Case Report

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Burden of Motor Neuron Diseases in a Tertiary Care Center of Eastern Nepal: A Case Series with Literature Review

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Abstract

A Motor Neuron Disease (MND) is a collective term for progressive neurological disorders that affect primary motor neurons. The primary aim of our study was to explore the spectrum of MNDs, their sex distribution, the prevalence of different subtypes, diagnostic modalities, and interventional strategies to alter the natural course of the disease. This study was conducted from May 2020 to July 2023, over a period of three years, at our tertiary care center. During this time, we identified a total of five cases of Amyotrophic Lateral Sclerosis (ALS), four cases of Progressive Bulbar Palsy (PBP), and one case of Progressive Muscular Atrophy (PMA). The typical age of presentation was over 40 years, with one exception being an 18 years old male. There was a slight female predominance in terms of sex distribution. Regarding treatment, Riluzole remained the mainstay, though the treatment outcomes were not particularly favorable.

Keywords: Epidemiology; Motor neuron diseases; Nepal

Declarations

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INTRODUCTION

The Global Burden of Disease Study 2016 (GBD 2016) reported that the global incidence of motor neuron disease was 2.3 per 100,000 people and the prevalence was 5.9 per 100,000 people in 2016 [1]. Motor neuron diseases include amyotrophic lateral sclerosis, spinal muscular atrophy, hereditary spastic paraplegia, primary lateral sclerosis, progressive muscular atrophy, and pseudobulbar palsy. Amyotrophic Lateral Sclerosis (ALS), the most common motor neuron disease, is clinically characterized by extensive paralysis leading to death generally by respiratory failure, with 50% of patients dying within 15–20 months after diagnosis [2]. Pathophysiology of ALS involves complex interplay between genetic and environmental factors which is not well understood, making the management approach a constantly evolving topic in neurology. Currently, there is no cure for these diseases [3].

Here, we report a few cases of these rare disorders.

CASE REPORT

CASE 1

A 62-year-old female, came up with weakness of right hand for nine months that worsened over time involving forearm. Within three months of the symptoms, she also started experiencing weakness of left hand, which was insidious in onset and gradually progressive. There was decreased bulk of muscle in both hands severe enough to impair her daily activities like dressing, eating and so on. There was no issue with her lower limb. History of pain, fever, head and neck trauma, difficulty chewing or swallowing, difficulty walking, headache, restricted neck movement and vomiting were negative. Higher mental function was grossly intact. on motor examination, there was bilateral decrease in bulk of muscle in upper arm with normal tone. Tone and bulk of muscle was normal in lower limb. Neck flexion was 4/5, power in right hand and elbow was 2/5 and in left elbow was 1/5 whereas in left hand was 2/5, dorsiflexion in right and left limb was 4/5.Power in foot and knee of right and left side was 4/5. Deep tendon reflex was 1+ in right and left bicep brachii, 2+ in right and left triceps, 2+ in right knee and 3+ in left knee, 1+ in right and left ankle and plantar reflex was mute. Co-ordination and gait was normal and Romberg's test was negative. Sensory examination findings were not very significant.

Non-contrast Magnetic Resonance Imaging (MRI) of cervical spine was performed which revealed global disc protrusion at multiple levels, C 4-5, C 5-6 and C 6-7 with mild spinal canal stenosis along with degenerative changes. Because of rapidly progressing bilateral upper limb weakness and distal extremities wasting, Motor Neuron Disease, most probably Amyotrophic lateral sclerosis (ALS) was suspected and advised for Electromyography (EMG).

After confirmation of the diagnosis, twice daily oral dosing of triluzole 50mg was prescribed and patient was advised to follow-up after two months, as needed. On, follow-up, she has noticed some degree of improvement in her symptoms and is able to give continuity to her daily routine activities with minimal difficulty. She is currently on same medication since past six months and doing well with it.

CASE 2

A 70-year-old female visited with history of right lower limb weakness gradually progressive over six years which was followed by right upper limb weakness developed within two years. The weakness, to start with, though mild, it eventually worsened to a state where she could not continue her daily routine activities. There was no history of pain, fever, head and neck trauma, difficulty chewing or swallowing, difficulty walking, headache, neck rigidity and vomiting. Patient, further, complaints of insomnia. On focused clinical examination, there was progressive right sided hemiparesis with spasticity and hyperreflexia in all limbs. Based on the clinical presentation of the disease. Motor Neuron Diseases most probably slow variant type of ALS was suspected. Because of age factor of the patient, to rule out any space occupying intracranial mass MRI in axial, coronal and sagittal T1 and T2, FLAIR and DWI weighted scans of the brain on 0.3T was performed but findings were normal. Ultrasonography (USG) abdomen revealed fatty liver and atrophied uterus. Bilateral Carotid Doppler study was done which revealed non-obstructing calcified plaque at left carotid bulb measuring 2.6 mm along with calcified plaque at right External Carotid artery measuring about 3.1 mm. Grade I diastolic dysfunction with normal ejection fraction (LVEF:60%) was noted on echocardiographic examination. Hemoglobin level was 12.1 g/dL, glycosylated hemoglobin (HbA 1 C) was 4.7%. Thyroid function test, complete blood count and electrocardiographic findings were within normal limits. Electromyography was advised.

With the confirmation of diagnosis, twice daily oral dosing of tab. riluzole 50mg, along with clonazepam 0.5mg once daily at bed time were given. On, follow-up, proxy visit was made by her son, who reported mild improvement in symptoms Continuation of existing treatment was

advised.

CASE 3

A 55-year-old female came up with rapidly progressing weakness of both arms since six months. It gradually progressed to weakness of hip, thigh and neck with decreased muscle bulk in both arms. There was swallowing and walking difficulty and patient was not able to carry out her daily routine activities. There was no history of pain, fever, head and neck trauma, difficulty chewing or swallowing, difficulty walking, headache, neck rigidity and vomiting. On examination, there was rapidly progressing weakness of all limbs more pronounced at proximal part of upper limb. There was associated wasting of muscles, hyperreflexia and dysphagia.

Motor Neuron Disease most likely ALS was suspected which was confirmed with EMG and Nerve conduction study.

Following the confirmation of diagnosis, twice daily oral dosing of tab. riluzole 50mg was given and patient was called to follow-up after three months. After two months, proxy visit was done by her son who reported that weakness had worsened to a state where patient was unable to even swallow.. The drug was continued and patient was consulted to gastro surgeon for Percutaneous Endoscopic Gastrostomy (PEG), as a part of palliative care. With the best of our effort and resources we used, patient deceased after one month because of respiratory failure.

CASE 4

A 80-year-old male presented to us with chief complaints of progressive difficulty in swallowing and change in voice for past one year. There was no history of pain, fever, head and neck trauma, headache, neck rigidity and vomiting. Past history is significant for COVID-19 and hypothyroidism. Also, there is history of surgery for peptic ulcer disease 30 years back.

Plain MRI brain was performed which revealed age related mild diffuse cerebellar and cerebral atrophy. Based on the clinical presentation of the disease, diagnosis of motor neuron disease most likely Progressive Bulbar Palsy (PBP) was made.

Twice daily dosing of riluzole 50mg was given and patient was called for follow-up after three months. On follow-up visit, there was progressive dysarthria and dysphagia along with cognitive decline, most likely progressive bulbar palsy with dementia. Riluzole was continued and clonazepam 0.25 mg along with Nortriptyline 50 mg, to be taken at bed time were added.

CASE 5

A 55-year-old female presented with progressive weakness of upper and lower limb for nine months and swelling of leg for four days. On detailed inquiry, she gave history of progressive weakness of limbs affecting right lower limb at first followed by right upper limb, left lower limb and left upper limb associated with difficulty in walking. She also gave difficulty in swallowing occasionally. She did not have recent head, neck or back trauma, abnormal body movement, loss of consciousness or alteration of bowel and bladder habit. On general examination, there was bilateral pitting edema over legs. There was no pallor, icterus, cyanosis, clubbing, lymphadenopathy and hydration status was normal. Vitals were within normal limit. On Glasgow, scale assessment, the patient revealed spontaneous eye opening, followed command and was oriented with verbal speech. No apparent signs of meningeal irritation and no gross deficit of higher mental function were observed. Cranial nerve examination findings were within normal limits. On motor examination, there was normal tone of muscles and power was 4/5 in all four limbs. There was hyperreflexia in right and left upper arms while deep tendon reflexes could not be elicited in lower limbs due to edema. No sensory deficit was seen, cerebellar and gait assessment was normal. Other systemic examinations were within normal limit.

Laboratory examinations were significant for raised thyroid stimulating hormone (26 mIU/mL), hypoalbuminemia (1.7g/dL). Grade I diastolic dysfunction with normal ejection fraction (LVeF:60%) was noted on echocardiography. Glycosylated hemoglobin level, renal function test and carotid Doppler study were within normal limit.

A diagnosis of motor neuron disease with hypothyroidism and hypoalbuminemia was made. Twice daily dosing of riluzole 50 mg and thyronorm 25 mcg once daily on empty stomach was advised. Physiotherapy and high protein diet was recommended.

CASE 6

A 62-year-old male was referred to us from Ear Nose and Throat (ENT) outpatient department for progressive difficulty is swallowing and speech since last month. There was no history of pain, fever, headache and neck trauma. Additionally, there was negative history for difficulty in walking, headache, neck rigidity and vomiting. controlled with insulin. There is history of recently treated left sided chronic otitis media. On examination, gag reflex was absent. There was presence of tongue fasciculation with absent jaw jerk. A case of motor neuron disease most likely

progressive bulbar palsy was suspected.

MRI brain with venogram reveals microvascular ischemic changes (Fazekas II), age related parenchymal volume loss and prominent perivascular space was seen. Upper GI Endoscopy findings were normal. Left sided true vocal cord palsy was observed with Laryngoscopy.

Twice daily dosing of riluzole 50mg was given and patient was called for follow-up after three months. Unfortunately, patient never returned back.

CASE 7

A 48-year-old male presented to us with progressive difficulty in swallowing along with nasal regurgitation over four months. There was no history of pain, fever, head and neck trauma, difficulty walking, headache, restricted neck movements and vomiting.

Higher mental function was grossly intact. Cranial nerve examination was normal except for absent gag reflex. No abnormality was detected on both motor and sensory examination as well as on cerebellar and gait assessment. Having excluded local organic cause of dysphagia with the help of upper GI endoscopy, we reached a final diagnosis of motor neuron disorder, possibly progressive bulbar palsy.

Patient was advised 50mg of Riluzole, twice a day and a follow up visit at three months was recommended. Upon follow up, the patients condition had deteriorated. We continued with the same medication and sought a gastroenterology opinion for palliative care inorder to improve the patients quality of life.

CASE 8

A 66-year-old female came up with chief complaint of weakness of right upper limb along with dysphagia for three months. Patient has history of left cerebellar hemorrhage, right basal ganglia hemorrhage and subsequent left sided hemiparesis eight years back. Patient is a known case of hypertension. There was no history of pain, fever, head and neck trauma, difficulty chewing or swallowing, difficulty walking, headache, neck rigidity and vomiting. She had been a heavy smoker smoking about 15 sticks per day for 30 years corresponding to a pack year of 22.5, which she quit 10 years back. On examination of right upper limb, weakness and distal wasting with associated hyperreflexia was found.

MRI brain revealed multiple confluent discrete T2/FLAIR high signals in bilateral periventricular white matter and centrum semiovale without restriction suggestive of chronic ischemic changes (Fazekas grade II). Age related cerebral atrophy, right maxillary sinusitis and concha bullosa was also revealed. MRI Cervical spine showed global disc bulge at multiple level.

A diagnosis of motor neuron disease, ALS type, was made. Patient was advised twice daily dose of 50mg of Riluzole. At three months, patients son reported major improvement in other complaints except for dysphagia, which had worsened. Same medication was continued and gastrosurgery consultation was sought for percutaneous endoscopic gastrostomy (PEG) in order to manage worsening dysphagia.

CASE 9

A 18-year-old male was referred for weakness of right hand since nine months. It began with mild weakness and had progressively worsened with decreased muscle bulk to the degree that it started impairing his daily activities. There was no history of pain, fever, trauma to head and neck, difficulty in chewing, swallowing and walking. Neck rigidity, vomiting and headache were also negative. No neurological deficit was noted on neurological examination.Higher mental function was grossly intact. There was decreased muscle bulk in right arm and forearm and normal in left arm and lower limb. Power was 4/5 in forearm and 3/5 in hand and normal (5/5) elsewhere. Deep tendon reflexes were elicited normally in both upper and lower limbs. Sensory examination, co-ordination and gait assessment and cerebellar examination were normal.

MRI right brachial plexus revealed normal findings. MRI cervical spine showed disc bulge at multiple level with mild spinal canal stenosis.

A diagnosis of motor neuron disease most probably progressive muscular atrophy was made. Cap. pregabalin 75mg one tablet at bed time for six weeks was given. Together with it, physiotherapy was advised and patient was called for follow-up.

CASE 10

A 50 years old female presented with progressive weakness of bilateral upper limb over one and half month. She further gave history of loss of muscles bulk in hands and progressive dysphagia, since then. Symptoms were more pronounced in right upper limb and were predominantly motor deficit. There was no issue with her lower limb. Personal history is significant for being an alcoholic, consuming alcohol regularly five to ten units per day since past 12 years. There was no history of pain, fever, head and neck trauma, difficulty chewing or swallowing, difficulty walking, headache, neck rigidity and vomiting.

MRI Cervical spine was performed but did not reveal any

significant findings. Gastroenterology consultation was done and subsequently Upper GI Endoscopy revealed multiple antral ulcers which was treated with triple therapy. Alcohol induced peripheral neuropathy with bulbar palsy of paraneoplastic origin was suspected and confirmed with Nerve Conduction Velocity (NCV) and Electromyography.

Pregabalin 75mg oral capsule, at night time for six weeks, along with 100mg oral thiamine twice daily was prescribed. Patient was advised to quit alcohol. Exercise and physiotherapy was recommended and follow up at two months was advised. On follow-up after two months, patient had stopped consuming alcohol; however, there was worsening of motor palsy involving both upper limbs. Speech had become nasal and unclear. Dysphagia has also worsened and patient complained of regurgitation. On Examination gag reflex was absent. While existing medications continued, gastroenterology and gastro surgery consultations were sought for palliative procedures to improve the patient's quality of life.

DISCUSSION

Motor neuron disease, is a rare neurodegenerative disease, which can affect motor neurons of both upper and lower extremities [4]. Within three years of observation at our tertiary care center, we found total of ten cases of motor neuron diseases. Amyotrophic lateral sclerosis was the commonest one followed by progressive bulbar palsy and we also reported one case of progressive muscular atrophy. The experience gathered from our case series suggests that the age group mostly affected by the disease was after 40 years of age, though we did have a single case in an 18 year old child.

Pathophysiology of MND involves both genetic and environmental factors, hence, definitive cure for the diseases lie in understanding the molecular genomics and treating accordingly [5]. SOD1, TARDBP, OPTN, TBK1 and NEK1 are the genes commonly associated with the diseases [6]. However, neither was genomic profiling feasible in our setting, nor did we have facility for targeted gene therapy. Nerve conduction velocity assessment with Electromyography remains the mainstay of diagnostic modalities for the motor neuron diseases.

Regarding the treatment stratergy, riluzole remains the only medication with demonstrated efficacy and regulatory approval for treatment of MND, mainly ALS. We used the same drug in our center, as well. Riluzole is based on the concept of excitotoxicity and it blocks the release of glutamic acid along with inhibiting post-synaptic effect of glutamate by blocking N-methyl-D aspartate (NMDA) receptor [7].

Understanding the immunopathogenesis and molecular genomics of the diseases and intervention at molecular level is the only hope for these groups of patients. Trials for genetic interventions like anti-sense RNA codon of SOD-1 gene is going on; however, despite decades of trials and research, MND still remains incurable [8].

CONCLUSION

More than half (6 out of 10) of the patients enrolled in the case series were females. Age of presentation in males was at relatively younger age compared to female. We did come across an unusual case of an 18 years old male patient. The distribution of disease in decreasing order of frequency was amyotrophic lateral sclerosis, progressive bulbar palsy and progressive muscular atrophy.

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