Inusual ictal paralysis due to inhibitory motor seizures mimicking a cerebral transient ischemic attack: two cases and a brief review of epileptic ictal paralysis

Brief historical development of inhibitory motor seizures

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Abstract

Negative phenomena can occur with seizures, but inhibitory motor seizures are rare and may lead to misdiagnosis. Two adults with focal inhibitory motor seizure (ictal paralysis) have been evaluated, and taken together with the clinical history, the results from these investigations suggest focal inhibitory seizures as the underlying etiology. The mechanisms of negative motor phenomena during a seizure are not well understood, but ictal negative motor phenomena have been reported in a frontal, central, or parietal epileptogenic focus. Inhibitory motor seizures must be differentiated from transient ischemic attacks. A brief review of some of the possible underlying physiological mechanisms of these unusual features is of interest.

Sintesi

Le crisi epilettiche possono manifestarsi con sintomi negativi, tuttavia le crisi motorie inibitorie sono eventi rari che possono portare ad errore diagnostico. Due casi di pazienti adulti con deficit motori conseguenti a crisi motorie inibitorie sono stati esaminati, la loro storia clinica insieme ai risultati delle indagini diagnostiche depone per crisi motorie inibitorie dal punto di vista eziologico. Il meccanismo fisiologico delle crisi motorie inibitorie non è ben conosciuto, ma deficit motori focali sono stati riportati in casi focus epilettogeno in regione frontale, centrale e parietale. Le crisi motorie inibitorie entrano in diagnosi differenziale con gli attacchi ischemici transitori. Una breve revisione dei possibili meccanismi fisiologici implicati in queste inconsuete manifestazioni cliniche costituisce elemento di interesse.

Keywords: inhibitory motor seizures, ictal paralysis, epileptic hemiplegia, negative seizures, focal atonic seizures, inhibitory seizure, negative myoclonus.

Introduction

Transient hemiplegia or hemiparesis is a rare but important presentation of seizures that is frequently misdiagnosed as cerebral transient ischemic attack (TIA). Two types of seizure-related hemiplegia have been described. The first, Todd described post-epileptic paralysis which he called epileptic hemiplegia (subsequently called Todd’s paralysis), patients were noted to have a focal paralysis that was transient and lasted from minutes to days after an epileptic seizure (1). Todd held that some patients “who recover from a severe fit, or from frequently repeated fits of epilepsy, are often found to labor under hemiplegia, or other modifications palsy”. He believed that this resulted from “undue exaltation [horizontal ellipsis] resulting in] a state of depression or exhaustion” (2). The second, sudden weakness of a limb as a seizure manifestation in the absence of “motor convulsion” was first described by Gower as a “paroxysmal appearing palsy of an epileptic origin” (3). Higier described a paralytic equivalent of epilepsy without disturbance of consciousness, were the paralysis appeared to be part of the epileptic seizure (4). He described as a “paralytic equivalent of epilepsy without disturbance of consciousness in the form of status hemiparalyticus” (5). Higier’s ictal paralytic phenomenon (inhibitory epilepsy) has also called inhibitory motor seizures (6).

Unlike post-epileptic paralysis, inhibitory motor seizure is rare and not well known, and inhibitory motor seizure has only rarely been analyzed systematically. A differentiation between the two phenomena is usually difficult because both may have associated seizures; it is interesting that Todd noted flaccid paralysis in many cases but in two cases he described the paralysis preceding the seizure. It is possible that they represented not post-ictal but ictal paralysis. Inhibitory motor seizures mimicking TIA are manifested as a paroxysmal paralysis of the face, arm, leg,
or hemibody, and weakness are not preceded by tonic or clonic activity in the affected extremity, consciousness typically is not impaired, and full function of the paretic or paralysis extremity returns.

I describe two cases of ictal hemiplegia which presented clinically as cerebral transient ischemic attack but later proved to be due to inhibitor motor seizures, and resolved with anticonvulsant treatment. Epileptic ictal paralysis, together with cerebral ischemia and migraine accompaniment, is listed in the differential diagnosis of focal limb weakness. Over the years, I have learned that numerous non-vascular disorders can mimic TIIAs. Thus, clinicians should consider seizures in the setting of unexplained deficits. I discuss possible mechanisms as to how inhibitory seizure are generated in partial epilepsies.

**Patient 1**

A 20-year-old, right-handed male with a history of type 1 diabetes, presented with acute left hemiparesis and was also slightly confused. Weakness was not preceded by tonic or clonic activity in the affected extremity and the patient experienced paresthesias in the whole left hand ipsilateral to weakness, immediately preceding the weakness. There was no history of head trauma, seizure, or migraine headache. Few minutes after symptom onset, the blood sugar level was 210 mg/dL. Because of the acute limb weakness, he was sent to the Emergency Room immediately. At presentation he was aware, and the neurological examinations revealed spontaneous verbal expression, left hemiparesis predominant in the arm, left central facial palsy, and gaze palsy to the left side.

Symptomatology was identical to hemiparesis of vascular origin, and right hemispheric ischemia was suspected. Neuroimaging with both non-contrast head computed tomography scan and magnetic resonance revealed no structural brain abnormality. Magnetic resonance venography showed no significant abnormality. The patient was
considered for acute thrombolytic therapy (with tissue plasminogen activator, tPA).
Over the next minutes, he improved clinically, showing gradual and complete resolution of his left hemiparesis. After admission to the Emergency Room about 3 hours from the onset, the neurological deficits resolved completely. Even though no EEG was performed at the time of presentation, an interictal EEG was consistent with ictal paralysis. The first interictal awake scalp EEG revealed periodic epileptiform discharges that had a clear right centro-fronto-temporal predominance, and tending to diffuse over both hemispheres. The follow-up EEG showed a decreased of epileptic discharges. The last EEG was normal. Electrocardiogram, transthoracic echocardiography, color-Doppler imaging of the carotid and vertebrobasilar arteries were reportedly normal. Magnetic resonance imaging of the brain performed on the nineth day was normal. The diagnosis of epilepsy was made. The subsequent 2 years have been seizures free. Thereafter, he had not other seizure episodes until age 22, when he had an episode characterized by transient prolonged weakness which involved the right arm without clonic movements in the same arm, and during this episode he appeared slightly confused with initially abnormal behaviour. Two hours later, the neurological deficits resolved completely. For the reason given above, he was admitted to Department of Neurology. Intercital neurological examination was normal. Intercital EEG revealed normal background activity and intermittent spike wave complex and sharp wave over left frontotemporal region. The following tests were negative: magnetic resonance imaging, hypercoagulable screening, lactic acid, mitochondrial DNA screening for MELAS and MERFF syndrome. Carbamazepine monotherapy was started. He was put on carbamazepine controlled release 200 mg two times a day.

Patient 2
A 86-year-old, right-handed women with a past medical history of hypertension and endarterectomy of the right internal carotid artery, who was receiving antiplatelet therapy, presented with several minutes of decreased responsiveness, difficulty in speaking, and inability to move her right side. These symptoms occurred a two times and lasted several minutes each. When presenting in the Emergency Room 2 hours later, symptoms had totally regressed. A non-contrast head CT scan demonstrated no acute hemorrhage. The gradual disappearance of the symptomatology within 15 minutes was indicative of a transient ischemic attack (TIA). The patient was admitted to the neurologic unit. Work-up investigating the etiology of the embolic event was non-contributory. The carotid was fully patent by duplex studies. In the following days four episodes has occurred characterized by acute aphasia and right hemiparesis, with no convulsive movements of the extremities. Over the next five to ten minutes, she improved clinically, showing gradual and complete resolution of her symptoms. In summary, this patient presented with unusual recurrent attacks that occurred on the same side. However, during the paralytic
stage, no EEG had been recorded, and the following EEGs were normal. She was discharged home with no definite diagnosis. One day later, the same patient presented two episodes characterized by sudden-onset right-side weakness and slurred speech. The attacks lasted about 15 minutes. For the reason given above, she was admitted to Department of Neurology. Since transient right-sided episodes were occurring several times, epileptic seizures were suspected. Intercritical EEGs was normal. After 10 day, she was discharged with diagnosis of epilepsy. Her discharge medications included: aspirin 100 mg per day, carbamazepine controlled release 200 mg two times a day, valsartan 160/Hydrochlorothiazide 12,5: 1/2 tablet per day, barmidipine hydrochloride administered once daily in the morning in a dose of 10 mg. No further episodes occurred after carbamazepine monotherapy.

Discussion

Inhibitory motor seizures is a subject that provokes strong reactions, perhaps largely due to the relative lack of evidence and the surfeit of opinions. Inhibitory seizures of various types have been described in literature, and epileptic ictal paralysis is an interesting special presentation of inhibitory seizures. The purpose of this paper is to describe aspects of negative seizures characterized by paralysis affecting only one side of the body. As a matter of fact from the clinical point of view, a hemiparetic seizure can lead to problems of differential diagnosis especially if it is prolonged. Hemiplegia with the onset of seizures should prompt investigation to exclude a progressive hemispheric disorder such as vascular events, space-occupying lesions and encephalitides. An epileptic seizure, by definition, indicates a positive electrical phenomenon. Seizures are most commonly associated with positive phenomena such as tonic, clonic or myoclonic movements, automatisms, paresthesias and hallucinations. Negative phenomena can occur with seizures, examples of negative seizures phenomena include speech arrest, aphasia, amnesia, amnesia, numbness, deafness, atonic seizures, neglect, and alien hand syndrome. Loss of awareness or muscle tone such as limb paralysis (inhibitory motor seizures) is less commonly described, and these seizures are separate entities (6) and should be differentiated from TIAs (8). Ictal paralysis may be misdiagnosed as transitory ischemia, when the patient is not known to have epilepsy and does not have tonic or clonic motor activity (7-8), and it responds to anticonvulsant treatment (8). The diagnosis of TIA is difficult at best and is frequently made from the patient's history, rather than from clinical observation (9), and TIA could be wrong in up to 30% of such cases (10). Although weakness of appendicular muscles has rarely been reported to result from transient inhibitory seizures, other inhibitory seizure symptoms such as speech arrest and aphasia are well documented (11-12-13-14-15-16-17). Terms that have been used to describe ictal paralysis include somatic inhibitory seizures, atonic partial seizures, focal akinetic seizures, hemiparetic seizures, focal inhibitory seizures, ictal paralysis, and non-convulsive seizures paralysis. The agreed definition by Abou-Khalil et al. was inhibitory motor seizure to specifically indicate the motor component (6). However, a limb paralysis is rarely reported as an ictal phenomenon (18), and prolonged limb paralysis has been reported in a few patients with a past history of convulsive epilepsy, but not as the first presentation (6-19). Unlike other partial seizure symptoms which usually last less than 3 min, ictal focal motor inhibition can last relatively longer, often more than 5 min. Although a transient focal motor deficit due to inhibitory seizures is a long-recognized phenomenon, relatively little is known about its pathogenesis. Some of the possible underlying physiological mechanisms of these unusual features are of interest. As regards the physiopathological mechanism of hemiparetic seizures, Penfield and Rasmussen (20) and Penfield and Jasper (21), observed that cortical stimulation may have a negative effect with evidence of paralysis. Sensory symptoms at onset suggest initial or early involvement of the primary sensory cortex, second sensory area, or supplementary sensory cortex (21-29). Luders et al. suggested that the secondary somatosensory area plays an important role in motor integration by supplying direct sensory feedback (22). The clinical manifestations of inhibitory seizures are usually focal or lateralized, and the epileptiform dischargers contralateral centroparietal or centro-temporo-parietal (23-24). Although the exact site of origin of seizures giving rise to focal atonic phenomena has not been well established, electrical stimulation of a retrorolandic supplementary sensorimotor area can cause inhibition of voluntary control (25). Focal seizures may inhibit normal neural function and produce a variety of negative phenomena that are topographically related to the site of ictal activity. Examination of published case reports suggests that seizures with ictal paralysis are exclusively simple partial, however ictal paralysis may be missed in seizures with altered consciousness (6).

The distinction between ictal and postictal paralysis may not always be clear. In patients also experiencing partial
motor seizures, the inhibitory phenomena may be difficult to differentiate from Todd's paralysis. Fisher suggested the following criteria for diagnosis of "non-convulsive seizures paralysis" (7): a) focal paralysis immediately preceding convulsive movements in a limb, b) focal paralysis without a convulsion, identical to deficit after convulsive seizures, c) simultaneous convulsive seizures in one limb and paralysis in another limb, d) occurrence in some paralytic spells of an aura which precedes other epileptic seizures, e) seizure discharge in EEG during an episode of paralysis, f) episodes of paralysis in a clinical setting where seizures are expected (brain tumor) rather than other phenomena, g) control of the episode with anticonvulsants and failure with other treatments, h) absence of other conditions that can account for transient attacks of focal weakness. Hemiplegia (negative motor symptom) were first presentation and constant components of the attacks that occurred in my patients. Diagnosis of ictal paralysis were favored. My patients satisfied several criteria proposed by Fisher: "focal paralysis without a convulsion, identical to deficit after convulsive seizures", "control of the episode with anticonvulsants and failure with other treatment", "absence of other conditions that can account for transient attacks of focal weakness". These are to be differentiated from postictal or Todd's paralysis in view of the fact that the paralysis did not follow convulsive movements.

**Bri I development of inhibitory motor seizures**

In 1827 Bravais in his description of the unilateral seizures also called attention to the paralysis which followed the attack (subsequently called Todd's paralysis), and he used the term "hemiplegia epileptique". In 1855 Todd making no reference to Bravais, described the paralysis as "epileptic hemiplegia" and added the idea that the paralysis is due to exhaustion of the neurons. Robertson in 1869 supported Todd's explanation that the paralysis is due to exhaustion.

Sudden weakness of limb as a seizure manifestation in the absence of "motor convulsion" was first described by Sir William Gowers, in 1881 he objected to the Todd-Robertson hypothesis as the explanation for all cases (26). Gowers referred to several patients who had experienced transient sensorimotor attacks with limb paresis, and he attributed these to lowered activity in motor centers due to inhibition (3). Gowers postulated active inhibition as an alternative mechanism, and he found no relation between the duration or degree of convulsion and the subsequent weakness and argued that a severe weakness that may also exist in a limb after a slight focal seizure is difficult to explain as an effect of exhaustion. In 1916 Higier described an ictal paralytic equivalent of epilepsy, where the paralysis appeared to be part of the epileptic seizure (4).

Wilson (1929) observed a patient during repetitive attacks of transient sensory loss and paresis involving the limbs on the left side (27). Penfield and Erickson (1941) were the first to suggest that an epileptic discharge involving the cortical motor area may produce inhibition or paralysis (28). Penfield and Rasmussen (1950) observed inhibition of voluntary movements of leg and arm upon stimulation of the lower end of the sensorimotor strip just above the fissure of Sylvius (29). Penfield and Jasper (1954) showed stimulation of the supplementary motor area also produces inhibition of voluntary movements (21). Lennox (1960) observed an 11-year-old child who had recurrent transient attacks of right arm paresis in the absence of convulsive movement or headache (30). Periods of muscular inhibition, strictly and only related to a diffuse or focal spike, without preceding myoclonia, were described by Tassinari et al. in 1968 and again by Tassinari in 1981, under the term "spike-related epileptic silent periods" (31-32). The term "negative myoclonus", introduced by Shahami and Young in 1976 extends this definition to any brief, jerky interruption of tonic muscular activity, which causes a sudden postural lapse (33).

Marsden et al. in 1982 speculated that motor cortex activity could provoke muscular contraction as well as inhibition (34). Luders et al. in 1992 demonstrated impaired ability to perform specific voluntary movement or to sustain a voluntary contraction in 17 of 41 individuals undergoing cortical stimulation of the premotor area (35). Negative motor areas have been identified in the lateral aspects of the frontal lobe (primary negative motor area) and in the fronto-mesial regions encompassed in the supplementary motor area (supplementary negative motor) (Luders et al. 1987, 1995; Lim et al. 1994).

In epileptic patients undergoing presurgical evaluation, high frequency (50 Hz) cortical electrical stimulations of negative motor areas through subdural electrodes produced sustained negative motor responses such as motor arrest, inability to perform a voluntary movement or to maintain a voluntary muscular contraction (Penfield and Welch, 1949, 1951; Luders et al. 1987, 1995; Fried et al. 1991; Lim et al., 1994; Hanakawa et al., 2001) (36). Matsumoto et al. in 2000 observed epileptic discharges in the positive arm motor area of the right precentral gyrus and in its rostral area, but not in the negative motor area. They hypothesized epileptic activity probably inhibited...
the spinal motoneuron pool without eliciting excitatory activity in the corticospinal pathway (37). Atonic seizure are currently defined as epileptic attacks characterized by a sudden loss or diminution of muscle tone which may be fragmentary, confined to a segment or massive (38). Atonic seizure is usually seen in patients with generalized epilepsy, and belongs to generalized seizure in the Classification of Epileptic Seizures by the International League Against Epilepsy in 1981 (39).

References

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