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Case Series

Pathology Section

Adult Wilms Tumour Cases Masquerading as Renal Cell Carcinoma

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ABSTRACT

Wilms tumour is the most common paediatric renal tumour but is extremely rare in adults. The real incidence of this tumour is unavailable in literature as majority are only case reports because of its rarity. We present 3 cases of Wilms tumour that occurred in male patients in 3-5 decade of life following Kilton's criteria. There are no strict guidelines for its management. NWTS suggested combination therapy of surgery, radiation and chemotherapy were found to be beneficial to reduce recurrence and metastasis. We present 3 cases of Wilms tumour in a 12 year study, which occurred in adult males with characteristic histology and Stage I and III disease at diagnosis.

Keywords: Kilton's criteria, Renal cell carcinoma, Triphasic Wilms

Wilms tumour is the 5th most common malignancy in children [1] and accounts for 7% of all tumours of that age group and noted for its good therapeutic response with a survival rate of 75% at 5 years [2]. Its incidence said to be 1 in 10,000 with slight female preponderance and 70% of them occur below the age of 5 years [3]. Majority are unilateral tumours and less than 10% cases are bilateral [3]. About 10% cases exhibit syndromic presentation with associated congenital anomalies. The cause for development of these tumours is attributed to two genes *WT1* and *WT2*, both are represented on the small arm of chromosome 11 in positions 13 and 15 respectively. Its occurrence in adults is rare; majority in literature are case presentations rather than studies except for a few.

CASE SERIES

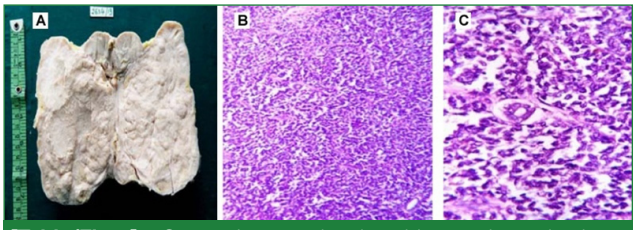
In our study on adult nephrectomy specimens with patient consent, between years 2005-2017; a span of 12 years in a teaching hospital in rural setup, there were a total of 62 nephrectomies performed on tumourous kidneys in adults. The most common tumour was renal cell carcinoma and its various histological subtypes (48 cases). The others were renal oncocytoma (3), angiomyolipoma (4), transitional cell carcinoma and squamous cell carcinoma; two cases of each arising from renal pelvis. three of these cases clinically and radiologically diagnosed as renal cell carcinoma were histologically confirmed as Wilms tumours.

Case-1

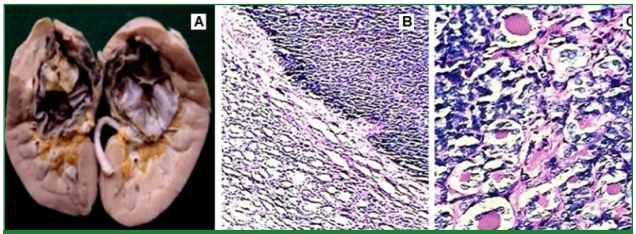
A 24-year-old male presenting with pain and palpable mass in left loin since 15 days. Left radical nephrectomy with perihilar lymphnode resection was done on provisional clinical and ultrasound diagnosis of renal cell carcinoma. The lower pole of left kidney showed a tumour mass of 17x12x8 cm size encroaching upon renal pelvis [Table/Fig-1].

Case-2

A 29-year-old male patient presented with pain in left loin, burning micturition and fever of 10 days duration. There was no mass palpable per abdomen and no haematuria. All his vitals, haematological profile and urine tests were normal. CT-scan of left kidney revealed a well defined



[Table/Fig-1]: Case-1-Image showing blastemal predominant Wilms tumour (PAS-), with a primitive tubules in 24 years old male patient. a) Gross; b) H and E (x100); and c) H and E (x400).



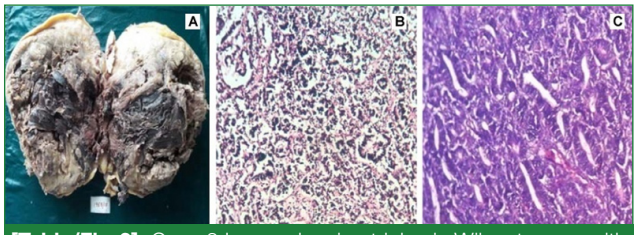
[Table/Fig-2]: Case-2-Image showing cystic Wilms tumour with primitive blastema and epithelial component in 29 years old male patient. a) Gross; b) H and E (x100); and c) H and E (x400).

fluid filled multilocular cystic lesion with hyperdense area of haemorrhagic attenuation in upper pole. A provisional diagnosis of cystic renal cell carcinoma was made [Table/Fig-2].

Case-3

A 53-year-old male patient admitted with the chief complaints of abdominal pain, mass in left loin and haematuria of 5 days duration. On CT-scan there was a mass of 25x20 cm in left kidney with arterial encasement and pseudo aneurysm formation along with internal solid/cystic/haemorrhagic areas, there were blood clots in bladder, no regional lymphadenopathy, no solid organ/bony metastases and no renal vein/IVC involvement but, there was varicocoele on same side [Table/Fig-3].

The present cases were diagnosed as Wilms tumours on histology basing on Kilton's criteria [4] on nephrectomy specimens. Two of the cases presented with pain in loin with large palpable masses at presentation except the predominantly cystic Wilms tumour that occurred in 29 years old male. Case 2 and 3 both had been radiologically evaluated from another diagnositc centre and referred to our hospital for surgical procedure. All histologically showed triphasic growth pattern with variable amounts of the three components; no anaplasia noted (favourable histology) in any of these cases and no heterologous differentiation either in epithelial or stromal component. Differential diagnosis included undifferentiated renal cell carcinoma and peripheral neuro ectodermal tumour for Case 1, cystic renal cell carcinoma and cystic partially differentiated nephroblastoma for Case 2. Case 3 showed classical triphasic pattern on initial sampling. IHC was not needed in Case 1 or Case 2 as both the cases showed classical triphasic histology on further sampling and histopathological examination. *WT1* gene mutation was confirmed only in one of these patients due to financial constrains. There were no other anomalies in these patients; all were treated as per NWTS-G3 guidelines (surgery and chemotherapy: actinomycin D, vincristine and doxorubicin for 15 months) [Table/Fig-4]. Follow-up was available in case 3 only, where there was no metastasis after 1 year of treatment. Other two cases could not be followed-up.



[Table/Fig-3]: Case-3 Image showing triphasic Wilms tumour with epithelial and blastemal components in 53 years old male patient. a) Gross; b) H and E (x100); and c) H and E (x400).

DISCUSSION

Nephroblastoma/Wilms tumour was named after the 19th century German surgeon Carl Max Wilhelm Wilms [5], is the most common malignant renal tumour in children [6]. According to Beckwith and Bennington, Wilms tumour represents a piece of developing kidney, persisted at an embryonic stage where growth is continuous and excessive and the differentiation is abortive and imperfect [7].

According to Bove and Mc Adams, Wilms tumour arises from nephrogenic rests. Nephrogenesis is essentially complete by 35 weeks of gestation; after which the blastemal cells usually disappear. Persistent nephrogenic blastema in postnatal life; either of perilobar or intralobar location are the source of Wilms tumour in later life [8].

Total 240 cases of Wilms tumour in adults have been reported in a recent study [9]. Kilton L et al., reported 35 cases of adult Wilms' tumour based on the Kilton criteria given by Kilton L et al., [4]. These include: patient's age >15 years, presence of primary renal neoplasm, presence of primitive blastemal spindle or round cells, with attempt at formation of embryonal tubules or glomerular structures, no areas diagnostic of renal cell carcinoma and pictorial confirmation of histology [6,10,11].

Kilton L et al., postulated the guidelines to diagnose Wilms tumour in adults as there are many other tumours occurring in adults that mimic Wilms tumour. They have selected only 35 cases as real adult Wilms tumour out of 195 documented cases strictly basing on the 6 criteria proposed [6,10,11].

Cystic Partially Differentiated Nephroblastoma (CPDN) and Cystic Wilms tumour are a spectrum of related clinical and pathologic entities. While CPDN is better differentiated and considered as benign, Cystic Wilms tumour is less differentiated and malignant. However, CPDN may show aggressive behaviour and has a tendency for recurrence following surgery due to the presence of blastemal cells in septa, despite the usual benign course of the tumour [12]. In the present study the case clinically suspected as cystic renal cell carcinoma was initially diagnosed as CPDN on core

Clinical Findings	Radiographic Findings	Histomorphology
Case 1: 24/Male, pain and palpable mass in left loin since 15 days	Left kidney, lower pole mass, 17x12x8 cm, encroaching on renal pelvis-? Renal cell carcinoma	Blastemal predominant Triphasic Wilms, No anaplasia.
Case 2: 29/Male, pain in left loin, fever and burning micturition since 10 days	Well defined multilocular cystic lesion with hyper dense are as in upper pole of left kidney-? Cystic Renal cell carcinoma	Cystic Wilms primitive blastemal and epithelial component, No anaplasia.
Case 3: 53/Male, pain and mass in left loin and haematuria since 5 days	Left kidney mass of 25x20 cm with arterial encasement and pseudo aneurysm formation-Renal cell carcinoma	Triphasic Wilms, No anaplasia.

[Table/Fig-4]: Case details

needle biopsy but, on nephrectomy the diagnosis of Wilms tumour was made, as it fulfilled Kilton's criteria [4].

Core needle biopsies are risky as wrong diagnosis is more than just a possibility because of patchy distribution of the components and should not be encouraged. Metanephric adenoma should be differentiated from adult Wilms tumour that exhibit mainly epithelial differentiation. A blastemal predominant Wilms tumour mimics small, blue round cell tumours like lymphoma, peripheral neuro ectodermal tumour and rhabdomyosarcoma; rarely metastatic small cell tumours from lung, immature teratoma, and primary renal cell sarcoma [10]. Renal cell carcinoma with sarcomatous areas should be distinguished from mesenchymal component of Wilms' tumour [13].

The NWTSG classifies Wilms tumour based on the presence of anaplasia, the revised SIOP histologic classification grades Wilms tumour into three risk groups:

Low risk group: Cystic partially differentiated nephroblastoma.

Intermediate risk group: Regressive, epithelial, stromal, mixed types, or focal anaplastic nephroblastoma.

High risk group: Blastemal type or diffuse anaplastic nephro blastoma.

The prognosis of high risk group (unfavorable histology) is very poor in adult Wilms tumour, but that of a low risk group or the epithelial histology is as in children [11].

Clinically and radiologically Wilms tumour resembles renal cell carcinoma [4]. Ultrasound observation of a rapidly growing abdominal mass, with heterogonous contrast uptake, that is surrounded by a pseudocapsule on CT is suggestive of Wilms tumour [10]. Most adults present with flank pain and haematuria and have a history of weight loss and of a sudden drop in performance status, in contrast to the palpable boggy mass which is more common in children. Adult Wilms tumour is larger in size, ill-defined, with areas of necrosis and haemorrhage [14]. About ten cases of extra-renal adult Wilms tumour were documented in the literature, four in the retroperitoneal region, two each in the ovary and endometrium; one each in ovotestis and prostate [4]. The majority of adult Wilms tumour patients are diagnosed in Stage II /III and die of metastatic disease [10]. Two of our cases (2 and 3) are of Stage I disease with no capsular infiltration or nodal spread. Case 1 was a Stage III tumour with capsular infiltration and two positive lymph nodes. After surgery and chemotherapy follow-up was possible in patient with Stage III disease and found to be disease free after 1 year.

Wilms tumour in adults has a worse prognosis than in the paediatric population, a phenomenon for which there is no adequate explanation [15] and as randomised trials couldn't be performed as it is rare. National Wilms Tumour Study (NWTS) and other studies have recommended multimodal therapy for the disease with surgery, chemotherapy (actinomycin D, vincristine and doxorubicin) for 15 months and tumour bed irradiation (4500 cGy) after surgery. Less aggressive therapy with two drugs is advised in Stage 1 and 2 disease [10]. The NWTSG has recommended preoperative chemotherapy under certain circumstances like presence of extensive symptomatic lung metastasis and for patients with refractory/recurrent disease. The results were encouraging. Use of cisplatin or cisplatin compounds; found to improve the prognosis of recurrent Wilms tumour in adults [10]. Recently, it has been reported that the overall survival is 83% with primary nephrectomy followed by adjuvant combination chemotherapy [16].

CONCLUSION

Wilms tumour in adults is a rarity and present as bulky variegated, irregular masses that clinically and radiologically appear like renal cell carcinoma. Core needle biopsies may result in erroneous diagnosis as they may not be adequate or represent the entire lesion; also as histological overlaps exist between various tumours that occur in adults, hence, thorough grossing and sampling is mandatory. In our study all patients were males, showed predilection for left kidney, mainly presented with pain and mass lesion and exhibited triphasic histology,

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