

التصوير المتقدم للجهاز العصبي في تشخيص مرض الميتوكوندريا في الأطفال

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توطئة للحصول على درجة الماجستير
في طب الأطفال

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Advanced Neuroimaging Technique In Diagnosis of Mitochondrial Disease In Children

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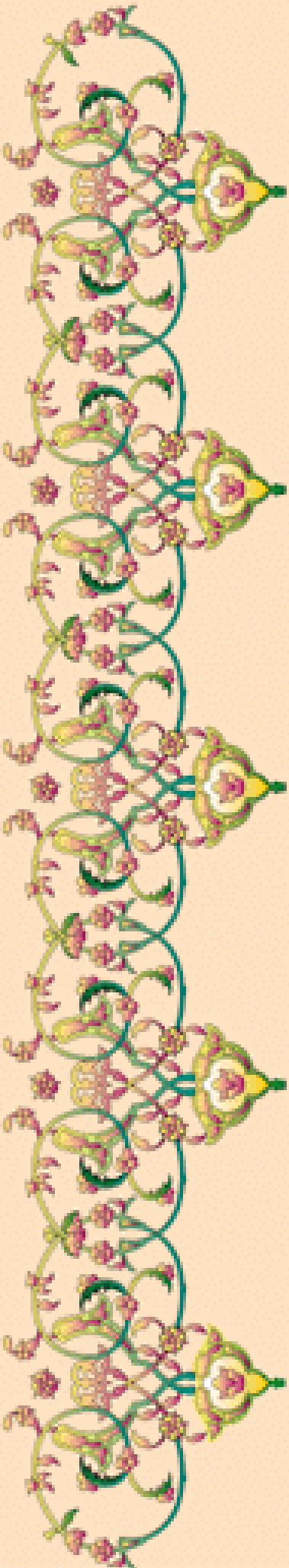
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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

" قَالُوا سُبْحَانَكَ لَا
عِلْمَ لَنَا إِلَّا مَا
عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْحَكِيمُ "

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Dedication

*To my parents ,to my Husband ,to
my friends , to my sisters ,to my
sons Eyad and Malek
And To all suffering children .*

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LIST OF ABBREVIATIONS

ALT	Alanine transferase
AST	Aspartate transferase
ATP	adenosine triphosphate
Cho	Choline
Co Q10	coenzyme Q10
CPEO	Chronic progressive external ophthalmoplegia
Cr	Creatine
Cyt c	cytochrome c
DPT	Diphtheria, pertussis, tetanus
ETC	electron transport chain
IUGR	Intra uterine growth retardation
KSS	Kearns-Sayre syndrome
LHON	Leber Hereditary Optic Neuropathy
MD	Mitochondrial disease
MDC	mitochondrial disease criteria
MELAS	Mitochondrial Encephalopathy, Lactic Acidosis and Stroke like episodes
MERRF	Myoclonic Epilepsy, Ragged Red Fibers
MI	Myo-inositol
MILS	Maternally inherited Leigh syndrome
mmol	Milli-molecule
MnSOD	Mitochondrial manganese superoxide dismutase
MRI	Magnetic Resonance Imaging
MRS	Magnetic Resonance spectroscopy

LIST OF ABBREVIATIONS

msec	millisecond
mtDNA	Mitochondrial DNA
NAA	N-acetylaspartate
NARP	Neuropathy, Ataxia, Retinitis Pigmentosa
nDNA	Nuclear DNA
NO	nitric oxide
ONOO	peroxynitrite
<i>OXPPOS</i>	oxidative phosphorylation
PEO	progressive external Ophthalmoplegia
ppm	Part per minute
ROS	reactive oxygen species
rRNAs	ribosomal RNAs
TE	Time to echo
tRNAs	transfer RNAs

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Introduction

The clinical recognition of mitochondrial disease is often a challenging endeavor. Genetically based, primary mitochondrial dysfunction presents as a heterogeneous group of disorders, which together are now recognized to constitute the most common neurometabolic disorder of childhood. **(Sanderson et al.,2006).**

Epidemiologic studies of mitochondrial disease are limited by disease heterogeneity and underdiagnosis. Prevalence figures are less accurate than incidence figures in estimating mitochondrial disease frequency due to the high childhood mortality of these disorders. **(Dimauro and Davidzon.,2005).**

Mitochondrial diseases are usually progressive and multisystemic. Typically affected organs are those with a high energy demand, including skeletal and cardiac muscle, endocrine organs, kidney, nonmucosal components of the intestinal tract, retina, and the central nervous system. However, virtually any organ or tissue can be involved. **(Dimauro and Davidzon.,2005).**

As a general rule, the involvement of 3 or more organ systems without a unifying diagnosis should raise

Introduction

suspicion for mitochondrial disease. Although effective treatments remain elusive, definitive diagnosis is crucial for permitting appropriate symptom management, as well as accurate prognostic and recurrence-risk counseling. **(Dimauro and Davidzon.,2005).**

Mitochondrial disease may present with “any symptom in any organ at any age, but some symptoms and signs truly are more suggestive of a mitochondrial disorder than others. **(Munnich et al.,1996)**

These features warrant the initiation of a baseline diagnostic evaluation for mitochondrial disease. **(Richard et al.,2007).**

In contrast, there are a multitude of nonspecific symptoms that frequently occur in infants and children with mitochondrial disease but have a broad differential diagnosis, and more often lead to other clear diagnoses. **(Richard et al.,2007).**

Thus, the nonspecific symptoms, particularly if they occur in isolation, do not indicate a mitochondrial problem per se. **(Richard et al.,2007).**

However, when they are present in combination, the likelihood of a mitochondrial disorder increases, particularly if the nonspecific features involve different