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Surgery for Wilms Tumour in Children in a Tertiary Centre in Hong Kong: A 15-year Retrospective Review

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Abstract ***Objective:*** To study the surgical aspect in the management of Wilms tumour in children. ***Methods:*** A retrospective study was conducted for all children who underwent nephrectomy for Wilms tumours in a university teaching hospital in Hong Kong from January 1996 to June 2011. ***Results:*** A total of 13 children (6 boys and 7 girls) were studied. The median age at diagnosis was 37 months (range, 9 months-10 years). Two children had stage I disease, 4 had stage II disease, 4 had stage III disease, 1 had stage IV and 2 had stage V disease. Pre-operative chemotherapy was given to children with stage III or above disease. The median tumour size was 10 cm (range, 5 to 17 cm). Unilateral radical nephrectomy was performed in children with unilateral disease. Children with bilateral disease underwent nephron-sparing surgery. Lymph node biopsies were performed in 8 cases while 1 had positive lymph node involvement. There was no intraoperative tumour rupture. Intraoperative complications including small bowel injury (n=1), diaphragmatic injury (n=1) and major bleeding that required transfusion (n=2). Post-operatively, all children received chemotherapy. Children with advance disease also received radiotherapy. There was no post-operative surgical complication. At a median follow-up of 76 months, all children survived and 2 children had distant tumour recurrence. ***Conclusion:*** This study provides updated surgical experience in the management of Wilms tumour. Zero intraoperative tumour ruptured rate was achieved. With multidisciplinary management, the long term outcome of Wilms tumour was excellent.

Key words Children; Surgery; Tumour; Wilms

Introduction

Although Wilms tumour (WT) or nephroblastoma is the third commonest solid tumour in childhood, the incidence of WT is only 8 cases per million in children under age 15 in the United States (US) and the incidence is even lower in Asia.[1-3] With the advances in surgery, chemotherapy and radiotherapy, the 5-year survival rate of children with WT exceeded 90% in localised disease and was about 70% in metastatic disease.[4]

According the National Wilms Tumour Study 4 (NWTS-4), surgical complications caused morbidity to the patients and affected the disease prognosis.[5] Among various surgical complications, intraoperative tumour spillage was regarded as a significant complication. Surgical spill correlated strongly with local recurrence and resulted in upstaging and more extensive chemotherapy and radiation therapy.[5]

In Hong Kong, the majority of paediatric renal tumours was managed in the three paediatric surgical centres.[6] We herein report our surgical experience in the management of WT.

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Methods

A retrospective review of all children who underwent nephrectomy for WT in the Prince of Wales Hospital from January 1996 to June 2011 was conducted. Basic epidemiological data including sex of the patient, age at presentation, location of the tumour and staging of the tumour were studied. Surgical aspects on the management including the need for pre-operative biopsy, the approach of surgery and any surgical related complications were studied. The prognosis including the survival rate and any tumour recurrence were also reviewed.

NWTS-staging of WT was used (Table 1). For stage I or II tumour, primary radical nephrectomy was performed. For stage III, IV and V tumour, tumour biopsy was performed and neoadjuvant chemotherapy was given. Following nephrectomy, all children received chemotherapy according to protocol. Since 2003, our centre adopted NWTS-5 protocol. In brief, children with stage I & II disease received vincristine and actinomycin D for 18 weeks. Children with stage III & IV disease received vincristine, actinomycin D and doxorubicin for 24 weeks. Radiotherapy was given to the children with stage III or above disease.

Table 1 NWTS staging of Wilms tumour

I	Tumour confined to the kidney and completely resected. The renal capsule is intact, and the tumour was not ruptured prior to removal. No renal sinus extension. There is no residual tumour.
II	Extracapsular penetration, but is completely resected. Renal sinus extension or extrarenal vessels may contain tumour thrombus or may be infiltrated by tumour.
III	Residual nonhematogenous tumour confined to the abdomen: lymph node involvement, any tumour spillage, peritoneal implants, tumour beyond surgical margin either grossly or microscopically, or tumour not completely removed. Tumour biopsied before removal.
IV	Haematogenous metastases to lung, liver, bone, brain, etc.
V	Bilateral renal involvement at diagnosis.

Results

Over the 15-year study period, 13 children underwent nephrectomy for the WT. The sex distribution was similar (male: female, 6:7). The median age at diagnosis was 37 months (range, 9 months-10 years). Five tumours were located on the left side while 6 were located on the right side. Two children had bilateral disease. None of the child had syndromic disease that predisposed to the development of Wilms tumour (Table 2).

Two children had stage I disease; 4 had stage II disease; 4 had stage III disease; 1 had stage IV and 2 had stage V disease. Nine children presented with abdominal mass. Four children had haematuria and 1 child had abdominal pain at presentation. One child had hypertension pre-operatively. The median tumour size was 10 cm (range, 5 to 17 cm).

Pre-operative computer tomography (CT) detected the presence of tumour thrombus in the renal vein (RV) in 2 cases and in both RV and inferior vena cava (IVC) in 2 cases. After pre-operative chemotherapy, only 1 child had residual thrombus at the RV and IVC which required thrombolectomy.

Two children had pre-operative tumour rupture. One of the children had the bilateral tumour and underwent ultrasound guided tumour biopsy pre-operatively. The tumour ruptured after biopsy and she received embolisation of the tumour for haemostasis. Regarding the other child with pre-operative tumour rupture, the pre-operative CT suggested the tumour had ruptured. Laparotomy showed moderate amount of blood stained peritoneal fluid with multiple peritoneal tumour deposits. Pathology report confirmed the tumour was ruptured with breakage of the renal cortex.

Upper transverse laparotomy or bilateral subcostal laparotomy was performed in order to achieve adequate exposure (Figure 1). One child underwent laparoscopy at the beginning of the operation but was converted to laparotomy before any attempt in tumour mobilisation. Contralateral kidney was examined in all cases. Lymph node biopsy was performed in 8 cases. Positive lymph node involvement was present in 1 case. Radical nephrectomy was successfully performed in all unilateral tumours. Regarding the 2 children with bilateral disease, one underwent unilateral nephrectomy and nephron sparing surgery for the contralateral kidney. Another child underwent bilateral nephron-sparing surgery. There was no intraoperative tumour rupture or tumour spillage. There were 4 intraoperative complications. One child had small bowel injury during laparotomy. One child had a small diaphragmatic tear during dissection. Two children had major bleeding from the RV and IVC respectively (Table 3).

Table 2 Demographic data and clinical characteristic of children with Wilms tumour

Case number	Sex	Age (months)	Symptoms and signs	Side	Biopsy	Thrombus	Stage	Lymph node biopsy	Histology
1	M	9	Mass	Bilateral	Yes	No	V	Negative	Unfavourable
2	F	38	Mass, Haematuria	Right	Yes	IVC, RV	III	Not taken	Favourable
3	M	54	Haematuria	Left	No	No	II	Not taken	Favourable
4	M	42	Mass	Right	No	No	IV	Negative	Favourable
5	F	24	Pain	Bilateral	Yes	No	V	Not taken	Favourable
6	F	19	Mass	Right	Yes	RV	III	Positive	Favourable
7	F	34	Mass	Left	No	No	II	Negative	Favourable
8	F	12	Mass	Right	No	No	I	Negative	Favourable
9	M	36	Mass, Hypertension	Left	Yes	RV	III	Negative	Favourable
10	F	36	Haematuria	Right	Yes	IVC, RV	III	Not taken	Favourable
11	M	39	Haematuria	Left	No	No	II	Negative	Favourable
12	F	24	Mass	Left	No	No	II	Negative	Favourable
13	M	120	Mass	Right	No	No	I	Not taken	Favourable

IVC-inferior vena cava, RV-renal vein

Table 3 Children with surgical complications or recurrence

Case number	Surgical complications	Recurrence
6	Diaphragmatic injury	Mediastinal
10	Small intestine laceration, bleeding from inferior vena cava	–
11	–	Lung, liver and right tibia
13	Bleeding from renal vein	–

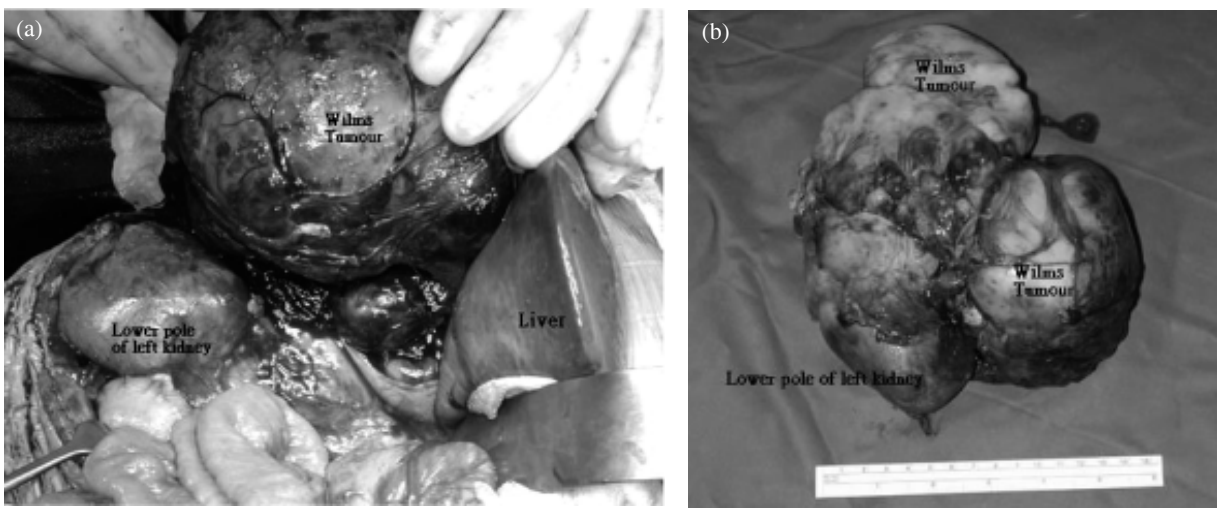

Figure 1 Wilm's tumour arising from the upper and middle pole of left kidney.

The median operative time was 175 minutes (range, 150 to 345 minutes). Six children required transfusion. Seven children were supported in the intensive care unit for 1 to 2 days post-operatively. No post-operative surgical complication such as intestinal obstruction or wound infection was identified. Twelve tumours had favourable histology and 1 tumour had unfavourable histology. At a median follow-up of 76 months (range, 6 months to 15 years), all children survived.

There was no local tumour recurrence. Two children had distant recurrence. One child had mediastinal recurrence and underwent surgical excision of the recurrent tumour. One child had distant metastasis to lung, liver and tibia. They were all in clinical remission after chemotherapy and radiotherapy.

Renal function was preserved in all cases even in children with bilateral disease. One child with stage V disease had mild scoliosis and supraventricular tachycardia.

Discussion

Surgery is the cornerstone of the management of WT. Although the incidence of surgical complications had decreased, complications did produce short term and long term morbidities.[5] Excision of a large tumour in a small peritoneal cavity had the inherent risk. The aim of the surgery is to achieve complete tumour removal without spillage of tumour content. Management of Wilms tumour differs between Europe and the US. In Europe, according to the Society of Paediatric Oncology (SIOP) protocol, all children with presumptive WT will receive chemotherapy before nephrectomy. In US and Canada, the Children Oncology Group (COG) adopts the NWTS protocol which advice for primary nephrectomy.[4] COG recommends neoadjuvant chemotherapy only in cases where the tumour is deemed unresectable at surgical exploration, bilateral, occurring in a solitary kidney or associated with vascular involvement above the hepatic veins. In our centre, we adopt a risk-stratified protocol resembling the NWTS protocol. Upfront nephrectomy was performed whenever it was surgically feasible.[7]

Although COG advocates primary nephrectomy, in stage V disease, it recommends pre-operative tumour biopsy. Pre-operative chemotherapy can be tailored according to the histological result.[8] However, tumour biopsy is not without risk.[9] In our series, 1 child with grade V disease had tumour ruptured after ultrasound guided tumour biopsy. The child presented with shock 2 days after the biopsy. Haemostasis was achieved through transarterial embolisation of the tumour feeding vessels. Although transarterial embolisation was rarely performed in the management of childhood tumour, it was reported to be feasible in life-threatening bleeding from Wilms tumour.[10] She subsequent underwent unilateral radical nephrectomy and nephron sparing surgery over the contralateral kidney. She remains well post operatively with no recurrence of tumour.

Transverse laparotomy is the preferred mode of skin incision. The frequency of complications was higher after Median laparotomy.[11] In the principle of surgical oncology, adequate surgical exposure is the key-factor for safe and complete tumour removal. There were limited publications on laparoscopic excision of WT. In those studies, all patients had received pre-operative chemotherapy.[12,13] The aim of chemotherapy is to shrink the tumour and the formation of a fibrous capsule. The capsule may decrease the risk of tumour rupture. In our series, 1 case started with laparoscopy, but we decided to proceed to laparotomy because we thought it was impossible to perform nephrectomy safely in a small place without tumour spillage.

Radical nephrectomy is the gold standard of surgical treatment in unilateral disease. Partial nephrectomy is only practiced in selected cases because the risk of renal failure after unilateral nephrectomy is low and often the tumour is too large to allow partial nephrectomy.[14-16] In bilateral disease, the risk of renal failure approach 15% for children with bilateral disease at 15 year post-operatively.[17] Nephron-sparing surgery is the principle of surgery. Bilateral nephron-sparing surgery was reported to be feasible in 50% of bilateral cases.[18,19] In this series, 1 child with stage V disease still had extensive unilateral tumour after chemotherapy and he underwent unilateral radical nephrectomy. Nephron-sparing surgery was safetly performed in the contralateral kidney. Although pathological reports showed the tumour extended to the margin in some of the specimens, there was no tumour recurrence and renal failure so far.

Knowing the rarity of the incidence of Wilm's tumour in Hong Kong, according to international experience, the presence of surgical expertise was an important factor to minimise the surgical complications.[11,20] Except the first case in this series, each operation were performed by at least 2 specialists experienced in tumour resection. Throughout the 15-year study period, there was no change in the surgical technique, approach and equipments. We did not have a single case of intraoperative tumour spillage. Availability of expertise was probably one of the reasons of zero tumour rupture rate.

Although we did not have a single case of tumour spillage, we did encounter other surgical complications. One child had laceration of small intestine during laparotomy. Careful dissection was needed because the intestine was displaced by the huge tumour. The laceration was repaired and there was no leakage or stricture post-operatively. One child had massive bleeding from the renal vein. The tumour was located at the right side. Right sided tumour had a known increased risk in vascular dissection because of the close proximity of IVC and renal vein, and the distorted anatomy by the huge tumour. Another child had bleeding from IVC during thrombolectomy.

One child had diaphragmatic injury. She had multiple peritoneal seedling and the tumour was adherent tightly to the dome of the diaphragm and surrounding tissues. A small piece of diaphragm was resected en-bloc with the tumour. Resection of a small piece of diaphragm was an acceptable and a well-known complication in surgical resection of the WT.[5,20]

Intestinal obstruction (IO) was reported to be the commonest surgical complication after surgery for WT.[21] Although in this small series we did not encounter a single case of intestinal obstruction, education to the parent and the patient about this potential risk is mandatory because IO can be presented years after the initial operation.

NWTS-4 showed that local tumour recurrence rate was higher if lymph node biopsy was not performed for children with stage I disease.[5] The recurrence rate was not statistically different in stage II/III disease. In our series, lymph node biopsy was routinely performed if any perihilar or para-aortic lymph node was palpable. Regarding the 2 cases with tumour recurrence, in 1 child who had multiple peritoneal deposits, the lymph node biopsy showed tumour involvement. In another child with stage II disease, 2 enlarged and firm para-aortic lymph nodes were identified during operation and were sampled. However, pathology reports only showed benign lymph nodes. Regarding the cases that lymph node biopsy was not performed, only one had stage I disease. In this case, we did intend to perform lymph node biopsy. However, no lymph node was palpable. Since he has the shortest follow-up duration in this series, continuous surveillance is needed to look for the possibility of local recurrence.

Besides surgical morbidities, chemotherapy and radiotherapy may lead to a number of late complications.[22] Knowing the improved survival of Wilms tumour, the direction of treatment were to decrease the intensity of chemotherapy and to identify the high risk patient.[4] In one of the early cases in this series, a child with stage III disease received 54 weeks of chemotherapy. Since 2003, we adopted the NWTS-5 protocol and children with stage III disease received 24 weeks of chemotherapy only. Recent study suggested that loss of heterozygosity on chromosome 1p and 16q was associated with increased risk of recurrence and mortality in children with favourable histology WT.[23] A more intense chemotherapy protocol was adopted if these abnormalities were identified.[23] In our centre, cytogenetic assessment was not performed. In future, it may become the integral part of the treatment protocol. Cardiotoxicity, scoliosis and secondary malignancy are well known complications from anti-WT treatment. A close follow-up is required to identify these potential complications as the children grow up.

Conclusion

This study provides updated surgical experience in the management of WT. In the presence of surgical expertise and risk stratified management, zero intraoperative tumour ruptured rate can be achieved. With multidisciplinary treatment, the long term outcome of WT was excellent and all children survived.

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