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Kennedy's Disease, a Mimic of Amyotrophic Lateral Sclerosis: A Case Report

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Abstract Kennedy's disease is an adult-onset, X-linked recessive trinucleotide, polyglutamine disorder, caused by expansion of a polymorphic CAG tandem-repeat in exon 1 of the androgen-receptor (AR) gene on chromosome Xq11-12. We report a case of 60 year old non-diabetic, normotensive, non-smoker, non-alcoholic male presenting with gradual onset and progressive difficulty in swallowing, nasal intonation of speech, generalized wasting and weakness with cramps and fasciculation without any sensory symptoms for around one year. Examination revealed gross emaciation, bilateral gynaecomastia, nasal speech with absent gag reflex, wasted and fasciculating tongue, wasted limb muscles with widespread fasciculation, bilateral postural tremor without any cognitive and sensory impairment. Investigation revealed elevated serum CPK. Electro-diagnostic (EDX) features are consistent with a slowly progressive and very chronic degeneration of the anterior horn cells and dorsal root ganglia (absent SNAP). MRI of the brain and cervical spine revealed no abnormality. Ultimately the genetic analysis confirmed the case as Kennedy's disease.

Keywords: *Kennedy's disease; amyotrophic lateral sclerosis; Bulbar and spinal muscular atrophy*

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1. Introduction

Kennedy's disease, also known as Bulbar and spinal muscular atrophy (BSMA) is an adult-onset, X-linked recessive trinucleotide, polyglutamine disorder, caused by expansion of a polymorphic CAG tandem-repeat in exon 1 of the androgen-receptor (AR) gene on chromosome Xq11-12 **[1]**. Pathogenetically, mutated AR accumulates in nuclei and cytoplasm of motor neurons, resulting in their degeneration and loss [2]. Phenotypically, both muscle and motoneurons are affected, manifesting as weakness and wasting of the facial, bulbar and limb muscles, associated with endocrinologic disturbances [3,4,5]. There may be mild hyper-CK-emia, abnormal motor and sensory nerve conduction studies, and neuropathic and myopathic alterations on muscle biopsy.

The gold standard for diagnosing BSMA is genetic analysis, demonstrating a CAG-repeat number >40. No causal therapy is available, but symptomatic therapy should be provided for tremor, endocrinologic abnormalities, sensory disturbances, or muscle cramps. The course is slowly progressive, the ability to walk lost only late in life, only few patients require ventilatory support, and life expectancy only slightly reduced [2].

2. Case Presentation

A 60 year old, normotensive, non-diabetic, non-smoker, non-alcoholic male, mechanical engineer presented to us with the complaints of gradual onset and progressive difficulty in swallowing (more for liquid than solid together with nasal regurgitation) and nasal intonation of speech for 1 year. The patient also complained of generalized wasting of the muscles along with twitching for almost the same duration. He had difficulty in getting out of chair, climbing stairs, combing hairs and even eating foods. On query he admitted to have cramps long before the onset of his symptoms. There was no history of tingling, numbness, paresthesia, ocular problem or bladder bowel dysfunction. He does not give history of similar illness in any of his family members. On examination the patient is grossly emaciated, weighing 35 kg, having bilateral gynaecomastia (Figure 1). Neurological examination revealed a normal higher psychic function with a nasal intonation of speech. Cranial nerves examination revealed no abnormality except a wasted tongue with fasciculation (Figure 2) and an absent gag reflex (but normal palatal movement). Prominent fasciculation was noted in the facial muscles particularly in the masseter muscles. The jaw jerk was absent. Motor

examination revealed bilateral postural tremor more on the right than left without any rigidity. The bulk of muscles is markedly reduced more in the proximal group than the distal with prominent fasciculation. The power is 3/5 in the proximal group and 4/5 in the distal groups in all limbs. All deep tendon reflexes were absent with bilateral flexor plantar response. All modalities of sensation were intact. There was no cerebellar sign or sign of meningeal irritation. Gait was normal. Other system examination revealed no abnormality except gynaecomastia bilaterally. Investigations revealed a modestly elevated serum CK (1603), normal brain and cervical spinal cord on MRI. NCS revealed reduced CMAP amplitude in the motor nerves and absent SNAP (Figure 3). Needle EMG revealed increased insertional activity, polyphasic, high amplitude, long duration MUAPs with reduced recruitment.

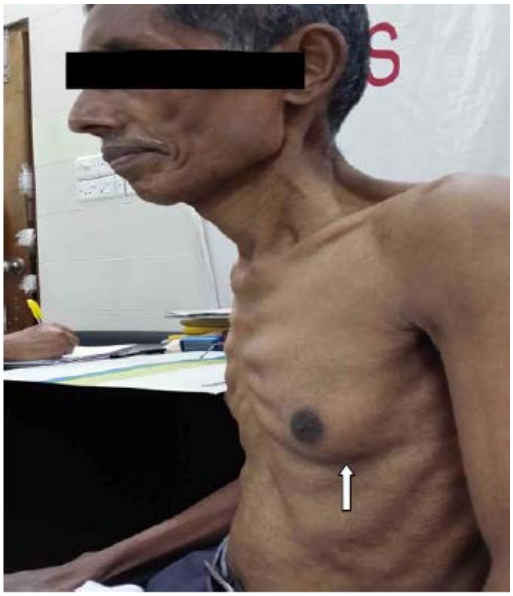

Figure 1. Gynaecomastia and emaciation

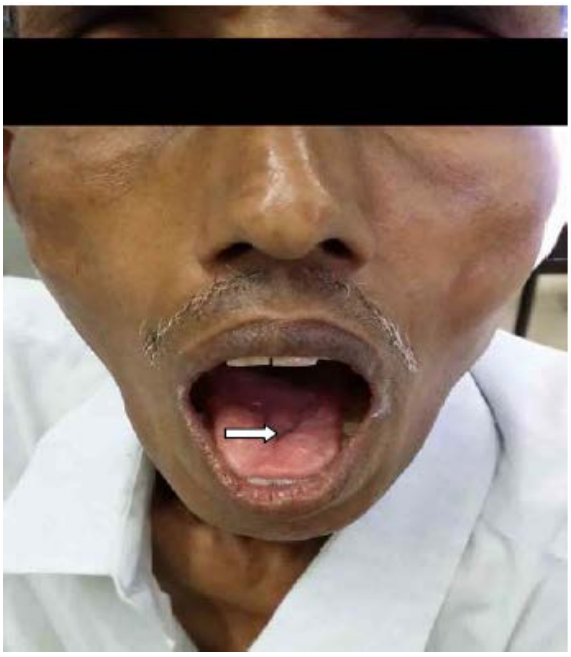

Figure 2. Wasted tongue

3. Discussion

Pathogenetically, mutated AR accumulates in nuclei and cytoplasm of motor neurons, resulting in their degeneration and loss. Phenotypically, patients present with amyotrophic, proximal or distal weakness and wasting of the facial, bulbar and limb muscles, occasionally sensory disturbances, and endocrinologic disturbances, such as androgen resistance, gynecomastia, elevated testosterone or progesterone, and reduced fertility. There may be mild hyper-CK-emia, abnormal motor and sensory nerve conduction studies, and neuropathic and myopathic alterations on muscle biopsy.

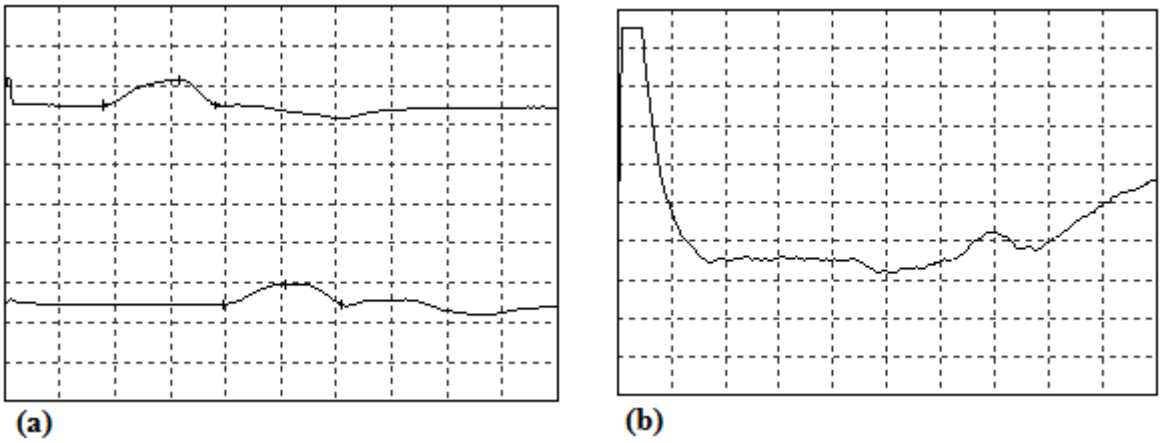

Figure 3. (a) Reduced Median CMAP amplitude, (b) Absent Ulnar SNAP

The gold standard for diagnosing BSMA is genetic analysis, demonstrating a CAG-repeat number >40. The course is slowly progressive, the ability to walk lost only late in life, only few patients require ventilatory support, and life expectancy only slightly reduced. The **diagnosis should be suspected** in any male patient with motor neuron disease who presents with proximal and bulbar weakness, a positive family history, facial fasciculations, gynaecomastia and absence of signs of pyramidal tract disease (spasticity) and whose EDX studies show abnormal sensory studies in addition to the typical widespread neuropathic pattern on needle EMG [6,7]. An unusually elevated CK level is often an important clue as well. **The gold standard** for diagnosing Kennedy's disease is genetic analysis. We, therefore, performed the genetic analysis which established the case as Kennedy's disease.

4. Conclusion

We presented this case because correct diagnosis is important both for prognosis and for its value in genetic counseling. Despite prominent bulbar weakness and the corresponding risk of aspiration, longevity usually is not affected.

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