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CORRELATION BETWEEN BRAIN MAGNETIC RESONANCE IMAGING CHANGES AND CLINICAL PROGRESSION OF AMYOTROPHIC LATERAL SCLEROSIS

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Abstract

Amyotrophic lateral sclerosis is a progressive neurodegenerative disease, with clinical symptoms and signs of central and peripheral motor neuron damage.

To find a correlation between brain changes verified by magnetic nuclear resonance with the degree of progression of the neurodegenerative disease.

A total of 15 patients were included in the study, who underwent a clinical and neurological examination; electromyography, neuroimaging studies (MR of the brain and spinal cord), examination of a panel of paraneoplastic antibodies in order to exclude a paraneoplastic etiology of the disease, and lumbar puncture with cytochemical analysis and electrophoresis of the cerebrospinal fluid.

Signal changes of the corticospinal tracts were seen in two patients, in whom the clinical picture was dominated by bulbar symptomatology.

Brain parenchyma changes recorded by the magnetic nuclear resonance are not a specific indicator of disease progression.

Keywords: amyotrophic lateral sclerosis, magnetic resonance imaging

Introduction

Amyotrophic lateral sclerosis (ALS) is a progressive, neurodegenerative disease based on the progressive degeneration of motor neurons in the brain, the brainstem and the spinal cord. Clinically, the disease presents with symptoms and signs of damage to both upper and lower motor neurons. Signs of a lesion of the upper motor neuron (UMN) are: spasticity, tendon hyperreflexia, dysarthria and dysphagia, while signs of damage to the lower motor neuron (LMN) are muscle atrophy (skeletal muscles and tongue), fasciculations, muscle cramps, dysphagia, dyspnea.

As the disease progresses, so do the symptoms, and the patients who have bulbar symptoms often develop emotional incontinence, that is, pseudobulbar affect. [1]

Most of the patients have the so-called spinal form of ALS, which is manifested by weakness of the limbs, while in 1/3 of the cases the onset is with predominantly bulbar symptoms - bulbar form of ALS. In a small percentage of cases, the so-called non-motor symptoms of the type of cognitive disorders (so-called behavioral variant of frontotemporal dementia) can develop.

The onset of symptomatology is usually between 55 and 75 years of age, with men being more often affected (ratio men : women = 1.3 : 1). Meanwhile, the average age of onset of the disease in men is around 55 years old, while in women it is 60 years old. People in whom the disease occurs under the age of 55 have a longer life expectancy, that is, the disease has a slower progression. [2]

The annual incidence of amyotrophic lateral sclerosis ranges from 0.6-1.8, while the prevalence is 4-6 cases per 100,000 inhabitants.

In terms of etiology, 90% of the ALS cases occur sporadically. The exact cause is unknown, but it is thought to be a disorder of protein metabolism, excessive stimulation of neurons (excitotoxicity), oxidative stress, neuroinflammation and dysfunction of the mitochondrial system. The age and the family history are known risk factors.

In 10% of the cases, there is a familial occurrence, thus about 25 genes associated with the disease are known. The inheritance pattern is autosomal dominant, but there are also cases of autosomal recessive as well as X-linked inheritance. In the most cases of familial ALS, a mutation of the C9ORF72 gene has been found, which also causes frontotemporal dementia. The second most common is mutation of the gene for the SOD1 gene, while the mutations of TARDBP and The FUS gene are not that common.

Depending on the clinical presentation, there are several subtypes of ALS. In 85% of the cases, the clinical picture is dominated by symptoms and signs of lesions of the UMN and LMN, that is, amyotrophy, muscle weakness and signs of degeneration of the corticospinal tracts in the lateral columns of the spinal cord.

Less common are the cases where there are signs of damage only to the lower motor neuron, with muscle weakness and atrophy, the so-called Progressive muscle atrophy. If the clinical picture is dominated by symptoms and signs of damage to the bulbar region (the muscles of the tongue, pharynx, larynx, mimic muscles), in that case it is progressive bulbar paralysis. In a small number of patients, the clinical picture shows symptoms and signs of damage to the corticospinal pathways, and that form of ALS is called Primary Lateral Sclerosis. [3]

Diagnosis

The diagnosis of amyotrophic lateral sclerosis is mostly clinical. Several diagnostic criteria are used in the practice.

The most commonly used criteria for diagnosis are the El Escorial criteria published in 1994 and which are based on the presence of: lower motor neuron degeneration (clinical, electrophysiological and neuropathological); upper motor neuron degeneration (clinical) and progressive worsening of symptoms and signs in one or more body regions. [4]

The clinical diagnosis, without pathological confirmation, distinguishes several types of ALS, namely:

- Clinically definite ALS- when there are symptoms and signs of upper and lower motor neuron lesions in three regions,
- Clinically probable - presence of symptoms and signs of an upper and lower motor neuron lesion in at least two regions
- Clinically possible- presence of symptoms and signs of upper and lower motor neuron lesions in at least one region or signs of upper motor neuron lesions in two or more regions or signs of lower motor neuron lesions.
- Clinically suspected ALS - if symptoms and signs of a lower motor neuron lesion are present.

Revised El Escoria criteria incorporating laboratory findings are the 1998 Arlie House criteria; The 2000 Awaji-shima criteria are based on electrophysiological findings. [5]

In patients who have prominent signs of damage to the corticospinal tracts on magnetic nuclear resonance, there may be mild cortical atrophy and changes in the signal of the pyramidal tracts as a result of Wallerian degeneration of the same.

These changes give an increased signal of the corticospinal tracts in T2 pulse and FLAIR sequence of the magnetic nuclear resonance of the brain, especially in the part of the posterior limb of internal capsule, brainstem and spinal cord, but this sign is neither sensitive nor specific for ALS. [6]

Superficial siderosis of the sulcus centralis as a result of intracellular iron accumulation secondary to microglial phagocytosis of degenerated neurons causes hyposignal in that region (motor band sign) [7].

Another indirect MRI sign of fat-suppressed sequences is the so-called bright tongue sign, which is due to fatty conversion of degenerated muscles of the tongue as a result of chronic denervation. [8]

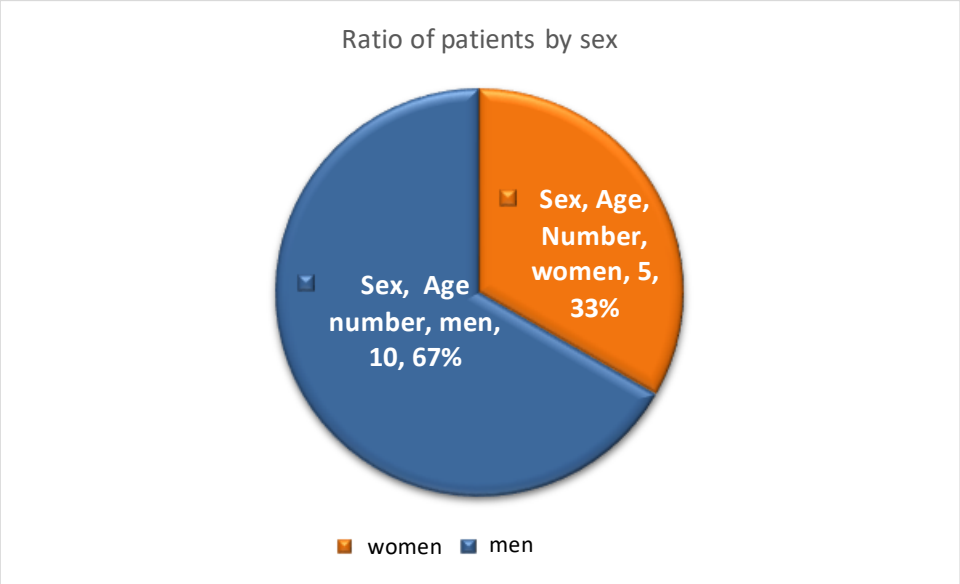
In relation to the course and progression of the disease, three stages are commonly used in the clinical practice to assess the progression.

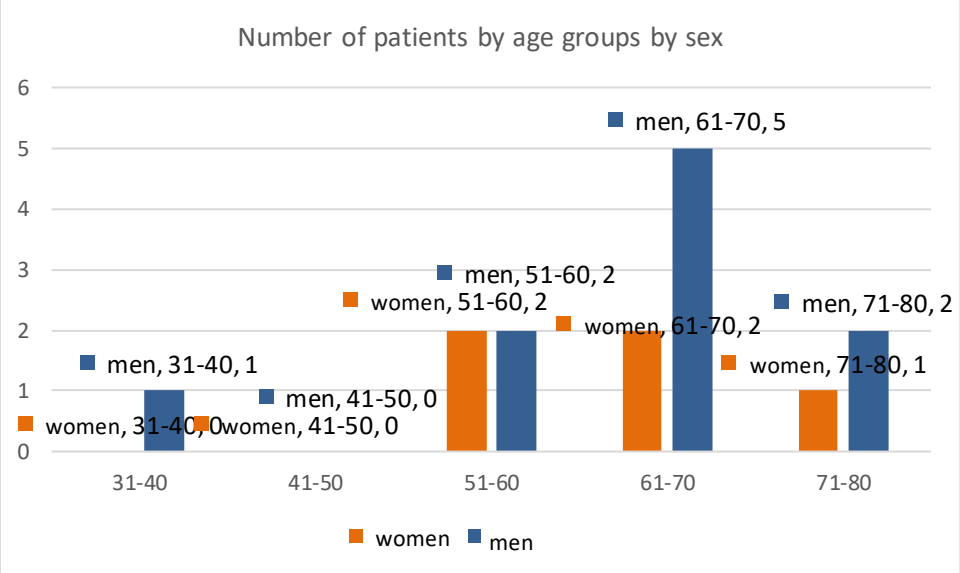
Early stage, where the clinical picture is dominated by muscle weakness (mainly in one region), problems with speech and swallowing, muscle cramps, feeling of muscle stiffness. In the intermediate stage, patients show symptoms and signs of involvement of other body regions. In addition to muscle weakness, they manifest difficulties in breathing, chewing and swallowing, with a loss of body weight, they manifest depression or anxiety.

In the final stage, patients manifest generalized muscle weakness, movement is extremely limited, and due to respiratory muscle weakness, they need non-invasive ventilation, tracheotomy and gastrostomy.

Material and methods

In our research study, 15 patients with a definitive diagnosis of amyotrophic lateral sclerosis were included, out of which 10 were men, 5 were women. The age of the patients was from 35 to 73 years old, and the average age for men was 60.7 years old, while for women it was 64.2 years old.





Regarding family history, none of the patients had a positive family history of diagnosed ALS, in previous or successive family generations.

Regarding the possible occupational exposure to heavy metals or organic/inorganic chemical compounds, three of the patients were occupationally exposed to non-metals or chemical compounds, while in the remaining 12 patients there is no data on exposure to toxins, heavy metals or organic/inorganic compounds.

All participants in our study underwent a clinical and neurological examination, routine blood tests (blood count, glycaemia, degradation products, protein status, liver enzymes, thyroid hormones)

and a panel for paraneoplastic antibodies in order to exclude other causes of amyotrophy or paraneoplastic amyotrophic syndrome.

From the neurological symptoms, the presence of bulbar symptoms (dysarthria and speech impediments, chewing and swallowing difficulties), muscle weakness, muscle cramps, and breathing difficulties were analyzed.

The neurological examination included an examination of the cranial nerves (with reference to the caudal group-mimic muscles, the position of the palatal arches, examination of the palatal and the pharyngeal reflex, the mobility of the tongue; the presence of fibrillations or fasciculations or atrophy of the tongue, examination of motility (gross motor strength , the trophicity, the tone of skeletal muscles, the presence of fasciculations in the skeletal muscles), examination of muscle-tendon reflexes, the presence of pathological reflexes and the mandibular reflex response, examination of the superficial and the deep sensitivity and the sphincter function.

Based on the clinical symptoms, dysarthria was present in 11 patients; dysphagia of solid and liquid food was present in 8 patients. Muscle weakness, presented as brachial diplegia, was present in 2 patients; muscle weakness of the type of monoparesis of the upper or lower limb was present in 4 patients, paraparesis was manifested by 2 patients, while quadriparesis was present in 3 patients. Four of the patients had no motor deficits in the limbs.

Denervation of the tongue, presented with fibrillations or fasciculations, was registered in 11 patients.

gender/age	dysarthria	dysphagia	muscle weakness	atrophies/fasciculations of tongue
m 35 years	+	+	**brachial diplegia**	+
m 58 years	/	/	**left-sided flaccid monoparesis**	/
m 61 years	+	+	**quadriparesis**	+
m 65 years	/	/	**diplegia brachialis/later quadriparesis**	/
m 72 years	/	+	**quadriparesis**	+
f 69 years	+	+	/	+
f 55 years	+	+	/	+
f 73 years	+	/	**paraparesis**	/
f 54 years	+	+	/	+
m 65 years	/	/	**monoparesis of the right upper limb**	/
m 72 years	+	/	**monoparesis of the left lower limb**	+
m 63 years	+	/	**paraparesis**	+
m 55 years	+	/	**quadriparesis pp paraparesis**	+
f 69 years	+	+	**monoparesis of the left lower limb**	+
m 61 years	+	+	/	+

Table 1. Neurological symptoms and signs in patients included in the study

All patients underwent electromyography using the needle technique as well as neurographic examinations. The tested muscles were: m genioglossus, m deltoideus, m biceps brachii, m triceps brachii, m oponenspollicis, m interosseus dorsalis I, m quadriceps femoris, m tibialis ant, m extensor dig brevis and m gastrocnemius.

Electromyographic examination of the paraspinal muscles was not performed in our study. In the neurographic examinations, motor conduction velocities of n medianus, n ulnaris, n peroneus profundus and n tibialis were analyzed. In all subjects, the neurographic examinations, that is, the motor speeds of implementation were normal, so the possibility of a possible form of motor axon peripheral neuropathies was excluded.

The presence or absence of spontaneous denervation activity (fibrillation potentials, positive sharp waves, fasciculations) was recorded in the examined muscles; the specimen type (neuropathic or myopathic), the percentage of polyphasia, and the degree of specimen reduction were analyzed.

gender/age	denervation activity in upper limbs	denervation activity in lower limbs	denervation activity of the tongue
m 35 years	+	+	+
m 58 years	+	+	/
m 61 years	+	+	+
m 65 years	+	+	/
m 72 years	+	+	+
f 69 years	+	/	/
f 55 years	+	/	+
f 73 years	+	+	+
f 54 years	/	+	+
m 65 years	+	+	+
m 72 years	+	+	+
m 63 years	+	+	+
m 55 years	+	+	/
f 69 years	+	+	+
m 61 years	+	+	+

Table 2. Presence of denervation activity in skeletal muscles and tongue muscles registered by electromyography.

MR-verified corticospinal pathway signal changes were present in only two patients . Both patients had bulbar (pseudobulbar) symptomatology with limb weakness and denervation findings in all body regions confirmed by electromyography.

Discussion

Our research study included 15 patients with a clinically definitive diagnosis of amyotrophic lateral sclerosis (according to the El Escorial criteria). All patients underwent a physical and detailed neurological examination, routine biochemical blood tests, lumbar puncture with cytochemical analysis, and cerebrospinal fluid electrophoresis.

Muscle weakness, presented as monoparesis, diparesis, paraparesis or quadriparesis was present in 11 patients, while 4 of them had no motor deficit. Bulbar symptomatology dominated in these patients, presented as dysphagia of solid and/or liquid food, dysarthria, increased mandibular reflex response, atrophy, fibrillations and fasciculations of the tongue.

Regarding the electrophysiological studies, denervation activity of the type of fibrillation potentials, positive sharp waves and fasciculations, registered on the skeletal muscles of the upper limbs

was present in 14 patients; denervation of lower limb muscles was registered in 13 patients, while active denervation of tongue muscles was registered in 4 patients.

As for the magnetic nuclear resonance changes of the enhanced signal type of the corticospinal tracts registered in T2 and FLAIR pulse sequences changes were registered ин only in two patients. In these patients, the clinical picture was dominated by bulbar (pseudobulbar) symptomatology.

Conclusion

Amyotrophic lateral sclerosis is a progressive neurodegenerative disease, which is mainly diagnosed by clinical examination, neuroimaging studies and electrophysiological studies. The assessment of the disease progression is mainly performed clinically and electrophysiologically.

Magnetic nuclear resonance is not a specific indicator of the progression of the disease, considering that the findings of cortical atrophy of the motor cortex as well as changes in the signal of the corticospinal pathways are not specific to this disease.

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