

Case Reports

Head and Arm Tremor in X-linked Spinal and Bulbar Muscular Atrophy

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Abstract

Background: X-linked spinal and bulbar muscular atrophy (SBMA) is a rare adult-onset neuronopathy. Although tremor is known to occur in this disease, the number of reported cases of SBMA with tremor is rare, and the number with videotaped documentation is exceedingly rare. Our aim was to describe/document the characteristic signs of tremor in spinal and bulbar muscular atrophy.

Case Report: We report a case of a 58-year-old male with a positive family history of tremor. On examination, the patient had jaw and hand tremors but he also exhibited gynecomastia, progressive bulbar paresis, and wasting and weakness primarily in the proximal limb muscles. The laboratory tests revealed an elevated creatine phosphokinase. Genetic testing was positive for X-SBMA, with 42 CAG repeats.

Discussion: Essential tremor is one of the most common movement disorders, yet it is important for clinicians to be aware of the presence of other distinguishing features that point to alternative diagnoses. The presence of action tremor associated with muscle atrophy and gynecomastia should lead to a suspicion of SBMA.

Keywords: Tremor, Kennedy's disease, X-linked spinal and bulbar muscular atrophy, CAG repeats

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Introduction

X-linked spinal and bulbar muscular atrophy (SBMA) is a slowly progressive, degenerative disorder of the lower motor neurons caused by an expanded cytosine, adenine, guanine (CAG) repeat length in the first exon of the gene encoding the androgen receptor, located on chromosome X (Xq11–12).^{1–8} Phenotypically, patients present with weakness and wasting of the facial, bulbar, and limb muscles, sensory disturbances, and endocrinological abnormalities. Although tremor is known to occur in this disease, the number of reported cases of SBMA with tremor is rare, and the number with videotaped documentation is exceedingly rare. Our aim was to describe/document the characteristic signs of tremor in spinal and bulbar muscular atrophy.

Case Report

A 58-year-old male presented with postural and kinetic, non-alcohol responsive hand tremor for 15 years. This was followed in the last 3 years by numbness in both hands and feet, cramps in the neck and legs, and proximal weakness of the legs and masseter muscles. Family history

revealed that his two brothers and one daughter also had tremors. Past medical history was significant for high blood pressure, diabetes mellitus, systemic lupus erythematosus, and cutaneous porphyria. He was taking oral agents for his diabetes (metformin 850 mg per day), and chloroquine (250 mg twice a day). Examination revealed gynecomastia, mild facial diplegia with temporal bilateral muscular atrophy, tongue fasciculations, lower extremity hypopallesthesia, muscle wasting and weakness primarily in the proximal limb muscles, and generalized areflexia. He had a jaw tremor when his mouth was both open and closed, and low-frequency postural and kinetic tremors in the distal upper limb muscles, which did not interfere with his activities of daily living. There was no resting tremor (Video 1). His blood examinations revealed an elevated creatine phosphokinase (CPK) level of 734 (normal range: 38–190). Electromyography showed chronic sensory axonal polyneuropathy. Spiral drawn of our patient is impaired due to both hands tremor (Figure 1). Genetic testing was positive for X-SBMA, with 42 CAG repeats. Owing to cramps, he was started on carbamazepine 200 mg t.i.d., with moderate benefit.



Video 1. Physical examination of our patient: gynecomastia, mild facial diplegia with temporal bilateral muscular atrophy, tongue fasciculations, positional and action hands tremor, and normal gait. Videotape segment showing gynecomastia, mild facial diplegia with bilateral temporal muscular atrophy, tongue fasciculations, jaw tremor, absence of rest tremor, postural and kinetic tremors of the hands, and normal gait.

Discussion

Previous reports in the literature reveal that tremor is a common feature in patients with SBMA, and that while the tremor mimics that of essential tremor, the pathophysiology and degree of responsiveness to alcohol, propranolol, and other drugs such as gabapentin is different.^{2,7} In essential tremor, which is considered to be generated by a central mechanism, the movement is always associated with electromyography (EMG) grouping activities at the same frequency, and it is resistant to external perturbation, such as weight loading.⁷ In SBMA, two different mechanisms might contribute to tremor generation: mechanical oscillation and reflex mechanisms.⁷ In support of this, in SBMA tremor frequency is affected by postural changes and weight loading, suggesting

that it might be considered a reflex tremor, mediated through reflex loops between peripheral nerves and the central nervous system, similar to the stretch reflex.⁷ In addition, the presence of sensory neuropathy in some patients might also contribute to reflex tremor.² On the other hand, because motor units are markedly decreased in SBMA, the muscle spindle feedback might also play an important role in the generation of tremor due to motor unit synchronization.⁷ Motor symptoms have been attributed to the accumulation of mutant androgen receptors in the nucleus of lower motor neurons, which is more profound in patients with a longer CAG repeat. The CAG repeat size and the age at onset are usually different between patients with motor- and sensory-dominant SBMA phenotypes, indicating that a longer CAG repeat (≥ 47) is more closely linked to the motor-dominant phenotype, and a shorter CAG repeat (< 47) is linked to the sensory-dominant phenotype.³ The presence of tremor in SBMA could thus be a clinical feature that predicts shorter CAG repeats of the androgen receptor gene.

With regard to female carriers, about 50% of the cases do not present with clinical manifestations.¹ The other half may present with fasciculations, minimal distal weakness, muscle cramps, tremor, and elevated CPK later in life.² Treatment is symptomatic, and muscular cramps may respond to tizanidine, baclofen, gabapentin, valproic acid, and quinine.⁴ Although it has been reported in animal models of SBMA are responsive to androgen-reducing treatments, no significant benefit has been reported in clinical trials in humans.^{5,6}

In our patient, other common causes of action tremor have been excluded, such as hyperthyroidism, hypoglycemia, alcohol, and medication. We recognize that the presence of a family history of tremor might make us suspect essential tremor. However, the high prevalence of tremor in SBMA reported in large series^{2,3,7,8} suggests that tremor is intrinsically related to SBMA. The lack of biological

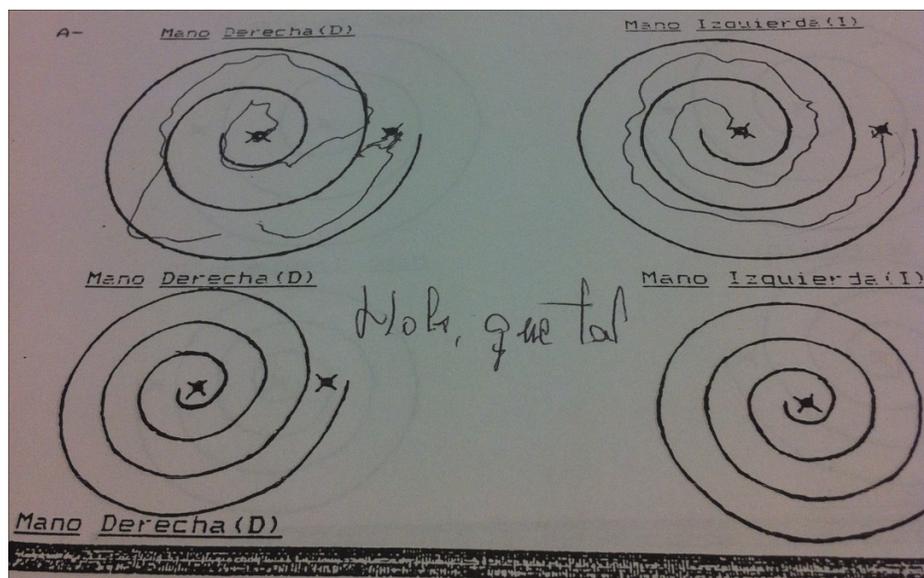


Figure 1. Picture of spirals according to Clinical rating Scale for tremor of our patient. Spirals drawn by our patient.

markers of essential tremor and SBMA-related tremor, besides EMG features, make this differentiation difficult.

In conclusion, essential tremor is one of the most common movement disorders, yet it is important for clinicians to be aware of the presence of other distinguishing features that point to alternative diagnoses. The presence of action tremor associated with muscle atrophy and gynecomastia should lead to a suspicion of SBMA.

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