

***Oncologic and functional outcome of children
With bone sarcomas treated with chemotherapy
and limb salvage surgery.***

Thesis

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Dedication

With all my love,

To my mother

Abstract

This is a retrospective study of the record of 86 patients with pathologically proven bone tumors and they were treated with chemotherapy. They were all treated in National Cancer Institute (NCI) and Cairo University Hospital over the period of 13 years from January 1993 to January 2006. The overall survival of all studied cases was 71.4%. Functional outcome was calculated according to MSTs scoring system and 70% of our patients had functional outcome of more than 70%. Various prognostic factors and chemotherapy toxicities were analyzed.

Key words: bone sarcomas, functional outcome, overall survival, prognostic factors.

List of contents

1- List of tables.....	I-II
2- List of figures.....	III-IV
3- List of abbreviations	V-VI
4- Introduction	1
5- Aim of the work	3
6- Review of literature	4
▪ Malignant bone tumors.....	4
▪ Osteosarcoma.....	6
▪ Ewing's sarcoma.....	38
▪ Chondrosarcoma.....	53
7- Patients and methods	55
8- Results	64
9- Discussion	90
10- Summary and conclusion	106
11- Recommendation	110
12- References	111
13- Arabic summary	

List of tables

Table	Subject	Page
1	Chemotherapy criteria according to NCI toxicity	61
2	Clinicopathologic characteristics of studied cases	64
3	Frequency of metastases at presentation	68
4	Frequency of chemotherapy protocols.	70
5	Frequency of the types of surgery performed	72
6	Tumor necrosis in studied cases	72
7	Functional outcome among studied cases	73
8	Types of recurrence in studied cases.	74
9	Causes of death in deceased cases	75
10	Toxicity related to OSGIV protocol	76
11	Toxicity related to OSGIII protocol	76
12	Toxicity related to OSGII protocol,	77
13	Toxicity related to OSGI protocol	77

Table	Subject	Page
14	Toxicity related to Ewing sarcoma protocol.	78
15	Correlation between DFS and age	80
16	Correlation between DFS and sex	80
17	Correlation between DFS and pathologic subtypes	81
18	Correlation between DFS and tumor size.	82
19	Correlation between DFS and tumor site	82
20	Correlation between serum LDH level and DFS	83
21	Correlation between serum ALP level and DFS	85
22	Correlation between chemotherapy protocol and DFS	86
23	Correlation between delay in chemotherapy and DFS	87
24	Correlation between type of salvage surgery and DFS	87
25	Correlation between tumor necrosis and DFS	88
26	Serum tumour markers among studied cases	69
27	Frequency of delay in chemotherapy	71

List of Abbreviations

ALP	-----	Alkaline phosphatase
CCG	-----	Children's Cancer Group
CNS	-----	Central nervous system
COSS:	-----	Cooperative Osteosarcoma Study
CT	-----	Computed tomography scan
DFS	-----	Disease Free Survival
EFS	-----	Event free survival
E	-----	Etoposide
ESF	-----	Ewing Sarcoma Family of Tumors
FDG-PET	-----	Fluorine-18 fluorodeoxy glucose positron emission tomography
GM-CSF	-----	Granulocyte-macrophage colony stimulating factor
HDMTX	-----	High dose methotrexate
IESS	-----	Intergroup Ewing's Sarcoma Study
IFX	-----	Ifosfamide
LDH	-----	Lactic dehydrogenase
L- MTP-PE	-----	Liposome-encapsulated muramyl tripeptide –phosphatidyl ethanolamine
LOH	-----	Loss of heterozygosity
MTX	-----	Methotrexate
MRI	-----	Magnetic resonance imaging

VI *List of abbreviations*

MSTS-----	Musculoskeletal Tumor Society
NSE-----	Neuro specific enulase
OS -----	Over all survival
OSG-----	Osteosarcoma Group
POG-----	Pediatric Oncology Group
PET -----	Positron emission tomography
PNET -----	Primitive neuroectodermal tumor
RB-----	Retinoblastoma
SIOP -----	International Society of Pediatric Oncology

List of figures

Figure	Subject	Page
1	Age distribution among studies cases	65
2	Sex distribution among studied cases	65
3	Frequency distribution of the presenting symptoms.	66
4	Frequency distribution of primary site of the tumor.	67
5	Frequency distribution of tumor size	67
6	Frequency distribution of histologic subtypes	68
7	Frequency distribution of metastatic cases at presentation	69
8	Frequency distribution of chemotherapy protocols	70
9	Type of surgery performed in the studied cases	71
10	Tumor necrosis among studied cases	72
11	Functional outcome among studied cases	73
12	Types of recurrences in the studied cases	74
13	Cause of death in died patients	75
14	Kaplan- Meier curve for OS among all cases	79
15	Kaplan- Meier curve for DFS among all cases	79
16	Kaplan- Meier curve for correlation between DFS and age.	80

IV *List of figures*

17	Kaplan- Meier curve for correlation between DFS and sex.	81
18	Kaplan- Meier curve for correlation between DFS and pathologic subtypes	81
19	Kaplan- Meier curve for correlation between DFS and tumor size.	82
20	Kaplan- Meier curve for correlation between DFS and different tumor sites	83
21	Kaplan- Meier curve for correlation between LDH level at initial presentation and DFS.	84
22	Kaplan- Meier curve for correlation between LDH level at end of therapy and DFS	84
23	Kaplan- Meier curve for correlation between ALP level at initial presentation and DFS	85
24	Kaplan- Meier curve for correlation between ALP level at end of therapy and DFS	85
25	Kaplan – Meier curve for correlation between DFS and 3 different osteosarcoma protocol	86
26	Kaplan – Meier curve for correlation between DFS delay in chemotherapy.	87
27	Kaplan – Meier curve for correlation between DFS and type of limb salvage surgery	88
28	Kaplan – Meier curve for correlation between DFS and tumor necrosis	88
29	OSG III chemotherapy protocol	59
30	OSG IV chemotherapy protocol	60
31	Frequency of delay in chemotherapy	71
32	DFS of non metastatic cases at presentation	89

IV *List of figures*

INTRODUCTION

Primary bone tumors are the sixth most common group of malignant neoplasm in children. In adolescent and young adults; they are the third frequent neoplasm exceeded only by leukemia and lymphomas. (*Sluga et al., 2006*).

Only one half of the bone tumors in childhood are malignant, of these; osteosarcoma is the most frequent, accounting for 35% of all primary sarcomas of bone and 56% of malignant bone tumors in the first two decades of life, Ewing's Sarcoma family of tumors (Ewing's Sarcoma and Peripheral Primitive Neuro Ectodermal Tumor) are the second most common primary osseous malignancy in childhood and adolescence (*Stiller et al., 2006*).

The survival of patients with malignant bone sarcomas has improved dramatically over the past 30 years, largely as a result of chemotherapeutic advances. Before the era of effective chemotherapy, 80 to 90 percent of patients with osteosarcoma developed metastatic disease despite achieving local tumors control and died of their disease. It was surmised and subsequently demonstrated that the majority of patients had subclinical metastatic disease at diagnosis, even in absence of metastatic disease. (*Bruland et al., 2005*).

Despite the fact that osteosarcoma is not very chemotherapy – sensitive, chemotherapy can successfully eradicate these deposits if initiated at a time when disease burden is low. As a result, all patients with osteosarcoma are treated with adjuvant chemotherapy, although

the optimal timing (ie.,preoperative or postoperative) is controversial (**Duffaud et al.,2000**).With modern therapy, approximately two thirds of patients with non metastatic extremity osteosarcoma will be long term survivals, up to 50 percent of those with limited pulmonary metastases may be cured of their disease, and long term relapse – free survival can be expected in about 25 percent of those who present with metastatic disease overall.(**Kager et al., 2003**).

Surgical management has evolved in parallel with emergence of effective chemotherapy. Although complete extirpation of the tumor remains the primary objective, the nature and scope of the approach taken to accomplish this goal has changed, with an emphasis on more conservative surgery in order to maintain function. Functional outcome depends not only on the extent of resection and the amount of muscle that is removed, but also the quality of the reconstruction and its associated complications. Limb – sparing surgery rather than amputation is now possible in the majority of patients, particularly when preoperative (neoadjuvant) chemotherapy is used. (**Ferguson et al., 2001**)

Aim of Work

Is to detect the oncologic and functional outcome of children who were newly diagnosed as primary bone sarcomas at National Cancer Institute (NCI) and Cairo university hospital, over a period of 13 years from January 1993 to January 2006. All the children attained limb salvage surgery as a type of local control of the tumor and they were treated with chemotherapy. In addition, various prognostic factors were analyzed to detect their significance.