شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم

شبكة المعلومـــات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

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قبلت الرسالة وتوصي اللجنة بطبع الرسالة على نفقة الكلية وتداولها مع باقي الجامعات

Central Involvement in Hereditary Motor and Sensory Neuropathy: A Clinical, Electrophysiological, Genetic, Posturographic and Imaging Study

Thesis

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By

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LIST OF ABBREVIATIONS

µm	:	micrometer
µV	:	Microvolt
95% CI	:	Confidence interval
AEP	:	Auditory evoked potentials
ALS	:	Amyatrophic lateral sclerosis
BAEP	:	Brainstem auditory evoked potentials
BAER	:	Brainstem auditory evoked response
BOS	:	Base of support
C1,2 etc	:	Condition
CDP	:	Computerized dynamic posturography
CIDP	:	Chronic inflammatory demyelinating polyneuropathy
CMAP	:	Compound muscle action potential
CMT	:	Charcot-Marie-Tooth
CMTD	:	Charcot-Marie-Tooth Disease
CNS	:	Central nervous system
COG	:	Centre of gravity
CPG	:	Central pattern generators
CT	:	Computerized tomography
CX32	:	Connexin 32
dB	:	Decibel
del	:	Deletion
DNA	:	Deoxynucleic acid
DSD	:	Dejeine-Sottas disease
dup	:	duplication
EEG	:	Electroencephalogram
EGR2	:	Early Growth Response 2
EM	:	Electron microscope
EMG	:	Electromyography
EP	:	Evoked potentials
FA	:	Friedreich's ataxia
FD	:	Field-dependent
FI	:	Field-independent
FSP	:	Familial spastic paraplegia
GM	:	Ganglioside M

HMSN	:	Hereditary motor and sensory neuropathy
HMSNCA	:	Hereditary motor and sensory neuropathy with cerebellar atrophy
HNPP	:	Hereditary neuropathy with liability to pressure palsy
HSP	:	Hereditary spastic paraplegia
HU	:	Initials of the original patient
HZ & KHZ	:	Hertz & kilo hertz
IG	:	Immunoglobulin
Inv	:	Inversion
IO P100	:	Interocular P100
IQ	:	Intelligence Quotion
KDa	:	Kilo Dalton
LLAEP	:	Long-latency auditory evoked potentials
LMNL	:	Lower motor neuron lesion
LOS	:	Limits of stability
m/sec	:	meter/second
mA	:	Milliampere
MAG	:	Myelin-associated glycoprotein
Mb	:	Million base pairs
MBP	:	Myelin basic protein
MCT	:	Motor coordination (control) test
Min-Max	:	Minimum-Maximum
MLAEP	:	Middle-latency auditory evoked potentials
mm	:	millimeter
MMSE	:	Mini-Mental State Examination
MNCV	:	Motor nerve conduction velocity
MRC	:	Medical Research Counsel
MRI	:	Magnetic resonance imaging
m-RNA	:	messenger
msec	:	Millisecond
MUAP	:	Motor unit action potentials
mV	:	millivolt
n	:	Number of observations
N-CAM	:	Neural cell adhesion molecule
NCV	:	Nerve conduction velocity
NS	:	Not significant
P/D	:	Proximal / distal
P2	:	Protein 2

PCR	:	Polymerase chain reaction
PLP	:	Proteolipid protein
PMP22	:	Peripheral myelin protein
PN	:	Peripheral neuropathy
PNS	:	Peripheral nervous system
PO/MPO	:	Myelin protein zero
Pref	:	Preference
P-VEP	:	Pattern reversal visual evoked potentials
RNA	:	Ribonucleic acid
SD	:	Standard deviation
SEP	:	Somatosensory evoked potentials
SNAP	:	Sensory nerve action potential
SOM	:	Somatosensory
SOT	:	Sensory organization test
SS	:	Somatosensory
SSR	:	Sympathetic skin response
SVR	:	Slow vertex response
T	:	Translocation
UMNL	:	Upper motor neuron lesion
Vest	:	Vestibular
VIS	:	Visual
VOR	:	Vestibulo ocular reflex
VOT	:	Vestibulo-ocular tract
VSR	:	Vestibulo spinal reflex
VST	:	Vestibulo spinal tract

CONTENTS

INTRODUCTION

INTRODUCTION

Hereditary motor and sensory neuropathy (HMSN) or Charcot-Marie-Tooth disease (CMT) is the most common inherited disorder of the peripheral nervous system with an incidence of 40:100000.[1] It is the most common disorder giving rise to the syndrome of peroneal muscular atrophy.[2] It is characterized by distal muscle weakness and wasting, primarily of the legs and later the arms, foot deformity, diminished or absent tendon reflexes and mild to moderate sensory loss.[1] However, complex forms are known to occur in HMSN. By the complex forms it is meant that patients with HMSN may have features denoting involvement of other parts of the nervous system rather than those of the periphral neuropathy and/or cutaneous and retinal changes etc.[2] In this context, as far as the clinical aspect is concerned, it is noticed that some patients have a multitude of symptoms that may reflect more than mere peripheral nerve involvement, for instance, balance problems, bulbar symptoms, episodic neurological complaints, mental and intellectual changes and even personality changes. These clinical situations which are actually confronted by the physician, warrant meticulous investigation of the nervous system both centrally and peripherally.

Diagnosis of HMSN depends on the clinical features, mode of inheritance, nerve conduction studies, neuropathological findings and definition of the underlying genetic defect. The latter is the main basis for classification.[3] However, diagnostic difficulties may be encountered in

some instances, especially in absence of the most diagnostic tool (molecular genetic study), which is not available as a routine laboratory test yet. One of these difficulties is the presence of associated manifestations as cerebellar dysfunction, which may raise the possibility of Friedreich's ataxia or involvement of cranial nerves and pyramidal tracts, which may draw the attention to metabolic neuropathies as metachromatic leucodystrophy. Moreover, the immune mediated neuropathies have gained much popularity nowadays and should be differentiated from HMSN when suspected.

Severe disability is not expected in the usual forms of HMSN. Ambulation must be encouraged and is not usually lost.[4] However, in complex forms considerable disability may take place (due to ataxia, balance problems, pyramidal and cranial nerves dysfunction, etc) and represent a challenge in the rehabilitation practice. Consequently, the patient may need only physical therapy to correct deformities, preserve joint mobility or use orthotic devices. Otherwise, the treatment may extend to a more comprehensive rehabilitation program for special problems as balance disorders. Therefore, detection of these associated features (whether they are manifest or not) is an integral part of the diagnosis.

Therefore, based on the fact that peripheral as well as central involvement can take place in HMSN, it is beneficial to utilize several investigative tools to diagnose CNS involvement. This will definitely increase the number of the diagnosed cases and detect the extent of the lesion, which in