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CASE REPORT | OLGU SUNUMU

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Acetazolamide-associated lingual myokymia: A reversible peripheral nerve hyperexcitability phenotype

Asetazolamid ile ilişkili lingual miyokimi: Geri dönüşümlü bir periferik sinir hipereksitabilitesi fenotipi

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ABSTRACT

Myokymia is a motor phenomenon within the spectrum of peripheral nerve hyperexcitability, characterized by fine, rhythmic, and often sustained involuntary muscle contractions. Clinically, it manifests as superficial undulation or "rippling" and is defined electromyographically by brief, grouped motor unit discharges. This case report presents a 23-year-old female with idiopathic intracranial hypertension who developed clinically isolated lingual myokymia shortly after the initiation of acetazolamide therapy. The diagnosis of lingual myokymia was confirmed by characteristic spontaneous, grouped motor unit discharges on genioglossus needle electromyography. To the best of our knowledge, this is the first detailed case of acetazolamide-related lingual myokymia reported from Türkiye, and it aims to contribute to the differential diagnosis of drug-induced focal peripheral nerve hyperexcitability.

Keywords: Acetazolamide, focal peripheral nerve hyperexcitability, idiopathic intracranial hypertension, lingual myokymia, needle electromyography.

ÖZ

Miyokimi, periferik sinir hipereksitabilitesi spektrumunda yer alan ve kas liflerinde ince, ritmik, çoğu zaman sürekli seyreden istemsiz kasılmalarla karakterize edilen bir motor fenomendir. Klinik olarak yüzeyel dalgalanma ya da "rippling" şeklinde gözlenir ve elektromiyografik olarak kısa süreli, gruplanmış motor ünite deşarjları ile tanımlanır. Bu vaka raporunda, asetazolamid tedavisine başlandıktan kısa bir süre sonra klinik olarak izole dil miyokimisi gelişen, idiyopatik intrakraniyal hipertansiyonu olan 23 yaşında bir kadın hasta sunulmaktadır. Dil miyokimisi tanısı, genioglossus iğne elektromiyografisinde karakteristik spontan, gruplanmış motor ünite deşarjları ile doğrulanmıştır. Bu olgu bilinen kadarıyla, Türkiye'den bildirilen ilk ayrıntılı asetazolamid ilişkili lingual miyokimi vakası olup ilaç kaynaklı fokal periferik sinir hipereksitabilitesinin ayırıcı tanısına katkı sağlamayı amaçlamaktadır.

Anahtar sözcükler: Asetazolamid, fokal periferik sinir hipereksitabilitesi, idiyopatik intrakraniyal hipertansiyon, lingual miyokimi, iğne elektromiyografi.

Myokymia is a manifestation of peripheral nerve hyperexcitability characterized by fine, rippling, and often continuous involuntary muscle contractions generated by single or grouped motor unit discharges. Electrophysiologically, it is defined by brief, rhythmically recurring motor unit potentials (MUPs) and can be distinguished from other forms of involuntary muscle activity, such as fasciculations, tremor, and neuromyotonia, by these features.[1,2] Myokymia may be associated with central or peripheral nervous system disorders, including multiple sclerosis, brainstem lesions, radiation-induced neuropathy, Guillain-Barré syndrome, and autoimmune potassium channelopathies.[3,4] Drug-related myokymia has been reported only rarely and, in the literature, is largely limited to a small number of cases involving antipsychotics, immunomodulatory agents, or treatments that affect ion channel function.[5]

Acetazolamide, a carbonic anhydrase inhibitor, is widely used in the treatment of idiopathic intracranial hypertension (IIH), epilepsy, and certain hereditary channelopathy phenotypes. Its effects on neuronal excitability are mediated through indirect mechanisms involving acid-base balance, ionic conduction, and membrane potential.[6] Data suggesting that acetazolamide may trigger myokymia are extremely limited.[7] Lingual myokymia, in particular, is a clinically

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striking phenotype due to its rarity and since it raises concern for motor neuron diseases and brainstem pathologies in the differential diagnosis.

In this case report, we present a case of isolated lingual myokymia with a reversible course following acetazolamide therapy and discuss the possible pathophysiological mechanisms in light of the clinical and electrophysiological findings. Written informed consent was obtained from the patient for the publication of this case report and the accompanying images.

CASE REPORT

A 23-year-old woman with no known prior neurological or systemic disease presented with complaints of episodic bilateral throbbing headache associated with neck pain and blurred vision that had been ongoing for several weeks. She reported experiencing 4-5 attacks per month over the preceding three months and described the headaches as having a motion-sensitive character. There were no associated symptoms of nausea or vomiting, involuntary body movements, or motor or sensory deficits. Her medical history was unremarkable, and she was not using any medications. Neuro-ophthalmological evaluation revealed bilateral papilledema; funduscopic examination was otherwise normal. Cranial imaging studies performed to evaluate potential secondary causes, including ischemic, metabolic, infectious, demyelinating, and neurodegenerative etiologies, were unremarkable. Brain magnetic resonance imaging (MRI) demonstrated findings consistent with partial empty sella, along with marked dilatation of the perioptic subarachnoid cerebrospinal fluid spaces and increased tortuosity of the bilateral optic nerves. The opening pressure measured during the lumbar puncture was 28 cmH_2O, and cerebrospinal fluid analysis was biochemically and cytologically normal. Based on the clinical, radiological, and laboratory findings, and after exclusion of secondary causes, a diagnosis of IIH was established. Acetazolamide 500 mg twice daily was initiated, and the patient reported symptom relief. Within 48-72 h of starting the medication, she noticed involuntary, rippling movements on the tongue that persisted even at rest. The symptoms became more prominent during speech and interfered with eating. She denied associated generalized muscle stiffness, painful cramps, weakness, dysphagia, sensory deficits, autonomic symptoms, or generalized muscle activity during sleep. Neurological examination revealed intact cranial nerves, with no tongue atrophy or deviation; however, prominent, non-rhythmic rippling movements of the intrinsic tongue musculature were observed at rest, particularly along the lateral and anterior surfaces, as shown in Figure 1. Laboratory investigations revealed normal serum sodium, potassium, calcium, and magnesium levels. Complete blood count and thyroid function tests were within normal limits. To rule out brainstem and cranial nerve involvement in the differential diagnosis, contrast-enhanced and non-contrast brain MRI and MR angiography/venography were performed, and all examinations were found to be normal. Peripheral blood autoimmune serology was sent and returned negative for voltage-gated potassium channel (VGKC)-complex antibodies (including contactin-associated protein-like 2 and leucine-rich glioma-inactivated 1) and for an extended neural/paraneoplastic antibody panel (Hu, Yo, Ri, Amphiphysin, and GAD65). Needle electromyography (EMG) of the tongue demonstrated intermittent, grouped bursts of spontaneous MUPs with a waxing-waning morphology and semi-rhythmic grouped discharges on multichannel recordings obtained from the intrinsic genioglossus muscle. These bursts consisted of short trains of MUPs lasting approximately 30-60 ms and recurring at irregular intervals, findings most consistent with myokymic discharges rather than isolated fasciculations or continuous neuromyotonic activity. The electrophysiological findings were thus interpreted as classic myokymic activity, as shown in

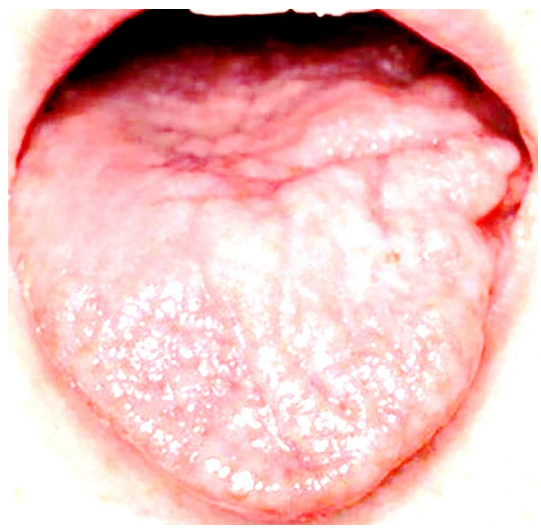

Figure 1. Clinical photograph obtained with the tongue fully protruded, showing prominent undulating/rippling movements of the intrinsic tongue musculature, particularly along the lateral and anterior surfaces. The mucosal surface texture and vascular pattern are preserved, with no evidence of ulceration or focal atrophy.

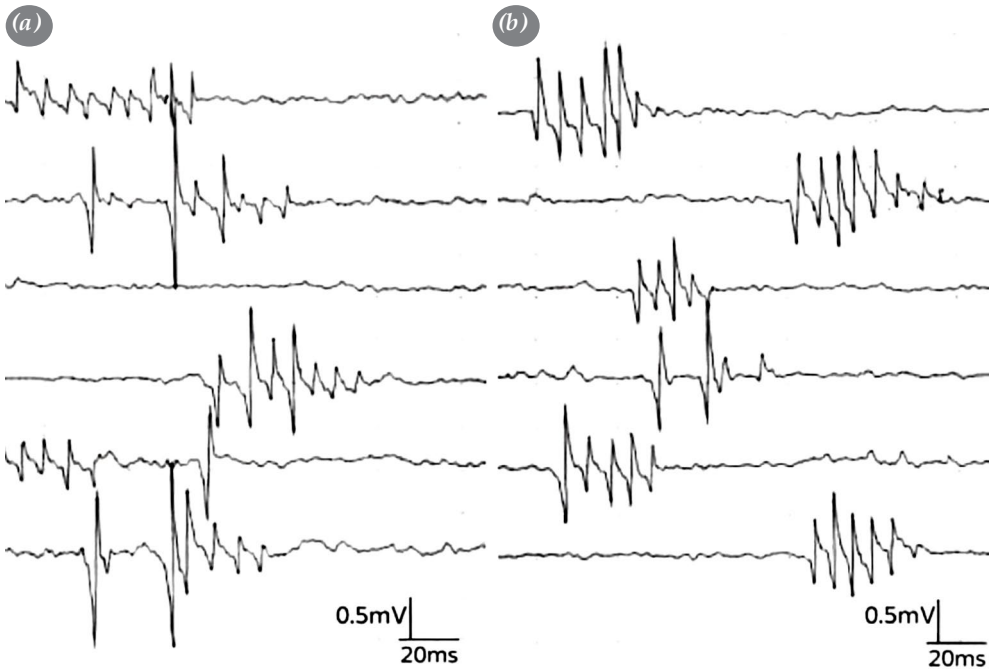

Figure 2. (a) Needle electromyography of the tongue demonstrating grouped myokymic discharges. Left panel: multiple channels from intrinsic tongue/genioglossus needle sampling showing intermittent, grouped bursts of spontaneous motor unit potentials with waxing-waning morphology. **(b)** Right panel: additional recording epoch from the same muscles demonstrating similar semi-rhythmic grouped discharges. Calibration parameters: Band-pass filtering 10 Hz-10 kHz, sensitivity 100 µV/div, sweep speed 20 ms/div, and a sampling rate ≥ 10 kHz.

Figure 2a, b. Given the suspected triggering role of acetazolamide, the medication was discontinued, and diuretic therapy was initiated. A marked reduction in lingual movements was observed within the first 24 h after drug withdrawal, and complete resolution of symptoms occurred within 72 h. During six months of clinical follow-up, there was no recurrence of myokymia, and neurological examinations remained normal.

DISCUSSION

This case report demonstrates clinical and electrophysiological evidence of isolated lingual myokymia closely associated with acetazolamide administration. The rapid and complete resolution of symptoms after discontinuation of the drug meets key criteria for a probable adverse drug reaction and supports a causal relationship between acetazolamide exposure and the onset of myokymic activity. Although the literature reports variable effects of acetazolamide on peripheral nerve excitability, the contrasting findings indicate that the electrophysiological effects of acetazolamide are likely context-dependent, shaped by individual susceptibility, baseline ion channel function, and regional axonal characteristics.

Acetazolamide inhibits carbonic anhydrase and may lead to metabolic acidosis and altered bicarbonate/CO_2 balance. Secondary changes in transmembrane ionic gradients, especially potassium handling, may lower the axonal threshold for spontaneous discharge.[8] These effects may not cause systemic electrolyte abnormalities, as local perineuronal or periaxonal ionic shifts can occur without changes in serum levels. Interindividual differences in ion channel expression, function, or tissue buffering capacity may determine whether acetazolamide stabilizes or destabilizes membrane excitability. This variability explains why acetazolamide can improve symptoms in some channelopathy syndromes but worsen or trigger myokymia in others.[9]

Myokymia is characterized by a decrease in the action potential threshold and an increased tendency for repetitive discharges due to impaired membrane stability in peripheral motor axons. At the

electrophysiological level, this process is associated with K^+ accumulation in the periaxonal space, decreased conductivity in voltage-gated K^+ channels, and modulation of pH-sensitive ion currents; ultimately, the refractory period is shortened, and semi-rhythmic, grouped motor unit discharges occur in the 5-150 Hz range, lasting 30-60 ms.[10] The mild-moderate metabolic acidosis induced by acetazolamide through carbonic anhydrase inhibition can increase the probability of spontaneous discharge by affecting Na^+/K^+-ATPase activity and axonal repolarization kinetics via intracellular pH reduction and CO_2 retention.[10,11] This mechanism may explain the clinically significant hyperexcitability in lingual muscles, which have intense motor innervation and require high-frequency fine motor control.

In the literature, myokymia has been predominantly described in limb or facial muscles, while reports with cranial muscle involvement and detailed quantitative parameters are limited. Gutmann[11] defined myokymia within the spectrum of peripheral nerve hyperexcitability, characterizing it on needle EMG by grouped, semirhythmic MUPs; intraburst frequency is generally reported to be between 5 and 150 Hz, distinguishing it from neuromyotonia, which shows higher-frequency, continuous discharges. In our case, the genioglossus muscle exhibited 30-60 ms bursts of waxing-waning, semirhythmic, grouped discharges, consistent with the classic myokymic organization described by Gutmann, whereas the absence of high-frequency, prolonged, continuous activity clearly distinguishes it from neuromyotonia. In Jamieson and Katirji's[12] series of idiopathic generalized myokymia, EMG recordings from limb muscles demonstrated intraburst frequencies mostly between 20 and 80 Hz, interburst intervals of 2-10 Hz, and burst durations typically ranging from 50 to 200 ms. In our case, the burst duration of 30-60 ms falls at the lower limit of this range, suggesting that cranial muscles may display shorter myokymic trains and highlighting potential physiological differences compared to limb muscles. Oh et al.[13] reported 30-100 Hz intraburst frequencies with short myokymic trains in facial and limb muscles of patients with dermatomyositis and VGKC antibody-associated conditions, while neuromyotonic discharges were longer and higher frequency. In our patient, the focal, short-duration bursts confined to the tongue, without evidence of systemic hyperexcitability, support a diagnosis of focal cranial myokymia rather than a generalized neuromyotonic syndrome. In a case of post-radiation lingual myokymia, the genioglossus muscle exhibited classic grouped spontaneous MUP discharges; however, quantitative burst duration and frequency were not reported.[14] Therefore, our case provides a unique contribution by quantitatively defining lingual myokymia in terms of burst duration, both morphologically and temporally. Compared to previous reports focused on limb or facial muscles, our case is distinguished by cranial muscle involvement, shorter burst duration, and clear electrophysiological differentiation from neuromyotonia, filling a gap in the literature by providing quantitative data on cranial muscle-specific myokymic activity.

In conclusion, this case report reveals lingual myokymia as a rare but potentially reversible side effect of acetazolamide; it highlights the critical importance of a detailed drug history and targeted needle EMG in cases of newly diagnosed focal myokymia. Further mechanistic and case-series studies are needed to identify the genetic, metabolic, and microenvironmental factors that enhance susceptibility.

Author Contributions

E.D.U., N.D.Ç.: Concept and design, data collection and processing, analysis and interpretation, literature search, writing, critical review; E.D.U.: Supervision.

Conflict of Interest

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