Nephroblastoma in adults. Clinical and histopathological features of two incidental Wilms' tumors

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KEY WORDS

Wilms' tumor ◗ nephroblastoma in adults ◗ rare kidney tumors ◗ incidental tumor

ABSTRACT

Nephroblastoma (Wilms' tumor) – the most common malignant renal tumor in childhood is extremely rare in adults. Early diagnosis is difficult and usually made by pathologic examination of a surgical specimen. The possibility of successful treatment and therefore prognosis of nephroblastoma in adults is poorer when compared with results in children. Here authors report 2 cases of nephroblastoma incidentally diagnosed in adult age and demonstrate the diagnostic challenges and distinct histopathological features of nephroblastomas in the adult age group.

Authors present results of imaging diagnostic techniques and histopathological as well as immunohistochemical findings.

As a result of analysis of clinical data, histopathological findings, and immunohistochemical results both analyzed patients were regarded as cases meeting criteria of favorable histology with low or intermediate risk of progression.

INTRODUCTION

Wilms' tumor (nephroblastoma) is the most common malignant kidney tumor in children and accounts for 6% of all childhood malignancies [1, 2, 3]. Nephroblastoma is a very rare tumor in the adult age group. Only 3% off all Wilms' tumors are diagnosed in age over 16 and only near 300 cases have been reported in the world medical literature [2, 3, 4, 5]. This rare phenomenon was described by Polish authors also [6, 7, 8, 9]. The overall results of treatment and prognosis of nephroblastoma in adults are generally less favorable than in children.

In the presented paper the authors report two cases of incidentally diagnosed Wilms' tumors in adults and describe the tumor's characteristic histopathological and immunohistochemical features. Both cases demonstrate diagnostic and therapeutic challenges of childhood neoplasms, but occurring in adults.

CASES REPORTS

Case 1

Patient T.T. 25-year-old male was admitted to the department of urology due to aching pain in the right flank. Patient reported right side trauma caused by falling into a drainage catch pit a week earlier. He denied hematuria. General examination revealed mild tenderness located in right flank and mid abdomen. Routine laboratory tests (full blood count, urine examination, renal function tests) were within normal range. Chest x-ray did not reveal any ribs fracture.

A trans-abdominal ultrasound revealed a right kidney measuring 110 x 42 mm, with a hypoechoic mass, 40 mm in diameter, located in its lower part. The left kidney measuring 100 x 58 mm with an 8 mm hyperacoustic shadow (stone). All other abdominal organs were normal.

Computed tomography due to provisional diagnosis of right kidney hematoma was made. CT scan revealed a heterogenic, irregular hypoattenuated mass in the lower part of the right kidney measuring 60 x 73 x 88 mm with calcified areas and with contrast enhancement ranging from 37 to 47-62 HU. Scan analysis suggested intrarenal hematoma, neoplasm, or hemorrhage into the tumor mass. CT presentations of the other abdominal viscera were radiologically normal.

The patient underwent conservative treatment with provisional diagnosis of renal hematoma. On the 4th day, due to increasing pain located in mid abdomen and suspicion of recurrent intrarenal hemorrhage as well as the non-homologous picture of CT scan, inspection of the right retroperitoneal space and subsequent right radical nephrectomy were performed. Surgical procedure was done by transperitoneal approach. Nephrectomy with adrenalectomy and lymphadenectomy has been done because of large hematoma in the lower part of kidney, 8 cm long parenchymal tearing reaching renal collecting system, and due to the result of intra-operational histopathological examination revealing neoplasmic cells.

Pathological examination of the specimen revealed subcapsular renal tumor with a diameter of 5 cm with multiple solid nodular areas and foci of hemorrhage. Blastemic component with epithelial elements comprised 50% of the area. Immunohistochemical staining were as follows: vimentin (+), WT1 (+), proliferation index Ki67(+) up to 40%. No evidence of cellular anaplasia. The histopathological diagnosis of low-risk nephroblastoma was established.

The postoperative course was uneventful. On the 7th day after surgery the patient was admitted to the Oncology and Hematology Clinic for systemic polychemotherapy

Case 2

Patient A.B., 34-year-old male was admitted to department of urology from a local hospital due to aching loin pain radiating to scrotum with tenderness and enlargement of the left testis. Patient presented with hematuria for a week and reported mild lower back injury half a year before. General condition of the patient was

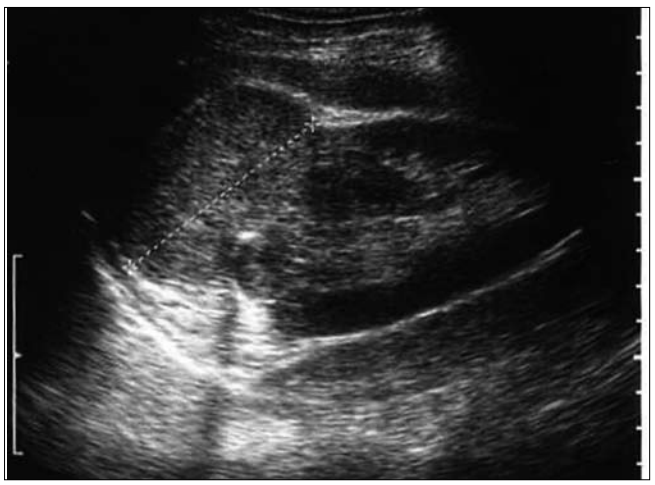

Fig. 1. Case I. Transabdominal ultrasound examination revealing a right kidney with a hypoechoic mass, 40 mm in diameter, located in its lower part.

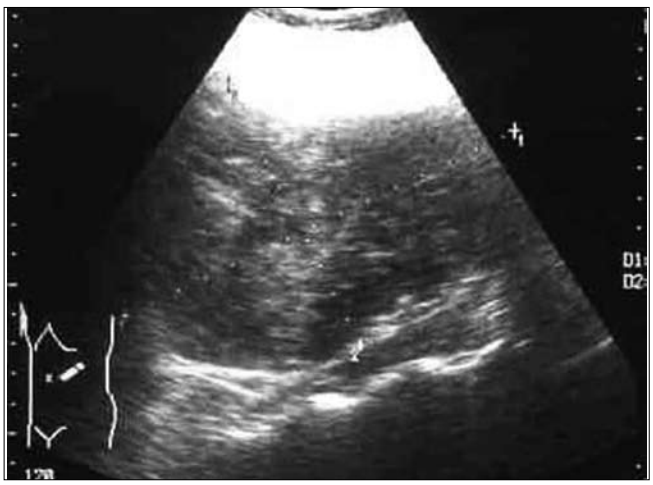

Fig. 3. Case II. Transabdominal ultrasound examination revealing blurred and irregular image of the left kidney.

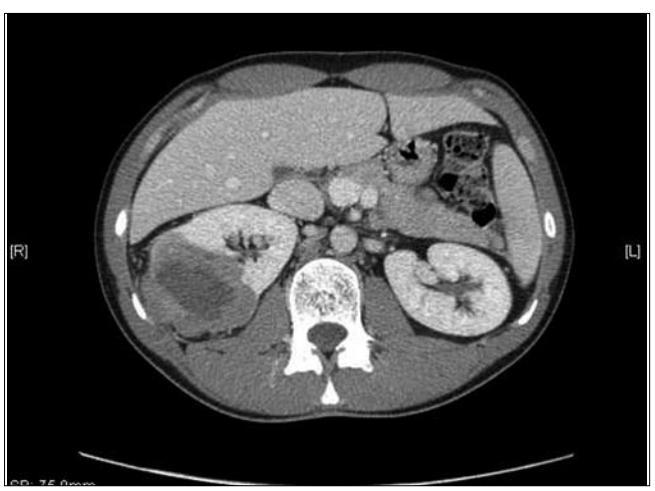

Fig. 2. Case I. CT scan of the right kidney: heterogenic, irregular hypoattenuated mass in the lower part measuring 60 x 73 x 88 mm with calcified areas. Contrast enhancement 37 to 47-62 HU.

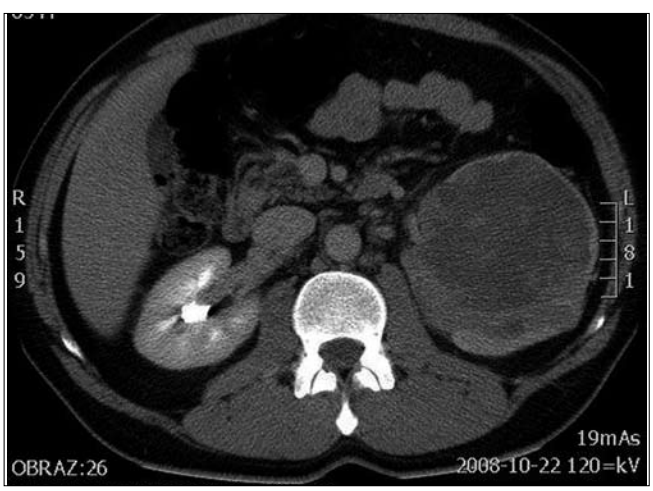

Fig. 4. Case II. CT scan revealing heterogenic, irregular hypoattenuated bulk mass in central part of left kidney, measuring 100 x 100 x 120 mm with infiltration of perirenal fat. Contrast enhancement 35 HU to 55-60 HU.

good. Routine laboratory tests were normal but urine examination revealed plenty of RBCs in high power field. An ultrasound examination showed normal right kidney measuring 115 x 55 mm and irregular left kidney measuring 125 x 59 mm with blurred image. The other abdominal organs were normal.

CT scan revealed heterogenic, irregular hypoattenuated bulk mass in central part of left kidney measuring 100 x 100 x 120 mm with contrast enhancement ranging from 35 HU to 55-60 HU and infiltration of perirenal fatty tissue. Scan suggesting disintegration of renal tumor mass with enlargement of para-aortal lymph nodes.

Left radical nephrectomy has been performed because of provisional diagnosis of hemorrhage into a disintegrated renal tumor mass. Inspection of left retroperitoneum revealed left kidney with tumor measuring 10 cm, occupying lower and central part of an organ and small amount of renal parenchyma in the upper part with small visible noduli. At cross-section of the specimen, focal hemorrhages were found.

Pathological examination of the specimen revealed a polycystic tumor measuring 11 cm and almost completely covering the kidney without microscopic evidence of capsular, renal pelvis, nor ureteral infiltration and subcapsular renal tumor of 5 cm in diameter with multiple solid nodular areas and foci of hemorrhage. Prevailing blastemic component with area of epithelial differentiation. Immunohistochemical reactions were as follow: NSE - neuron specific enolase (+), cytokeratin AE1/AE3 (+), S-100 (+), weak expression of WT1, proliferation index Ki67(+) 20-40% depending on the field, vimentin (-), chromogranin (-), synaptophysin (-). No evidence of metastases in lymph nodes and left adrenal gland. Postoperative course was uneventful and the patient was admitted to department of oncology for adjuvant chemotherapy.

DISCUSSION

Wilms' tumor (nephroblastoma) originates from embryonal metanephric blastema. It is the most common malignant renal tumor in childhood. The average age at diagnosis is 3.5 years. Synchronous bilateral Wilms' tumors account for 6% of all nephroblastomas. Some syndromes are associated with increased risk of such tumor. Among them are syndromes as: Beckwith-Wiedemann, Dash, Perlman, Soros, familial Wilms' tumor type 1 and 2, and WAGR (Wilms tumor [a tumor of the kidneys], aniridia (absence of the colored part of the eye, the iris), genitourinary anomalies, and mental retardation. Nephroblastomas can develop in association with inborn genitourinary defects like cryptorchidism, hypospadia, hemihypertrophy, and aniridia. Nephroblastoma is very rarely found in adults, but some advanced age cases (72- and 99-year-old) has been reported [13, 14]. The estimated incidence of Wilms' tumor in

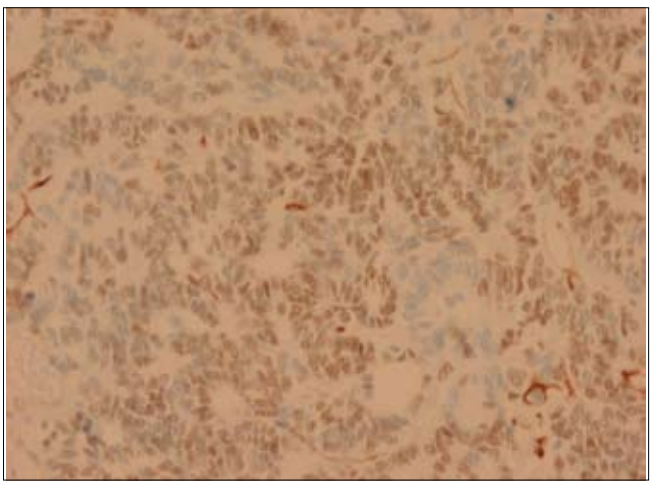

Fig. 5. Case I. Prominent immunoexpression of the WT1 studied in paraffin-embedded tissue section (20x).

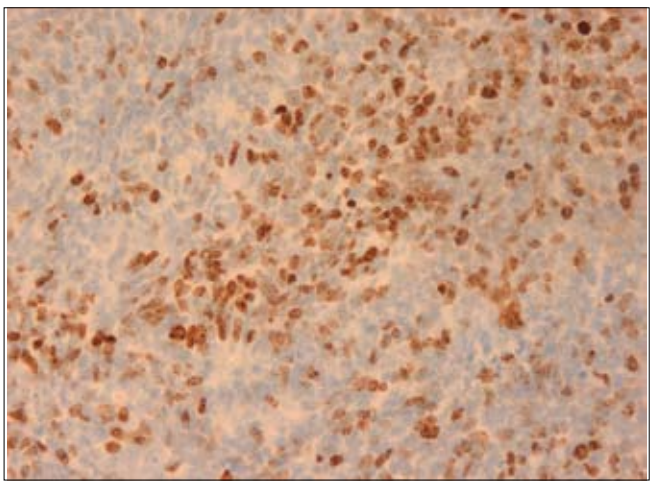

Fig. 7. Case I. Patterns of Ki67 immunostaining, expression of Ki67 40% (20x).

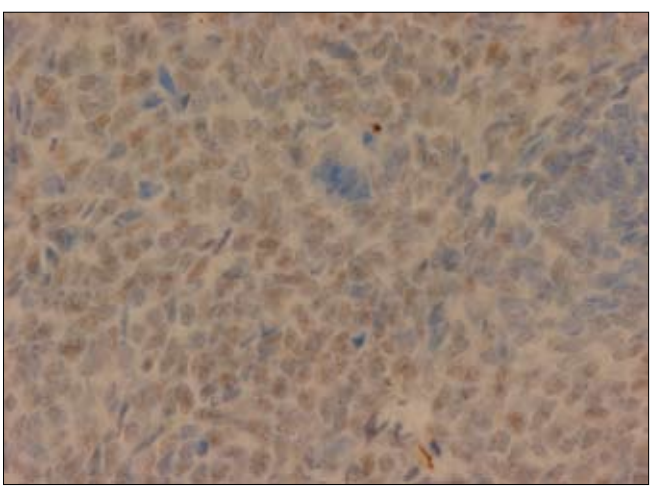

Fig. 6. Case II. Weak immunoexpression of the WT1 studied in paraffin-embedded tissue section (40x).

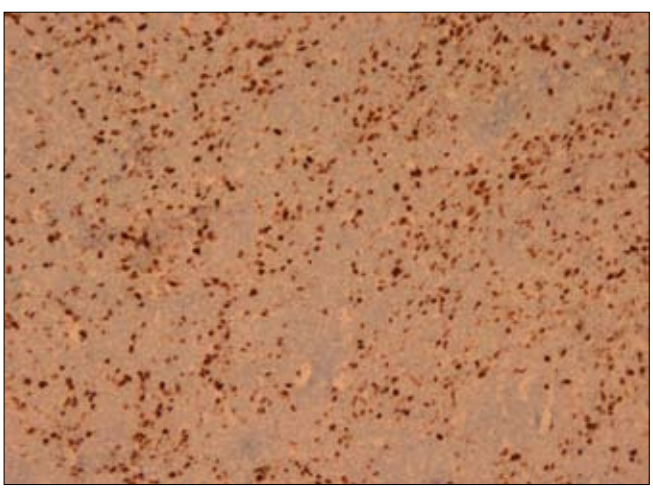

Fig. 8. Case II. Patterns of Ki67 immunostaining, expression of Ki67 20-40% (10x).

adults is about 0.2/1 mln/year [14, 16]. There is widely recognized opinion that in adults, nephroblastoma has less favorable histology and a worse prognosis than in the child age group [14, 16]. For instance, E. Mitry and co-workers analyzed a group of 143 patients and concluded that life span after diagnosis was 1 to 5 years and 2 times longer in female than in male group [14]. In advanced stages tumor gives hematogenous and lymphogenous metastases and in 40% of cases involves the renal vein. The most common manifestation of Wilms' tumor at diagnosis are abdominal mass, fever, hematuria, and is often accompanied by hypertension and coagulopathy [1, 2, 3, 4]. Tumor appears as a solid or polycystic mass. Histologic characteristic is the most important prognostic indicator and histopathological criteria for child and adult group are the same.

Histopathological presentation of both described above specimens revealed high cellular tumors with blastemic, epithelial and stromal cells. Blastemic cells with uniform, oval nuclei without the appearance of hyperchromasia and no area of atypia. There were no cells in metaphase and proliferation index (Ki67 – based evaluation) did not overdraw 40%. Expression of WT1 is not a constant feature of all nephroblastomas and correlates with histology of given tumor. WT1 is expressed in areas of blastema and early epithelial differentiation, but could be absent in mature stromal and epithelial elements. The same situation was seen in our presented cases – WT1 expression evident in the first case and very weak in the second case. Other immunohistochemical findings like: nuclear

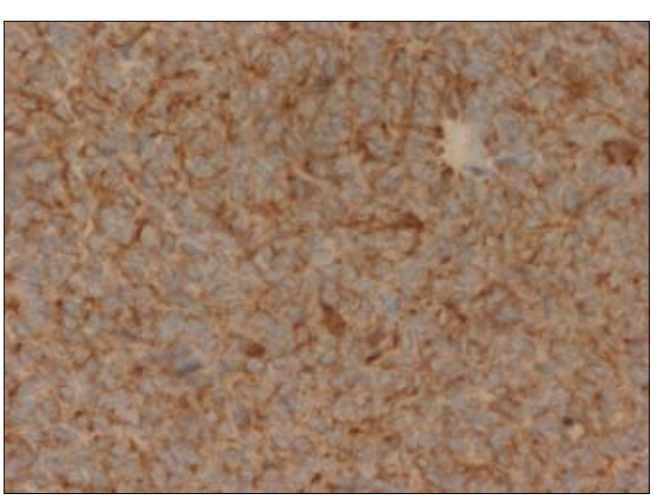

Fig. 9. Case II. Immunoreactivity for expression of cytokeratin AE1/AE3 (40x).

specific enolase, cytoceratin, S-100, vimentin, synaptophysin, chromogranin correlated with light microscopy presentation. This is proof for heterogeneous structure of this tumors with high admixture of epithelial and stromal elements.

Typical, „classic" histopathological presentation of Wilms' tumor is a "triphasic" tumor composed of undifferentiated metanephric blastema and spindle-shaped stromal cells surrounding nests of

epithelial cells. Epithelial component forms abortive glomerular and tubular structures which are present in various proportions. Beside this characteristic triphasic histologic appearance two- or even monophasic presentations can be found. Structural diversity can be emphasized by the presence of mature components like cartilage, osteoid, muscle or fatty tissue. In most cases (especially in children) surgical removal of the tumor is preceded by polychemotherapy. In such patients chemotherapy-induced changes are observed and then appropriate classification of prognostic value is used, including "regressive" histopathological changes of the specimen. For this reason, for staging and prognostic purposes, histologic classification covers two distinct subgroups: tumors that not require neoadjuvant chemotherapy (primary nephrectomy) and tumors which should be treated with neoadjuvant chemotherapy. Both are divided into tumors of low, intermediate or high risk. Presence of differentiated, mature elements and necrosis as well as anaplasia has a prognostic significance. Tumors are classified according to favorable versus unfavorable histology and finally patients are stratified into 3 groups [1, 18]. Treatment outcomes in adults with nephroblastoma with favorable histology are generally less successful than in children age group [3]. Due to its rarity, to be regarded as a nephroblastoma in adults, each Wilms' tumor must fulfill criteria defined by Kilton and coworkers: primary tumor in patient with age over 15, presence of blastemic cells and abortive renal tubules and glomeruli with no evidence of renal clear cell carcinoma [16, 17]. Additional diagnostic studies like immunohistochemical staining for expression of selected antigens (cytokeratins, desmin, vimentin, actin, WT1) are used to differentiate nephroblastoma from other rare tumors (renal sarcoma, mesoblastic nephroma, clear cell sarcoma CCSK, rhabdoid tumor of the kidney) [19].

Renal cell carcinoma accounts for over 90% of all kidney tumors in adults. Though it remains clinically occult for most of its course, a prevailing proportion of symptomatic patients is classified correctly and cured in early clinical stages. Rare kidney tumors occurring in adults, like those presented above, usually require additional treatment. For this reason, early diagnosis of Wilms' tumor in adults should help introduce an adequate treatment protocol. (similar to the pediatric protocols introduced by NWTSG – National Wilms Tumor Study Group and SIOP – Société Internationale d'Oncologie Pédiatrique) and to achieve better outcome [5]. Nephroblastoma in adults still has worse prognosis than in childhood, which was explained by different histological factors and different tumor biology in both age groups [9, 4, 5, 20, 21]. Age is an adverse prognostic factor even in neuroblastoma with favorable histology [22]. Up to now, there is no uniform algorithm of treatment of Wilms' tumor in adults, but some consensus exists that adults should be cured in the same way as children [16]. It seems that the best approach in such patients is nephrectomy followed by combination chemotherapy with or without radiotherapy. Unfortunately, lack of large patient groups and absence of randomized controlled data preclude general conclusions for standard therapy in adult patients [4, 8, 9]. The latest papers suggest that introduction of pediatric protocols into adult age group can give positive outcomes especially in low risk cases with favorable histology nephroblastomas [3, 5]. It is not only the author's opinion that diagnostic difficulties are the main reason for worse prognosis. Analysis of medical literature revealed that nephroblastoma in adults was accurately diagnosed preoperatively in only a few adult cases [9, 23]. Mainly, patients were operated due to suspicion of renal cell carcinoma, inflammatory kidney tumor or even kidney hematoma and delay of diagnosis was 5 months [21].

Clinical presentation and imaging studies are not able to distinguish the real type of kidney tumor in adults because of lack of characteristic radiologic features discriminating nephroblastoma and other renal neoplasms [4, 24]. Presence of intra-tumoral polycystic structures and focal necrosis additionally complicates interpretation of radiological findings [7]. Imaging studies (USG, CT) of both presented patients did not suggest Wilms' tumor and the most spectacular is the first case (patient T.T.) in which tumor was diagnosed during evaluation of uncomplicated flank injury. Both patients met the diagnostic criteria of Wilms' tumor in adults given by Kilton and co-workers and adjuvant polychemotherapy protocol was started after surgery. In both cases histopathological examination confirmed definitive character of the lesions and final diagnosis of Wilms' tumor with triphasic pattern and low risk, favorable histology was made.

Immunohistochemical and histopathological features of both cases justified their classification as nephroblastomas with "classic" triphasic histology. In spite of this favorable microscopic diagnosis we should remember that Wilms' tumor in adults still has a worse prognosis than in childhood.

CONCLUSIONS

1. As presented in literature, rare kidney tumors are usually diagnosed incidentally.
2. Literature data and presented cases indicate that Wilms' tumor in adults should be taken into consideration in young patients presenting with a large kidney mass, fast tumor growth, and unusual imaging findings.
3. Panel of additional laboratory techniques, like immunochemistry studies, are helpful in microscopic differential diagnosis of tumors poorly differentiated or with atypical histology.
4. It is widely accepted opinion that the chance for successful treatment of nephroblastoma depends on correct histopathological confirmation of the disease but prognosis of Wilms' tumor in adults still remains serious.

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