



## A Case with Cramp-Fasciculation Syndrome

### Kramp-Fasikülasyon Sendromlu Bir Olgu

Cramp-Fasciculation Syndrome

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#### Özet

Kramp-fasikülasyon sendromu periferik sinir hipereskitabilite sendromlarından biridir ve kas ağrısı, kramplar ve egzersiz intoleransı ile seyrederek. Fasikülasyon ve kramplar hem sağlıklı kişilerde hem de Amyotrofik Lateral Skleroz gibi fatal seyirli hastalıklarda görülebilir. Biz 27 yaşında, iki yanlı gastrocnemius-soleus kaslarında 3 yıl önce kramp ve fasikülasyonları başlayan, profesyonel futbol oyuncusu bir erkek hasta sunduk. Tüm laboratuvar ve elektrofizyolojik incelemeler sonrasında hastaya kramp-fasikülasyon sendromu tanısı konuldu. Bu yazının amacı kramp-fasikülasyon sendromunu nadir bir olguyu sunmak ve bu sendromun benign ya da ciddi bir patolojik sürecin ön bulgusu olup olmadığının tartışılmasıdır.

#### Anahtar Kelimeler

Kramp Fasikülasyon Sendromu; Periferik Sinir Hipereskitabilite; Fasikülasyon; Kramp; Isaac's Sendromu

#### Abstract

Cramp-fasciculation syndrome is one of the peripheral nerve hyperexcitability disorders and presents muscle aching, cramps, stiffness and exercise intolerance. Fasciculation and cramps can be seen both in healthy individuals and in those with fatal diseases, such as Amyotrophic Lateral Sclerosis. We present a 27-year-old male patient, professional soccer player with fasciculations and cramps in bilateral gastrocnemius-soleus complex. The patient complained about having to stop playing soccer because of muscle cramps and twitches in both calves, which had started 3 years earlier. After completing all laboratory and electrophysiological examinations, the patient was diagnosed as cramp-fasciculation syndrome. The aim of this paper was to present a rare case of cramp-fasciculation syndrome and discuss if the syndrome is benign or pioneer of a severe pathological process.

#### Keywords

Cramp Fasciculation Syndrome; Peripheral Nerve Hyperexcitability; Fasciculation; Cramp; Isaac's Syndrome

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## Introduction

In 1948 Denny-Brown et al. [1] defined the fasciculation-cramp syndrome as being characterized by cramps, fasciculation, and muscle aches which frequently become more intense with exercise, and which might be accompanied by muscle weakness and muscular atrophy. In 1978 Hudjon et al. [2] described this syndrome as muscular pain-fasciculation syndrome, whereas Blexrud et al. [3] described it as benign fasciculation syndrome. At the present time, peripheral nerve hyperexcitability (PNH) refers to a group of disorders characterized clinically by muscle twitching (myokymia and fasciculations), muscle cramps, muscle stiffness and pseudomyotonia (delayed muscle relaxation after muscle contraction), of which the primary PNH are Isaac's syndrome, cramp-fasciculation syndrome and Morvan syndrome. Cramp fasciculation syndrome identifies a disorder characterized by a less prominent PNH than is shown in Isaac's syndrome [4]. These disorders may come from the effects of auto-antibodies against voltage gated potassium channels (VGKC).

We presented a case diagnosed as cramp-fasciculation syndrome and discussed if the syndrome is benign or pioneer of a severe pathological process.

## Case Report

The patient was a 27-years-old male professional soccer player. For 3 months he had not played soccer because of a sport injury, when he had played at the big derby. He complained about having to stop playing in his team because of muscle cramps and twitches in both calves, which had begun 3 years ago. The patient reported that the cramps occurred only in response to extreme effort during matches; the symptoms did not occur while training. Cramps interrupted his performance in matches and he had to cut out every game. Twitching occurred constantly when he was awake. He was concerned that people would see him twitching and had stopped wearing shorts. His cramps and twitches affected his calves alone.

The patient also reported that he always had to wait nearly 5 minutes to urinate after going to the bathroom and that when he was in stressful situations the muscles of his face twitched. He reported that he could never sleep the night before a soccer match. The patient's history revealed that 2 years earlier anxiety had led him to begin taking serotonin reuptake inhibitors after consulting a psychiatrist. Because of abulia, he discontinued the medication.

His neurological examination was normal except for fasciculation in the gastrocnemius-soleus complex and vivid deep tendon reflexes (Video 1). The patient's hemogram, sedimentation, C reactive protein, fasting glucose level, hemoglobin A1c, urea, creatinine, alanine aminotransferase, aspartate-glutamyltransferase, creatinine kinase, sodium, potassium, magnesium, ionized calcium, chloride, vitamin D 25-hydroxy, ferritin, vitamin B12, homocysteine, lactate dehydrogenase, total protein, albumin, cholesterol, HDL, LDL, triglyceride, TSH, free triiodothyronine (T3), total T3, free thyroxine (T4), total T4, thyroid peroxidase anti-core (anti-TPO), hepatitis B antibody, hepatitis B antibody, hepatitis C antibody, HIV antibody values and paraneoplastic panel were all normal. A chest X-ray revealed no abnormality. The tumour markers were all negative, but serum and cerebrospinal fluid testing for voltage-gated potassium channel anti-

bodies, and whole-body Positron Emission Tomography (PET) scan could not be pursued. No pathology was observed during the patient's lumbo-sacral magnetic resonance imaging.

Electromyographic examination showed that the patient's nerve conduction studies were normal except for the presence of after-discharges of tibial nerve in the motor conduction studies. Denervation potentials were not observed in any of the 4 extremities. Fasciculation potentials were observed in both gastrocnemius muscles with needle electromyography (EMG) and surface electrodes. In the examination of gastrocnemius muscles at rest, the morphologically normal different motor unit potentials (MUPs) were firing constantly at low frequency. No pathological findings were observed during voluntary contractions. The needle EMG of muscles which are innervated by cranio-bulbar, cervical, thoracic and lumbar regions were found normal.

## Discussion

Fasciculations are a normal experience for healthy people. The prevalence of benign fasciculation is high 1% in the general population. Epidemiological studies indicate that fasciculation potentials are frequently seen in men [1]. Cramp-fasciculation syndrome is a rare condition and is thought to be related to peripheral nerve hyperexcitability. Cramps and fasciculation symptoms should first be distinguished from the symptoms of such fatal diseases as amyotrophic lateral sclerosis (ALS). Many patients have cramps and fasciculations during the first stages of ALS. Cramp-fasciculation syndrome is diagnosed by eliminating all other possible diagnoses.

Fasciculation other than motor neuron disease can be observed in various illnesses and situations. For example it can be seen in cases of excessive use of alcohol, caffeine, cola, tea, and tobacco, and in cases of stress, acute viral infection, rarely poliomyelitis or late-stage myelitis, hyperthyroidism, compression of the nerve body or root, cervical spondylosis, syringomyelia, thyrotoxicosis, tetanus, high-dose anti-cholinesterase use, fasciculation-cramp syndrome, focal and generalized neuropathies, and acute dermatomyositis. Mitsikostas et al. [5] found that in normal people fasciculations were noticeably correlated to the body weight and height and to the anxiety level. A history of regular tiring exercise is also common feature in many cases. Blexrud et al. [3] undertook follow-up examinations of 121 patients with benign fasciculation after 2 and after 32 years later. The results showed that none of the patients had ALS in the following years. On the other hand, De Carvalho M et al. [6] reported that 3 patients with benign fasciculation eventually went on to develop ALS. Singh et al. [7] also reported 4 cases who were initially diagnosed as a cramp-fasciculation syndrome, but who finally progressed to ALS. Therefore they suggest that a diagnosis of cramp-fasciculation syndrome should not be considered secure without minimum follow-up 4-5 years.

The existence of denervation potentials is the first thing to examine when differentiating benign fasciculation electrophysiologically. It must be emphasized that benign fasciculation syndrome is a condition which generally affects young adults. When fasciculation occurs in the elderly, ALS should be considered. While benign fasciculation is observed in certain muscles focally, generalized fasciculation occurs in ALS; however, ALS occurs

focally during its early stages and then generalized fasciculation occurs. The electrodiagnostic criteria for the diagnosis of ALS was reviewed and reported that malign fasciculation has a complex morphology and unstable characteristics, whereas benign fasciculation has a basic morphology and stable characteristics [8].

Isaac's syndrome is an antibody-mediated potassium channel disorder characterized by painful muscle cramps, muscle rigidity, slow relaxation following muscle contraction (pseudomyotonia), hyperhidrosis, and autoantibodies against VGKC, a dendrotoxin-sensitive fast potassium channel. Autoantibody-mediated VGKC dysfunction leads to hyperexcitability of the peripheral nerves. In our case, there were no other clinical features of Isaac's syndrome, except for cramps and fasciculations.

The findings suggest that the presented case had fasciculation-cramp syndrome and because he has no other characteristics than the fasciculations and cramps in the gastrocnemius-soleus complex in his neurological examinations. The patient's electrophysiological examinations also showed that there were no denervation potentials or pathological MUP findings. The presence of after-discharges was supposed to be associated with cramp-fasciculation syndrome. In conclusion, this case emphasizes the importance of clinical and electrophysiological evaluations for the concepts of cramp and fasciculation.

#### **Competing interests**

The authors declare that they have no competing interests.

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