

CASE REPORT
OPIS PRZYPADKU

CLINICAL-MORPHOLOGICAL FEATURES OF WILMS' TUMOUR: ANALYSIS OF LITERATURE DATA AND A CASE FROM PRACTICE

Victor D. Urzhumov¹, Nana M. Pasiyeshvili², Nataliia V. Kapustnyk², Mykhailo S. Myroshnychenko³,
Iryna V. Borzenkova⁴, Dmytro V. Molodan³, Victor N. Grinevich¹

¹ MILITARY MEDICAL CLINICAL CENTRE OF THE NORTHERN REGION, KHARKIV, UKRAINE

² PUBLIC NONPROFIT ORGANIZATION OF THE KHARKIV DISTRICT COUNCIL «REGIONAL CLINICAL PERINATAL CENTRE», KHARKIV, UKRAINE

³ KHARKIV NATIONAL MEDICAL UNIVERSITY, KHARKIV, UKRAINE

⁴ PUBLIC NONPROFIT ORGANIZATION OF THE KHARKIV DISTRICT COUNCIL, «REGIONAL CLINICAL HOSPITAL», KHARKIV, UKRAINE

ABSTRACT

Wilms' tumour, or nephroblastoma, is a malignant tumour, originating from nephrogenic germ cells that copy histology of developing kidneys and often contain cells at different stages of their differentiation. The article analyses clinical-morphological features of Wilms' tumour, which is typical for childhood and seldom occurs in adults. The authors suppose that one of the causes of Wilms' tumour development can be maternal complications, which arise during pregnancy, leading to inhibition of glomerulogenesis and tubulogenesis in the offspring kidneys, an increase the number of foci of primitive (immature) tissue, from which this tumour, as it is known, can originate. The described case from practice of Wilms' tumour is of particular interest because of an untypical age category, when the above pathology was diagnosed, demonstrates necessity of a multidisciplinary approach to its identification and necessitates its inclusion into the differential diagnostic line for the detection of kidneys tumours in adults.

KEY WORDS: Wilms' tumour, clinical picture, morphology, case from practice

Wiad Lek 2019, 72, 10, 2050-2055

INTRODUCTION

Nephroblastoma, or Wilms' tumour, is a malignant tumour, originating from nephrogenic germ cells that copy histology of developing kidneys and often contain cells at different stages of their differentiation [1]. The first description of a nephroblastoma was made in 1872 by D.J. Eberth. In 1879 W. Osler informed about his own 2 observations of a nephroblastoma. In 1899 the German surgeon M. Wilms made the fullest review of the available literature about nephroblastoma and added description of his own 7 clinical observations. His description of the clinical picture of nephroblastoma was so accurate that during subsequent years doctors with an increasing frequency preferred the term «Wilms' tumour» compared with the term «nephroblastoma» [2].

Wilms' tumour affects one in 10,000 children and accounts for 5% of all childhood cancers. More than 80% of children are diagnosed with Wilms' tumour under the age of five years, and the median age at diagnosis is 3.5 years [3]. In children, Wilms' tumour is by far the most common (85% of cases), followed by renal cell carcinomas (3-5%), mesoblastic nephroma (3%), clear cell sarcoma of the kidney (3-4%), rhabdoid tumour of the kidney (2%) and miscellaneous rare tumours (2%) [4]. Black African children have an increased prevalence of Wilms' tumour compared with whites [5]. The global experience lists isolated cases of Wilms' tumour in adults,

they making less than 1% of all renal tumours. Only 70 new cases of Wilms' tumour in adults are diagnosed in Europe each year [3].

Wilms' tumour develops with the same frequency in boys and girls, equally affecting both kidneys [1].

As it is known, in the kidneys development process the metanephrogenic blastema areas, which form the secretory apparatus of this organ, should disappear completely after 36 weeks of pregnancy, but an insignificant part of the nephrogenic blastema remains functioning at birth in 1% of babies [6]. Our previous complex morphological studies on autopsy material of the kidneys revealed the above areas in all cases (13 fetuses and 15 newborns at 37-40 weeks of gestation) too [7].

Nephroblastoma is known to develop frequently from preserved embryonal foci of the immature renal tissue. This phenomenon was described in literature as persistence of nephrogenic blastema or nephrogenic rests [8]. It is currently believed that nephrogenic rests give rise to approximately 30-40% of Wilms' tumours, and they are found in up to 99% of bilateral Wilms' tumours [9, 10]. Nephrogenic rests may be single, multiple or diffuse. Multiple or diffuse nephrogenic rests are also referred to as nephroblastomatosis [11].

Nephroblastomatosis was described at first in 1961, when L. Hou and R. Holman used this term for defining a renal lesion in newborns characterized by an enlargement and

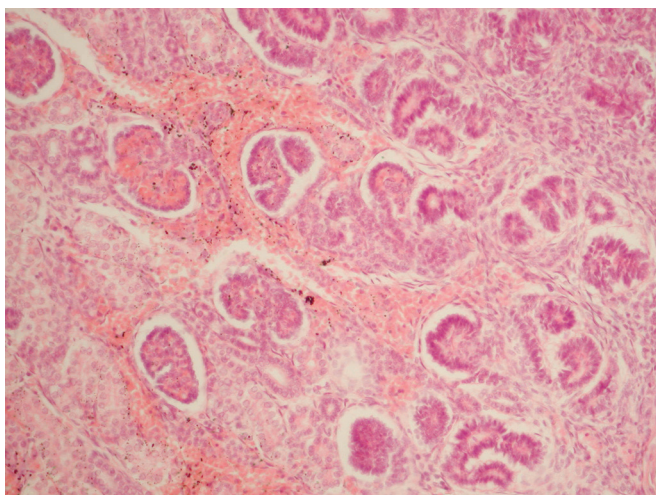


Fig. 1. Foci of the immature tissue in the newborn kidney developing in conditions of maternal iron deficiency anemia. Staining with haematoxylin and eosin, $\times 200$.

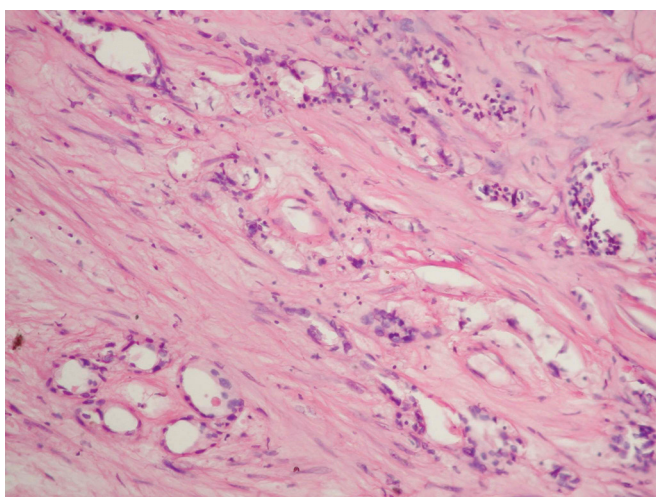


Fig. 3. Prevalence of the mesenchymal component over the epithelial one in the tumour. Focal infiltration of immune cells. Connective tissue disorganization. Staining with haematoxylin and eosin, $\times 200$.

an increased lobulation of the organ. But later the term «nephroblastomatosis» was used for describing multifocal or diffuse nephrogenic rests in one or both kidneys [8].

Morphologically, several variants of nephroblastomatosis are separated: perilobar, intralobar and mixed [12]. In perilobar nephroblastomatosis embryonal nephrogenic rests are localized along the renal cortex periphery; in intralobar nephroblastomatosis they prevail in the renal parenchyma [8]. Nephrogenic rests are classified histologically as dormant, sclerosing, hyperplastic or neoplastic. Dormant and sclerosing rests are usually microscopic and are not considered to have any malignant potential. Hyperplastic and neoplastic rests are grossly visible as small tan nodules surrounded by normal parenchyma [9].

So far the aetiology of Wilms' tumour has not been sufficiently studied [13]. Some scientists believe that maternal diseases and effects of ionizing radiation during the first half of pregnancy belong to causative factors for development of this tumour [13].



Fig. 2. The kidney with an adjacent tumour.

REVIEW AND DISCUSSION

Complications that appear in the mother in the course of her pregnancy can be, from our viewpoint, one of the causes for development of Wilms' tumour in the posterity. For example, our study of clinical and experimental material revealed that different degrees of severity of maternal pre-eclampsia and iron deficiency anaemia [7, 14], experimental chronic intrauterine and mixed hypoxias, experimental maternal subacute abdominal infectious-inflammatory process caused by *Escherichia coli* [15, 16] resulted in inhibition of glomerulogenesis and tubulogenesis and an increased number of foci of the immature tissue (fig. 1), thus making the development of Wilms' tumour in such children more probable.

According to data of G.R. Bunin et al., maternal use of hair-colouring products, maternal vaginal infection, parent's tea drinking, a high mean child birth weight and an old maternal age can serve as risk factors for development of Wilms' tumour [17].

A few studies have mentioned some hypothetical risk factors for Wilms' tumor such as occupational, environmental and life style factors [5].

Approximately 5% of patients with Wilms' tumor have an underlying predisposing genetic syndrome and over 50 such syndromes have been described [3]. It is known that a high risk of development of this tumour is observed in patients with some WT1-associated syndromes (including WAGR and Denys-Drash), Perlman syndrome, mosaic variegated aneuploidy and Fanconi anaemia with biallelic BRCA2 mutation. A moderate risk of nephroblastoma

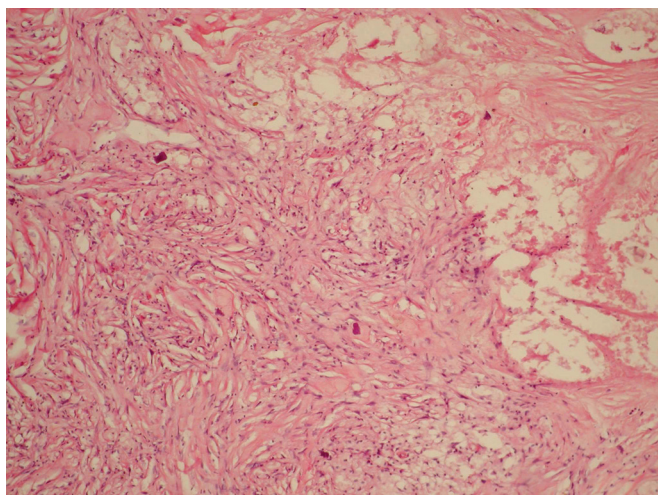


Fig. 4. Myoid, mesenchymoid proper and lipoblastic structures in the mesenchymal component of the tumour. Foci of necrosis and dystrophic calcification. Connective tissue disorganization. Staining with haematoxylin and eosin, $\times 100$.

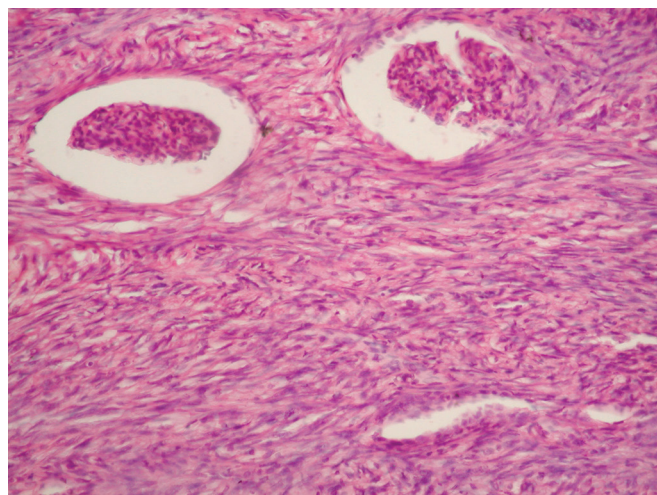


Fig. 5. Wilms' tumour. Glomerular and tubular structures. Staining with haematoxylin and eosin, $\times 200$.

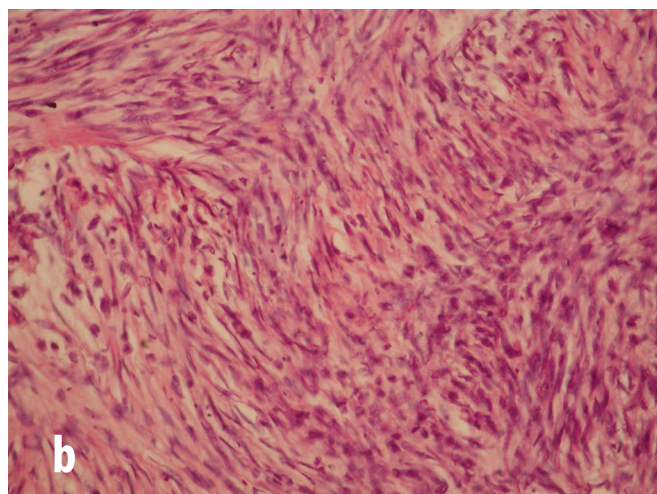
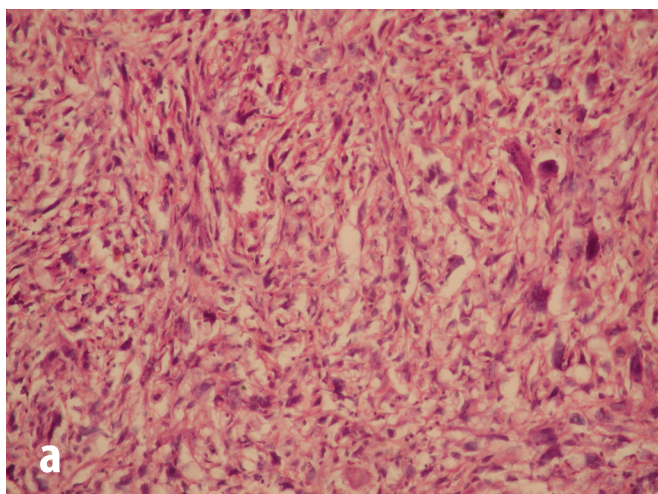


Fig. 6. The undifferentiated type of mesenchymal Wilms' tumour, represented by myosarcoma and fibrosarcoma areas. Staining with haematoxylin and eosin, a), b) $\times 200$.

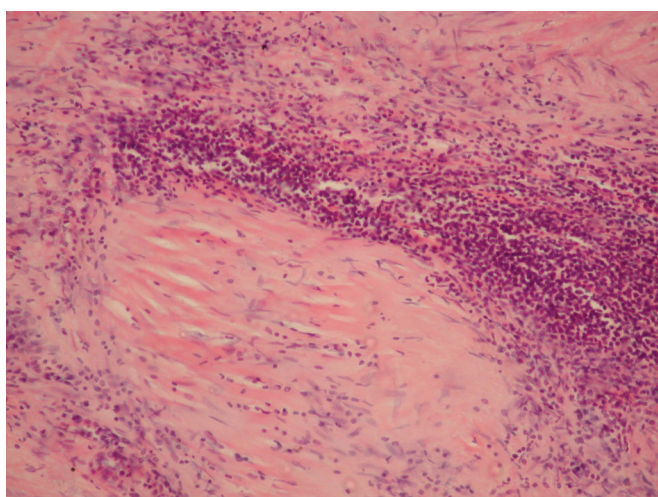


Fig. 7. Disorganization of the connective tissue, immune infiltration in the tumour tissue. Staining with haematoxylin and eosin, $\times 200$.

development is found in patients with Fraser and Beckwith-Wiedemann syndromes, which result from disomy of 11p15, and Simpson-Golabi-Behmel syndrome. The group of a low risk for development of the above tumour is made up of cases with isolated hemihypertrophy, Bloom's and Li-Fraumeni syndromes, congenital hyperparathyroidism combined with jaw tumours, Mulibrey nanism and other chromosomal aberrations [6, 10].

At the initial stages of the disease any symptoms and signs of Wilms' tumour in children are usually absent or minimal [13]. This tumour is more commonly diagnosed by parents, when they wash or dress their children, palpating a tumour mass in the abdominal cavity or detecting an enlarged or asymmetrical abdomen. Children may suffer from an abdominal pain, haematuria and an acute abdomen. In rarer cases anaemia, hypertension caused by an excessive production of renin and polycythaemia due to production of erythropoietin by the tumour occur in chil-

dren [1]. As the tumour grows, its clinical manifestations augment. The rates of the tumour enlargement are different. Its slow growth during many months is possible, but more frequently it enlarges rapidly, gradually compressing or pushing away surrounding tissues [10, 13]. Often the tumour grows through a fibrous capsule of the kidney and encroaches upon the surrounding fat and adrenal gland, grows into the diaphragm, large intestine, spleen, liver, pancreas tail, intestinal mesentery and retroperitoneal lymph nodes [1].

Adult Wilms' tumour is different in many ways when compared with the paediatric one: adults present with local pain and haematuria usually, in contrast to a palpable boggy mass which is a more common presentation in children; adult Wilms' tumour is larger and ill-defined without sharp margins and with areas of necrosis and haemorrhages. Extension into the adjacent retroperitoneum is often present; adult Wilms' tumour has a more aggressive clinical course and a worse prognosis. Metastasis rates for adults and children were respectively 29% and 10%. The lungs are the commonest sites for a spread of metastases, other sites include the liver, bone, lymph nodes, skin, orbit and the contralateral kidney. Unlike the paediatric population, majority of the adult patients are operated primarily. It is not possible to achieve a safe diagnosis in adults by imaging studies alone [18].

An important part in diagnosing Wilms' tumour in children and adults is played by morphological methods of examination. It is difficult to make the histological diagnosis of nephroblastoma, taking into consideration the various morphological structure of this tumour [19]. Clinicians need a rapid and correct assessment of results of examination of the biopsy material or operated tissues by pathologists in order to choose and carry on adequate diagnostic and treatment measures.

Macroscopically, the tumour looks like a well-defined node, it can achieve a large size and is located under a capsule or near the renal hilum. Consistency of the tumour depends upon maturity of its components. On its sections the tumour varies from whitish-gray to pale brown; it has foci of fresh and old haemorrhages, sometimes with macerations and cysts. Also, the above tumour may contain areas of osseous and cartilaginous tissues as well as foci of calcification [20].

Morphologically, nephroblastoma is a combination of epithelial and mesenchymal elements with different extents of differentiation, thereby making this tumour extremely variable. [2]. The epithelial component is represented by a mesonephral blastema with formation of tubules as well as glomerular and cystic structures with different degrees of differentiation. The mesenchymal component is represented by a connective tissue with structures having different tissue differentiation: myoid (leiomyoblastic and rhabdomyoblastic), mesenchymoid, lipoblastic (of the type of embryonic lipoma and/or hibernoma), chondroblastic as well as osteoblastic and neuroectodermal [2].

Some scientists isolate three components in the structure of Wilms' tumour: blastemic, mesenchymal and epithelial

[10]. In a part of cases Wilms' tumour may not contain all three above components. Proportions of the tumour components may differ, therefore it has 3 variants: typical nephroblastoma, characterized by equal volumes of its epithelial and mesenchymal components; nephroblastoma with prevalence of the epithelial component; nephroblastoma with prevalence of the mesenchymal component. In each of these variants the pathologist should determine the degree of differentiation of the prevailing component [2].

Monoclonal antibodies against Wilms' tumour 1, vimentin, CD 56, CD 57, cytokeratin 22, cytokeratin 18, cytokeratin 8, epithelial membrane antigen, smooth muscle actin and actin are useful markers for an accurate diagnosis of Wilms' tumour [21].

The prognosis varies. Patients under two years have a more favourable prognosis. The prognosis is unfavorable in cases of the tumour growing outside the limits of the renal capsule, a large size of the tumour, its metastases, anaplasia of the tumour tissue revealed by enlargement of nuclei in cells, their hyperchromia and appearance of patterns of atypical mitoses [1, 2].

CLINICAL CASE

Taking into account that Wilms' tumour occurs in adults infrequently, we would like to give here our analysis of the case from practice with development of the above tumour in a 45-year-old male, who was hospitalized in April of 2019 to the Military Medical Clinical Centre of the Northern Region. Computed tomography of his thoracic and abdominal organs and small pelvis revealed that the middle and lower thirds of the right kidney contained a multinodal cystic-solid formation with the subcapsular spreading and fine areas of calcification. The above formation was intimately adjacent to the lateral inferoposterior segment of the right hepatic lobe and the inferior pudental vein; a spherical formation, 9×8 mm in size, was visualized in the inferoposterior segment of the right hepatic lobe. The patient underwent laparotomy, removal of his right kidney with the tumour and some part of his ureter. The operated material was sent to the pathology department for morphological examination and pathology identification.

Macroscopic examination determined a slightly reduced kidney with an adjacent tumour, which had the subcapsular localization in the hilum region (fig. 2). The tumour was soft in some places and had dense consistency in others; on sections it was whitish-yellowish and reddish-brownish color.

Microscopic examination revealed structure of Wilms' tumour, characterized by prevalence of its mesenchymal component over the epithelial one (fig. 3), the latter being actually undetectable in some part of visual fields (fig. 4). The epithelial component was characterized by formation of glomerular and tubular structures (figs. 3, 5); the latter ones were both without any lumen and with a well-formed lumen. In some part of visual fields the epithelium produced a secretion into the lumen of ducts, therewith making such structures look like a gland.

The mesenchymal component revealed an aggregate of myoid (leiomyoblastic and rhabdomyoblastic), mesenchymoid proper and lipoblastic structures (fig. 4) with prevalence of the specific volume of myoid ones.

A.O. Prylutsky et al. note that prevalence of myoid structures in the mesenchymal component of Wilms' tumour demonstrates augmentation of its malignancy, it being caused by a high proliferative activity of muscle elements and their capacity for vascular invasion [19].

In the course of our further analysis of the microslides a few visual fields revealed the differentiated mesenchymal type, where mesenchymal derivatives did not have any morphological signs of a malignant growth. But most visual fields demonstrated the undifferentiated type of mesenchymal Wilms' tumour, represented by myosarcoma and fibrosarcoma areas (fig. 6).

Some places of the mesenchymal component of Wilms' tumour contained foci of dystrophic calcification (fig. 4), signs of disorganization of the connective tissue up to the development of extensive necrosis (figs. 3, 4, 7), focal infiltration of immune cells (figs. 3, 7).

CONCLUSIONS

The article has analysed clinical-morphological features of Wilms' tumour, which is typical for childhood and rare in adults. One of the causes of Wilms' tumour development can be maternal complications, which arise during pregnancy, leading to inhibition of glomerulogenesis and tubulogenesis in the offspring kidneys, an increase the number of foci of primitive (immature) tissue, from which this tumour, as it is known, can originate. The described case from practice of Wilms' tumour is of particular interest because of an untypical age category, when the above pathology was diagnosed, demonstrates necessity of a multidisciplinary approach to its identification and necessitates its inclusion into the differential diagnostic line for the detection of kidneys tumours in adults.

REFERENCES

1. Memjanova FN, Jalilov JJ. Opukhol Vylmsa [Wilm's tumour]. The Bulletin of emergency medicine. 2011;1:80-83. (Ru)
2. Zhurilo IP, Grona VN, Litovka VK, Abdullin RF, Latyшов KV, Muzaliov AA. Diagnostyka ta likuvannya nefroblastomy u ditey [Diagnostics and treatment of nephroblastoma in children]. Neoplasm. 2007;1:121-125. (Ru)
3. Szychot E, Apps J, Pritchard-Jones K. Wilms' tumor: biology, diagnosis and treatment. Translational pediatrics. 2014;3(1):12-24.
4. Vujanić GM, Sandstedt B. The pathology of Wilms' tumour (nephroblastoma): the International Society of Paediatric Oncology approach. Journal of clinical pathology. 2010;63(2):102-109.
5. Woldeab WE, Nyongole OV, Frank B. Wilm's tumor: Presentation and outcome at Kilimanjaro Christian Medical Center. The Journal of Medical Research. 2016; 2(4):114-117.
6. Kulyova SA, Imyanitov EN. Opukhol Vylmsa: syndromalnaya y molekulyarnaya dyagnostyka [Wilm's tumor: syndrome-based and molecular diagnostics]. Onkopediatria. 2017;4(4):283-289. (Ru)

7. Sorokina IV, Myroshnychenko MS, Kapustnyk NV, Simachova AV, Ivanova AA. Morfometrycheskaya otsenka sostoyaniya pochek plodov y novorozhdennykh, razvyyavshykh v uslovyakh maternoy zhelezodefitsytnoy anemyy [Morphometrical evaluation of fetuses and newborns kidneys status developing under maternal iron deficiency anemia conditions]. Wiadomości Lekarskie. 2018;LXXI(7):1222-1230. (Ru)
8. Chililova AM, Kachanov DYu, Mitrofanova AM, Konovalov DM, Sukhov MN, Tereshchenko GV, et al. Bylateralnyy dyffuznyy gyperplastichesky perylobarnyy nefroblastomatoz: sobstvennoe klynycheskoe nablyudeniye [Bilateral diffuse hyperplastic perilobar nephroblastomatosis]. Pediatric hematology/oncology and immunopathology. 2015;14(4):37-43. (Ru)
9. Lowe LH, Isuani BH, Heller RM, Stein SM, Johnson JE, Navarro OM, et al. Pediatric renal masses: Wilms tumor and beyond. RadioGraphics. 2000;20:1585-1603.
10. Huppmann AR. Educational case: Wilms tumor. Academic pathology. 2018;5:1-5.
11. Lonergan GJ, Martinez-Leon MI, Agrons GA, Montemarano H, Suarez ES. Nephrogenic rests, nephroblastomatosis and associated lesions of the kidney. RadioGraphics. 1998;18:947-968.
12. Sharoyev TA, Sokolova IN, Ivanova NM, Rubanskaya MV, Koshechkina NA, Panferova TR. Nefroblastomatoz u detey: obzor lyteratury y sobstvennye materyaly yssledovaniya [Nephroblastomatosis in children: review of literature and the authors' study findings]. Cancer urology. 2009;4:19-24. (Ru)
13. Grigoryev KI, Boyechenko EI. Nefroblastoma u detey [Nephroblastoma in children]. Meditsinskaya sestra. 2013;2:22-29.
14. Sorokina IV, Myroshnychenko MS, Kapustnyk NV, Khranova TO, Dehtiarova OV, Danylchenko SI. Morfologicheskaya kharakterystyka soedynitelnykh pochek donoshennykh plodov y novorozhdennykh ot materey, beremennost kotorykh oslozhnylas preeklampsyey razlychnoy stepeny tyazhesty [Morphological characteristics of kidneys connective tissue of mature fetuses and newborns from mothers, whose pregnancy was complicated by preeclampsia of varying degrees of severity]. Wiadomości Lekarskie. 2018;LXXI(3/1):579-587. (Ru)
15. Sorokina I, Myroshnychenko M, Kapustnyk N. Pathology of the urinary system organs in children population of Ukraine: its past, present and future. Regional Innovations. 2017;4:35-42.
16. Sorokina IV, Myroshnychenko MS, Ivanova MD. Morfologicheskyye osobennosti pochek plodov y novorozhdennykh ot materey s podostrym ynfektsyonno-vospalytelnyy protsessom v bryushnoy polosty, vyzvannym Escherichia coli (eksperymentalnoe yssledovaniye) [Morphological features of kidneys in fetuses and newborns from mothers with subacute infectious-inflammatory process in the abdominal cavity caused by Escherichia coli (experimental study)]. Kidneys. 2018;7(1):18-25. (Ru)
17. Bunin GR, Kramer S, Marrero O, Meadows AT. Gestational risk factors for Wilms' tumor: results of a case-control study. Cancer research. 1987;47:2972-2977.
18. Varma AV, Malukani K, Rihal P, Nandedkar SS. Adult Wilms' tumor: a case report with review of literature. Journal of cancer research and therapeutics. 2015;11(4):934-936.
19. Prylutsky AO, Chernyshenko AS, Prylutsky OO. Patomorfologiya neepitelialnogo komponenta pukhlyny Vylmsa (nefroblastomy) [Pathomorphology of nonepithelial component of Wilms tumor (nephroblastoma)]. Morphology. 2007;1(4):120-121. (Ua)
20. Morgoshia TSh, Kokhanenko NYu. Vklad legendarnogo khyrurga y onkologa Maksa Vylmsa (1867-1918) v klynycheskuyu medytsynu (k 150-letyuy so dnya rozhdeniya) [The contribution of the legendary surgeon and oncologist Max Wilms (1867-1918) to clinical medicine (on the 150th anniversary of his birth)]. Russian journal of pediatric hematology and oncology. 2018;5(1):103-105. (Ru)

21. Vasei M, Moch H, Mousavi A, Kajbafzadeh A. Immunohistochemical profiling of Wilms tumor. *Applied immunohistochemistry and molecular morphology*. 2008;16(2):128-134.

Conflict of interest:

The Authors declare no conflict of interest.

Authors' contributions:

According to the order of the Authorship.

ORCID numbers:

Victor D. Urzhumov – 0000-0002-8648-7758
Nana M. Pasiyeshvili – 0000-0002-8016-4288
Nataliia V. Kapustnyk – 0000-0002-4875-398X
Mykhailo S. Myroshnychenko – 0000-0002-6920-8374
Iryna V. Borzenkova – 0000-0002-0701-5286
Dmytro V. Molodan – 0000-0002-7679-8288
Victor N. Grinevich – 0000-0002-6232-5949

CORRESPONDING AUTHOR

Mykhailo S. Myroshnychenko

Kharkiv National Medical University
str. Svetlaya27A, apt. 70, 61129, Kharkiv, Ukraine
tel: +380501699763
e-mail: msmyroshnychenko@ukr.net

Received: 21.04.2019

Accepted: 17.09.2019