neurocritical care society Neurocrit Care (2012) 16:139–144
DOI 10.1007/s12028-011-9624-6

PRACTICAL PEARL

Involuntary Craniofacial Lingual Movements in Intensive Care-Acquired Quadriplegia

A. M. Cartagena · M. Jog · G. B. Young

Published online: 31 August 2011

Abstract
Background The syndrome of involuntary craniofacial lingual movements in the setting of acute intensive care-acquired quadriplegia (critical illness neuromyopathy) following sepsis-associated encephalopathy has not been previously described. We suggest a localization and treatment for this disabling condition.
Methods Three patients (2 female) from our center were quadriplegic from critical illness neuromyopathy when they developed involuntary craniofacial lingual movements following sepsis-associated encephalopathy.
Results Extensive investigations failed to identify an etiology for the abnormal movements. Movements were of large amplitude, of moderate speed, and semi-rhythmic in the jaw, tongue, and palate, persistent and extremely bothersome to all patients. Injection with Botulinum toxin type A was very beneficial.
Conclusions Involuntary craniofacial lingual movements in the setting of flaccid quadriplegia following sepsis-associated encephalopathy are consistent with focal craniofacial brainstem myoclonus and constitutes a new syndrome. Botulinum toxin type A treatment maybe helpful in treatment.

Keywords Myoclonus · Critical illness neuromyopathy · Sepsis · Neurocritical care

Introduction

Abnormal involuntary cranio-facial lingual movements (ICFLM) in the setting of acute ICU-acquired quadriplegia (critical illness neuromyopathy) [1] has not been previously described. We report three patients who developed abnormal movements of their jaw, tongue, and palate following severe sepsis, and multi-organ failure requiring intensive care support. All patients went on to develop flaccid quadriplegia diagnosed as critical illness neuromyopathy (CINM); eventually all patients developed ICFLM. We describe each patient as well as a possible treatment for this debilitating condition.

Case 1

A 50 year-old female was admitted to the ICU after she overdosed on psychiatric medications: quetiapine, hydromorphone, and temazepam. On initial presentation she was found to be hypotensive, febrile, and acidotic. Her initial ICU course was complicated by multi-system organ failure, severe sepsis, and delirium. By her second week in the ICU her metabolic derangements began to clear but her encephalopathy persisted and her speech became unintelligible. It was during this metabolic improvement that both a flaccid quadraparesis and abnormal cranio-facial lingual movements were noted. Electrodiagnostic studies performed 3 weeks after her presentation to hospital showed

Electronic supplementary material The online version of this article (doi:10.1007/s12028-011-9624-6) contains supplementary material, which is available to authorized users.

A. M. Cartagena (✉) · M. Jog · G. B. Young
Department of Clinical Neurological Sciences, Schulich School of Medicine, The University of Western Ontario, 339 Windermere Rd, Rm B7-005, London, ON N6A 5A5, Canada
e-mail: acartage@uwo.ca

M. Jog
NPF Centre of Excellence, Movement Disorders Program, Schulich School of Medicine, The University of Western Ontario, London, ON, Canada

evidence of critical illness myopathy. Her delirium was initially treated with haloperidol; maximum daily dose of 8 mg. Five days after exposure to haloperidol she began to have abnormal face, tongue, and jaw movements (Video 1). Haloperidol was discontinued and her movements did not improve (Summary in Table 1).

Magentic resonance imaging (MRI) was obtained in to diagnose a potential etiology for these movements. Findings were non-diagnostic and felt to be representative of posterior reversible encephalopathy syndrome (PRES) (Fig. 1). These findings later improved (Fig. 2) and no structural lesion was ever identified.

Several weeks later she remained in a persistent quadriparetic state with uncontrollable ICFLM that were very bothersome to her and her family. Various treatments were tried including tetrabenazine, clonazepam, and valproic acid; after lack of success Botulinum toxin A (BoNT A) was injected as a therapeutic agent with marked improvement (Video 2). Several weeks after the initial injection the movements returned.

Case 2

A 46-year-old male was initially admitted to a community hospital for severe pancreatitis secondary to hypertriglyceridemia. He developed multi-system organ failure and rhabdomyolysis with a CK $>$ 250,000 U/l (normal $\leq$ 167 U/l). His condition rapidly deteriorated and he required ventilatory support. While in the intensive care unit (ICU) he had various complications including recurrent gastro-intestinal bleeding, acute renal failure requiring hemodialysis, and a cardiac arrest. By his 11th day in the ICU setting he was noted to have minimal response to pain and poverty of movement. Electromyographic (EMG) testing and nerve conduction studies (NCS) were consistent with critical illness neuropathy/myopathy as the cause for his flaccid quadriplegia. Approximately 4 weeks after his diagnosis of CINM he developed abnormal jaw and tongue movements (ICFLM) (Summary in Table 1).

His movement disorder was treated successfully with BoNT A after therapeutic failure with benzodiazepines. Again, several weeks after his initial injection his ICFLM returned.

Case 3

A 45 year-old female was treated for gram negative sepsis in the ICU. She had a history of breast cancer that had been treated with chemotherapy and surgery. While on chemotherapy she developed febrile neutropenia, septic shock, and acute renal failure. She eventually went into a coma-like state requiring prolonged ventilator support. MRI brain showed abnormal signal in the globus pallidi (Fig. 3). In the midst of her third week in the ICU she eventually regained consciousness but was in a quadriplegic state. She was diagnosed with CINM. It was approximately 2 weeks after her onset of flaccid quadriplegia that a neurologic examination revealed ICFLM (Table 1). After several months the ICFLM persisted and a pseudobulbar affect developed with mood swings of emotional lability involving periods of persistent crying and then of perceived happiness.

No treatment modality was initiated for her abnormal movements.

Discussion

Our three cases share several features: (1) each patient emerged from a septic encephalopathy quadriplegic from CINM when the abnormal movements began—extensive investigations did not identify a cause for their ICFLM; (2) ICFLM were pseudorhythmic, continuous, large amplitude, random, subsided with sleep, and were aggravated by stress and anxiety; (3) ICFLM responded to BoNT A injections. Only Case 1 had brief exposure to a dopamine blocking medication (haloperidol); the movements however, were not typical of and the exposure was too brief to produce tardive phenomena. The hypothesis that these movements may have been caused by a toxin such as an antibiotic was also reviewed. These patients were on various courses of antibiotics and a common one was not identified that fit into the temporal pattern of their ICFLM presentation. Moreover, myoclonus of this severity has not yet been associated with antibiotics.

One case report was identified in the literature as describing a locked-in-state and associated abnormal craniofacial movements [2]. Duffy et al., described a 64 year-old gentleman who developed tetraplegia and mutism after a basilar artery thrombosis. A year after his presentation "synchronous, involuntary movement(s) of soft palate and tongue" were noted. The movements were further described as "incessant" with variable intensity.

ICFLM localizes best to the brainstem and comes closest to being described as segmental myoclonus. The clinical impression of myoclonus is based on the rhythmicity and speed of the movements; furthermore patients were conscious, aware of their surroundings, and had intact eye movements. Neuroanatomically a lesion in the ventral pons or lower brainstem would spare vertical and horizontal ocular movements. An injury to a specific cranial nerve (CN) is not in keeping with this clinical presentation. An injury to CN 7 would not entirely explain the motor involvement of the jaw (CN 5), the tongue (CN 12), and the sternocleidomastoid and trapezius (CN 11). Case 3 also exhibited a type of eye

Table 1 Medical details of cases including their treatment with botulinum toxin A (BoNT A)

	Concurrent illnesses	Neurologic examination	Imaging	Investigations	Treatment with BoNT A
Case 1: 50 year F	Sepsis, multi-system organ failure, delirium CINM	Movements: Persistent "no–no" head movements with intermittent jaw opening and closing. Tongue was protruding. Movements were of large amplitude, chaotic, and involuntary. There was facial diplegia and inability to close the jaw. The ICFLM disappeared during sleep Exam: Responses to yes/no commands were appropriate. Jaw-jerk was pathologically brisk. Extra-ocular movements were full. Tongue was not atrophic. There was flaccid quadriparesis and areflexia with preserved ability to minimally elevate shoulders and perform some finger flexion. Mute plantar reflexes.	MRI brain: initial changes in thalamus and pons consistent with PRES, these changes subsequently resolved on repeat imaging	CSF: protein 2,948 mg/l ($n \leq 400$ mg/l), no cells, repeat samples showed persistently elevated protein CSF electrophoresis revealed IgG elevation 198 mg/l ($n \leq 64$ mg/l) with elevated albumin (1,185 mg/l; $n \leq 300$ mg/l), negative oligoclonal banding EEG: moderate to severe encephalopathy, no seizure activity Muscle biopsy: nonspecific myopathic Specialized pertinent negatives: AntiNR1/Anti-NMDA, ANA, ENA, anti-GM1/GD1a/b, GQ1b, JC virus, HIV antibody, porphyria screen	Total: 400 units Right sternocleidomastoid (80 units) Left splenius capitus (80 units) Lateral pterygoid (50 units/each) Trapezius (50 units/each) Digastrics (10 units/each) Genioglottis (10 units/each)
Case 2: 46 year M	Multi-system organ failure, sepsis, rhabdomyolysis, CINM	Movements: Persistent lateral involuntary movements of face, jaw, and tongue. The ICFLM were rhythmic and wide amplitude and disappeared during sleep. Exam: Patient was alert with purposeful eye movements and consistent yes/no response via eye closure. Horizontal and vertical pursuit was saccadic. There was facial diplegia with inability to close mouth. Gag reflex was absent. Muscle tone was flaccid with wasting, areflexia and mute plantar responses.	MRI brain and full spine unremarkable	CSF: protein 720 mg/l and no nucleated cells CSF electrophoresis not done EEG: no seizures Muscle biopsy: nonspecific myopathic	Total: 90 units Lateral pterygoids (30 units each) Digastrics (10 units each) Tongue (5 units in two sites)
Case 3: 45 year F	Sepsis, febrile neutropenia, multi-system organ failure, CINM	Movements: There were involuntary dyskinetic face, tongue, and neck movements. ICFLM disappeared during sleep. Exam: Patient had conjugate roving eye movements with unrestricted gaze. Eye movements were slow with intermittent saccades, occasional 'reverse ocular dipping'. Preserved oculocephalic reflexes. Patient inconsistently obeyed commands. Flaccid quadriparesis with areflexia.	MRI brain showed abnormal signal in the globlus pallidi, left worse than right.	CSF: protein 1950 mg/l CSF electrophoresis revealed IgG elevation 190 mg/l ($n \leq 64$ mg/l) with elevated albumin (691 mg/l; $n \leq 300$ mg/l), negative oligoclonal banding EEG: no seizures Muscle biopsy: nonspecific myopathic Negative anti-Hu	N/A
Case 4: Late 50's year M	Intra-abdominal sepsis, CINM	Flaccid quadriplegia with constant tongue, jaw and lateral head movements. ICFLM disappeared during sleep.	N/A	N/A	N/A

CINM Critical illness neuro-myopathy, *ICFLM* involuntary craniofacial lingual movements, *MRI* magnetic resonance imaging, *PRES* posterior reversible leukoencephalopathy syndrome, *CSF* cerebrospinal fluid, *EEG* electro-encephalogram

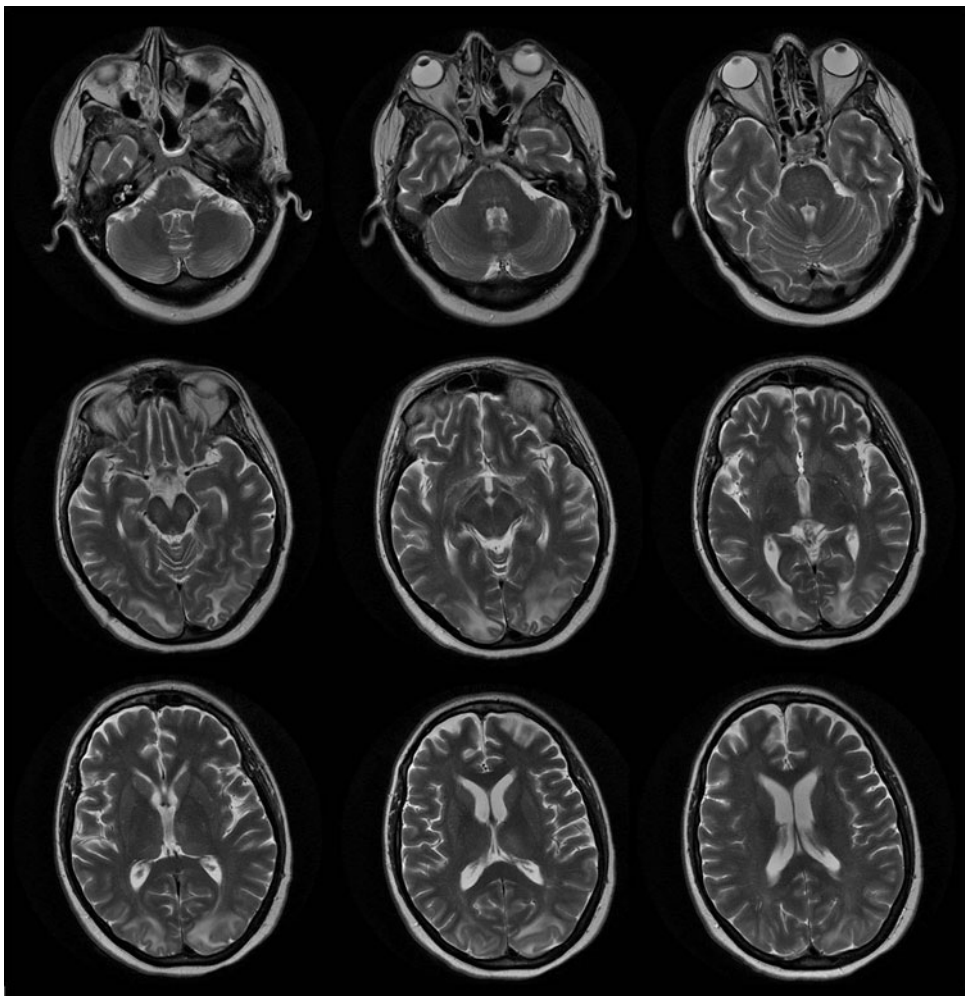

Fig. 1 Case 1—Axial T2 weighted magnetic resonance imaging (MRI). There is subtle T2 hyperintensity in the left thalamus, posterior fossa, cerebral peduncles, basis pontis and pontine tegmentum and in the subcortical white matter of both occipital poles

movement abnormality similar to ocular bobbing which localizes to the pons. Although, another potential neuroanatomic localization for these myoclonic movements could be the basal ganglia or specifically the globus pallidi our group tends to favor the involvement of the pons. The globus pallidi however, has been implicated in myoclonus and palatal tremor and was abnormal in one of our patients (Case 3).

Certainly an argument can be made for movement disorders originating from the pons as this has been well reported in the recent literature [2–7]. Bauer et al. in 1980 [5] initially described involuntary motor phenomenon seen in patients with locked-in-syndrome. These patients were conscious, had vertical gaze spared, and had various inexplicable movements and reactions such as extensor and flexor spasms, mimicking pain and crying reactions, and even screaming. Other motor phenomena noted were whining, moaning, groaning, sighing, and even yawning. In 2000 a case report by Dietrichs et al. [3.], described jaw-opening dystonia secondary to a pontine lesion. Periodic limb movements during sleep following a pontine infarct have also been reported [4]. Furthermore in addition to the report previously mentioned by Duffey et al., Lee et al. [6] describe another patient with involuntary tongue movements following a pontine stroke. The tongue movements were rhythmic periodic contractions involving the whole tongue from side to side with a sideward tongue deviation—these movements also disappeared during sleep.

In summary the movements of ICFLM syndrome may in fact be segmental brainstem myoclonus. In segmental brainstem myoclonus the jerky involuntary muscle contractions occur via contiguous segments of brainstem, and have previously been described in association with brainstem injury [8, 9]. Although, in our patients there was no structural brainstem injury on MRI we hypothesize that an injury likely occurred as a consequence of severe metabolic and septic injury. All patients suffered metabolic compromise and cortical as well as brain stem structures are vulnerable to such compromise.

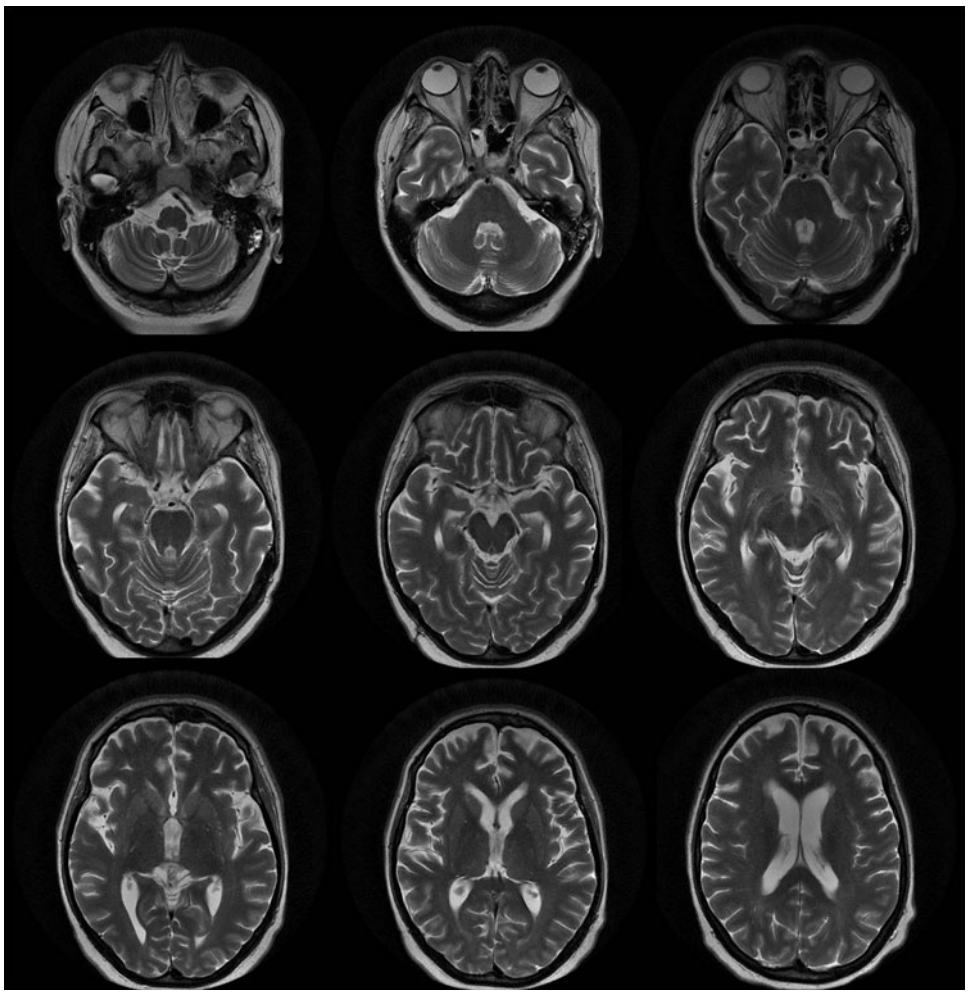

Fig. 2 Case 1—Axial T2 weighted magnetic resonance imaging (MRI). Findings seen on previous MRI are now resolved

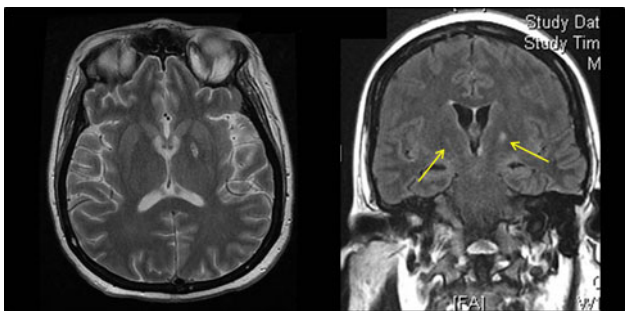

Fig. 3 Case 3—Axial T2 weighted magnetic resonance imaging (MRI) and coronal fluid attenuated inversion recovery (FLAIR). Focal signal change is seen in the globus pallidi; left worse than right (*arrows*)

Sepsis-associated encephalopathy (SAE) is a term used to describe multifocal brain dysfunction as a complication of infection without evidence of direct brain infection [10]. Often patients with SAE will also have critical illness neuromyopathy [10, 11]. The pathophysiology is thought to be from ischemic, excitotoxic or oxidative stress, or activation of apoptotic mechanisms [12]. It is possible that such injury occurred in our patients.

Although, the observed movements were localized to the craniofacial region, quadriplegia may have fictitiously hidden abnormal limb movements.

Conclusion

The development of abnormal involuntary movements after severe critical illness has never been described. We describe a new syndrome that is best characterized as brainstem myoclonus. BoNT A was beneficial in greatly diminishing the speed and amplitude of these movements; its facility of use, and lack of significant metabolic side effects is such that it needs to be considered in treatment of these complex disorders.

References

1. Schweickert WD, Hall J. ICU-acquired weakness. Chest. 2007; 131:1541–9.
2. Duffey P, Jenkins N, King D. Palatal tremor and orofacial stereotypies within the locked-in syndrome. Mov Disord. 2007;22: 593–5.

3. Dietrichs E, Heier MS, Nakstad PH. Jaw-opening dystonia presumably caused by a pontine lesion. Mov Disord. 2000;15:1026–8.
4. Kim JS, Lee SB, Park SK, Han SR, Kim YI, Lee KS. Periodic limb movement during sleep developed after pontine lesion. Mov Disord. 2003;18:1403–5.
5. Bauer G, Gerstenbrand F, Hengl W. Involuntary motor phenomena in the locked-in syndrome. J Neurol. 1980;223:191–8.
6. Lee PH, Yeo SH. Isolated continuous rhythmic involuntary tongue movements following a pontine infarct. Parkinsonism Relat Disord. 2005;11:513–6.
7. Kellett MW, Young GR, Fletcher NA. Painful tonic spasms and pure motor hemiparesis due to lacunar pontine infarct. Mov Disord. 1997;12:1094–6.
8. Cassim F, Houdayer E. Neurophysiology of myoclonus. Neurophysiol Clin. 2006;36:281–91.
9. Yoshikawa H, Takamori M. Benign segmental myoclonus: electrophysiological evidence of transient dysfunction in the brainstem. J Clin Neurosci. 2001;8:54–6.
10. Young GB, Bolton CF, Archibald YM, Austin TW, Wells GA. The electroencephalogram in sepsis-associated encephalopathy. J Clin Neurophysiol. 1992;9:145–52.
11. Jackson AC, Gilbert JJ, Young GB, Bolton CF. The encephalopathy of sepsis. Can J Neurol Sci. 1985;12:303–7.
12. Wilson JX, Young GB. Progress in clinical neurosciences: sepsis-associated encephalopathy: evolving concepts. Can J Neurol Sci. 2003;30:98–105.