Non CNS pediatric malignancies in Mosul

Khalil I. Mahmood*, Likaa Fasih Al-Kzayer, Sahar K. Omar*****
*** Department of Medicine, Nineveh College of Medicine, University of Mosul; ** Pediatric oncologist in Ibn Al-Atheer Pediatric Hospital;*** Department of Pediatrics, College of Medicine, University of Mosul.**

(Ann. Coll. Med. Mosul 2010; 36 (1 & 2): 86-91).
Received: 30th Sept 2009; Accepted: 9th Feb 2011.

ABSTRACT

Objectives: To find out the types of pediatric malignancies in patients from Mosul, their age and sex distribution as well as the death rate among these diseases with special emphasis on acute lymphoblastic leukaemia.
Patients and methods: A survey which was conducted in Mosul pediatric wards of oncology in Alsalam, Ibn Sina general hospitals and Ibn Alatheer hospital for pediatric diseases on 228 children of both sexes, their ages were less than 12 years from year 2001-2007. The clinical data were taken from their case sheets regarding age, sex, clinical presentation at time of admission and the lab tests including tissue biopsy as well as bone marrow examination.
Results: The commonest 3 types of these malignancies were acute lymphoblastic leukaemia (ALL) (43.4%), lymphoma (19.5%) and neuroblastoma (7.9%). The mean age of presentation was 65 months; the majority of cases were between 13 months - 6 years. Males predominate in a ratio of 1.28/1. Regarding ALL the main clinical features at presentation were fever, pallor, bone pain and bleeding. All cases were treated as inpatients. Death rate was high (35.08 %), the commonest causes were sepsis, bleeding and progressive disease.
Conclusion: There were different types of malignancies in children in Mosul, the commonest were ALL, Lymphoma and neuroblastoma, with high death rate.

Keywords: Pediatric, malignancies.

الخلاصة

أهداف البحث: لمعرفة أنواع الأمراض السرطانية عند الأطفال في الموصل كذلك الأعراض السريرية لكل نوع مع تشديد خاص على ابيضاض الدم.
التصميم والمشاركون: دراسة وصفية أجريت على ٢٢٨ طفلا في ردهات الأطفال في مستشفيات السلام وابن سينا وابن الأثير والتي تعالج فيها سرطانات الأطفال لكلا الجنسين وأعمارهم أقل من ١٢ سنة بين عامي ٢٠٠١-٢٠٠٧. وأخذت المعلومات من سجلات المرضى فيما يخص العمر، والجنس والأعراض السريرية وقت دخول المستشفى مع الفحوصات المختبرية التي أجريت ومن ضمنها الخزعة النسيجية وفحص نخاع العظم.
النتائج: تبين ان الأمراض السرطانية الثلاثة الأكثر انتشارا عند الأطفال هي: ابيضاض الدم (٤٣,٤%)، السرطانات اللمفاوية (١٩,٥%) وسرطان الغدد الكظرية (٧,٩%) وكان معدل عمر الأطفال وقت الدخول الى المستشفى هو ٦٥ شهرا ومعظم الأعمار كانت تتراوح بين ١٣ شهرا -٦ سنوات ومعظم الحالات كانت من الذكور بنسبة الذكور\الإناث (١.٢٨ \١). بالنسبة لابيضاض الدم كانت أهم الأعراض السريرية وقت الدخول الى المستشفى هي الحمى، الشحوب، ألم في العظام والقابلية على النزف. جميع الأطفال المرضى بالسرطان أدخلوا المستشفى وعولجوا فيه. كانت نسبة الوفيات عالية (٣٥,٠٨%) وأهم أسباب الوفيات كانت خمج الدم، النزف، متلازمة تحلل الورم وتقدم المرض.

الاستنتاج: أهم الأمراض السرطانية عند الأطفال في الموصل هي ابيضاض الدم، السرطانات اللمفاوية وسرطان الغدد الكظرية. نسبة الوفيات كانت عالية.

Cancer in children is not common. Around 1 child in 500 develops cancer by 15 years of age and each year there are 120-140 new cases per million children aged under 15 years[1].

While in adults about 80% of cancerous diseases pertain to the respiratory, gastrointestinal and reproductive organs; only <5% of cancerous diseases of children are manifested in these organs. Furthermore, the histopathology of pediatric neoplasia differs markedly from that of adults: in children embryonal and immature cells can be found at very different stages of development which perpetually proliferate and rarely mature[2].

The most common pediatric cancers may be classified into 5 categories on the basis of the involved tissue or organ system: the lymphohematopoietic system, the nervous system, the embryonal group, connective tissue, and gonadal system. Accordingly, paying particular attention during physical examination to “blood, brain, belly, and bone” manifestations—the four Bs—is helpful in eliciting evidence of malignancy.

Abnormalities of the hematopoietic system manifest as pallor, which indicates anemia, bleeding from orifices, petechiae, purpura, and ecchymosis, which indicate thrombocytopenia or disseminated intravascular coagulation. Cellulites or other evidence of infection, which indicates leucopenia, skin nodules, which indicate leukocytosis, and other abnormalities of the formed elements of the blood. Abnormalities of the lymphatic system include lymphadenopathy, superior vena cava syndrome, or respiratory distress when the patient is in a supine position, suggesting an upper anterior mediastinal mass or thymic enlargement. Enlargement of the cervical lymph nodes is common in children with infection and in patients with lymphoma. Persistent or progressive enlargement of lymph nodes, often painless, is suggestive of lymphoma and indicates the need for biopsy. Abnormalities of the embryonal system usually are apparent on physical examination as organomegaly or an abdominal mass. However, an unexplained mass in any area of the body should be considered malignant until proven otherwise. Retinoblastoma usually manifests as a white pupillary reflex rather than the usual red reflection from incident light. In neonates, “blueberry muffin” spots on the skin may be neuroblastoma. A sacrococcygeal mass usually is a teratoma that may undergo malignant transformation if it is not removed [3].

Worldwide cancer mortality rates have decreased for children since the 1950s as a result of improvements in treatment and the resulting increased survival rates. In the 1950s, childhood cancer mortality rates were stable at approximately 80 per million. The cancer mortality rate for 0- 19 years old began declining in the 1960s and by the late 1990s had decreased to less than 30 per million. Declines in mortality for the leukemias began in the early 1960s, with rates decreasing from 30 to 35 per million to less than 10 per million by the late 1990s. For NHL, declining mortality began in the late 1960s, with rates decreasing from 6 to 7 per million to less than 2 per million by the 1990s. Mortality from kidney tumors (primarily Wilms' tumor) decreased by 80% over a similar time period from approximately 4 per million to less than 1 per million. Mortality rates also declined for Hodgkin's disease, with rates decreasing from approximately 3 per million in the 1950s and early 1960s to approximately 0.4 per million in the mid-1990s[4].

Aims of the study

The study was conducted on patients who selectively live in Mosul, to:

1- Find out the relative frequency of different pediatric malignant disease.
2- Determine the age and sex distribution of these diseases.
3- Discuss the clinical presentation of ALL as prototype of these diseases.

4- Study the percentage of death among treated patients and the causes of their death.

Patients and methods

A random sample of 228 children with different malignant diseases, other than C.N.S malignancies, who were from Mosul city and registered in pediatric oncology wards in Alsalam, Ibn Sina and Ibn Alatheer Hospitals between January 2001 and December 2007 were included in this study. They were admitted to the centre and managed as inpatient for the purpose of diagnosis and treatment, at least in the phase of induction of remission. The data taken from all patients and recorded in isolated files. The case records were analyzed, including age, sex, signs and symptoms at the time of presentation and the final diagnosis of each patient. Z1 proportion test was used to study the significance in the difference of male/female ratio and a test value of more than 1.96 is considered to be significant.

Acute lymphoblastic leukemia (ALL) was taken as prototype for studying the clinical features at the time of presentation. Required investigations for each case were done according to the disease type, such as complete blood picture, E.S.R, different types of imaging studies, bone marrow aspiration and biopsy, tumor markers….etc and the histological diagnosis was confirmed by pathologists in all cases.

C.N.S neoplasms were excluded from the study because they were managed in a different centres; however histiocytosis - X and connective tissue tumors of borderline malignancy were also included in this study.

Results

The most common malignancy was acute lymphoblastic leukemia and it accounted for 43.4 % of all cases. The least common were retinoblastoma and malignant fibrous histiocytoma, and each accounted for 0.4 % of all cases as shown in table 1.

The mean age of presentation of all patients was 65.16 months, the oldest age group were those presented with germ cell tumor (132.5 months), while the youngest was that found to have retinoblastoma (16 months) as shown in table 1.

The majority of cases had an age range of 13 months - 6years (131 patients) (57.45%). No case had been diagnosed in the neonatal period, there were 7 patients between 2-12 months (3%) and there were 90 patients more than 6 years (39.5%)

Males were 128 while females were 100 (1.28/1), that is a higher male ratio, the male ratio was clearly higher in the first four common diseases which were a statistically significant differences as calculated by Z1 proportion test, however the female ratio is higher for the less common diseases as shown in table 1.

Fever was the most common presenting complaint among patients with acute lymphblastic leukemia, and was present in 61.6% of patients at the time of diagnosis, followed by pallor (45.45%), bleeding tendency (33.33%), abdominal pain (35.35%), lymphadenopathy, (30.30%), hepatomegaly and/or splenomegaly (22.22%), fatigue and weight loss (18.18%) as shown in table 2.

Eighty patients (35.08%) died of all malignancies due to different causes. Serious infections (like pneumonia, gastroenteritis and septicemia), bleeding (mainly intracranial), progressive disease (resistance to treatment, metastasis and development of complications despite treatment) and tumor lysis syndrome were the major causes of death, however sepsis was the leading cause of death in 46 patients (57.5%) followed by other causes as shown in table 3.

Table (1): Types of malignancies, mean age of presentation and gender of patients.

	Malignancy	Number of patients	%	Mean age in months	males	females
1	Acute lymphoblastic leukemia	99	43.4	66	63 (63.6%)	36 (36.4%)
2	Non Hodgkin lymphoma	45	19.5	64	26 (57.7%)	19 (42.3%)
3	Neuroblastoma	18	7.9	39.27	13 (72.2%)	5 (27.8%)
4	Hodgkin's lymphoma	16	7.0	76.25	9 (56.25%)	7 (43.75%)
5	Acute myelogenous leukemia	14	6.1	68.28	5 (35.7%)	9 (64.3%)
6	Wilms tumour	10	4.4	60.80	3 (30%)	7 (70%)
7	Rhabdomyosarcoma	6	2.4	42.33	3 (50%)	3 (50%)
8	Histiocytosis	4	1.8	41.50	1 (25%)	3 (75%)
9	Chronic myeloid leukaemia	3	1.3	68.66	1 (33.3%)	2 (66.6%)
10	Osteogenic sarcoma	3	1.3	94	1 (33.3%)	2 (66.6%)
11	Hepatoblastoma	2	0.9	17	1 (50%)	1 (50%)
12	Germ cell tumour	2	0.9	132.50	0 (0%)	2 (100%)
13	Unclassified leukaemia	2	0.9	87	0 (0%)	2 (100%)
14	Primitive neuroectodermal tumor	2	0.9	108	0 (0%)	2 (100%)
15	Retinoblastoma	1	0.4	16	1 (100%)	0 (0%)
16	Malignant fibrous histiocytoma	1	0.4	61.00	1 (100%)	0 (0%)
	Total	228	100		128 (56.14%)	100 (43.86%)

Table (2): Signs and symptoms of patients with ALL.

Signs and symptoms	No of patients	%
Fever	61	61.61%
Pallor	45	45.45%
Bleeding tendency (nasal, cutaneous and intracranial)	33	33.33%
Bone pain	35	35.35%
Abdominal pain	31	31.31%
Lymphadenopathy	30	30.30%
Hepato and/or splenomegaly	22	22.22%
Fatigue and weight loss	18	18.18%

Table (3): Causes of death of patients.

	Disease	Bleeding	Sepsis	Progressive disease	Tumor lysis syndrome	Total
1	Acute lymphoblastic leukemia	11 (39%)	16 (57%)		1 (14%)	28
2	Non Hodgkin lymphoma	1 (5%)	14 (74%)	2 (10.5%)	2 (10.5%)	19
3	Neuroblastoma		2 (40%)	3 (60%)		5
4	Hodgkin's lymphoma	1 (50%)	1 (50%)			2
5	Acute myelogenous leukemia	2 (18.18%)	7 (63.6%)		2 (18.18%)	11
6	Wilms tumor		2 (40%)	3 (60%)		5
7	Rhabdomyosarcoma		1 (25%)	3 (75%)		4
8	Histiocytosis		1 (100%)			1
9	Chronic myeloid leukemia					0
10	Osteogenic sarcoma			1 (100%)		1
11	Hepatoblastoma			1 (100%)		1
12	Germ cell tumor					0
13	Unclassified leukemia					0
14	Primitive neuroectodermal tumor		2 (100%)			2
15	Retinoblastoma					0
16	Malignant fibrous histiocytoma			1 (100%)		1
	Total	15 (18.75%)	46 (57.5%)	14 (17.5 %)	5 (6.25%)	80(100%)

Discussion

Malignancy is a serious problem, and after excluding C.N.S tumors, the relative frequency of different malignancies was nearly similar to that of other localities and among the total pediatric patients treated in Mosul as reported by Mosul cancer registry in year 2008, with acute lymphoblastic leukemia was the most frequent one among all other malignancies [2,5-8,15]. But this study disagrees with another study done by AL-Jumaily which found that lymphoma was the commonest type of malignancy during the period 1991-1998; a difference that is probably due to the effect of prohibited weapons used against Iraq at that time as that study showed [16].

In general, malignancies were more common in male children than in females in Mosul and this was especially true for leukemias, lymphomas and neuroblastom. The first 5 years of age was the most common age of the presentation of cancers in Mosul children and this age requires particular attention when such diagnosis is considered and this finding was similar to that found by others .[8,9]

The clinical presentation of malignant disease in Mosul children was more or less the same as that written in text books[10,11], this was largely because the pathogenesis of the clinical picture was the same anywhere, and this was especially true for acute lymphoblastic leukemia, where fever was the commonest complaint followed by pallor, bone pain and bleeding.

The death rate in all cases was 35.08% compared to less than 30% found by others [2] and if acute leukemia was taken as a prototype, the death rate was significantly higher than that in developed countries [2,13,14], and this was explained by the difficulties related to management including availability of diagnostic equipments, chemotherapeutic agents, effective radiotherapy machines and lack of stem cell transplantation as well as difficulties related to follow up of patients.

Sepsis and bleeding were the major causes of death especially in leukemias and lymphomas and this was the same as that found by other studies[12,14], while another study found that chemotherapy related toxicity and resistant disease where the major causes of death [13] and this is due to improvement in the diagnosis and treatment of sepsis with this latter group.

Conclusion

1- Leukemia is the most common malignancy among Mosul children and it accounted for 43.4% of all cases followed by Non-Hodgken lymphoma (19.5%) and neuroblastoma (7.9%).
2- Age and sex distribution in malignant diseases and clinical features were more or less similar to those elsewhere.
3- The death rate in general was high, which was due to the difficulties related to management and follow up of patients, and the commonest causes of death were sepsis, bleeding and progressive disease.

References

1. Lissauer. T, Clayden. G. Illustrated text book of pediatrics. Third edition, Mosby, 2007. chapter 21, Malignant Diseases: 347-360.
2. P. Imbach· T. Kühne· R. Arceci. Pediatric Oncology. Second Edition, 2004. Springer-Verlag Berlin Heidelberg New York. Introduction, Incidence and Management of Childhood Cancer : 3-6.
3. Nina S. Kadan-Lottick: Epidemiology of Childhood and Adolescent Cancer. In: Robert M. Kliegman, Richard E. Behrman, et al editors: Nelson Text Book of Pediatrics,18th ed, W B Saunders, 2007: 1105-1109.
4. Malcolm A. Smith and Lynn A. Gloeckler Ries: Childhood Cancer: Incidence, Survival, and Mortality. In: A. Pizzo, David G. Poplack: Principles and Practice of Pediatric Oncology, 4th Edition , Lippincott Williams & Wilkins Publishers, 2001:7.
5. Thomas W. McLean Marcia M. Wofford: Oncology. In: Robert M. Kliegman, Richard E. Behrman: Nelson Essentials Of Pediatrics, 5th ed, W B Saunders, 2006: 725-726.
6. Parkin DM, Stiller CA, Drapper GJ, Bieber CA. The international incidence of childhood cancer. Int J Cancer 1988; 42: 511-520.

7. Gurney JG, et al: Incidence of cancers in children in the united states. Cancer 1995; 75:2186.
8. Yacoub AAH, Al-Sadoon IO, Hassan GG and Al-Hemadi M: Incidence and pattern of malignant disease among children in Basrah with specific reference to leukemia during 78 the period 1990- 1998. Medical journal of Basrah University 1999;17:33.
9. Kusumakumary P., Rojimon Jacob, Rema Jothirmayi, M.K. Nair. .Profile of malignancies: A ten years study. Indian Pediatrics 2000;37: 1234-1238.
10. Donald H. Mahoney, Jr. acute lymphoblastic leukemia. In: Julia A. McMillan , Catherine D et al editors: Oski's Pediatrics: Principles and Practice,3rd Edition, Lippincott Williams & Wilkins Publishers,1999:327.
11. Judith M. Sondheimer, MD. Current Essentials Pediatrics. first Edition, The McGraw-Hill Companies, 2008. Chapter 8, Oncology: p.149.
12. Slats A M, et al: Causes of death in childhood acute lymphoblastic (ALL) and myeloid leukemia. Archives of Disease in Childhood 1992; 67:1378-1383.
13. Ulla M. Saarinen-Pihkala, Carsten Heilmann, et al: Pathways Through Relapses and Deaths of Children With Acute Lymphoblastic Leukemia. Journal of Clinical Oncology 2006; 24(36): 5750-5762.
14. Bo Lantz, Jan Adolfsson, Bengt Lagerlöf, Peter Reizenstein: Causes of Death in Leukemia and Lymphoma with Modern Treatment.: Acta Haematol 1980;63:61-67
15. Al-Ramadhani A.H. and Ismail A.M.: Cancers in children:Cancers in Mosul 2008; 17:31-65.
16. Al-Jumaily S .The prohibited weapons and malignant disease of children in north of Iraq: Annals college of medicine Mosul 2000;26 (1 and 2):35-40.

