SOFT TISSUE SARCOMA

An essay

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الأورام السرطانية في الأنسجة الرخوة

رسالة مقدمة من

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توطئة للحصول على درجة الماجستير
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المقـــدمة

ينشأ الورم عندما تنمو خلايا جزء من الجسد و تخرج عن نطاق التحكم ، و على الرغم من وجود عدة أنواع من الأورام ، فالكل يبدأ بسبب نمو خارج عن التحكم في خلايا غير طبيعية .

خلايا الجسد الطبيعية تنمو و تنقسم و تموت بنظام ثابت ، ففي خلال السنوات الأولى من حياة الإنسان ، تنقسم الخلايا أسرع حتى يصبح الإنسان يافعاً ، و بعد ذلك تنقسم هذه الخلايا فقط لتحل محل الخلايا الميتة و التالفة في معظم أنحاء الجسد .

تخـــتلف خلايا الأورام عن الخلايا الطبيعية في تكـــــوين خلايا غير طبيعـــية وتستمر في النمو و الانقسام .

خـــلايا الأورام تنتج بسبب خلل في الحمض النووي و الذي يوجد في كل خلية لتوجيه أنشـــطتها ، و في معظم الأوقات التي يتلف فيها الحمض النووي يكون الجسم قادراً على إعادة بنائه مرة أخرى ، و لكن في خلايا الأورام لا يمكن إعادة بنائه ، و الإنسان يمكنه وراثة حمض نووي به خلل مما يؤدي إلى وراثة الأورام .

و يتلف الحمض النووي للإنسان بالتعرض إلى عوامل بيئية معينة مثل التدخين .

و تعد الأورام السرطانية في الأنسجة الرخوة أوراماً نادرة ، حيث تمثل ١ % من أورام الكـــبار ، و ١٥ % من أورام الأطفال .

لم يتم التعرف على سبب معين للإصابة بالأورام السرطانية فـي الأنسجة الرخوة في معظم المـصابين ، و لكن توجد علاقة واضحة بين عوامل بيـــــــئية معينة و حـدوث مثل هذه الأورام ، و من ضمنها التعرض للإشعاعات المتأينة .

و يوجد أكثر من ٥٠ نوع من هذه الأورام ، و التي يتم تشخيصها بالجينات الوراثية و معايير شكلية أخرى .

و الطريقة التي يتم بها التعبير عن طريقة انتشار الورم تسمى التصنيف ، و يتم هذا التصنيف بدراسة عينات من الورم و عمل الأشعات مـــثل أشعة الرنين المغناطيـــسي و الأشعـة المقطعية و المسح الذري .

و تصنيف الورم يحدد الطريقة التي تتم بها طريقة العلاج سواء كـان علاجاً جراحياً أو إشعاعياً أو كيماوياً أو الجمع بين أي منها .

هدف الرسالة

إن الهدف من الرسالة هو مراجعة الأنواع المختلفة للأورام السرطانية في الأنسجة الرخوة ، و تشخيص و علاج كل نوع .

محتويات الرسالة

ملخص الرسالة

يمثل علاج الأورام السرطانية في الأنسجة الرخوة تحدياً للجراحين ؛ حيث أصبح في الإمكان ـ مع مراعاة بعض الاحتياطات ـ المحافظة على الطرف المصاب بالورم بعد تطور العلاج المصاحب للجراحة (الكيميائي و الإشعاعي) ؛ في حين كان بتر الطرف المصاب هو العالج السائد في الماضي كمحاولة للحفاظ على حياة المريض.

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List of Abbreviations

AIDS : Acquired immunodeficiency syndrome
AJCC : American Journal Committee on Cancer
ATF1 : Activating transcription factor 1 gene
ATM : Ataxia telangiectasia mutated gene
BRCA 1, 2 : Breast cancer, early onset, genes 1 and 2
CNB : Core-needle biopsy
CT : Computed tomography
DFSP : Dermatofibrosarcoma protuberans
DNA : Deoxyribonucleic acid
ERG : V-ets avian erythroblastosis virus e26 oncogene-related gene
ETS : Ewing's sarcoma translocation genes
ETV1, 4, 6 : ETS variant genes 1, 4, and 6
EWS : Ewing's sarcoma breakpoint region 1 gene
FDG : Fluoro - deoxy D - glucose
FKHR : Forkhead homolog 1 gene
FLI1 : Friend leukemia virus integration 1 gene
FNAB : Fine-needle aspiration biopsy
GU : Genitourinary
HHV-8 : Human herpes virus - 8
HIV : Human immunodeficiency virus
IGF 1 R : Insulin-like growth factor type 1 receptor
KIT : V-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog gene
LMS : Leiomyosarcoma
MDM2 : Human homolog of murine double minute 2 gene
MFH : Malignant fibrous histiocytoma
MRI : Magnetic resonance imaging
NCI : National Cancer Institute
PAX 3, 7 : Paired box homeotic genes 3 and 7
PDGFR alpha : Platelet-derived growth factor receptor alpha
PET : Positron emission tomography
PNET : Primitive neuroectodermal tumours
RB1 : Retinoblastoma gene
RMS : Rhabdomyosarcoma
RT : Radiotherapy
SSX1, 2, 4 : Synovial sarcoma, x breakpoint genes 1, 2, and 4
STS : Soft tissue sarcoma
SYT : Synovial sarcoma translocation gene
TNM : Tumour, lymph node and metastasis
TP53 : Tumor protein 53 gene
VEGF : Vascular endothelial growth factor
WT1 : Wilms tumor 1 gene

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Ahmed Abdel-Hameed

AIM OF THE WORK

The ongoing study is designed to review recent literature about the different types of soft tissue sarcoma, diagnosis and management of each type.

INTRODUCTION

Cancer develops when cells in a part of the body begin to grow out of control. Although there are many kinds of cancer, they all start because of out-of-control growth of abnormal cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of person's life, normal cells divide more rapidly until the person becomes an adult. After that, cells in most parts of the body divide only to replace worn-out or dying cells and to repair injuries. Because cancer cells continue to grow and divide, they are different from normal cells. Instead of dying, they outlive normal cells and continue to form new abnormal cells .Cancer cells develop because of damage to DNA. This substance is in every cell and directs all its activities. Most of the time when DNA becomes damaged the body is able to repair it. In cancer cells, the damaged DNA is not repaired. People can inherit damaged DNA, which accounts for inherited cancers. Many times though, a person's DNA becomes damaged by exposure to something in the environment, like smoking. *(1)*

Soft tissue sarcoma comprises a group of relatively rare but anatomically and histologically diverse neoplasm. These tumours share a common embryonic origin, arising primarily from tissues derived from the mesoderm, with the notable exception of neurosarcomas, primitive neuroectodermal tumours (PNET) and possibly Ewing sarcomas which are thought to arise from tissues of ectodermal origin. Despite the fact that the skeleton and somatic soft tissue account for as much as 75% of total body weight, neoplasms of the soft tissues are comparatively rare، accounting for 1% of adult malignancies and 15% of pediatric malignancies. *(2)*

No specific etiologic agent is identified in the overwhelming majority of patients with soft tissue sarcoma. There are a number of recognized associations between specific environmental factors and subsequent development of sarcoma. Exposure to environmental toxins has been limited with development of this specific sarcoma: mesothelioma (asbestos) and hepatic angiosarcoma (thorotrast and vinyl chloride). Ionizing radiation has been indicated as a cause of sarcoma arising in soft tissue and bone. The latent period averages approximately 10 years but ranges between 2 and 30 years, and the

prognosis is usually poor. The epidemiologic relationship between the development of soft tissue sarcoma and inherited syndromes associated with predisposition to sarcoma has been appreciated for more than two decades. Neurofibromatosis, tuberous sclerosis, basal cell nevus syndrome and pediatric patients with familial retinoblastoma have a 13 q chromosomal deletion and an increased incidence of osteosarcoma and other second primary neoplasms including soft tissue sarcoma. Sarcomas rarely develop from preexisting benign soft tissue tumours. *(3)*

There are over 50 subtypes of this disease, which are currently diagnosed by genetic and morphological criteria. Those most frequently seen include liposarcoma, leiomyosarcoma, malignant fibrous histiocytoma (MFH), fibrosarcoma, and synovial sarcoma. *(4)*

The process of finding out how far the cancer has spread is called staging. In sarcoma staging, doctors also evaluate the appearance of the tumour under the microscope and judge how fast the cancer seems to be growing. The information needed to stage sarcomas includes biopsies, imaging tests of the main tumour (usually with CT or MRI scans), and imaging tests of other parts of the body where the cancer may have spread.

When examining the biopsy sample, the pathologist takes into account the number of cells that are actively dividing and how closely the cancer resembles normal tissue. He or she determines the cell type and grade and estimates how rapidly it will grow and spread. The stage of a sarcoma is the most significant factor in determining each patient's prognosis and in selecting treatment options. *(5)*

Most of sarcomas could be treated with surgical excision, chemotherapy, radiotherapy, or combination of all. *(1)*

Chapter I

Classification of Soft Tissue Sarcoma

Earlier classifications have been largely descriptive and have been based more on the nuclear configuration than the type of tumour cell. Terms such as round cell, spindle cell or pleomorphic sarcoma should be discouraged because they are meaningless and convey little information as to the nature and potential behavior of a given tumour. *(6)*

More recent classifications have been based on the line of differentiation of the tumour, that is the type of tissue formed by the tumour rather than the type of tissue from which the tumour arise.

The World Health Organization proposed classifications, these classifications based on different tumour categories, ranging from fibrous, adipose, and muscle tumour to tumour of uncertain histological type and tumour that cannot be further classified. The last category includes 5-15 % of all sarcomas depending on the quality of available material, the experience and knowledge of the examining pathologist. *(7)*

Classification of soft tissue tumour into benign and malignant groups is not meant to imply that malignant soft tissue tumour tend to originates from their benign counterparts. In fact, malignant transformation of benign soft tissue tumour is an extremely rare event, with the exception of the occasional transformation of neurofibroma to malignant schwannoma.

The various tumour types are named according to histological type of predominant cellular element, that is, the resemblance of the tumour to normal tissue or its embryonic counterpart.

Malignant fibrous histiocytoma and liposarcoma are the commonest soft tissue sarcoma in adult, while rhabdomyosarcoma, neuroblastoma and extra skeletal Ewing's sarcoma are the most frequent soft tissue sarcoma in childhood. *(6)*