Wilms' tumour

Synonym: nephroblastoma

What is Wilms' tumour?

Wilms' tumours are the most common intra-abdominal tumours of childhood. A Wilms' tumour is an undifferentiated mesodermal tumour of the intermediate cell mass (primitive renal tubules and mesenchymal cells). It may be sporadic or familial.

How common is Wilms' tumour? (Epidemiology) [1]

Wilms tumour is the second most common extracranial solid tumour and the most common malignant renal tumour in children. It accounts for 5% of all childhood malignancies and 80% of all diagnosed renal cancers in children and teenagers. Most cases are diagnosed in children under the age of 5 years.

In the United States and Canada, the estimated incidence is about 9 per million children under 15 years old, affecting 1 in 10,000 children. Similar rates are reported in Europe, Australia, and New Zealand, with lower rates in Asia, Central and South America.

Most cases are unilateral, with 5–10% of cases affecting both kidneys. Bilateral Wilms' tumours are more common in children with underlying genetic syndromes.

More than 15 different syndromes are associated, including:

- WAGR (Wilms tumour, aniridia, genitourinary abnormalities, and a range of developmental delays).

- Denys-Drash (Wilms tumour, diffuse mesangial sclerosis leading to early-onset renal failure, and intersex disorders that can range from ambiguous to normal-appearing female genitalia in both XY & XX individuals).
- Beckwith-Wiedemann (embryonal tumours, macrosomia, macroglossia, hemihypertrophy, visceromegaly, omphalocele, neonatal hypoglycaemia, and ear creases/pits).

Only 10% of cases are associated with an underlying constitutional mutation, and therefore the aetiology of most cases is unknown

Familial Wilms' tumour[2]

Hereditary Wilms' tumour (either bilateral tumours or a family history of the neoplasm) is uncommon. Several different families with Wilms' tumours have been identified. All are transmitted in an autosomal dominant manner, caused by mutations in one of at least three genes:

- One related to the WT1 gene on chromosome 11 (11p13) - (includes those patients with WAGR) - encodes a protein which is a transcriptional repressor downregulating IGF-II, an insulin-like growth factor.
- Other families (including those with Beckwith-Wiedemann syndrome) have a different mutation - of the WT2 gene on chromosome 11 (11p15.5).
- Other gene mutations, thought to be on chromosome 16 (WT3-16q) and/or chromosome 1p can also cause the tumour.[3]

Symptoms of Wilms' tumour (presentation)[1]

- Children are usually asymptomatic at initial diagnosis. In most cases, a parent will identify an abdominal mass upon bathing or dressing their child, or a mass will be palpated during a routine well-child visit or non-related consultation.
- However, up to 35% of patients can present with either haematuria, hypertension, fever, or loin pain.
- Rarely, a child can present with an acute abdomen in the setting of tumour rupture and bleeding into surrounding tissue.

- If the diagnosis is clinically suspected, an initial ultrasound of the abdomen with doppler is indicated, followed by referral to a paediatric general surgeon and oncologist for additional work-up and treatment.

Screening for Wilms' tumour

A recommendation for surveillance of children at high risk (familial or associated conditions) included:[4]

- Surveillance should only be offered after review by a clinical geneticist.
- Surveillance should be carried out by renal ultrasound every 3-4 months.
- Surveillance should continue until 5 years of age in all conditions except Beckwith-Wiedemann syndrome, Simpson-Golabi-Behmel syndrome and some familial Wilms' tumour pedigrees, when it should continue until 7 years.

Diagnosing Wilms' tumour (investigations)[5]

- Useful laboratory tests include FBC, renal function and electrolytes and urinalysis.
- Genetic studies may reveal the chromosomal abnormalities consistent with the condition.
- Initial imaging of a renal mass usually includes abdominal ultrasound to identify the organ of origin.
- This is followed by cross-sectional chest/abdominal/pelvis imaging with either CT or MRI to further evaluate the primary site and to identify any metastases. These scans also evaluate the status of the contralateral kidney, tumour involvement of the renal veins or inferior vena cava, presence of retroperitoneal adenopathy, preoperative tumour rupture, and the existence of ascites.
- Imaging characteristics are not always correlated with operative or pathologic findings and should not replace surgical exploration and tissue analysis for local and disease staging.

- Advances in imaging such as 3-D computer reformatting and printing models may assist in planning operative approaches, particularly when nephron sparing surgery is appropriate.

Staging of Wilms' tumour [6]

Stage I	Tumour limited to the kidney and completely excised. Renal capsule is intact. The tumour is not ruptured before or during removal. The vessels of the renal sinus are not involved. There is no residual tumour apparent beyond the margins of excision.
Stage II	Tumour extends beyond the kidney but is completely excised. No residual tumour is apparent at or beyond the margins of excision. There may be: Regional extension of the tumour - ie penetration through the outer surface of the renal capsule into the perirenal soft tissue or more than 1-2 mm of tumour invasion into the renal sinus. Vessels outside the kidney are infiltrated or contain tumour thrombus. The tumour was biopsied or there was local spillage of tumour confined to the flank.
Stage III	There is residual tumour confined to the abdomen. There may be one or more of the following: Tumour-positive lymph nodes in the renal hilus, the periaortic chains, or other intra-abdominal sites on biopsy. There has been diffuse peritoneal contamination by the tumour - eg, spillage of tumour beyond the flank before or during surgery or by tumour growth penetrating through the peritoneal surface. Implants are found on the peritoneal surfaces. Tumour extends beyond the surgical margins, either microscopically or grossly. Tumour is not completely resectable because of local infiltration into vital structures.
Stage IV	Haematogenous metastases - beyond stage III - eg, to the lung, liver, bone, or brain.
Stage V	Bilateral renal involvement at initial diagnosis. Attempt to stage each side according to the above criteria on the basis of extent of disease prior to biopsy. Four-year survival was 94% for those patients whose most advanced lesion was stage I-II; 76% where it was stage III.

Management of Wilms' tumour[7]

- For most patients, nephrectomy followed by chemotherapy (regimes include vincristine, dactinomycin and doxorubicin, sometimes with additional cyclophosphamide) can be curative.
- Routine postoperative radiotherapy to the flank is beneficial in patients with a stage III tumour.
- Patients with massive, nonresectable unilateral tumours, bilateral tumours, or venacaval tumour thrombus above the hepatic veins should be considered for pre-operative chemotherapy because of the risk of initial surgical resection.

Wilms tumour develops in association with an underlying germline predisposition in 10% to 15% of cases. A genetics referral is recommended for all children with Wilms tumour who have a positive family history of cancer, bilateral kidney involvement, or presence of syndrome-specific features.

Prognosis[7]

Wilms tumour is a curable disease in most affected children. Since the 1980s, the 5-year survival rate for Wilms tumour with favourable histology has been consistently greater than 90%. This favourable outcome occurred with changes in therapy that included reductions in the length of therapy, dose of radiation, extent of fields irradiated, and the percentage of patients receiving radiation therapy.

The prognosis for patients with Wilms tumour depends on the following:

- Histopathological features of the tumour (favourable or anaplastic).
- Stage of disease at diagnosis.
- Molecular features of the tumour such as 1q gain and loss of heterozygosity of 1p and 16q. 1q gain, affecting 28% of Wilms tumours, is the most powerful predictor of outcome and is associated with an adverse outcome. Loss of heterozygosity of 11p15 and loss of imprinting of 11p15 is associated with relapse in very low-risk patients who do not receive chemotherapy.

- Age at presentation is commonly between 2 and 5 years, and the incidence of Wilms tumour in children older than age 10 years is rare. Older age is associated with an adverse prognosis.

There is an increased risk of second tumours in survivors of Wilms' tumour. Second tumours include bone and soft tissue sarcomas, breast cancer, lymphoma, gastrointestinal tumours and melanoma. Acute leukaemias may also occur.

References

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Last updated by: Dr Colin Tidy, MRCGP 20/07/2023	
Peer reviewed by: Dr Krishna Vakharia, MRCGP 20/07/2023	**Next review date:** 18/07/2028

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