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CASE SERIES

Wilms tumour with poor response to pre-operative chemotherapy: A report of 2 cases

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Abstract

Introduction: Majority of Wilms tumour (WT) responds well to pre-operative chemotherapy. In Malaysia, incidence of WT is rare with only two cases reported per one million populations yearly. This case report is to highlight on the awareness of WT in an Asian population and highlight two cases and challenges faced after pre-operative chemotherapy. *Case Report:* In this case series, we report on two cases of WT which had poor response to pre-operative chemotherapy. Both cases underwent surgery after pre-operative chemotherapy and recovery was uneventful during a two-year follow-up. *Discussion:* Both patients had chemotherapy prior planned surgery, but had unfortunate poor tumour response. The tumour progressed in size which required a radical nephrectomy. The histology report for the first case had more than 60% blastemal cells remaining despite giving pre-operative chemotherapy with no focal anaplasia. This showed poor response to chemotherapy evidenced by the high number of blastemal cells. The second case was a stromal type WT which is known for poor response and may lead to enhancement of growth and maturation induced by chemotherapy. These were the possible reason of poor response of WT in these two cases.

Keywords: Child, Wilms tumour, kidney neoplasm

INTRODUCTION

Incidence of WT in Malaysia is rare with less than 2.5 cases per million populations yearly and 5-7% of all childhood cancers in a White Caucasian population.[1,2] An audit by Cheah *et al*. recorded only 37 cases over a 22-year period which translates to 1.6 cases per year in a Malaysian university hospital.[2] To include the incidence in children, as WT is a childhood cancer. This case series describes the challenges faced to manage two cases of intermediate risk Wilms Tumour with poor response to pre-operative chemotherapy and its possible reasons for the poor response to chemotherapy.

CASE 1

An eight-month old baby boy presented with a left renal mass for two months. Thoracic, abdominal and pelvic staging computed tomography (CT) scan showed a large left heterogenous mass arising from the mid to lower pole of right kidney measuring 7.3cm x 6.2cm x 7.7cm with no evidence of lymph node involvement (Fig. 1A). There was no evidence of distant metastases to the lungs and other abdominal solid organs from the CT scan. In view of large tumour and risk of tumour spillage, decision was made for pre-operative chemotherapy first and a CT guided percutaneous biopsy was performed which histopathological results confirmed the diagnosis of WT. Pre-operative chemotherapy was commenced with actinomycin D and vincristine for 4 weeks. Radiological reevaluation of CT abdomen 6weeks later revealed an enlargement of the mass to 7.5cm x 7.7cm x 10.3 cm which is approximately 70% volume increment from the original size. Subsequently, the child underwent an elective radical nephrectomy. With careful dissection, an en-bloc resection

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was performed with no rupture of tumour (Fig. 1B). The resected specimen (Fig. 1C) weight at 450grams showed mixed type WT with 20% necrosis, 60% blastema, 25% epithelium and 15% stroma (Fig. 3A). There were no features of anaplasia (extreme nuclear and cytologic atypia). Blastemal components were positive to WT-1 stains (Fig. 3B). Resected margins were clear with no tumour invasion beyond the renal capsule with no lymph node involvement. Features were consistent with intermediate risk nephroblastoma of mixed type. Section of the renal pelvis show no malignant infiltration into the renal sinus fat, vessels or urothelium. Section of the ureteric and blood vessel margin is clear. Post-operative recovery was uneventful and the patient was treated as a stage III WT (SIOP classification). Post-operative chemotherapy (vincristine, actinomycin D and doxurobicin) was continued with addition of 14.4Gy, 8 fractions of right flank radiotherapy over 1.5 weeks. Till current (2 years post-operatively), there were no evidence of tumor recurrence on subsequent follow-up visits.

CASE 2

A 9 months old baby boy presented with an incidental finding of a mass in the abdomen. An urgent CT staging thoracic, abdomen and pelvis was performed. CT staging of the thoracic abdomen and pelvis revealed a well-defined heterogeneous enhancing mass arising from the anterior aspect of the right kidney measuring 7.3cmx8.5cmx9.6cm with no evidence of local infiltration or suspicious lymph nodes (Fig. 2A). There was no evidence of distant metastases to the lungs and other abdominal solid organs from the CT scan. Similar to the first case, due to large tumour and risk of tumour spillage, decision was made for pre-operative chemotherapy first and a CT guided percutaneous biopsy was performed which histopathological results confirmed the diagnosis of WT. Pre-operative chemotherapy was commenced with actinomucin D and vincristine for 4 weeks. Radiological reevaluation of the CT abdomen 6 weeks later showed enlargement of the mass to 10cmx8.5cmx11cm which was 60% greater than its original size. A radical nephrectomy was performed and the right renal mass was successfully removed en-bloc without

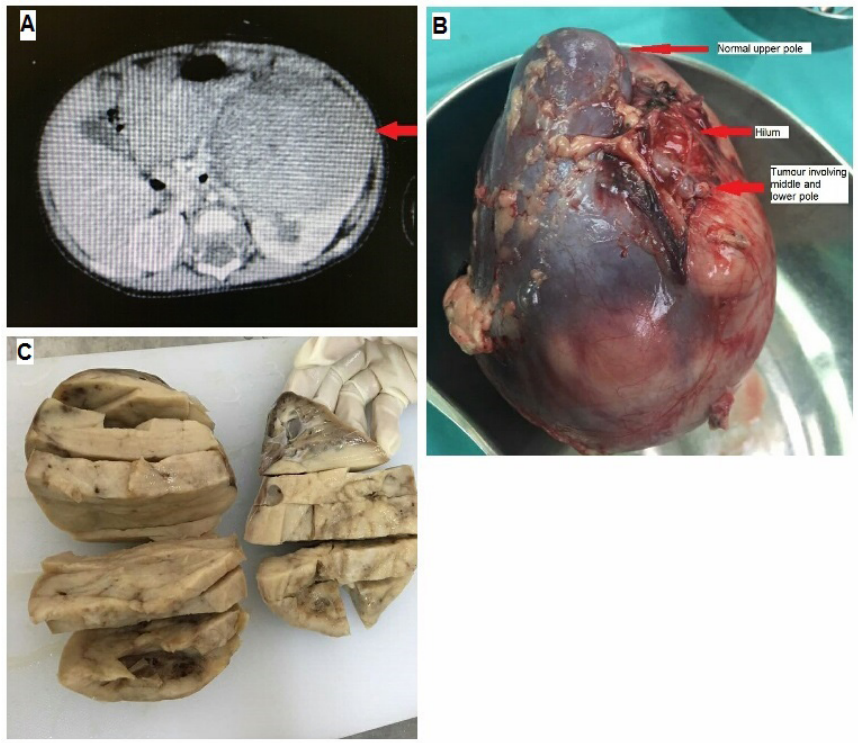

FIG. 1: (A) Contrast enhanced CT abdomen of Case 1 showing large left heterogeneous renal mass involving the upper pole (red arrow). (B) Intra-operative findings of left renal mass with involvement over the upper, middle and lower pole (red arrow). (C) Gross specimen showing a solid cream tan renal tumour involving the entire kidney.

any tumour rupture (Fig. 2B). Macroscopic examination revealed a 650grams cream tan solid renal mass (Fig. 2C) Several enlarged para-aortic lymph nodes seen, excised and biopsied. Histopathology results showed a triphasic growth pattern, composed of predominantly 70% stromal, 20% epithelial and 10% blastemal cells (Fig. 3C) and positive for WT-1 stains (Fig. 3D). Additional staining with was performed for the epithelial component which tested negative for Myogenin stains. There were no areas of necrosis which indicated poor response to chemotherapy. Resected margins were clear with no tumour invasion beyond the renal capsule and no lymph node involvement. Section of the renal pelvis show no malignant infiltration into the renal sinus fat, vessels or urothelium. Section of the ureteric and blood vessel margin is clear. Presence of involvements with triphasic growth components were features consistent of nephroblastoma, stromal type predominantly. Similarly, post-operative recovery was uneventful and the patient was treated as a stage III WT (SIOP classification). Post-operative chemotherapy (vincristine, actinomycin D and doxurobicin) was continued with addition of 14.4Gy, 8 fractions

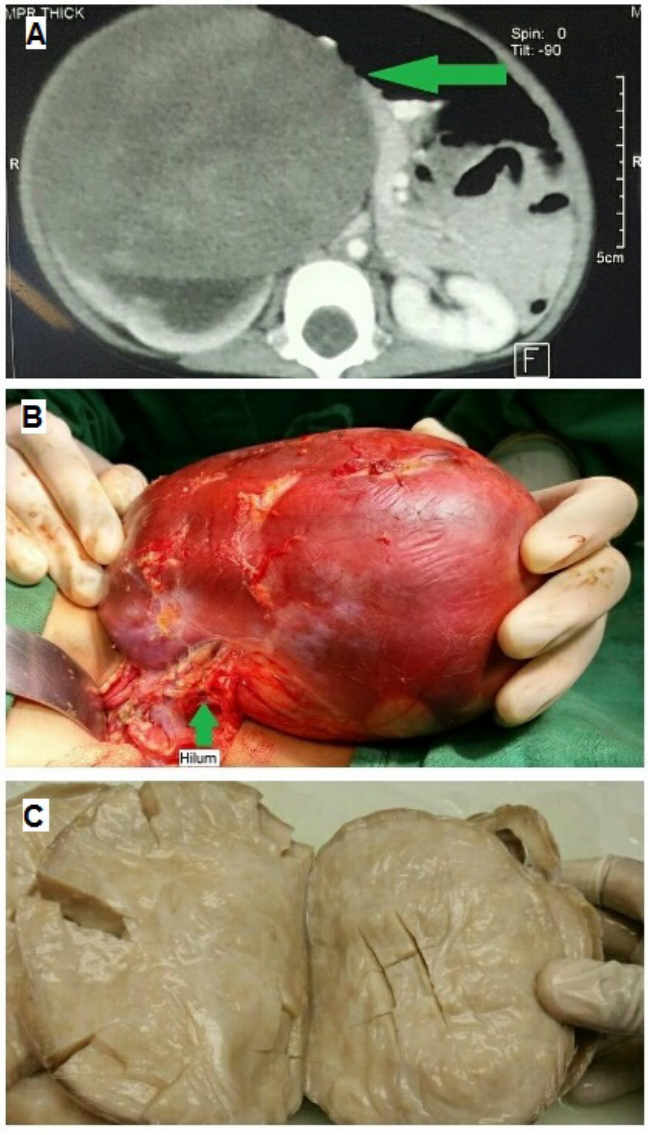

FIG. 2: (A) Contrast enhanced CT abdomen of Case 2 showing large right heterogeneous renal mass displacing surrounding structures (green arrow). (B) Intra-operative findings of right renal mass involving the entire kidney. (C) Gross specimen showing a solid cream tan renal tumour.

of right flank radiotherapy over 1.5 weeks. Till current (2 years post-operatively), there were no evidence of tumour recurrence on subsequent follow-up visits.

DISCUSSION

Majority of WT normally respond to pre-operative chemotherapy with a 90% overall five year survival especially in patients with favourable histology.[3] The benefit of pre-operative chemotherapy reduces the incidence of rupture and tumour spillage, reduced relapses and fewer post-operative complications.[4] Patients with mixed type histology WT is reported to have a good pre-operative chemotherapy response with more than 70% of patients achieving 40% or more reduction of tumour size. In large trials by SIOP (Society of Paediatric Oncology), it is shown that pre-operative chemotherapy reduces the tumour size and may down-stage the disease by causing necrosis to the affected draining lymph nodes.[5] Patients with focal or diffuse anaplasia have a poorer response towards pre-operative chemotherapy which is an unfavourable histology in WT.[5]

In the first case of mixed type nephroblastoma, there was only 20% of necrosis with 60% blastemal cells remaining in the histopathology specimen depicting poor response to pre-operative chemotherapy. In patients pre-treated with chemotherapy, the amount of remaining blastemal cells is of prognostic significance.[6] A high percentage of viable blastemal cells are associated with a reduced relapse-free survival (58.4% versus 86.7%) which is seen in blastemal subtype histology.[7] Due to the lack of facilities, the authors were not able to proceed with genetic testing to ascertain if there were any tumour-specific loss of heterozygosity for chromosome 1p or 16q which is associated with an adverse outcome in favourable histology Wilms Tumour.[8]

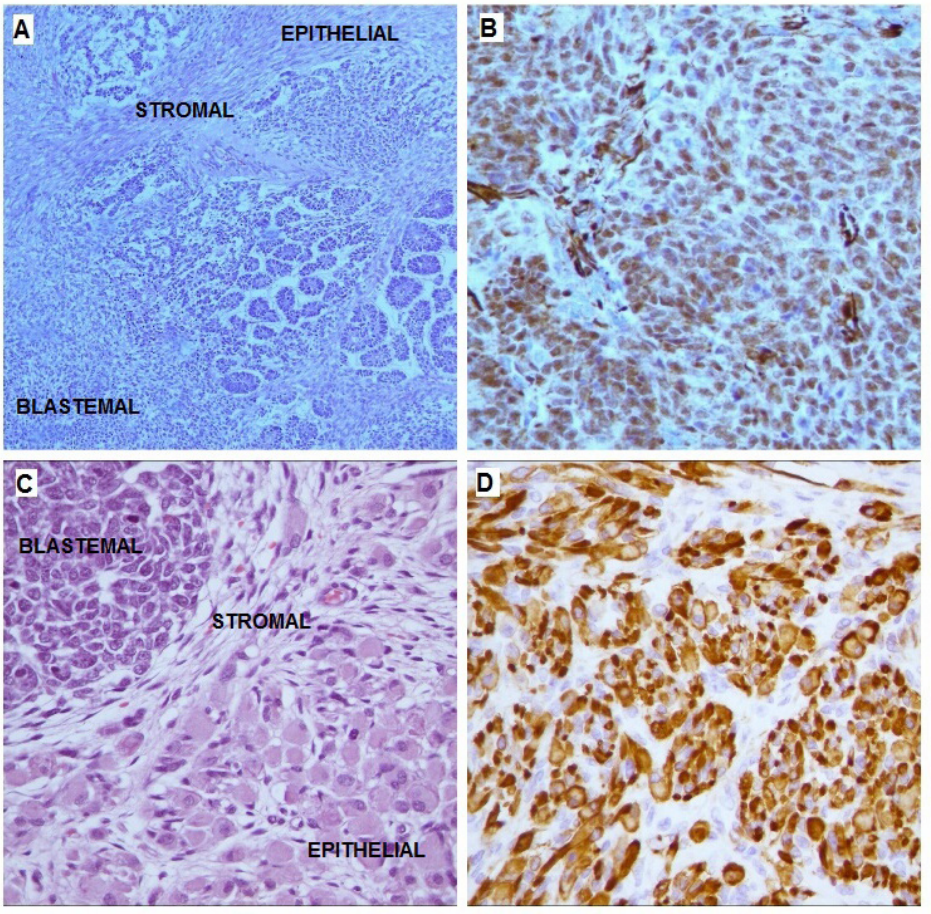

FIG. 3: (A) Microscopic specimen of Case 1 which shows all three types of cell components of blastema, epithelial and stromal cells positive for (B) WT-1 staining. (C) Microscopic specimen of Case 2 which shows all three types of cell components of blastema, epithelial and stromal cells positive for (D) WT-1 staining.

In the second case of stromal subtype nephroblastoma, there were no areas of necrosis which showed even poorer response to chemotherapy. The first possible reason for poor response is which chemotherapy usually eradicates blastema followed by the least differentiated epithelial cells. Tumour histology was predominantly stromal type in origin and led to poor response of chemotherapy to the stromal type cells. Secondly, chemotherapy may also lead to cancer cell maturation especially in the stromal component. Therefore, it was also possible that chemotherapy further enhanced the maturation of stromal cells leading to an increase in size of tumour.[9] Sandeep *et al*. reported 7 cases of bilateral WT (over period of 11 years) which were not responsive to pre-operative chemotherapy. Similarly, there was one case of stromal type with teratoid features which also showed poor response to chemotherapy.[10]

The authors acknowledge the long-term benefits of pre-operative chemotherapy (increase in 5-year survival with a longer relapse free period) and advocate its use. This is based on the initial study SIOP 2 and 6 which showed that pre-operative chemo and radiotherapy had benefits in reducing intra-operative tumour spillage (5% in chemoradiation group vs 20% in the upfront surgery).[11] Subsequently studies in SIOP 6 identified that a risk-adapted therapy which selectively limits the use of radiotherapy in accordance to patient risk resulted in high cure rates with an 82% 2-year disease free rate and 89% 5-year survival rate.[11] This had led to the current treatment with pre-operative chemotherapy which the optimal duration was established as 4 weeks of vincristine and actinomycin D from the SIOP 9 study. The study revealed that there was no added survival benefit of 4 weeks versus an extended duration of pre-nephrectomy chemotherapy of 8 weeks (2-year event free survival rate 84% and 82% respectively; 5-year survival of 90% and 87% in both groups).[12] However, in cases of minimal response after upfront chemotherapy multidisciplinary meetings is important to determine the subsequent treatment. This is essential to ensure that such cases are detected early and may be offered for upfront surgery as tumours as soon as possible.

Ethical consent: This case report is registered in accordance with the National Malaysia Medical Research (NMRR-17-1806-37676). As this is a case report with patient anonymity, no ethics approval was needed by the Malaysian Ministry of Health Research Ethics Committee.

Conflict of interest: The authors declare no conflict of interest.

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