RETROSPECTIVE ANALYSIS OF CLINICOPATHOLOGIC AND MANAGEMENT ASPECTS OF SOFT TISSUE SARCOMA

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By

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Rana El-Sayed Mohamed Mohamed Hegazy

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LIST OF ABBREVIATIONS

Abb.	Full term
AJCC	American Joint Committee on Cancer
ASPS	Alveolar soft part soft tissue sarcoma
CD68	Cluster of differentiation 68
CDK	Cyclin dependent kinase
CTH	Chemotherapy
CCSST	Clear cell sarcoma of soft tissue
CTV	Clinical target volume
CT	Computed tomography
CNB	Core needle biopsy
CKs	Cytokeratin
DFS	Disease Free Survival
DFSP	Dermatofibrosarcoma protuberance
DSRCT	Desmoplastic round cell tumor
EBRT	External Beam Radiotherapy
EGFR	Epidermal Growth Factor R
EHE	Epitheliod hemangioendothelioma
EMA	Epithelial membrane antigen
EORTC	European Organization for Research and Treatment of Cancer

ES	Epithelioid Sarcoma
ESMO	European Society of Medical Oncology
FAP	Familial Adenomatous Ployposis
FISH	Fluorescence in situ Hybridization
FNAB	Fine Needle Aspiration Biopsy
FNCLCC	National Federation of French Cancer Centers
GIST	Gastrointestinal Stromal Tumors.
GTV	Gross Target Volume
HHV8	Human Herpes Virus 8
HIV	human immunodeficiency virus
HILP	Hyperthermic Isolated Limb Perfusion
HPF	High Power Field
IHC	Immunohistochemistry
ILP	Isolated Limb Perfusion
IMRT	Intensity Modulated Radiotherapy.
IMT	Inflammatory myofibroblastic Tumor
KS	Kaposi Sarcoma
LMS	Leiomyosarcoma
LPS	Liposracoma
MDT	Multidisciplinary team
MFH	Malignat Fibrous Histiocytioma

MPNST	Malignant Peripheral Nerve Sheath Tumor
MRI	Magnetic Resonance Imaging
mTor	Mammalian Target of Rapamycin
NCCN	National Comprehensive Cancer Network
NCRP	National Cancer Registry Programme
NF-1	Neurofibromatosis Type 1
NF-2	Neurofibromatosis Type 2
ORR	Overall Response Rate
OS	Overall Survival
PAS	Periodic Acid Schiff
PCR	Polymer Chain Reaction
PDGF-a	Platelets Derived Growth Factor a
PET-CT	Positron Emission Tomography
PFS	Progression Free Survival
PM	Pulmonary Metastasis
RB-1	Retinoblastoma Tumor Suppressor gene
RT	radiotherapy
RTH	Radiotherapy
STS	Soft Tissue Sarcoma
Sarcoma NOS	Sarcoma Not Other Wise Specified
SDH	Succinate Dehydrogenase

SEER	Surveillance, Epidemiology, and End Results Program
SFT	Solitary Fibrous Tumor
TLE-1	Transducer Like enhancer of split 1
TNF- α	Tumor Necrosis Factor Alpha
UICC	Union for International Cancer Control
UPS	Undifferentiated Polymorphic Sarcoma
USTS	Undifferentiated Soft Tissue Sarcoma
USS	Ultra Sound Scan
VEGFR	Vascular Endothelial Growth Factor R
vWF	Von Willi brand Factor
WHO	World Health Organization
WLE	Wide Local Excision

INTRODUCTION

Soft-tissue sarcomas (STS) are a heterogeneous group of tumors that mainly arise from embryonic mesoderm with some neuroectodermal contribution and differentiate to non-epithelial extra skeletal tissue including muscle, fat and fibrous tissue. Almost 50 tumor subtypes of STS are present, and they can be anywhere in the body. **(Fletcher *et al*, 2013).**

STS are uncommon tumor group that represents approximately 1% of adult cancers with an annual incidence of the disease in the UK and USA, respectively, is of 3,300, and 10,000 **(Clinical Practice Guidelines Version 2013).**

They can occur all over the body; commonest sites are the extremities (50 %), trunk (15 %), retroperitoneum (15 %), and viscera (15 %). The most common histological subtypes in adults are liposarcoma and leiomyosarcoma **(Fletcher *et al*, 2013)**.

Whereas the cause of most sarcomas is not known, a few cases are associated with exposure to radiation (especially in presence of p53 germ line mutations) (Sorrell et al, 2013).Chemical exposure (e.g., to phenoxyacetic acids, chlorophenols, thorium oxide, vinyl chloride, and arsenic), or chronic lymphedema **(Sharma *et al*, 2012).**

Generally, low-grade tumors have tendency to recur locally or loco-regionally, with a low risk of distant spread; high-grade tumors can also recur locally but have a much higher propensity for distant failure. Extremity and trunk wall STS most commonly spread to the lungs when they metastasize, whereas retroperitoneal sarcomas generally have a pattern of loco-regional recurrence **(Colombo *et al*, 2012).**

The treatment for STS is largely dictated by the tumor grade, size, location of metastatic sites, and the histological subtype **(Casali *et al*, 2010).**

STS is best treated by multidisciplinary teams specialized in the management of these tumors**. (Rossi *et al,* 2013).** When the disease is localized, surgical resection with or without radiotherapy and chemotherapy is the treatment with curative intent.

Surgery is the mainstay of treatment in localized adult STS. The aim is the excision of the tumor surrounded by a cuff of healthy tissue all around, in order to have free resection margins at pathological examination **(Casali *et al,* 2010).** While the goal of surgery and radiotherapy is only local control of the tumor. Unfortunately, STS recurs usually as locally inoperable or metastatic disease, at this point systemic therapy has a prominent role in the multidisciplinary management of this tumor.

Cytotoxic chemotherapy has been the mainstay therapy for treating advanced-stage STS, giving an overall response rates of about 25% in the first-line setting **(Judson *et al,* 2012).** The aim of chemotherapy is to gain both local and systemic control, and it can be used for either curative or palliative intents.

The Anthracycline doxorubicin is the most commonly used agent as a first-line treatment of metastatic STS, and provide response rates of 12–24 % **(Volkova, *et al,* 2011).**

The survival of patients with soft tissue sarcoma is unsatisfactory. The disease-free survival has increased significantly over the recent decades due to the introduction of multidisciplinary approaches and with further standardization of surgery, radiotherapy and the use of systemic therapy. Patients commonly demonstrate a median survival ranging from 11 to 18 months from diagnosis of advanced disease **(Italiano *et al,* 2011).**

AIM OF THE WORK

The aim of the study is to investigate clinicopathologic and different management aspects of STS.