Adult Wilms' Tumor

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Introduction

Wilms' tumor or nephroblastoma, named after nineteenth-century German surgeon Carl Max Wilhelm Wilms, is an embryonal kidney tumor that occurs primarily in children. It is a rare tumor and represents 5–6 % of all childhood cancer cases in Europe and United States and is the most common pediatric primary malignant tumor of the kidneys [1]. The median age at diagnosis for children is 3–4 years, and 90 % of children are diagnosed before the age of 7 years [2]. In Europe and the United States, the incidence rate of Wilms' tumor in children (0–14 years) is about ten per million [3]. Approximately 510 children are diagnosed every year in the United States [4].

Wilms' tumor is extremely rare among the adolescent and adult population. Until 2004, only 300 cases had been reported in adults worldwide [5]. According to a population-based European epidemiological study from European cancer registries' study on cancer patients' survival and care (EUROCARE) project, which included data from years 1983 to 1994 from 67 cancer registries that covered a combined population of 100 million in 22 European countries, the overall crude incidence rate was 0.19 per million adults. The proportion of adult Wilms' tumor among all kidney cancers was 0.33 % or less in most registries. Recent data indicates that approximately 70 new cases arise in adults in Europe each year [2].

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Pathogenesis

Histopathology

The histology and cytology of Wilms' tumor in adults are similar to that of pediatric patients [6]. During embryonic development, the fetal kidney and collecting ducts from the ureteric bud and the metanephric mesenchyme or blastema form the stroma and proximal tubular structures, glomeruli, proximal and distal tubules, and loop of Henle (which requires mesenchymal to epithelial transition) [7]. The blastema usually disappears by 36 weeks of gestation. However, at birth approximately 1 % of infants retain residual blastema within their kidney [8, 9]. These abnormally persistent cells were defined by Beckwith as nephrogenic rests [8]. Interestingly, in 40 % of Wilms' tumor patients, nephrogenic rests can be identified. Nephrogenic rests are thought to be the precursor lesions of Wilms' tumors [10]. Although nephrogenic rests may regress or lie dormant, a proportion will proliferate and may undergo neoplastic transformation into Wilms' tumor.

Progression of disease is thought to result from the acquisition of stable somatic changes, either in the form of genetic mutations or epimutations [8, 10]. Morphologically, three major components are present in most tumors – undifferentiated blastema, mesenchymal stroma, and epithelial cells (Fig. 5.1). The blastema is extremely cellular and composed of small round to oval primitive cells or spindle

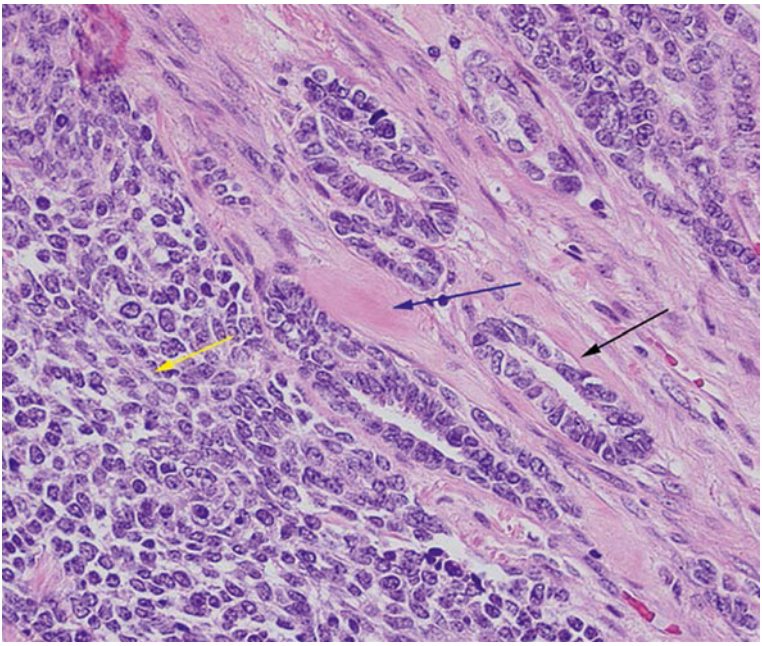

Fig. 5.1 Histopathology of Wilms' tumor. This image shows all the three components of Wilms' tumor – epithelial component (*black arrow*), blastemal component (*yellow arrow*), and mesenchymal component (*Blue arrow*) (Courtesy of Jennifer Beth Gordetsky, MD, Dept. of Pathology, UAB Birmingham, AL)

cells with scanty cytoplasm. The pattern of growth may be diffuse, nodular, cord-like, or basaloid. The mesenchymal elements usually have a spindle-cell fibroblastic configuration but may exhibit a varied differentiation, including smooth and striated muscle cells and neurons. The epithelial component is characterized by the formation of embryonic tubular or glomerular structures, which closely recapitulates the appearance of normal developing metanephric tubules and glomeruli. The key to recognizing Wilms' tumor in a biopsy is to identify these three components of the tumor in the renal mass; the most conspicuous being the blastemal component [11].

Immunohistochemistry (IHC) can provide supportive evidence with the presence of WT1 in the malignant blastemic and epithelial components. Additionally, IHC for cytokeratin, vimentin, desmin, and actin helps to distinguish Wilms' tumor from other malignancies such as renal sarcoma and clear cell sarcoma as well. Kilton and colleagues established diagnostic criteria for adult Wilms' tumor which include: [12]

- Primary renal neoplasm
- Presence of primitive blastemic spindle- or round-cell component
- Formation of abortive or embryonal tubules or glomerular structures
- No areas of tumor diagnostic of renal cell carcinoma
- Pictorial confirmation of histology
- Age >15 years

Blastemal-predominant Wilms' tumor is more aggressive than other types and confers poor outcomes. In contrast, epithelial and stromal component predominant tumors confer intermediate risk. Anaplastic features, i.e., the presence of substantial nuclear and mitotic atypia, have also been associated with a poorer outcome and resistance to chemotherapy [13].

Histologic Classification

The International Society of Pediatric Oncology (SIOP) approach classifies tumor into three prognostic risk groups (low, intermediate, and high) based on histology which captures chemotherapy-induced regressive changes and has allowed the use of tailored therapy (Table 5.1) [14]. In contrast, the National Wilms' Tumor Study Group (NWTSG) approach which is used by the Children's Oncology Group (COG) classifies Wilms' tumor into two groups based on presence or absence of anaplasia.

Genetics

Wilms' tumor is known to be genetically heterogeneous in the pediatric. Thus far, the paucity of data available in adults makes it difficult to determine whether Wilms' tumor in adults and children is biologically comparable and similar tumor entities occurring in a different age group as suggested by their morphological similarities. More research needs to be done to elicit the genetic landscape of adult Wilms'

Table 5.1 Histological subtyping and risk grouping of renal tumors in children according to SIOP initial treatment approach [14]

Low risk tumor	Intermediate risk tumor	High risk tumor
Mesoblastic nephroma	Epithelial type	Blastema type
Necrotic nephroblastoma	Stromal type	Diffuse anaplasia
Cystic partially differentiated nephroblastoma	Regressive type	Clear cell sarcoma of kidney
	Mixed type	Rhabdoid tumor of kidney
	Focal anaplasia	

Adapted from Vujanić et al. [14]

tumor. Wilms' tumor is generally a sporadic disease. Nevertheless, congenital disorders due to germline WT1 gene alterations that predispose to pediatric Wilms' tumor, like the WAGR (Wilms' tumor, aniridia, genitourinary anomalies, and mental retardation) syndrome, Denys-Drash syndrome (renal disease, male pseudohermaphroditism, and Wilms' tumor), and the Beckwith-Wiedemann syndrome (associated with microduplication mutations in the 11p11.5 regions of imprinting genes), do not seem to be associated with adult Wilms' tumor [15].

Somatic mutations in Wilms' tumor 1 (WT1) gene located on the short arm of chromosome 11 at position 13 (11p13), Wilms' tumor gene on the X chromosome (WTX; also known as AMER1), β-catenin (CTNNB1), and TP53 occur either singly or in combination in a third of cases (Fig. 5.2) [16–18]. Cytogenetic analysis of germline DNA from patients with the rare congenital WAGR syndrome detected deletion of band 13 of the short arm of chromosome 11, which led to the identification and isolation of WT1 tumor suppressor gene from that region [19, 20]. Data suggest that WT1 expression plays a role in metanephric stem cell differentiation [21]. Consistent with its vital role in the development of the kidney and gonad, in addition to predisposition to Wilms' tumor, WT1 germline mutations can engender genitourinary tract anomalies and glomerulosclerosis, leading to renal failure [22, 23]. The CTNNB1 or catenin (cadherin-associated protein) beta 1 gene encodes β-catenin and upregulates the WNT pathway leading to tumorigenesis. A positive correlation exists between CTNNB1 mutation and WT1 gene mutation with many WT1-mutated Wilms' tumors also harboring CTNNB1 mutations [24]. The WTX (Wilms' tumor on the X, Xq11.1) tumor suppressor gene is altered in 7–29 % of Wilms' tumors, with two-thirds of these tumor's carrying deletions of the entire WTX gene [16, 25–28]. The remaining one-third of WTX-mutated Wilms' tumors carry mutations such as nonsense mutations and insertions and deletions that cause frameshifts that can result in termination codons or missense mutations [24]. The WTX gene encodes a protein that negatively regulates the WNT pathway. WTX mutations appear to be equally frequent in tumors with and without mutations in WT1 [16, 28]. Although p53 tumor suppressor gene alterations are the most common genetic abnormality detected in adult tumors, they are rare in pediatric malignancies, including Wilms' tumor with the exception of the anaplastic histologic subtype of Wilms' tumor. This finding provides a biologic rationale for the poor outcomes in anaplastic tumors with current chemotherapy. Their p53-dependent apoptotic pathway may have become inactivated [29].

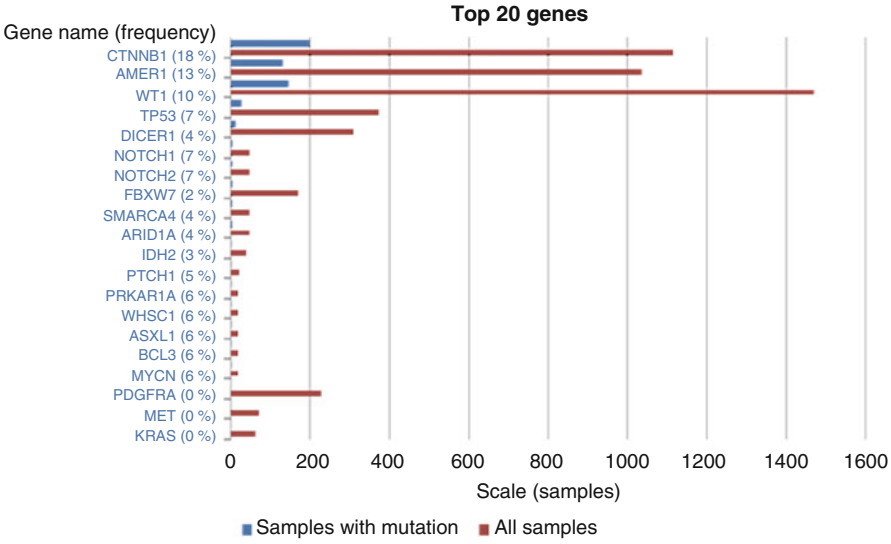

Fig. 5.2 Common somatic mutations in Wilms' tumor. CTNNB1, AMER1, WT1, and TP53 appear to be the most commonly mutated genes in Wilms' tumors (Courtesy of cancer.sanger.ac.uk and Forbes et al. COSMIC: exploring the world's knowledge of somatic mutations in human cancer 2014 [16–18])

Other loci, including 11p15, 1p, 2q, 7p, 9q, 14q, 16q, and 22, have also been implicated in the etiology of Wilms' tumor. Patients with LOH for chromosome 16q had relapse rates three times higher and a significantly higher mortality, i.e., more than ten times higher than patients without this alteration, suggesting that a gene within this site may be responsible for more aggressive biology [30]. National Wilms' Tumor Study (NWTS) Group-5 trial also identified that in favorable histology Wilms' tumors, the presence of both LOH of chromosome 16p and 1p was associated with an increased risk of relapse and death [31]. Genome loss at 4q and 14q has been identified for anaplastic tumors as well [32]. Additionally, gain of chromosome 1q observed in approximately 25 % of cases appears to be associated with poor survival as demonstrated in the NWTS-4 favorable histology cohort [33, 34].

Clinical Features

Clinical Presentation

Adult Wilms' tumor presents with flank or abdominal pain in approximately 80 % of patients. This is accompanied by nonspecific symptoms including weight loss, anorexia, gross or microscopic hematuria, and decline in performance status. Rarely, it can present as a palpable abdominal mass. The median age of diagnosis reported in adults with Wilms' tumor has varied between 18 and 34 years in different case

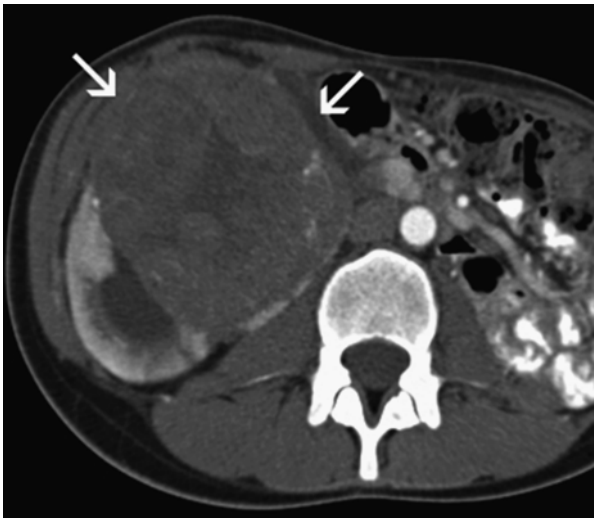

Fig. 5.3 The Wilms' tumor is shown by the *white arrows* (Courtesy of Mark Lockhart, MD Dept. of Radiology UAB Birmingham, AL)

series [35, 36]. In contrast, children typically present with an asymptomatic abdominal mass, malaise, pain, and either microscopic or gross hematuria. Approximately 25 % of children with Wilms' tumor have hypertension presumably due to increased renin activity [20].

Imaging

Imaging plays an important role in the early diagnosis of Wilms' tumor. Ultrasound is the most common method for initial diagnosis of Wilms' tumor. It is noninvasive and affordable [37]. However, it provides poor cross-sectional anatomical information and is less accurate than computerized tomography (CT) scan in tumor staging. Intravenous urography (IVU) can assess physiological or functional ability of the kidney(s) and is also helpful in preoperative differentiation between neuroblastoma and Wilms' tumor [38]. However, IVU is suboptimal to differentiate between solid tumors and benign lesions. CT and magnetic resonance imaging (MRI) are superior to conventional ultrasound and IVU in the preoperative evaluation of patients with Wilms' tumor, owing to their better accuracy and detail [37, 39]. CT chest may be performed to detect pulmonary metastases. CT scan provides excellent visualization of the renal mass, intravascular extension of tumor, and contiguous structures like vessels and lymph nodes along with status and function of the contralateral kidney. On CT, Wilms' tumor usually appears as a bulky, spherical intra-renal mass, usually with a well-defined rim of compressed renal parenchyma or surrounding pseudo capsule (Fig. 5.3) [39]. Some tumors may arise from the periphery of the cortex and grow in an exophytic manner. A heterogeneous mass replacing the kidney and displacing adjacent organs can also be observed. The tumor is hypodense as compared to the surrounding normal renal parenchyma on contrast-enhanced CT

scans with the areas of low attenuation coinciding with tumor necrosis, fat deposition, or both [40]. MRI may be superior to CT for determining the extent of intravascular involvement [41]. Wilms' tumor in adults can be indistinguishable from the more common adult renal neoplasm renal cell carcinoma [42].

Management

Staging

Available adult series report a higher incidence of advanced stage 3 or 4 disease in greater than 50 % of patients compared with the pediatric series where approximately one-third of children are classified as stage 3 or 4 disease [5, 43]. Staging investigations should include a CT scan of the chest and abdomen to detect pulmonary and hepatic metastases and to assess tumor extension, involvement of inferior vena cava, and function of the contralateral kidney. There are two main staging systems: a pre-chemotherapy, surgery-based system developed by the NWTS group and a post-chemotherapy-based system developed by the SIOP [14, 44]. Both staging systems are described in detail in Tables 5.2 and 5.3.

Table 5.2 Wilms' tumor pre-chemotherapy staging by the National Wilms' Tumor Study Group (NWTSG) [44]

NWTSG staging system (pre-chemotherapy)
Stage 1
Tumor is limited to the kidney and completely resected
Tumor was not ruptured before or during removal
Vessels of the renal sinus are not involved beyond 2 mm
There is no residual tumor apparent beyond the margins of excision
Stage 2
Tumor extends beyond the kidney but is completely excised
No residual tumor is apparent at or beyond the margins of excision
Tumor thrombus in vessels outside the kidney is stage 2 if the thrombus is removed en bloc with the tumor
Stage 3
Residual tumor confined to the abdomen
Lymph nodes in the renal hilum or the periaortic chains or beyond are found to contain the tumor
Diffuse peritoneal contamination by the tumor
Tumor extends beyond the surgical margins either microscopically or glossy
Tumor is not completely resectable because of local infiltration into vital structures
Stage 4
Presence of hematogenous metastases or metastases to distal lymph nodes
Stage 5
Bilateral renal involvement at the time of initial diagnosis

Table 5.3 Wilms' tumor post-chemotherapy staging by the International Society of Pediatric Oncology (SIOP) [14]

SIOP staging system (post-chemotherapy)
Stage 1
Tumor is limited to kidney or surrounded with fibrous pseudocapsule. If outside the normal contours of the kidney, the renal capsule or pseudocapsule may be infiltrated with the tumor, but it does not reach the outer surface and is completely resected (resection margins "clear")
The tumor may be protruding into the pelvic system and "dipping" into the ureter (but it is not infiltrating their walls)
The vessels of the renal sinus are not involved
Intra-renal vessel involvement may be present
Stage 2
The tumor extends beyond kidney or penetrates through the renal capsule and/or fibrous pseudocapsule into peri-renal fat but is completely resected (resection margins "clear")
The tumor infiltrates the renal sinus and/or invades blood and lymphatic vessels outside the renal parenchyma but is completely resected
The tumor infiltrates adjacent organs or vena cava but is completely resected
Stage 3
Incomplete excision of the tumor, which extends beyond resection margins (gross or microscopic tumor remains postoperatively)
Any abdominal lymph nodes are involved
Tumor rupture before or intraoperatively (irrespective of other criteria for staging)
The tumor has penetrated through the peritoneal surface
Tumor thrombi present at resection margins of vessels or ureter transected or removed piecemeal by surgeon
The tumor has been surgically biopsied (wedge biopsy) prior to preoperative chemotherapy or surgery
Stage 4
Hematogenous metastases (lung, liver, bone, brain, etc.) or lymph node metastases outside the abdominopelvic region
Stage 5
Bilateral renal tumors at diagnosis

Treatment

To achieve the best outcomes in adults, a multimodality approach using pediatric protocols which includes surgery (nephrectomy), chemotherapy, and radiation treatment is advocated.

Surgery: In children, there are two protocols (SIOP and COG) for the treatment of Wilms' tumor. The protocols differ on the timing of surgery (nephrectomy). The COG which took forward clinical trials run by NWTS in 1969 recommends resection of the primary tumor (nephrectomy) for precise pathologic assessment of tumor extent (stage) and histology before adjuvant chemotherapy is instituted. In contrast, the SIOP nephroblastoma group, which commenced its trials in 1971, favors

preoperative (neoadjuvant) chemotherapy to reduce the complications of surgery and tumor spillage, at the time of delayed nephrectomy which takes place 4–6 weeks after chemotherapy [22].

Most adult patients are treated with initial nephrectomy because in majority of patients the diagnosis is made unexpectedly after nephrectomy is performed for presumed RCC. Even when Wilms' tumor is diagnosed before nephrectomy, total nephrectomy is still recommended according to adult nephrectomy guidelines for any renal cancer. The surgery of choice is open total nephrectomy with lymph node sampling and immediate review by pathology [45]. A review of lymph node sampling has demonstrated a false-negative rate of more than 30 % [46]. Hence although formal lymph node dissection is not considered necessary, lymph node sampling is critically important during the surgical procedure regardless of benign appearing nodes on preoperative imaging or during surgery. Conversely, enlarged lymph nodes seen on preoperative imaging may be "reactive," and there is no definitive evidence that routine lymphadenectomy improves survival. The absence of node sampling may result in under-staging and undertreatment of the tumor as reported by NWTS group in 2005, which could result in an increase of relative risk of local recurrence [46–48]. The surrounding structures are infrequently invaded by Wilms' tumors. The en bloc excision of the tumor with closely adherent structures is necessary when they cannot be cleanly separated, e.g., hepatic invasion [46].

In the pediatric population, there was no difference in event-free or overall survival with immediate nephrectomy versus preoperative chemotherapy followed by nephrectomy in the United Kingdom Children's Cancer Study Group (UKCCS group) trial [49, 50]. In this trial, 205 pediatric patients (186 had confirmed Wilms' tumor) with newly diagnosed potentially resectable renal tumors were randomly selected to undergo immediate nephrectomy, or percutaneous renal biopsy, followed by 6 weeks of neoadjuvant vincristine and actinomycin-D chemotherapy followed by nephrectomy. There was no difference between the two groups in 5-year event-free survival (~80 %), although clinical downstaging was observed with neoadjuvant chemotherapy. In a subsequent report of 520 pediatric patients from the UKCCS group including the aforementioned trial and other off-protocol patients, delayed nephrectomy preceded by preoperative chemotherapy was reported to be associated with fewer surgical complications including tumor rupture and spillage compared with immediate nephrectomy (1 % versus 20.4 %) [15]. For patients with bilateral Wilms' tumor, surgical management is complicated and the risk of renal failure is a concern [46]. The treatment strategy relies on nephron sparing surgery after preoperative chemotherapy which often results in significant reduction of tumor size [51]. The incidence of end-stage renal disease is approximately 15 % at 15 years post-surgery [52].

Chemotherapy: Over the years, adopting pediatric regimens of chemotherapy for treating adults has proven to be effective in improving outcomes. Wilms' tumor is quite sensitive to chemotherapy with partial or complete responses seen in 40–60 % of metastatic tumors. The backbone of chemotherapy regimens for Wilms' tumor

comprises vincristine and actinomycin-D, which is administered as perioperative therapy for stage 1 and favorable stage 2 disease. Doxorubicin is added to this backbone, in high-risk stage 2, 3, and 4 disease. Ifosfamide, carboplatin, and etoposide (ICE) are generally reserved for recurrent advanced disease [45]. The duration of therapy requires further study. Currently, protocols are using 4–6 weeks of neoadjuvant chemotherapy followed by 4–6 months of adjuvant chemotherapy for operable localized disease. For recurrent metastatic disease, the ICE regimen and clinical trials may be considered.

The COG protocol recommends metastatic or "inoperable" cases be diagnosed by preoperative biopsy to receive preoperative chemotherapy based on histology. In their current protocol, children with stage 2 favorable histology Wilms' tumor are treated without doxorubicin. The recommendation for adults is to include doxorubicin in patients who harbor LOH at 1p and 16q, since this molecular subset of patients exhibit poor outcomes with the two-drug regimen. Vincristine intensity is also decreased in these guidelines as compared with current childhood protocols, as adults frequently develop severe neurological toxicities. Sperm banking in males or ovarian preservation in females could be considered immediately before instituting chemotherapy, especially when delivering regimens containing cyclophosphamide or carboplatin [53].

Radiation: Nephroblastoma is a radiotherapy-sensitive cancer as well. In general, radiation therapy is a component of treatment for more advanced stages of Wilms' tumor (stage 3–5). Minor differences in recommendations exist between the SIOP and COG protocol. According to SIOP, radiation therapy is also indicated as adjuvant therapy for node-positive and stage >2 with high risk disease. For the intermediate-risk group, the dose recommended is 15 Gray (Gy) with 15 Gy boost and for the high-risk group, 30 Gy with 5 Gy boost [36]. In the COG protocol, in addition to stage >3, radiation therapy is also recommended for stage 1–2 with unfavorable histology. Radiotherapy is usually instituted by day 14 post-nephrectomy although starting by day 30 is also considered acceptable [45]. Pulmonary radiotherapy is reserved for patients with evidence of pulmonary metastases on chest imaging.

Outcomes

Adults with Wilms' tumor were reported to have worse outcomes in the past as compared with pediatric patients, with historically recorded long-term survival rates of 18–27 % [54, 55]. These results are attributable in part to the fact that the disease usually presented at an advanced stage in adults. Patients with stage 3 and stage 4 diseases were reported to account for more than 50 % of most adult series. Byrd et al. demonstrated that the prognosis was worse in adults than in children even stage for stage. Uncorrected for histology, the recorded 3-year actuarial survival rates in adults were 48 % for stages 1–2 aggregated and 11 % for stage 4, with an

Table 5.4 Outcomes in adult patients with Wilms' tumor reported by different studies

Study (year)	Year	*n* (F/M)	Median age (years)	EFS (%)	OS,% 5 years	Ref. no.
Mitry et al. (2006)	1983–1994	133 (69/64)	34 (15–60)	N/A	47.3	[2]
Izawa et al. (2008)	1973–2006	128	26 (15–73)	N/A	68	[57]
Terenziani et al. (2004)	1983–2001	17 (11/6)	17.5 (16–29)	45	62.4	[5]
Kattan et al. (1994)	1973–1992	22 (14/8)	24 (16–40)	41	55	[35]
Reinhard et al. (2004)	1994–2001	30 (13/17)	25.4 (15–62)	57	83	[36]
Kalapurakal et al. (2004)	1988–2001	23 (13/10)	21.9 (16–51)	77.3	82.6	[58]
Arrigo et al. (1990)	1979–1987	27 (N/A)	24 (16–74)	NA	67	[56]

overall survival of 24 %. In contrast, children of that era had corresponding survival rates of 87 %, 53 %, and 74 %, respectively, also uncorrected for histology [43]. This prompted treating adults with protocols that were designed for and used in pediatric patients involving different modalities of treatment. Using pediatric protocol, the experience of Arrigo and associates with 27 patients between 1979 and 1987 yielded 3-year survival rates of 67 % when anaplastic tumors were included and 79 % when they were excluded (Table 5.4) [56–60]. This data represented an important improvement over prior results and led to the following recommendations: perioperative two-drug chemotherapy for patients with stage 1 disease and perioperative three-drug chemotherapy and adjuvant radiotherapy to the tumor bed (2,000 cGy) for patients with stage ≥2 disease [56]. Subsequently, other retrospective case series of patients reported similar long-term outcomes with multimodality therapy (Table 5.4) [2, 5, 35, 36, 56–58].

In one noteworthy study, a German group using the SIOP perioperative treatment protocol focused on 30 adult patients who were treated according to the SIOP 93-01 study. All of the patients had a central pathology review, and six tumors (13 %) were classified as having high-risk histology. Ten patients (33 %) were found to have distant metastases at the time of diagnosis. All patients underwent primary surgery, all received chemotherapy, and 14 of the 30 patients received radiation as well. At a median follow-up of 4 years, the event-free survival and the OS rates were 57 % and 83 %, respectively [36].

Treatment Toxicity and Monitoring

Neurotoxicity secondary to vincristine and hepatotoxicity or veno-occlusive disease (VOD) due to actinomycin-D is also reported in adults similar to children [36, 58]. The SIOP 9301 study done by the German group reported that 13 out of 27 (48 %) adults suffered from severe (grade 3–4) neurotoxicity, resulting in treatment delay,

dose reduction, or even discontinuation of treatment (40.7 %) [36]. In children, the incidence of VOD varies from 5 to 8 % [59–61]. If supportive management is initiated adequately and timely, it is mostly reversible. The SIOP 9301 also reported severe VOD in 1 out of 30 (3 %) adult renal tumor patients (27 Wilms' tumor and 3 clear cell sarcoma of the kidney) that resolved without residual effects [36]. Kalapurakal and his associates reported 23 adult Wilms' tumor patients of whom 3 (13 %) died after treatment-related liver toxicity, 3–6 months after treatment with actinomycin-D [58].

A late adverse effect associated with a cumulative dose of anthracyclines exceeding 300 mg/m^2 is cardiotoxicity. Anthracycline-mediated cardiotoxicity may be severe if pulmonary irradiation has been administered. Pulmonary irradiation can itself result in restrictive lung disease, whereas abdominal radiotherapy can cause fertility problems and impaired renal function. Renal dysfunction has been described after cyclophosphamide and carboplatin as well in adults [62–66]. Long-term survivors of Wilms' tumor have an increased risk of developing subsequent secondary malignant neoplasms (6.7 % at 40 years from diagnosis) [67]. Secondary malignancies can include bone and soft-tissue sarcomas, breast cancer, lymphoma, leukemia, and melanoma [51].

Toxicity monitoring should comprise of complete blood count and a complete metabolic panel before administration of each dose of chemotherapy. Disproportionate thrombocytopenia and signs of hepatotoxicity will alert the physician to the possibility of VOD. Monitoring for impaired renal function (both glomerular and tubular) as well as possible cardiac function by an echocardiogram (especially in cases with lung irradiation in combination with doxorubicin) or impaired lung function is recommended in patients bearing this risk. During and after therapy, tumor monitoring by chest and abdominal imaging is recommended periodically for 2 years, since most of the relapses occur within first 2 years of completion of therapy [5, 15, 35, 36, 56].

Conclusion

Over the years, the outcomes in the adult Wilms' tumor population have been steadily improving with the adoption of aggressive multimodality pediatric protocols. Further appropriate application of diagnostic and treatment strategies as applied to childhood Wilms' tumor patients and more effective cooperation with pediatric oncologists and pediatric surgeons are important steps in achieving even more improved outcomes. Better understanding of the molecular biology of the disease is critical to make further advances.

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Potential Conflicts

Ankit Madan: None

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