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Original Article

'EFFECT OF PREOPERATIVE CHEMOTHERAPY IN THE TREATMENT OF ADVANCED WILMS' TUMOR'

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Abstract

Introduction: The management of Wilms' tumor still remains a matter of great challenge to pediatric surgeons and also to pediatric oncologists. The tumor continues to be the subject of intensive investigations that with the aid of co-operative protocols by the National Wilms' Tumor Study (NWTS) have resulted in marked improvement in survival. Surgical excision remains the cornerstone of treatment of Wilms' tumor; however the dramatic improvement in overall survival is the result of coordinated use of surgery, chemotherapy and radiation therapy.

Materials and methods: This was a prospective study, started in September, 1999 and completed in November, 2000 in Pediatric Surgery department of Dhaka Shishu (Children) Hospital and Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. Preoperative chemotherapy was given to all the patients of advanced Wilms' tumor for four weeks with vincristine and actinomycin D according to the Societe Internationale d' Oncologie Pediatrique (SIOP) protocol (Herdrich K, 1982). The patients were followed up every 2 weekly by ultrasonography, LFT, Hb% and chest X-ray for one month. The size of the tumor as well as the metastatic lesions in the prechemotherapeutic and postchemotherapeutic ultrasonographic findings was compared after one month.

Results: After giving neoadjuvant chemotherapy, the size of the tumor was reduced in 08 patients and it was measured by USG after one month. The change in the metastatic lesions was also compared by USG at the same time. Two patients died during the course of neoadjuvant chemotherapy and nephroureterectomy was done in 08 patients. All the resected specimens were sent for histopathology. The reports revealed features of Wilms' tumor with favorable histology (FH) in 07 cases and unfavorable histology (UH) in 01 case.

Conclusion: It is evident from this study that advanced stage of Wilms' tumor, where operative treatment was not primarily possible, preoperative chemotherapy downsized the tumor significantly. It is then possible to perform nephroureterectomy.

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Introduction:

Childhood diseases are a matter of greatest concern for everyone. Although infectious diseases still top the priority, malignancy, which is always considered as a dreadful condition, is taking concern [1]. Despite many advances in the diagnosis and therapy of diseases, childhood malignancies remain as a great challenge for the medical personnel particularly in the developing countries because of lack of resources, advance stage of the disease and overall ignorance and poverty.

Wilms' tumor or nephroblastoma is an embryonal tumor of childhood. This constitutes the commonest intraabdominal solid tumor of childhood occurring 1 in 100000 children younger than 15 years[1,2] and male to female ratio are almost equal[3]. It presents usually in an apparently healthy child as a painless abdominal mass. The peak age of incidence is approximately 3-4 years[4]. Other presentations like hematuria, anemia or weight loss also may be the features.

The management of Wilms' tumor still remains a matter of great challenge to pediatric surgeons and

also to pediatric oncologists. The tumor continues to be the subject of intensive investigations that with the aid of co-operative protocols by the National Wilms' Tumor Study (NWTS) have resulted in marked improvement in survival [5]. Surgical excision remains the cornerstone of treatment of Wilms' tumor; however the dramatic improvement in overall survival is the result of coordinated use of surgery, chemotherapy and radiation therapy[4].

The management of advanced cases of Wilms' tumor is even more challenging. These include bilateral tumors, tumor with intracaval and atrial extension, advanced local tumors as inoperable and non-resectable ones and distal metastatic tumors. The diagnosis as well as treatment of these cases remains a matter of great difficulty. The multimodal treatment especially preoperative chemotherapy may reduce the extent of the disease that ultimately may help in further surgical excision- total or partial, reducing the morbidity and mortality of the disease[6]. Preoperative chemotherapy may cause shrinkage of the tumor before resection[5].

In the event, the tumor is too large or the child is too sick for surgery, needle biopsy should be performed, and the tumor considered at least stage- III for the treatment[5].

There have been some other studies on solid intraabdominal tumors in children in general but the challenges of management of advanced Wilms' tumor have not been addressed in our country. This study aims at findings a strategy for managing advanced Wilms' tumor.

Materials and methods:

This was a prospective study, started in September, 1999 and completed in November, 2000 and was carried out in Dhaka Shishu (Children) Hospital and BSMMU, Dhaka. the patients up to 12 years of age irrespective of sex with advanced Wilms' tumor admitted in the pediatric surgery wards of these two hospitals were included in this study. These include tumors with intracaval and atrial extension, advanced local tumors as inoperable and non-resectable ones (size more than 10cm X 9cm, with ultrasonographic evidence of liver and para-aortic lymph nodes involvement) which were subsequently checked by two consultants and distal metastatic tumors.

Patients with recurrent tumors, parents nonconsenting to the protocol and extremely moribund patients not capable of withstanding chemotherapy were excluded from this study.

Routine blood and urine examination with renal function tests (RFT), liver function tests (LFT), urinary Vanillyl Mandelic Acid (VMA), ultrasonography (USG) of the whole abdomen with particular attention to the kidneys, liver and lymph nodes, plain X-ray abdomen, intravenous urography (IVU) and chest X-ray was done for all patients. Computed tomography (CT) was not done in any case as it is a costly investigation and most of the patients were poor. Finally the diagnosis was confirmed by final needle aspiration biopsy (FNAB).

Preoperative chemotherapy was given for four weeks with vincristine and actinomycin D according to SIOP protocol (Herdrich K, 1982).The patients were followed up every 2 weekly by USG, LFT, Hb% and chest X-ray for one month.

The size of the tumor as well as the metastatic lesions in the prechemotherapeutic and postchemo-therapeutic ultrasonographic findings was compared after one month. Then post chemotherapy nephroureterectomy was done. All the resected specimens were sent for histopathological studies. The data was collected from all 8 patients.

Observation and results:

During our study period from September '99 to November 2000, total surgical admission in two hospitals was 4705 and Wilms' tumor patients were 22. So Wilms' tumor represented 0.47 % of total admission. Among them, 12 were having local tumors with small size (less than 9cm X 8cm) and 10 were advanced stages (size more than 10cmX9cm with hepatic and lymph node metastasis).

Table-I

Incidence of Wilms' tumor (n=22)

Tumors	Number	Percentage
Wilms' tumor	Local tumors- 12	54.55
	Advanced tumors-10	45.45

Table-II

Age distribution of advanced Wilms' tumor patients (n=10)

Age group	No. of patients	Percentage
0-2 years	1	10
2-4 years	7	70
4-6 years	2	20

Among the 10 patients of advanced Wilms' tumor 8 were males and 2 were females.

Table-III

Clinical presentations in the study population (n=10)

Symptoms	No of patients	Percentage
Abdominal lump		
Right	4	40
Left	6	60
Anorexia/weight loss	8	80
Fever	6	60
Jaundice	6	60
Abdominal pain	4	40

Table-IV

Ultrasonographic findings (n=10)

Metastasis	No. of patients	Percentage
Hepatic metastasis	5	50
Para aortic lymphadenopathy	3	30
Both	2	20

Table-V

Intravenous Urography findings (n=10)

Findings	No. of patients	Percentage
Non visualization of kidney	8	80
Distorted and displaced PCS	2	20

After giving neoadjuvant chemotherapy, the size of the tumor was reduced in 8 patients and it was measured by USG after one month. The change in the metastatic lesions was also compared by USG at the same time. Two patients died during the course of neoadjuvant chemotherapy and nephroureterectomy was done in 8 patients.

All the resected specimens were sent for histopathological studies. The reports revealed features of Wilms' tumor with favorable histology (FH) in 7 cases and unfavorable histology (UH) in 1 case. Postoperative results were uneventful and the patients were advised for postoperative chemotherapy. They were followed up for 2 months to 12 months. Recurrence of symptoms or any other complaints were not observed in any case.

P value of this study is less than 0.001.

Table-VI

Size of tumor before & after chemotherapy (n=10)

Pt. number	Prechemotherapy size cmxcm	Volume (cm^2)	Postchemotherapy size (after one month) cmxcm	Volume (cm^2)
1	11.5x12.7	146.05	7.4x8.8	65.12
2	10.6x11.5	121.9	7.2x7.9	56.88
3	10.9x11.8	128.62	6.2x7.1	44.02
4	15.1x15.9	240.09	Expired	
5	13.7x13.9	190.47	8.5x8.8	74.8
6	12.5x13.7	171.25	10.6x10.9	115.54
7	14.5x13.1	189.95	9.5x10.4	98.8
8	11.4x13.8	157.32	7.5x9.5	71.25
9	12.4x13.8	171.12	8.1x7.7	62.37
10	14.9x14.4	214.56	Expired	

Table-VII

Fate of metastatic lesions after chemotherapy (n=8)

Site of lesions	Disappearance	Diminution
Liver	3	2
Para-aortic lymph nodes	3	0
Both	1	1

Table-VIII

Histopathological reports (n=8)

Histology	No. of patients
Favorable histology (FH)	07
Unfavorable histology (UH)	01

Discussion:

Malignancy is the second most common cause of death after accident in the developed countries[7]. Wilms' tumor is the most common renal malignancy in childhood [8]. In Bangladesh two separate studies also suggested the occurrence of Wilms' tumor to be more common than others[9].

Because of the pervasive poverty, ignorance and lack of medical resources, many children present with advanced stage of Wilms' tumor. Many such patients are denied of their treatment because of their poor general condition and/or advanced stage of the disease.

There have been some studies on solid intraabdominal tumors in children in general but the challenges of

management of advanced Wilms' tumor have not been addressed in our country. Locally advanced (primarily inoperable tumors) have a high incidence of micrometastasis and runs the risk of tumor rupture and spillage in an attempt for excision[10]. It was presumed that since chemotherapy is effective in control of metastatic disease, it will also help the primary lesion to regress. The aim of the present study was to find out the rate of respectability of locally advanced Wilms' tumor after neoadjuvant chemotherapy. This study carried out with 10 patients of advanced Wilms' tumor of both sex aged between 9 months to 6 years admitted to the Pediatric Surgery department of Dhaka Shishu (Children) Hospital and BSMMU from September 1999 to November 2000.

It was not possible to determine the results of preoperative chemotherapy in advanced Wilms' tumor in Bangladesh with this study. But it may be possible to find out a strategy for the management. The study has been carried out in pediatric surgery department of only two hospitals.

Of the 10 patients with advanced Wilms' tumor, there was no associated anomaly found. Most of the patients were from 2 years to 4 years (Table-II).

For the preliminary diagnosis physical examination of the patient is very suggestive. USG was done to ascertain the origin, extent and physical nature of the lump and also the metastasis (Table-IV). IVU was done to assess the functional status of the kidney (Table-V). LFT and chest X-ray were done in all cases. CT was not done in any case. In keeping with SIOP recommendation, FNAB was done to obtain tissue diagnosis before preoperative chemotherapy.

Many of the diagnostic facilities available are not too much costly. So lack of facilities was not the common problem in most of the cases for delaying presentation to hospital. It is the lack of health awareness of poor parents and quacks. Also lack of awareness of the even qualified medical persons at primary level attending the unfortunate children with malignant abdominal tumor in this country causes delay in early detection and proper treatment although tumors have excellent prognosis and survival throughout the world.

Vincristine and actinomycin D were given preoperatively to all the patients for 4 weeks and the tumors were re-evaluated for resectability and metastasis (Table- VI & Table-VII) after one month. Two patients died during the course of chemotherapy and nephroureterectomy was done in 8 patients.

In this study it has been shown that the tumor found unresectable can be totally excised after cytoreductive chemotherapy. Therefore it can be advocated that preoperative chemotherapy should be given to all patient with Wilms' tumor when the tumor is in advanced stage and seems to be unresectable.

Conclusion:

It is evident from this study that advanced stage of Wilms' tumor, where operative treatment was not primarily possible, preoperative chemotherapy downsized the tumor significantly. It is then possible to perform nephroureterectomy.

We also found that this might be an option for the management of advanced Wilms' tumor.

It is therefore recommended that, parents should be educated properly so that they seek early medical service in cases of any abdominal lump symptomatic or asymptomatic; that the primary care physicians and general practitioners should remain alert with high degree of suspicion about the conditions presenting with abdominal mass and refer them to a specialized center for admission in a priority basis.

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