Original Article *Iran J Ped Hematol Oncol. 2016, Vol6.No3, 142-148*

Clinicopathologic characteristics of malignant abdominal tumors in children: 10 years experience

Soheila Zareifar MD [1,*], Sezaneh Haghpanah MD[1], Mohammad Reza Farahmandfar MD [1], Hamid Reza Forotan MD [2]

1. Hematology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.
2. Pediatric Surgery Department, Namazi Hospital, Shiraz University of Medical Sciences, Shiraz, Iran.
*Corresponding author: Soheila Zareifar, MD. Hematology Research Centre, Namazi Hospital, Shiraz University of Medical Sciences, Shiraz, Iran. E-mail: Zareifars@sums.ac.ir

Received: 10 November 2015 **Accepted:** 21 June 2016

Abstract
Background: Abdominal tumors are still a diagnostic problem in children. This study was conducted to assess the presentation and types of childhood intra abdominal tumors in children in Shiraz.
Materials and Methods: Participants of this historical cohort study consisted of 298 children aged between 1.5 months to 15 years old who were diagnosed with abdominal mass between March 2003 and March 2013. All patients referred to pediatric surgery wards of Namazi hospital affiliated to Shiraz University of Medical Sciences, Shiraz, Iran. Data extracted by checklist included patient's demographic data, type of malignancy, signs and symptoms at the time of presentation and duration of signs and symptoms.
Results: The majority of tumors were retroperitoneal followed by intra-peritoneal and pelvic masses. Wilms tumor was the most common tumor constituting 34% of all cases followed by neuroblastoma (24.7%), and non-Hodgkin lymphoma (12.7%). The most common signs and symptoms were abdominal pain (39.5%), abdominal distention (34.2%), palpable mass (27.5%), weight loss (19.4%), fever (16.7%), and vomiting (10.7%).
Conclusion: Better understanding of signs and symptoms of abdominal masses can facilitate early diagnosis and proper treatment of malignant abdominal tumors in children.
Keyword: Abdominal neoplasm, Pediatric, Peritoneal neoplasm, Retroperitoneal neoplasm

Introduction

Detection of an abdominal mass in a child is an alarming finding for both parents and practitioner, because of the possibility of malignant disorders. Any palpable mass felt during abdominal examination of a child should be regarded as malignancy until proven otherwise. A palpable mass may be a presentation of benign diseases, malignant tumors, or even tumor-like intra-abdominal inflammatory conditions (1- 3). In addition, some benign tumors in the abdomen or pelvis may need to make an immediate diagnosis and treatment (2-5). The first line of treatment in malignant abdominal tumors in children is surgical resection which is followed by chemotherapy with or without radiotherapy (4, 5). In some childhood intra-abdominal tumors, like Wilms tumor, current therapies and new agents have resulted in overall survival rates of greater than 90%. Dramatic improvements in survival rate have been achieved for children and adolescents with cancer (5).

The 5- year survival rates have improved to 88% in children younger than 15 years and from 47% to 77% for adolescents aged between 15 and 19 years and even to 70% to 90% for advanced-stage disease (3). The aim of this study was to assess the demographic data, clinical presentations, site, and extent of surgical resection, histopathology and outcome of intra-abdominal tumors in children younger than 15 years of age in a pediatric surgery ward of Namazi hospital, affiliated to Shiraz University of Medical Sciences, Shiraz,

Iran. This hospital is the main referral center for children with abdominal mass in southern of Iran.

Materials and Methods

In this historical cohort study, all children affected with abdominal mass (n=390) who were younger than 15 years and were registered and diagnosed during the time period of March 2003 to March 2013 at Namazi hospital of Shiraz University of Medical Sciences were evaluated until April 2014.

Forty five patients were excluded from the study because of incomplete medical records. The parents of two children refused further diagnostic and therapeutic measures and left the hospital. Forty-five patients were finally diagnosed as benign diseases and 298 children with malignancy were enrolled in the study. Consent forms were obtained from each participants and the Ethics Committee of Shiraz University of Medical Sciences confirmed the protocol (Grant number=82/1008).

Diagnosis was based on clinical and laboratory evaluation, pathology report, and radiology examination including ultrasonography, Computerized tomography scan (CT scan) or Magnetic resonance imaging (MRI).

Patients' data was extracted by checklist from medical records that included sex, age at diagnosis, age of death, age at diagnosis, signs and symptoms at the time of diagnosis, duration of symptoms, amount of resection of tumors, histology of tumors, tumor location, the presentation of metastasis at the time of diagnosis, chemotherapy, frequency of relapse or secondary metastasis, and mortality.

The pathological diagnosis was based on morphologic and immunohistochemical evaluation of tissue biopsies, which were confirmed by at least two pathologists.

Amount of resection in checklist is categorized into three groups: unresectable, subtotal resection (75% resection), near total resection (90% or more resection), and gross total resection. Sites of tumors in this study included retroperitoneal, intra-peritoneal, and pelvic tumors. The patients were followed till April 2014. The mean of duration of follow-up was 6.5 ± 2.3 years (1.5 - 9 years).

Statistical analysis

Data were statistically analyzed using SPSS (version 15). Results were expressed as mean ± standard deviation (SD) for age and duration of clinical presentations, and for other variables as percentage.

Results

The results can be divided into seven parts:

1. Sex and age distribution:

In the malignant group, there were 150 (50.3%) males and 148 (49.7%) females (Male/female:1.02/1). The age distribution of patients was 1.5 months to 15 years (Table 1) with a mean age of 4.8 ± 4.15 years.

2. Clinical manifestations:

Abdominal pain was the most common clinical presentation (n=118, 39.5%), followed by abdominal distension (n=102, 34.2%). Palpable masses detected by physicians or parents were found in 82 (27.5%) cases (Table 2). The duration of signs and symptoms was 2-180 days (mean: 40.2 ± 39 days).

One hundred eighty-four patients (61.7%) presented in advanced stage (stage III, IV). Ultrasound examination and abdominal CT- Scan assisted greatly in making the diagnosis. One hundred forty-two (47.6%) patients underwent total tumor resection, sub-total resection was performed in 46 (15.4%) cases, and unresectable tumors were detected in 110 (37%) subjects.

3. Origin of tumor:

The majority of tumors (62.4%, n=186) were retroperitoneal, which was followed by intra-peritoneal (26.2%, n=78), and pelvic masses (11.4%, n=34). The most common retroperitoneal malignancies were Wilms tumor (54%, n=102), and then NBL (38%, n=72), with peak incidence in the age group of 0-4 years

(79%), followed by 5-9 (15%), and then 10-15 years (6%). Retroperitoneal tumors were more common in females (58% versus 42%). NHL (n=34, 46%) and hepatoblastoma (n=26, 35%) were the most common intra-peritoneal malignancies with peak incidence in the age group of 0-4 years (43%), followed by 10-15 years (30%), and 5-9 years (27%). These tumors were three times more common in males than females. The most common pelvic tumors were embryonic RMS (53%, n=18), and then germ cell tumors (GCT) (31%, n=14). The peak incidence of pelvic masses was in the 10-15 year (53%) age group, 0-4 years (35%), and 5-9 years (12%). These tumors occurred almost equally in both sexes.

4. Tumor resection:

The tumors were resected totally in 142 cases (47.6%), sub-totally in 46 (15.4%), and unresectable in 110 subjects (37%). Children with inoperable tumors underwent percutaneous tro-cut or laparatomy for open biopsy.

5. Metastasis at the time of diagnosis:

Metastasis was detected in 88 cases (29.5%) in primary evaluation. In eight patients, there was more than one site of involvement. The most common sites of metastasis were bone marrow (n=38, 12.7%), lymph node (n= 32, 10.7%), liver (n=20, 6.7%), bone (n=14, 4.6%), and lungs (n= 2, 0.67%).

6. Pathological diagnosis:

Wilms tumor was the most common tumor constituting 34% of all cases, followed by NBL (24.7%), and NHL (12.7%) (Table III).

7. Treatment and outcome:

Surgical complications including wound infection and hemorrhage were demonstrated in 10 (3.35%) and 4 (1.34%) cases, respectively. Treatment was done in 294 patients (98.6%) according to pediatric standard protocols. Treatment was chemotherapy alone in 162 (55%) patients and combined chemotherapy and radiotherapy in 132 patients (44.9%).

Two cases of hepatoblastoma died before chemotherapy due to respiratory insufficiency and severe abdominal distension, and two patients tend to have treatment at another facility. At the end of the study, 78 patients (26%) were on chemotherapy and in 216 cases (74%) treatment were terminated. Of total 298 patients, 226 (76%) were alive at the end of the study and the overall mortality was 24% (n=72), regardless of the causes. The most common cause of death was secondary metastasis, which occurred during or after the treatment in 21% of patients (n= 62). Secondary metastases were seen mostly in NBL (32%, n=20), Wilms tumor (22.5%, n= 14), RMS (16%, n= 10), NHL (13%, n=8), and hepatoblastoma (10%, n=6). Chemotherapy induced febrile neutropenia and sepsis, led to death in 6 patients (2%). Local relapses occurred in 28 cases (9.3%). Regardless of stages at first presentation, the 5 year event free survival was 88.2% and 73.8% in Wilms tumor and NHL, but in NBL, RMS and in hepatoblastoma, it was 58.3%, 58%, and 33%; respectively.

Table I: Data of children with malignant abdominal mass younger than 15 years registered in Shiraz University of Medical Sciences during 2003-2013

Age group (%)	No. of cases	Male	Female	Death
0-4	186 (62.4%)	103 (57%)	83 (43%)	38 (53%)
5-9	62 (21%)	40 (64.5%)	22 (35%)	14(19.4%)
10-15	50 (17%)	26 (52%)	24 (48%)	20 (28%)

Table II: Major clinical presentations among 298 cases with malignant abdominal mass younger than 15 years registered in Shiraz University of Medical Sciences during 2003-2013

Clinical presentation	No. of cases	percentage
Abdominal pain	118	39.5%
Abdominal distension	102	34.2%
Palpable mass	82	27.5%
Weight loss	58	19.4%
Fever	50	16.7%
Vomiting	32	10.7%
Gross hematuria	24	8%
Bone pain	14	4.6%
Constipation	12	4%
Urinary problem	10	3.3%
Respiratory distress	8	2.6%
Diarrhea	6	2%
Weakness	6	2%
Jaundice	4	1.3%
Opsoclonus	4	1.3%
Virilization	2	0.67%

Table III: Pathological diagnosis among 298 patients with malignant malignant abdominal masses younger than 15 years of age registered in Shiraz University of Medical Sciences during 2003-2013

Diagnosis	No. of cases	Percentage
Wilm's tumor	102	34.2%
Neuroblastoma	74	24.8%
Non-Hodgkin lymphoma	40	13.4%
Hepatoblastoma	24	8%
Rhabdomyosarcoma	24	8%
Germ cell tumor	14	4.7%
Ewing sarcoma	6	2%
Hodgkin disease	6	2%
Hepatocellular carcinoma	2	0.67%
Gastrointestinal stromal tumor	2	0.67%
Adrenocortical carcinoma	2	0.67%
Clear cell sarcoma	2	0.67%

Discussion

There are few epidemiological studies on abdominal tumors in children. The present study showed that the majority of pediatric abdominal tumors was retroperitoneal, which was followed by intra-peritoneal and pelvic masses. The relative rarity of abdominal tumors and the vagueness of their symptoms, such as loss of appetite, pallor or recurrent fever which are often treated as general systemic illnesses prior to a more thorough examination of the child are the main reasons for delay in diagnosis. Therefore, taking a careful history and physical examination, baseline laboratory and correct imaging studies can provide sufficient information to determine the diagnosis or to choose the appropriate specialist. In this study, the most frequent sign was abdominal distention and the most common symptom was abdominal pain. Pourang's research (6) revealed palpable mass as the most common sign and abdominal distension as the most common symptom. The diagnostic possibilities depend on age, gender, location of the mass, physical evaluation, and presence or absence of other signs and symptoms (7- 9). The duration and character of the symptoms such as fever, weight loss, and fatigue should be noted too (3). Although great advances have been made in the cure rates of pediatric abdominal tumors, there is still an excessive delay between the first symptom and diagnosis.

According to the present study, this has been estimated as from one to three months in the average case.

Wilms tumor, NBL, RMS, and liver tumors comprise the majority of malignancies arising within the abdominal cavity (8). Knowledge of the spectrum of diseases allows the physicians to provide an appropriate differential diagnosis and suggests proper patient management (9). In the present study, Wilms tumor was the most common tumor constituting 34% of all cases, followed by NBL, and NHL which was similar to some other studies that reported most solid abdominal tumors arise from the kidney or adrenal gland in children older than one year (1, 5, 7, 10, 11). In a study by Pourang et al., (2011) in Iran, 19% of patients with abdominal mass were diagnosed as a case of Wilms tumor (6). Horcher et al., (1986) showed that NHL, hepatoblastoma, and RMS were the most common intra-abdominal tumors in children (10). In another study by Hanif in Pakistan, NBL was the most common tumor constituting 26.6% of all cases, followed by Wilms tumor (25.1%), NHL (15.5%), GCT and hepatoblastoma (9% each), RMS (4.4%), hepatocellular carcinoma (1.4%), and miscellaneous (6%) (11).

The first line of treatment in pediatric abdominal tumors is surgical resection whenever possible. According to this research, out of total 298 patients, tumors were removed completely in nearly half of cases. Some studies suggested that surgical resection more than 90% is associated with improved overall survival compared to less than 90% resection (12- 14). In many pediatric solid tumors, although the important clinical and biological prognostic factors currently used to determine treatment are the age of the patient at diagnosis, stage, tumor histology, and cytogenetic status, complete resection of tumor remains the cornerstone of treatment with minimal peri-operative mortality and morbidity to achieve cure (15-21).

This study also revealed that regardless of staging, Wilms tumor and lymphoma have better event free survival than other tumors. In a study in Iran, the 5-year survival rate of the patients with Wilms tumor was approximately 76±4% (21, 22). Nearly half of the patients with NBL, RMS and one third of the patients with hepatoblastoma survived 5 years after discontinuation of therapy.

Conclusion

Regarding the results of current study, it can be concluded that epidemiological pattern of the childhood abdominal mass in southern Iran is similar to that of other developing countries, in which Wilms tumor and NBL are the most common abdominal malignant pathological diagnosis. In addition, this study revealed that attention to uncommon signs and symptoms in history taking and physical examination together with laboratory tests may increase the physician's awareness and achieve better diagnosis of pediatric malignancies and would also be beneficial for the patient. Further and larger studies are needed to compare the effect of tumor's resection, stage, and response to treatment as the most significant prognostic factors in each type of childhood abdominal tumors.

Acknowledgements: We would like to express our special thanks to Sheryl Nikpour for English editing of the manuscript.

References

1. Groff DB. Pelvic neoplasm in children. J Surg Oncol. 2001; 77(1): 65-71.
2. Latawiec- Mazurkiewicz I, Juszkiewicz P, Pacunowski J, Kwas A, Rybkiewics M, Rudnicki J, et al. Tumors-like inflammatory abdominal conditions in children. Eur J Pediatr Sug. 2005; 15(1): 38-43.
3. Tasci Y, Kayikcioglu F, Vavusoglu D, Gokcin H. Splenosis mimicking pelvic mass. Obstet Gynecol. 2005; 106: 1167-9.

4. Young G, Toretsky JA, Campbell AB, Eskenazi AE. Recognition of common childhood malignancies. Am Fam Physician. 2000; 61(7): 2144-54.
5. Dumba M, Jawad N, McHugh K. Neuroblastoma and nephroblastoma: a radiological review. Cancer Imaging. 2015; 15(1): 5.
6. Pourang H, Sarmadi S, Mollaeian M, Sanii S, Nahvi H, Azarshahin M, et al. A review of 25 years experience in 461 cases of pediatric abdominal mass. IJBC. 2011; 2: 31-34.
7. Meyer JS, Harty MP, Khademian Z. Imaging of neuroblastoma and Wilms tumor. Magn Reson Imaging Clin North Am. 2002; 10: 257-302.
8. Schenk JP, Gunther P, Schrader C, Ley S, Furtwangler R, Leuschner I, et al. Childhood kidney tumors-the relevance of imaging. Radiologe. 2005; 45(12): 1112-23.
9. Chung EM, Biko DM, Arzamendi AM, Meldrum JT, Stocker JT. Solid tumors of the peritoneum, omentum, and mesentery in children: radiologic-pathologic correlation: from the radiologic pathology archives. Radiographics. 2015; 35(2): 521-46.
10. Horcher E, Helmer F. Benign and malignant intra-abdominal tumors in childhood. Wien Med Wochenschr. 1986; 136(10): 253-7.
11. Hanif G. Intra-abdominal tumors in children. J Coll Physicians Surg Pak. 2004; 14(8): 478-80.
12. Moon S.B, Shin H. B, Seo J.M, Lee S-K. Hepatoblastoma: 15-year experience and role of surgical treatment. J Korean Surg Soc. 2011; 81(2): 134–140.
13. Kieran K, Ehrlich PF. Current surgical standards of care in Wilms tumor. Urol Oncol. 2016; 34(1):13-23.
14. Dome JS, Graf N, Geller JI, Fernandez CV, Mullen EA, Spreafico F, et al. Advances in Wilms Tumor Treatment and Biology: Progress through International Collaboration. J Clin Oncol. 2015; 33(27): 2999-3007.
15. Sadeghian N, Sadeghian I, Mirshemirani A, Khaleghnejad Tabari A, Ghoroubi J, Abdollah Gorji F, et al. Types and frequency of ovarian masses in children over a 10-year period. Caspian J Intern Med. 2015; 6(4): 220-3.
16. Golden CB, Feusner JH. Malignant abdominal masses in children: quick guide to evaluation and diagnosis. Pediatr Clin North Am. 2002; 49: 1369–92.
17. Englum BR, Rialon KL, Speicher PJ, Gulack B, Driscoll TA, Kreissman SG, et al. Value of surgical resection in children with high-risk neuroblastoma. Pediatr Blood Cancer. 2015; 62(9): 1529-35.
18. Pham TH, Igbal CW, Grams JM, Zarrouq AE, Wall JC, Ishitani MB, et al. Outcomes of primary liver cancer in children: an appraisal of experience. J Pediatr Surg. 2007; 42(5): 834-9.
19. Rosenfield NS, Leonidas JC, Barwick KW. Aggressive neuroblastoma simulating Wilms tumor. Radiology. 1998; 166: 165-167.
20. Schmidt ML, Lukens JN, Seeger RC, Brodeur GM, Shimada H, Gerbing RB, et al. Biologic factors determine prognosis in infants with stage IV neuroblastoma: A prospective Children's Cancer Group study. J Clin Oncol. 2000; 18: 1260-68.
21. Pe rez CA, Matthay KK, Atkinson JB, Seeger RC, Shimada H, Haase Giml, et al. Biologic variables in the outcome of stage I and II neuroblastoma treated with surgery as primary therapy: A Children's Cancer Group study. J Clin Oncol. 2000; 18: 18-26.
22. Faranoush M, Bahoush GR, Mehrvar A, Hejazi S, Vossough P, Hedayatiasl AA, et al. Wilm's Tumor: Epidemiology and Survival. Res J Biol Sci. 2009; 4 (1): 86-89