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A REVIEW OF CAUSES, SYMPTOMS, DIAGNOSIS, AND TREATMENT OF MOTOR NEURON DISEASE (MND)

Eftikhaar Hasan Kadhum
Department of pharmaceutical science, College of Pharmacy, University of Thi-Qar, Thi-Qar, 64001, Iraq

Abstract: Motor neuron disease (MND) also called amyotrophic lateral sclerosis (ALS) is an adult-onset neurodegenerative defect characterized by loss of upper motor neurons (UMNs) and lower motor neuron (LMNs, anterior horn cells of the spinal cord and brainstem nuclei). The term MND is widely synonymous with ALS, reflecting the observation that most patients reveal combined LMN-related loss of muscle because of denervation (amyotrophy), and UMN degeneration of the lateral corticospinal tract and its cortical origins establishing as gliosis, or hardening (sclerosis). The average survival of patients is 3–5 years. However, there is several causes of this disease includes: genetics, mitochondrial dysfunction, apoptosis, oxidative stress, protein aggregation, reduced axonal transport… etc.

The symptoms of MND are includes the following: dysphagia, bulbar featuresdysarthria, excessive salivation and tongue fasciculations, muscle wasting, limb or muscle features focal weakness, muscle twitching, sensory impairment and muscle stiffness; respiratory features orthopnoea, rapidity of breath on exertion, early morning headache and fatigue or tiredness, depression, cognitive features behavioural change, emotional lability…. etc. Riluzole is the only drug licensed to treat MND.

Keywords: MND, ALS, neurons, PMA.

Introduction

Motor neuron disease (MND) also called amyotrophic lateral sclerosis (ALS) is an adult-onset neurodegenerative defect characterized by loss of upper motor neurons (UMNs) and lower motor neuron (LMNs, anterior horn cells of the spinal cord and brainstem nuclei) [1]. The term MND is widely synonymous with ALS, reflecting the observation that most patients reveal combined LMN-related loss of muscle because of denervation (amyotrophy), and UMN degeneration of the lateral corticospinal tract and its cortical origins establishing as gliosis, or hardening (sclerosis). 5–10% of ALS is hereditary (fALS) and sporadic (sALS), with an occurrence of 2–3 per 100,000 [2]. ALS is a mortal disease. The average survival of patients is 3–5 years [3]. The first symptoms typically occur in the limbs, but muscle fault may also begin in the bulbar region. Respiratory failure is the most common cause of death this happened because advanced weakness of the respiratory muscles. More than 50% of the motor neurons innervating a muscle may already be lost before the first clinical signs of muscle weakness become apparent [4]. In the Netherlands, approximately 1,700 people (prevalence 10.3 per 100,000) suffer from ALS. Approximately 500 people (incidence 2.8 per 100,000) in the Netherlands are diagnosed with ALS every year [5]. In Europe, the yearly crude incidence rate was estimated to be 2.7 per 100 000 person per year [6]. The term ALS was first described in 1874 by Jean-Martin Charcot [7]. The course of the disease is relentlessly progressive eventually leading to death, in most patients because of respiratory insufficiency, ninety percent of MND patients are sporadic cases and 10% are familial, often with an autosomal dominant

inheritance. The single effective drug is Riluzole, which has a modest effect on survival (3-6 months) [8]. The median existence of ALS is (3 years), and that of progressive spinal muscular atrophy (PMA) is possibly between 5 and 8 years, though a proportion of PMA patients display an ALS-like survival predicted by an early decline of vital ability (a respiratory measure) [9]. ALS is the term which categorizes the most common form of the illness and is often used synonymously with MND, motor neuron disease is heterogeneous neurodegenerative syndromes characterized by the progressive decline of upper (UMN) and/or lower motor neurons (LMN), leading to advancing muscular paralysis and death, it have been found that patients with (UMN) involvement 30% of patients with (ALS), and fair percentage of patients with primary lateral sclerosis have executive and memory deficits, recently it has been shown that pUMN and pLMN phenotypes exhibit significantly longer survival compared to classic ALS [10-13]. This holds true for patients with only lower motor neuron (LMN) signs is indistinct [14]. Progressive spinal muscular atrophy (PMA) is an adult-onset progressive LMN condition. There is still argument on whether PMA represents one end of the spectrum of motor neuron diseases or whether is a separate disease entity. In approval of the latter claim are the geneticm clinical and pathologic features that PMA shares with ALS [15-17]. Concerning their predictive significance, several studies have shown varied results in disease progression and survival [18-20].

Causes of MND

The obvious pathogenic of MND is not well known as it has not been entirely elucidated by medical research, however, several key factors can be noted including, genetics, mitochondrial dysfunction, apoptosis, oxidative stress, protein aggregation, reduced axonal transport, Inflammatory dysfunction and contribution of non-neuronal cells, shortages of neurotrophic factors and dysfunction of signaling pathways [21,22].

Atrophy of the anterior roots in the cervicothoracic spinal cord was seen in cases with certain lower motor neuron involvement. Cortical atrophy was clear in the limbic system including the temporal pole, amygdala and par hippocampus but usually spared the hippocampus in typical ALS – Dementia (ALS-D) cases [23]. Histological modifications included neuronal loss and gliosis with sponginess in layers II and III of frontotemporal cortices with main involvement of the limbic system including the anterior cingulated gyrus, anterior temporal and insular lobes, subiculum and amygdale in typical cases [23].

Symptoms

The symptoms of MND is includes the following: dysphagia, bulbar features dysarthria, excessive salivation and tongue fasciculations, muscle wasting, limb or muscle features focal weakness, foot drop, muscle twitching, cramps, sensory impairment and muscle stiffness; respiratory features orthopnea, rapidity of breath on exertion, sleep difficulties, early morning headache and fatigue or tiredness, depression, cognitive features behavioral change, emotional lability, hallucinations and misperception as well as desire for food loss and family history of MND as supporting issues. Moreover, there is potential symptoms such as dry mouth, ataxia, weight loss, bulk of legs and difficulty ascending stairs, which were identified through literature searches [24–26].

Diagnosis

This disease is commonly diagnosed late due to its disingenuous and heterogeneous presentation. Many patients access multiple health professionals and undergo investigations prior to a neurologist’s assessment [27]. The main role of MRI is to except mimics, and while brain and/ or spinal MRI is not always essential, it should be accomplished wherever a plausible other neuroanatomical explanation is present [28]. This is often the case in early-stage or focal disease, and in practice, many patients do undergo MRI. However, standard MRI sequences in MND may also reveal abnormalities along the corticospinal tracts or motor cortex (MBS), that support diagnostic suspicion. The MBS has been described in the amyotrophic lateral

sclerosis (ALS) and primary lateralizing sclerosis alternatives of MND. It results from an extra iron within the microglia of the primary motor cortex, which causes misrepresentation of the local magnetic field [29]. It is typically seen bilaterally and is best esteemed on axial SWI and gradient echo (GRE) sequences [30].

Treatment

Riluzole (2-amino-6-(trifluoromethoxy) benzothiazole, RP 54274) is the only drug licensed to treat MND, it is suggested that riluzole provides a 9% gain in the chance of surviving one year and adds approximately 2 months to patient survival [8].

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