

CASE REPORTS AND DISCUSSION: AMYOTROPHIC LATERAL SCLEROSIS

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CASE NUMBER 1. Mr. M. W., a 41-year old white male was admitted to the Victoria General Hospital with complaints of twitching in the left arm and legs, and weakness of the left hand. Seven to eight years prior to admission, the patient noticed dull muscle pain in his arms and legs, lasting four to five days at a time. The pain worsened as the day passed and was neither aggravated nor relieved by anything the patient did. The remissions lasted up to three months. The patient had no episodes of pain in the three years preceding the onset of the present symptoms

Six months prior to admissions, he noticed weakness in his left hand which gradually worsened. And, two months after the onset of this symptom, he noticed twitching of the muscles of his left arm and right leg, and to a lesser extent, the muscles of the other two limbs. He developed unsteadiness due to weakness in his right leg. On admission, he complained of cramps in his right calf and left hand.

His past, family, and personal histories were non-contributory.

On physical examination, the only abnormalities were neurological. Cerebral and cerebellar functions were normal. No cranial abnormalities were detected. Muscle power was markedly decreased in the left hand and wrist and moderately decreased in the left elbow. There was weakness of the right ankle extensors, right hip flexors, and the right knee flexors. There was noticeable wasting in the thenar and hypothenar eminences and on the dorsum of the left hand. Muscle tone was normal. Reflexes were generally hyperactive, especially those of the left arm, left leg, and right leg. Hoffman's sign was absent. Plantar and abdominal reflexes were normal. Sustained ankle clonus was present bilaterally. Gross fasciculations were present in the legs,

back, upper thoracic muscles, and left arm. There were no sensory abnormalities.

All laboratory investigations, including cerebral spinal fluid, were within normal limits. His hospital course was uneventful and he was discharged with no medications and with a diagnosis of Amyotrophic Lateral Sclerosis.

CASE NUMBER 2. Mr. L. M., a 40-year old white male was seen early in 1964 with a complaint of a dragging of his left leg and foot which had been getting progressively worse during the two months prior to examination. The only abnormalities found on examination were neurological in nature. The cranial nerves were normal. There were no sensory abnormalities about the face, head, or neck. The jaw jerk was increased and he had a mild palmo-mental reflex, more pronounced on the left. Examination of the motor system revealed atrophy of the muscles of the dorsum of both hands. Fasciculations were seen over both shoulder girdles, spreading to the upper thoracic muscles. There was weakness of elbow flexion and shoulder abduction on the left side. Weakness was also noted in the left leg, mainly in the pelvic muscles. Reflexes were greatly increased in the upper and lower extremities and more so on the left side. Hoffman's sign was present bilaterally and plantar responses were normal. Abdominal reflexes were normal. Pronounced clonus was present at the knees and ankles, more marked on the left. There were no sensory abnormalities. His gait was spastic and he dragged the left leg.

A lumbar puncture showed normal pressure and the C.S.F. was normal.

X-ray examination of the cervical spine revealed no evidence of an expanding or destructive lesion. There was slight disc degeneration at C6, C7, and there were bilateral short cervical ribs. A pantopaque myelogram was negative.

One month after the initial visit, sucking

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and pouting responses were present. No fasciculation or atrophy of the tongue were present at this time.

In the following year the patient was admitted to the Montreal Neurological Institute on two occasions, and the diagnosis of motor neuron disease was confirmed. Worsening of symptoms was seen in the six month interval between admissions to the Montreal Neurological Institute. On his second admission, the patient was started on a course of therapy consisting of A.C.T.H., Valium, and physiotherapy. Over the next two years, the patient's condition deteriorated steadily with progressive involvement of bulbar nerves.

Due to increasing difficulty in swallowing, the patient was admitted to the Victoria General Hospital in the summer of 1967. At this time, the patient was aphonic with marked dysphagia and regurgitation. He was conscious, mentally alert, and emotionally calm. He was able only to move his head. He was unable to blow out his cheeks or whistle but was able to smile. His tongue was markedly wasted and could not be protruded. Generalized muscle fasciculations and atrophy were present, with nearly complete paralysis of all muscle groups. Sensory examination showed no abnormalities. Only the biceps reflex was present in the arms, the patellar and ankle reflexes were normal and decreased respectively. The plantar responses were normal. Hoffman's sign was absent. Abdominal reflexes were absent.

A gastrostomy was performed after much consideration. Post operatively, he developed severe respiratory complications and gastric hemorrhage. He expired suddenly nine days after the surgery. There was no post mortem examination.

A discussion of Amyotrophic Lateral Sclerosis must include comments about nuclear Amyotrophies in general. The nuclear Amyotrophies include progressive Spinal Muscular Atrophy, Amyotrophic Lateral Sclerosis, and progressive Bulbar Paralysis. All these degenerative conditions have similar pathological substrates and are probably variants of the same process. They involve different areas of the nervous system and transitions between one group and another are quite common. Consequently, rigid separation of these entities cannot be maintained too strongly. These conditions are characterized mainly by disease of the anterior horn

cells of the brain stem nuclei with resulting symptoms of weakness, paralysis, atrophy, fasciculations, and reaction to degeneration in the muscles supplied by the nerves involved. In primary Spinal Muscular Atrophy, the site of involvement is almost exclusively the anterior horn cells of the spinal cord. On the other hand, the site may be only in the nuclei of the brain stem as in progressive Bulbar Paralysis. In Amyotrophic Lateral Sclerosis, the involved area includes the pyramidal tracts and the anterior horn cells, both in the spinal cord, and the corticobulbar fibers and motor nuclei of the brain stem. Another entity which should be included with the nuclear Amyotrophies is Primary Lateral Sclerosis which is characterized only by pyramidal tract disease that may persist for years before the appearance of anterior horn involvement.

Amyotrophic Lateral Sclerosis is regarded as the paradigm of the nuclear Amyotrophies, all other forms being regarded as variants of the disease.

ETIOLOGY: The disease affects males more than females and usually appears in the forty to fifty age group. The incidence is 1 per 150,000.

The exact cause is not known. Such factors as exertion and alcohol, lead or arsenic intoxication have been implicated. Previous infections such as syphilis and endemic encephalitis may play a part. In some cases, the onset of the disease is closely associated with trauma; but it is doubtful that this is ever the exciting cause. Most authorities agree that the disease is non-familial and non-hereditary, but some recent evidence suggests that heredity may account for a significant number of cases. Other recent evidence suggests that the disorder may be due to "slow virus" infection. Familial incidence has been found among the Chamorro natives on Guam and in other parts of the world, in at least twelve other nationalities. There are rare incidences where the disease occurs in families, especially the Bulbar type.

PATHOLOGY: Amyotrophic Lateral Sclerosis is a systemic disease affecting the corticospinal system from cortex to periphery and the anterior horn cells of the spinal cord. The Betz cells of the cortex are often involved to varying degrees. Degeneration of the pyramidal tract may be found only in the spinal cord or in the cord and brain stem, or

may be followed from the motor cortex throughout the length of the pyramidal tract. Degeneration of the brain stem nuclei involve especially the hypoglossal, vagus, facial, and trigeminal. The oculomotor nuclei are very rarely involved. Changes in the anterior horn cells, similar to those of progressive Spinal Muscle Atrophy, particularly affect the cervical cord. The large nerve fibers of the anterior roots and the large fibers of the pyramidal tracts in the spinal cord are particularly affected. Other fiber tracts may be affected; such as the cortical association tracts, the posterior longitudinal bundle, and the rubrospinal tract. Myelin and axis cylinder loss may occur.

SYMPTOMS: The symptoms develop gradually and are usually slow to be recognized. The earliest and most common symptom is muscle cramps preceding those of weakness and awkwardness of the hands and arms. In some cases, the presenting complaint may be weakness of the legs. In others, the presenting complaint may be difficulty in swallowing and with articulation or hoarseness indicating Bulbar involvement.

Classically, atrophy of the hand muscles develops first, usually bilaterally; but it may be unilateral. The small muscles of the hand, those of the thenar and hypothenar eminences, the interossei, and the lumbricals are initially affected, followed by atrophy of the arm and shoulder girdle muscles. In rare cases, the atrophy may begin in the lower limbs. Fasciculations are commonly present and are usually related to the extent and duration of disease. They may be localized and obvious or few and diffuse. They bear no relationship to the degree of atrophy or weakness, but are more pronounced the more severe the degree of illness. They may disappear when there is diffuse muscle atrophy. Despite the extensive skeletal muscle involvement, the sphincter control remains intact.

The arm and leg reflexes are overactive and ankle clonus may be present. Babinski's sign is usually present, but this is not constant. Abdominal reflexes may be normal, decreased, or absent. These changes are usually the first manifestations of pyramidal tract involvement.

Sensory changes are not found in the typical case; however, subjective sensory phenomena occur and are not infrequent. These include paresthesiae, cramp-like sen-

sations due to muscle spasticity, dull muscle aches, and feelings of numbness and coldness. Objective sensory changes are rare but have been recorded. These include central sensory disturbances of pain and temperature and loss of vibration sense and proprioception. Optic atrophy may occur.

Mental symptoms such as memory loss, difficulties in concentration and attention, and psychoses may be present. The mental picture is not uniform. The relationship of these mental changes to the disease is questionable.

Bulbar symptoms characterized by difficulties in phonation, swallowing, and chewing are prominent and occur as first evidence of the disease in twenty-five to thirty-five per cent of cases. All patients die as a result of Bulbar involvement.

The symptoms in all cases of Amyotrophic Lateral Sclerosis are a combination of atrophy, weakness, fasciculations, and pyramidal tract involvement. The nature and degree varying from patient to patient. Firstly, there is great variation in the intensity of involvement of the process; being more marked at times in the medulla, others in the cord, and still others in both. Secondly, there is wide variability in the involvement of the specific structures within the affected areas. The picture may be dominated by either anterior horn cell disease or pyramidal tract disease; or both of these may be of equal severity. In some cases, there may only be time for pyramidal tract involvement.

For the sake of clarity in clinical diagnosis the principal categories of Amyotrophic Lateral Sclerosis include:

1. The classical form characterized by atrophy of the hand and arm muscles, accompanied by or followed later by spastic weakness of the legs and bulbar symptoms. Atypical forms include the monoplegic type, or the hemiplegic type; types with involvement of shoulder girdles; cases with involvement first of the legs, thighs, or pelvic girdle. Eventually the atypical forms develop into the classical forms.

2. Bulbar type, with predominant involvement of the brain stem. This may be due to corticobulbar disease giving rise to a spastic small tongue, causing trouble with speech, and swallowing and characterized by increased jaw jerk, pathological mouth reflexes and emotional incontinence - the so called

"pseudo-bulbar palsy" picture. Only the brain stem nuclei may be involved leading to true bulbar palsy with weakness and atrophy and fasciculations of the tongue and characterized by difficulty in speech and swallowing. There may be a mixture of both bulbar forms.

3. Incomplete type, including cases of lateral sclerosis with or without fasciculations.

DIAGNOSIS: The diagnosis of Amyotrophic Lateral Sclerosis offers few difficulties in a well developed case. The clinical manifestations are not always uniform or stereotyped. Despite the varieties of the disease there is usually enough in the entire clinical picture to establish a clinical diagnosis with certainty.

Electromyography is an aid to diagnosis and may reveal fasciculations and fibrillations in involved muscles, reduction in the number and increase in size of motor unit potentials with normal motor conduction rates.

In the diagnosis, great care must be taken to differentiate this disease from Amyotrophic syndromes, which can resemble it. Generally there are two features which arouse suspicion that another amyotrophic syndrome is present. Firstly, the presence of root pain particularly in the shoulders and arms. For the most part Amyotrophic Lateral Sclerosis is a painless disease. Secondly, the presence of segmental atrophy and fasciculations confined to the shoulder and arm regions. Amyotrophic Lateral Sclerosis is usually a diffuse process except in the bulbar form. The atrophy and fasciculations are diffuse and not segmental.

The Amyotrophic Syndrome may be caused by a number of conditions.

1. **Cervical cord tumor.** This may simulate the disease but here sensory changes are present and pain is a common feature. In instances of cervical tumor, radiological examination may reveal erosion of the vertebrae; there may be evidence of subarachnoid block; spinal fluid protein may be increased; and the progression will be slower than that of Amyotrophic Lateral Sclerosis.

2. **Centrally herniated cervical disc.** This may mimic Amyotrophic Lateral Sclerosis very closely, since pain may not be present. This condition may be suspected if there is evidence of cervical disc degeneration and it can be established by myelogram

studies.

3. **Syphilitic meningomyelitis.** This condition is now rare, but may also simulate the condition closely. It occurs at an earlier age, is associated frequently with pain, and with positive serological reactions of spinal fluid.

4. **Syringomyelia.** This causes segmental atrophy and there are sensory changes which are not present in Amyotrophic Lateral Sclerosis.

Other conditions which may cause weakness and atrophy of the hand and arm muscles and thus be confused with Amyotrophic Lateral Sclerosis must also be considered; such as:

(a) **Median thenar neuritis** (carpal tunnel syndrome) which occurs most often in females, is usually unilateral, and the atrophy is confined to the thenar eminence with no fasciculations, and there are sensory disturbances in the distributions of the median nerve.

(b) **Ulnar neuropathy**, with weakness and atrophy of small hand muscles innervated by the ulnar nerve, but with sensory changes confined to the distribution of this nerve. Ulnar neuropathy may be bilateral.

(c) **Cervical rib and scalenus anticus syndrome** may cause atrophy of muscles of the hand and arm, may be bilateral and symmetrical. Important factors in differentiation here are pain, coldness in the affected areas, changes in the pulses, and radiological evidence of the presence of a cervical rib. Muscle atrophy is much less prominent than pain in these conditions.

Hyperthyroidism shares some features of Amyotrophic Lateral Sclerosis, such as wasting, muscle twitching, and hyperreflexia; but it is usually easily differentiated by other clinical signs and biochemical tests.

Syndromes resembling Amyotrophic Lateral Sclerosis have been reported in chronic mercurial poisoning, in triorthocresyl phosphate poisoning, and following both gastrectomy and polyarthritis, and finally as a non-metastatic manifestation of malignancy.

PROGNOSIS: The disease is steadily progressive and usually fatal in one to six years. The prognosis becomes more grave as the clinical picture becomes more complete. Benign forms, with a long life, are also reported. The degree of muscle fasciculation is a good indication of an advancement of the disease. Bulbar forms are more rapidly fatal than others. Death is due to bulbar paralysis with

respiratory failure or pneumonia. Intelligence and awareness are typically preserved to the end.

TREATMENT: There is no specific treatment for the disease. With Bulbar involvement a stomach tube may be necessary in order to feed the patient. Physiotherapy in the form of massage may help to keep the patient comfortable. Drugs are of no benefit. ACTH and Cortisone have been used with no success.

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