



Spinal and Bulbar Muscular Atrophy: Case Report and Diagnostic Overview

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Abstract

Spinal and bulbar muscle atrophy (SBMA), frequently known as Kennedy disease is an X-linked recessive disease. SBMA is characterized by bulbar and limb muscle weakness, atrophy and fasciculation, along with endocrine abnormalities leading to gynecomastia and infertility. The incidence of SBMA is 1/30,000 male births. It is caused by the repeated expansion of CAG on the X chromosome. The age of presentation depends on the numbers of CAG repeats, with an average of 43 years and the progression of the disease is slow, an estimated 2% decrease in muscle strength per year. Diagnosis of SBMA is made by NCS and needle EMG, which are a standard part of the evaluation of motor neuron disease. SBMA is often confused with other motor neuron disease, and definitive diagnosis is always required. We present a case of a 53-year-old male who presents with leg weakness and was initially treated as lumbar radiculopathy and was later diagnosed as SBMA.

Keywords: Spinal and bulbar muscle atrophy; Kennedy disease; Gynecomastia

Introduction

Spinal and Bulbar Muscle Atrophy (SBMA), frequently known as Kennedy disease, is an X-linked recessive, adult-onset, progressive degenerative disease of the Lower Motor Neuron Disorders (LMND). SBMA characterized by bulbar and limb muscle weakness, atrophy, and fasciculation. The weakness could be symmetrical or asymmetrical, involving proximal and distal muscles. Also, SBMA is associated with endocrine abnormalities due to resistance to androgen, causing defective spermatogenesis leading to gynecomastia and infertility [1].

William Kennedy first defined SBMA as a lower motor neuron and bulbar muscle degenerative disease in 1968. The incidence is 1/30,000 male births [2]. It is caused by the repeated expansion of CAG on the X chromosome. The age of presentation depends on the numbers of CAG repeats, with an average of 43 years but varying from 18 to 64 years. Weakness in the limbs, cramping, and tremors, as well as dysarthria, dysphagia, tongue fasciculation, and nasal speech, are the most prevalent complaints. The progression of the disease is slow, an estimated 2% decrease in muscle strength per year, measured by quantitative muscle testing (QMT) [3]. Therefore, until late disease, these patients have good function and mobility preservation; however, involvement in the gait and hip muscles can limit the patients to a wheelchair. Usually, they have a normal life span until the involvement of bulbar and respiratory muscles, resulting in aspiration [4]. Symptoms such as twitching of the muscle without loss of muscle strength are present in heterozygous females.

Since many of the clinical characteristics of SBMA are comparable to other neurodegenerative diseases such as Amyotrophic Lateral Sclerosis (ALS) and late-onset Tay-Sachs disease, a definitive diagnosis is always required [1]. We present a unique case of a 53-year-old Hispanic patient present in our institute.

Case Presentation

A 53-year-old right-handed Hispanic man with a history of essential tremor presented with a 6-7 month history of progressive weakness and cramps in his lower extremities followed by weakness in the upper extremities. Initially, he noticed difficulty in walking more than a block due to pain and weakness in his legs. Three months later, he developed pain in his lower back, and he realized that he could not lift his arms above his head at work because of weakness. He felt fatigued quickly with physical activity. His older brother reportedly had a similar weakness for some time.

On examination, he was alert and responsive. His neurologic examination showed normal

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Table 1: Sensory Nerve conduction study. **Sensory and Mixed nerve Conduction**

Nerve and Site	Onset Lat ms	Peak Lat ms	Amp μ V	Segment	Dist mm	CV m/s
Median.L to Digit II (Index figure).L						
Wrist	2.1	2.6	8	Wrist-Digit II (Index finger)	130	62
Wrist	2.1	2.5	8	Wrist-Digit II (Index finger)	130	62
Ulnar.L to Digit V (little finger).L						
Wrist	2.2	2.6	2	Digit V (little finger)- Wrist	110	51
Wrist	1.9	2.5	2	Digit V (little finger)- Wrist	110	57
Radial.L to Anatomical snuff box.L						
Forearm	1.3	1.8	19	Anatomical snuff box-Forearm	100	77
Forearm	1.3	1.9	22	Anatomical snuff box-Forearm	100	77
Sural.L to Ankle.L						
Lower leg	2.5	3.2	6	Ankle-Lower leg	140	56
Lower leg	2.7	3.3	6	Ankle-Lower leg	140	52
Median.R to Digit II (Index figure).R						
Wrist	2.1	2.7	7	Wrist-Digit II (Index finger)	130	62
Wrist	2.1	2.7	8	Wrist-Digit II (Index finger)	130	62
Ulnar.R to Digit V (little finger).R						
Wrist	2.2	2.7	3	Digit V (little finger)- Wrist	110	51
Wrist	2.1	2.6	3	Digit V (little finger)- Wrist	110	53
Sural.R to Ankle.R						
Lower leg	2.8	3.2	6	Ankle-Lower leg	140	50
Lower leg	2.8	3.3	6	Ankle-Lower leg	140	50

denotation, but dysarthria was noted. He had bilateral facial weakness, more prominent around the orbicularis oculi, and there were fasciculation and atrophy of the tongue. Other cranial nerves were normal. His motor examination showed wasting of the bilateral triceps, biceps, and deltoid muscles. Fasciculation was noted in the right deltoid, biceps and triceps. The tremor was observed in both hands and chin. Motor strength tested on the Motor Research Council (MRC) scale was as follows: Neck Muscles: Flexion 4/5, Extension 4+/5, Deltoid, Biceps, and Triceps 4/5 bilaterally.

Iliopsoas: Right 4 +/ 5, Left 4- /5 (limited due to the pain), Knee Flexion/ Extension 4 +/5, Foot Dorsi/Plantar Flexion: 4+ /5. Reflexes, Biceps/ Triceps, and Patella were 1+ bilaterally; Ankle Jerks were absent, No Babinski noted. He was able to walk without support. Cerebellar and sensory exam was normal.

Diagnostic workup: MRI of the cervical and lumbar spine was ordered to evaluate possible radiculopathy given the history of back pain with weakness. MRI of the Lumbar Spine reported bilateral L5 pars defects and mild degenerative changes. MRI cervical spine showed mild to moderate degenerative spondylosis of the cervical spine with no significant focal disc herniation. Because of bulbar symptoms and facial weakness, MRI of the brain was also ordered, and it was normal. In addition, comprehensive blood work and Nerve Conduction Study (NCS)/Electromyography (EMG) was performed. Blood work was significant for mildly elevated liver enzymes and CPK. The neuropathy panel was normal, including serum and urine immunoelectrophoresis.

Nerve conduction study (Table 1 and 2):

Sensory Nerve Conduction Studies showed low amplitudes,

normal peak latencies and Conduction Velocities (CVs) in the bilateral median and ulnar nerves; however, normal left radial and bilateral sural sensory responses were noted in the Lower Extremities (LE).

Motor Nerve Conduction Studies in multiple motor nerves in the left upper and lower extremities were normal in distal latencies, amplitudes, and CVs. There was no conduction block noted.

Needle EMG (Table 3) performed in three limbs, and thoracic paraspinal muscles showed widespread active denervation, including fibrillation, positive waves, and fasciculation potentials. In addition, limb muscles showed large Motor Unit Action Potentials (MUAPs) with increase polyphasic units, consistent with chronic re-innervation. MUAPs recruitment was also reduced in multiple muscles.

In Summary, the electrodiagnostic findings showed diffuse active and chronic denervation in multiple muscles of three limbs and in the thoracic paraspinal muscles, suggested Motor Neuron Disease (MND); however, low Sensory Nerve Action Potentials (SNAPs) are not typically seen in MNDs such as Amyotrophic Lateral Sclerosis (ALS) or its variant, Progressive Muscular Atrophy (PMA).

During his visit for electromyography, additional clinical examination showed gynecomastia and testicular atrophy. Clinical findings in conjunction with electrodiagnostic data were consistent with the diagnosis of Kennedy Disease, which was confirmed with gene testing.

Discussion

SBMA is a rare hereditary motor neuron disorder also associated with endocrine abnormalities. Typically bulbar weakness follows the

Table 2: Motor Nerve Conduction Study
Motor Nerve Conduction

Nerve and site	Lat ms	Amp mV	Segment	Dist mm	Lat Diff ms	CV m/s
Median.L to Abductor pollicis brevis (C8-T1).L						
Wrist	3.2	7.5	Abductor pollicis brevis (C8-T1)-Wrist	70	3.2	
Elbow	7	6.8	Wrist-Elbow	230	3.8	61
Axilla	9.3	6.4	Elbow-Axilla	160	2.3	70
Ulnar.L to Abductor digiti minimi m.(C8-T1).L						
Wrist	3.1	9.3	Abductor digiti minimi m.(C8-T1)-Wrist	70	3.1	
Below elbow	6.5	8.7	Wrist-Below elbow	220	3.4	65
Above elbow	8.5	8.1	Below elbow-Above elbow	120	2	60
Peroneal.L to Extensor digitorum brevis (L4-S1).L						
Ankle	3.9	7.1	Extensor digitorum brevis (L4-S1)-Ankle	90	3.9	
Fibula(head)	9.6	7	Ankle-Fibula(head)	280	5.7	49
Popliteal fossa	11.6	6.7	Fibula(head)-Popliteal fossa	100	2	50
Tibial.L to Abductor hallucis (S1-S2).L						
Ankle	3.9	6.4	Abductor hallucis (S1-S2)-Ankle	90	3.9	
Popliteal fossa	10.8	5.1	Ankle-Popliteal fossa	350	6.9	51
Median.R to Abductor pollicis brevis (C8-T1).R						
Wrist	3.1	7.8	Abductor pollicis brevis (C8-T1)-Wrist	70	3.1	
Elbow	7.4	6.5	Wrist-Elbow	230	4.3	53
Axilla	9.5	6.4	Elbow-Axilla	140	2.1	67

limb weakness; however, limb weakness is occasionally the presenting complaint. Involvement of the bulbar musculature may be expressed as difficulty in chewing, swallowing, and speaking [5].

Examination of the cranial nerves usually shows evidence of weakness in the facial, palatal, and tongue muscles. Fasciculations are seen easily in affected muscles. Muscle strength shows a classic pattern of proximal-greater-than-distal weakness, beginning in the legs. However, Ferrante and Wilbourn showed the variation of initial weakness ranging from symmetry to asymmetry, from proximal to distal predominant weakness, and from the upper extremity to lower extremity [6]. Reflexes are variable, ranging from normal to depressed and are usually absent at the ankles. Generally, no upper motor neuron dysfunction occurs in these patients [7]. The sensation is often clinically normal to the modalities of vibration perception, position sense, sharp touch, and light touch, despite the demonstration of abnormalities in electrophysiological studies [8,9].

Gynecomastia is probably the most common non-neurologic finding on examination, but it is not a criterion for diagnosis. Testicular atrophy and erectile dysfunction may be present and typically occur in advanced cases. The study by Alves et al. [10] defined the case of SBMA as tremors in extremities with weakness and fasciculation in limbs, atrophy, and fasciculation of the tongue, like our patient.

Diagnostic Work

Depending on the clinical presentation and positive family history, immediate genetic testing for SBMA may be performed to confirm the diagnosis, eliminating the other tests; however, usually, like in our patient, this is not the case. Our patient was initially evaluated and treated for lumbar radiculopathy and essential tremors. His older brother probably also had SBMA; however, the diagnosis was

never confirmed. In addition, appropriate initial testing is indicated because of associated conditions in these patients, such as diabetes mellitus, lipid disorders, and other endocrine disorders.

Some following differential diagnoses should be considered while performing diagnostic workup or if gene testing is negative.

1. Multilevel cervical spondylosis, if the patient does not show bulbar signs on presentation.
2. Early presentation of ALS without the manifestation of upper motor neuron signs yet.
3. Adult-onset of spinal muscular atrophy.
4. Late-onset Tay-Sachs disease (GM2 gangliosidosis).
5. Motor neuron syndromes with lymphoproliferative disorders: Lymphoma (Hodgkin or non-Hodgkin), multiple myeloma, chronic lymphocytic leukemia, Waldenstrom macroglobulinemia.
6. Motor neuron syndromes in lung, breast, and other cancers can produce an indirect paraneoplastic degeneration of the motor neurons.

The patients with SBMA and ALS usually have high Creatine Kinase (CK) level as it was noted in our patient [11] and high liver enzymes because of the rapid loss of muscle fibers secondary to denervation. Sometimes based on high CK, they are given the wrong diagnosis and treatment, such as inflammatory myopathy.

Electrodiagnostic studies

NCS and needle EMG are a standard part of the evaluation of SBMA and other motor neuron disease. EDX studies are most helpful when clinical findings to support the diagnosis of SBMA are limited.

In general, the electrodiagnostic evaluation includes multiple

**Table 3: Needle EMG.
Needle EMG Examination**

Muscle	Insertion Activity	Spontaneous Activity				Volitional MUAPs					
		Fiba	PSW	Fase	Other	Poly	Amp	Dur	Rate	Pattern	Effort
1 st dorsal interosseous (C7-T1).R	Increased	2+	2+	3+		Few	Incr	Incr	Normal	Min Red	Normal
Biceps brachii (C5-C6).R	Increased	1+	2+	2+	CRD	Few	Incr	Incr	Incr	Min Red	Normal
Triceps brachii (C6-C8).R	Increased	3+	3+	1+		None	Incr	Incr	Normal	Mod Red	Normal
Flexor carpi radialis (C6-C7).	Increased	3+	2+	2+	CRD	Few	SI Incr	SI Incr	Normal	Normal	Normal
Tibialis anterior (L4-L5).R	Increased	2+	3+	2+		Few	SI Incr	SI Incr	Normal	Mod Red	Normal
Gastrocnemius (Medial head) (S1-S2).R	Increased	2+	3+	1+		Few	Incr	Incr	Normal	Normal	Normal
Vastus Lateralis (L2-L4).R	Increased	1+	2+	1+	CRD	Few	Incr	Incr	Incr	Mod Red	Normal
Gluteus medius (L4-S1).R	Increased	2+	3+	0	CRD	Few	Incr	Incr	Incr	Min Red	Normal
T11 paraspinal.R	Increased	2+	2+	0		None	Normal	Normal	Normal	Normal	Normal
1 st dorsal interosseous (C7-T1).L	Increased	0	2+	2+		None	Incr	Incr	Normal	Normal	Normal
Biceps brachii (C5-C6).L	Increased	1+	2+	0	CRD	Few	Incr	Incr	Incr	Mod Red	Normal
Triceps brachii (C6-C8).L	Increased	2+	2+	2+	CRD	Few	Incr	Incr	Incr	Mod Red	Normal

motor and sensory conduction studies in two or three limbs and detail needle EMG of multiple muscles in three or four limbs, thoracic paraspinal region, and/or bulbar region.

Motor nerve conduction study is usually normal; however, loss of motor axons in severely atrophic muscles can cause reduction of the CMAP amplitude, and it may be associated with mild slowing of conduction velocity. Motor conduction block should be absent.

Sensory nerve conduction study is typically normal in MNDs; however, in SBMA, SNAPs are usually lower despite normal sensory examination like in our patient. The literature also supports these findings. Ferrante MA, Wilbourn AJ evaluated 19 patients with Kennedy's disease and found that the SNAPs abnormalities were high [6].

The Needle EMG examination is always abnormal. It shows combined features of acute and chronic denervation and reinnervation. Acute denervation findings include fibrillations and positive sharp waves. Fasciculations should be present in multiple muscles of the limbs and thoracic paraspinal. Chronic denervation and reinnervation findings include large-amplitude; long-duration, MUAPs with neurogenic recruitment, and a reduced interference pattern should be present in multiple muscles of limbs.

The EMG abnormalities noted in muscles of patients with SBMA or in other MNDs are not pathognomonic for the disease but can be seen in any disease-causing active and ongoing chronic denervation, such as in diffuse motor neuropathy or multilevel cervical and lumbar radiculopathy. However, the diagnosis should be suggested by the observation of similar abnormalities in many muscles of proximal and distal limbs, in the absence of radiologic abnormality of corresponding nerve root compression. In addition, denervation should be present in the thoracic paraspinal and bulbar muscles.

Histopathology examination reveals depletion of motor neuronal cell bodies in the brainstem and spinal cord. Muscle biopsy shows atrophy, splitting, centralized nuclei, and fiber degeneration of muscle fibers. There are also changes in the white brain matter that show frontal lobe hypometabolism [12].

In Summary, the EDX features of SBMA are consistent with diffuse, slowly progressive chronic degeneration of anterior horn cells

coupled with a sensory neuropathy/neuronopathy (degeneration of dorsal root ganglia).

Conclusion

The clinical findings of our case are compatible with the cases present in the literature and give an understanding that, although SBMA is uncommon, it must also be taken into consideration in the differential diagnosis of motor neuron disease [13]. In order to obtain the right diagnosis, it is important to avoid delaying the diagnosis and ineffective treatment. In addition, it is always necessary to assess the patients clinically with thorough neurological examinations, to perform necessary testing such as appropriate labs, neuroimaging (If indicated) and electrophysiological studies along with genetic testing. As SBMA is often confused with other neurodegenerative diseases, adequate diagnosis can prevent excessive delay in management and allow appropriate genetic counseling.

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