

Extrarenal nephroblastoma

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Introduction Nephroblastoma is one of the most common solid tumours in children. The occurrence of extrarenal nephroblastoma is exceedingly rare. What can be defined as extrarenal Wilms' tumor must satisfy the following criteria: histologically confirmed nephroblastoma and extrarenal location.

Material and methods Current data on extrarenal nephroblastoma based on a selective review of the literature.

Results The retroperineal location is reported to be typical in males, whereas the inguinal region is believed to predominate in females. There are no characteristic manifestations of extrarenal nephroblastoma. The symptoms depend on the location and stage upon diagnosis. US, CT and MRI are used to detect tumours in the retroperitoneal space, inguinal, sacro-coccal and scrotal area. However, extrarenal nephroblastoma does not show characteristic radiological features.

Conclusions In absence of typical clinical presentation or conclusive imaging tests, the diagnosis is based on histology after the resection of the tumor. The recommended management of the extrarenal nephroblastoma is similar to the treatment of intrarenal nephroblastoma.

Key Words: nephroblastoma ↔ extrarenal location

INTRODUCTION

Nephroblastoma, one of the most common solid tumours in children, constitutes 8-10% of all neoplasms in that group, ranking third after neuroblastoma and CNS tumours. The peak incidence occurs in pre-school children, between 1 to 5 years of age. About 70 new cases of the tumor are registered in Poland annually. Extrarenal nephroblastoma is rare in adults and children. Few as they are, there are still more reports on the tumor in children [1, 2, 3]. What can be defined as extrarenal Wilms' tumor must satisfy the following criteria: histologically confirmed nephroblastoma and extrarenal location [4].

Incidence

Extrarenal nephroblastoma was first reported in 1961 by Moyson et al., who described a chest

tumor in which the histological image resembled nephroblastoma [1]. About 300 cases of the disease have been reported around the world since then. In all of them, the tumor was located in the retroperitoneal space, excluding an intrarenal location [2, 3, 5].

The second most common location is the area of the pelvis minor, in particular the inguinal canal, the female reproductive organs (vagina, uterus), the round ligament of the uterus, the ovaries and the testicles [6, 7, 9, 10, 11]. Nephroblastoma was also found in the sacro-coccal area in children. From the embryological point of view, extrarenal nephroblastoma is frequently reported to be located in the vicinity of the fetal urogenital ridge and mesonephron, which might account for the location of the tumor in the organs mentioned above [12, 13].

The retroperineal location is reported to be typical of males [4, 9, 11, 12], whereas the inguinal region is believed to predominate in females [6, 7, 14, 15].

A case of extremely rare extrarenal nephroblastoma within the isthmus of the horseshoe kidney was described as well. Histology of the tumor revealed an association with teratoma and three cell types which typically form nephroblastoma: blastemal, stromal and epithelial [8, 9].

Although recent studies maintain that extrarenal Wilms' tumor most commonly occurs in children, according to multicentre research analyzing the data of 34 patients by Cooppe et al., the patients' age varied from 2 months to 56 years [4]. The occurrence of the tumor in men and women was comparable in the group of 4 adults and 3 teenagers. The remaining 27 patients were children below 10, predominantly between 1 to 4 years of age.

Embryogenesis

According to Becwith et al., nephroblastoma in a typical location can be classified as having either favourable or unfavourable histology [16]. In addition, one more category has been singled out by SIOP [Society of Pediatric Oncology] and NWTSS (National Wilms' Tumor Study) pathologists, comprising intermediate risk tumors [17].

The pathogenesis of extrarenal nephroblastoma has not as yet been thoroughly explained. Two causes of the pathology are taken into account. The tumor is believed to arise from mesonephric remnants or metanephretic tissue [8, 9, 13, 15, 18, 19]. Alternatively, it is assumed to originate in a teratoma, but this conception has not yet been confirmed [9].

Extrarenal nephroblastoma seldom contains elements of teratoma. However, mature teratoma was recognized in a teratoid Wilms' tumor found in the horseshoe kidney, even though other forms such as blastematous elements with abortive glomeruli, tubules and immature chondromatoid elements predominated. It was the presence of these three phases – blastemal, epithelial and stromal – that justified the diagnosis of a teratoid extrarenal Wilms' tumor [4, 8, 12, 20, 21]. It is claimed that extrarenal Wilms' tumor develops from mesonephric or pronephric remnants and its tissue is more primitive than the tissue of intrarenal nephroblastoma. According to Kaptur et al., between the 6th and 7th week of fetal development, a nexus between metanephric blastema and a ureteral bud is formed. Extrarenal nephroblastoma may arise from the ectopic blastematous cells [8, 18].

Another theory points to the role of the mesonephric duct in the pathogenesis of extrarenal nephroblastoma. Male urogenital structures such as the epididymis, vas deferens and seminal vesicles, as well as the female Gartner's duct, differentiate from the meso-

nephric duct. The Gartner's duct disappears by the 4th month of gestation. Yet, as was observed, it could remain beyond that time as juxtagonadal mesonephric glomeruli, which might be the cause of nephroblastoma in genitalia [13]. On the other hand, Roberts et al. identified the WT1 gene in 25% of patients with extrarenal nephroblastoma and suggested that the gene mutation might cause transformations of extrarenal mesonephric or pronephric splinters in Wilms' tumor [18].

Electron microscopy of Wilms' tumor showed protein elements, vimentin filaments, as well as cyto-keratin and epithelial antigen, which might suggest a relation between stroma, blastema and epithelium, also observed in intrarenal nephroblastoma. Most researchers emphasise the importance of histological differential diagnosis between extrarenal nephroblastoma and teratoma. [9, 10, 11, 19, 20, 21]

Clinical presentation

There are no characteristic manifestations of extrarenal nephroblastoma. The symptoms depend on the location and stage upon diagnosis. The most common presentation is nonspecific abdominal pain and, as in the case of intrarenal nephroblastoma, a palpable mass (Figure 1). Pelvic and retroperitoneal location is associated with gastrointestinal disorders, cachexia, haematuria, gynaecological haemor-



Figure 1. Large palpable mass of the abdomen.

rhage and in few patients even raised temperature. The clinical presentation depends mainly on the tumor size [3, 4, 12, 22, 23, 24].

Diagnosis

An accurate diagnosis is based on histology following tumor removal. US, CT and MRI are used to detect tumors in the retroperitoneal space, inguinal, sacrococcal and scrotal area. However, extrarenal nephroblastoma does not show characteristic radiological features.

Treatment

The treatment of extrarenal nephroblastoma, based on the guidelines for the management of intrarenal nephroblastoma, comprises of surgery, chemotherapy and radiotherapy. The commonly shared opinion is that the surgical removal of the tumor together with the organ it originates from and adjacent lymph nodes is the most important element of the therapy [3, 4, 9, 13].

Tumors in the retroperitoneal space, inguinal or sacrococcal area must be radically resected. Surgery is the treatment of choice and should be as radical as it is for intrarenal nephroblastoma. The whole area of resection should be carefully inspected and the enlarged lymph nodes from the area must be removed. Chemotherapy as adjuvant therapy was reported to have been used in all studies [12, 17]

Coopies at al. described 34 cases of extrarenal nephroblastoma [4]. Stage I amounted to 30%, II to 10%, III to 57% and IV to 3%. In all patients, two-year asymptomatic survival was observed in 82% of cases. Radiation therapy was used only when surgery was not possible. Radiation doses ranged from 20 Gy to 50 Gy. Postoperative treatment depends on the stage of the tumor and its histological result. Both factors (stage and histology) determine the choice of a chemotherapy regimen and aggressiveness of adjuvant therapy [17]. It seems controversial to refer to the TNM classification in cases of tumors unrelated to the organ. Therefore, other classifications are used. SIOP pathologists distinguish three risk groups: high, intermediate and low. Nephroblastoma – blastemal type, diffuse anaplasia, clear cell sarcoma, and rhabdoid tumor are all high risk tumors. Mesoblastic

nephroma, cystic partially differentiated nephroblastoma and complete necrotic nephroblastoma belong to the low risk group. As in all reports on extrarenal nephroblastoma, the TNM classification was referred to and the types of treatment, as well as the results, were be compared. The NWTS has recommended a modified classification of nephroblastoma for extrarenal nephroblastoma [16].

Stage 1 – organ-confined tumor, resected completely, no injury to a pseudocyst, clear surgical margin.

Stage 2 – regional tumor, biopsied before removal or invading blood vessels; resected completely, clear surgical margin.

Stage 3 – tumor not completely resected, regional lymph node metastasis present, tumor spread to the abdominal organs and peritoneum.

Stage 4 – hematogenous metastases.

In the past, tumor removal was not followed by standardized chemotherapy. Since the year 2000, chemotherapy regimens recommended by SIOP or NWTS have been introduced according to the stage and histological image of the tumor. In Poland, the chemotherapy regimen recently recommended by SIOP is used. In the case of the boy with extrarenal nephroblastoma reported by the authors, a three-agent therapy [actinomycin, vinkristine and doxorubicin], recommended for stage 3, was used after tumor resection. After that, the patient was treated with 20 Gy radiation [3].

According to both NWTS and SIOP pathologists, diffuse anaplastic changes generally predict a poor outcome and full recovery is achieved in 30% of cases [16, 17]. What also confers poor prognosis is a tumor mass above 250 mg, volume above 400 cm³ and lymph nodes metastases [17].

CONCLUSIONS

The occurrence of the extrarenal nephroblastoma is exceedingly rare. In absence of typical clinical presentation or conclusive imaging tests, the diagnosis is based on histology after the resection of the tumor. The recommended management of the extrarenal nephroblastoma is similar to the treatment used for intrarenal nephroblastoma.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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