بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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شبكة المعلومات الجامعية

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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MONA MAGHRABY

Clinical and genetic characteristics of patients with mucopolysaccharidosis disease

Thesis

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ABSTRACT

Background: The clinical spectrum of mucopolysaccharidosis (MPS) type I is variable and range from the mildest attenuated form (Scheie syndrome) and the severest form (Hurler syndrome). Patients with Scheie syndrome suffer, despite being attenuated, from variable musculoskeletal, ophthalmological, and cardiac symptoms that sometimes delay or hinder reaching a proper diagnosis.

Aim of the case report: To highlight the different presentation of a patient with Scheie syndrome.

Description: We report a 30-year-old girl with Scheie syndrome, the firstborn of first-cousin parents presented at the age of 7 years with arthralgia and limitation of movements of several joints and so misdiagnosed as juvenile rheumatoid arthritis. She also suffered from corneal cloudiness, short stature, and no coarse facial features. Her skeletal survey at that time showed no abnormality as well as her Echocardiography. The diagnosis of MPS was confirmed by low alpha L-iduronidase enzyme activity. She received enzyme replacement therapy (ERT), which was started late and on an irregular basis. Therefore, her disease continued to progress despite regular ERT, especially avascular organs like corneas

Conclusion: Scheie syndrome should be suspected in patients with rheumatoid like symptoms, especially in the presence of other MPS characteristic features like corneal cloudiness. Late start of treatment hinders the patient's chance of optimum ERT effect.

Keywords : ERT: Enzyme replacement therapy; GAGs : Glycosaminoglycan; MPS Mucopolysaccharidoses

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List of Abbreviations

ARSB	:	N-acetylgalactosamine-4-sulfatase gene
BBB	:	Blood-Brain Barrier
BiPAP	:	Bilevel positive airway pressure ventilators
C6S	:	chondroitin-6-sulfate
CNS	:	Central nervous system
CPAP	:	Continuous positive airway pressure
CSF	:	Cerebrospinal fluid
CT	:	Computed tomography
CTS	:	Carpal tunnel syndrome
DNA	:	Deoxyribonucleic acid
E.N.T	:	Ear nose throat
ECM	:	Extracellular matrix
ERT	:	Enzyme replacement therapy
FEV1	:	Forced expiratory volume in 1 second
FVC	:	Forced vital capacity
GAGs	:	Glycosaminoglycan
GALNS	:	N-acetylgalactosamine-6-sulfate sulfatase
GLB1	:	β-galactosidase
GVHD	:	Graft-versus-host disease
HGSNAT	:	Membrane bound lysosomal enzyme acetyl-CoA: a-glucosamine N-acetyltransferase
HLA	:	Human leukocyte antigen
HSCT	:	Hematopoietic stem cell transplantation
ICP	:	Intracranial pressure
ICV	:	Intracerebroventricular
IDS	:	Iduronate sulfate
IOP	:	Intraocular pressure
IQ	:	Intelligence quotient
JIA	:	Juvenile idiopathic arthritis

List of Abbreviations (Cont.)

KS	:	Keratan sulfate
LVH	:	Left ventricular hypertrophy
MPS	:	Mucopolysaccharidoses
MRI	:	Magnetic resonance imaging
NAGLU	:	N-acetyl-alpha-d-glucosaminidase
NMD	:	Nonsense-mediated mRNA decay
nmDMD	:	Nonsense mutations causing Duchenne muscular dystrophy
OME	:	Otitis media with effusion
OSA	:	Obstructive sleep apnea
QOL	:	Quality of life
rhASB	:	Recombinant human N-acetylgalactosamine-4-sulfatase
rhGALNS	:	Recombinant human N-acetylgalactosamine-6-sulfate sulfatase
rhGUS	:	Recombinant human beta-glucuronidase
SCRT	:	Stop codon read-through
TLR4	:	Toll-Like Receptor 4

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Introduction

Mucopolysaccharides are essential constituents of connective tissue, including cartilage and vessel walls. They are composed of long sugar chains, containing highly sulfated, alternating uronic acid and hexosamine residues, assembled into repeating units. The polysaccharide chains are bound to specific core proteins within complex macromolecules called proteoglycans. Depending on the composition of the repeating units, several mucopolysaccharides are known. Their degradation takes place inside the lysosomes and requires several acid hydrolases. Deficiencies of specific degradative enzymes are the cause of a variety of disorders, collectively termed mucopolysaccharidoses **(Neufeld and Muenzer et al., 1995).**

Mucopolysaccharidoses are a group of rare lysosomal storage diseases, each being related to a particular mutation responsible for a deficiency of glycosaminoglycan degrading enzymes, leading to an accumulation of glycosaminoglycans in tissues. Many of them are diagnosed in children or teenagers and have a severe prognosis because of organ failure, however, some of them have a more progressive presentation, with musculoskeletal symptoms at the forefront and a lifespan that nearly reaches that of the general population. These milder forms are more likely to be diagnosed in adults, in patients who have suffered for years and sometimes even decades with unrecognized mucopolysaccharidosis. Indeed, they can sometimes mimic