 4 years with median age for males and females of 37 and 43 months respectively.

Male to female ratio 1.3:1. Most of the tumours weighed between 501-1000 grams. Incidence is more on right side (53.6%) which is slightly more than that of left side(46.4%). Incidence for Wilms' tumour was almost equal (0.97:1) in series of Bennington. M:F ratio was 1.27:1 in the study conducted by B Guruprasad et al[11] which is similar to our study. In the series of Bernard[12] incidence of Wilms' tumour on left side 51.8% and 39.2% on right side.

D' Angio et al[13] found maximum incidence of Wilms' tumour below the age of 7 years (90%). Howard et al[14] reported 75% incidence between the age of 1 and 5 years

and 90% below the age of 7 years. In our study 71.3% cases were present below 7 years.

Our patients had lump in abdomen 85.7% of cases. Hematuria was present in 17.8% of cases and pain in abdomen 7.1% of cases. Constitutional symptoms like fever, weight loss were present in 10.7% of cases. This study was similar to the study conducted by V Hajgude et al[15] abdominal lump was found in 92.3% of cases, hematuria was present in 8.7% of cases pain in 8.7% of cases.

Out of the 28 cases WT1 immunostaining was moderate to strong positivity seen in 78.5% of blastemal component, 71.4% of epithelial component and 42.8% of stromal component which is weak in intensity. Our study was compared with S Goyal et al[16] in their study blastemal component showed 75% positivity with moderate to strong immunostaining, 80% positivity in epithelial component and 44.4% positivity in stromal component with weak immunostaining. According to Miwa et al.[17] WT1 protein is expressed at high levels in Wilms' tumours having wild type genotype and blastema / epithelial predominant histology. WT1 expression is limited to stromal component due to developmental arrest mediated by mutated WT1 gene. It appears that WT1 controls genes which mediate mesenchymal to epithelial transition during embryonic kidney development. In our study 20 cases showed moderate to strong nuclear WT1 positivity in blastema and epithelial components. This localization pattern of WT1 was comparable with that reported in foetal kidneys.

CONCLUSION

Overall survival of over 85% of patients with Wilms' tumour can now be achieved using combination therapy with chemotherapy, surgery and in some cases radiotherapy.[18] WT1 immunostaining helps to differentiate Wilms tumours from other paediatric renal tumours.

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