Clinical Neurophysiology Practice 3 (2018) 22–23

Contents lists available at ScienceDirect

Clinical Neurophysiology Practice

journal homepage: www.elsevier.com/locate/cnp

Editorial

Differentiating fasciculations from myoclonus in motor neuron disease

Diagnosis in neuromuscular medicine is usually confirmed following careful clinical and electrodiagnostic assessment. Occasionally, the neuromuscular physician encounters clinical phenomenology that may be unexpected, such as the presence of involuntary muscle movements in patients with suspected neuropathy or neuronopathy, which may obfuscate a clear diagnosis. In these situations, neuromuscular ultrasound may be helpful in reaching a diagnosis.

In this issue of Clinical Neurophysiology Practice, Inoue and colleagues report on the ultrasound and surface electromyography (EMG) findings of four patients with motor neuron disease (MND) with abnormal involuntary limb movements (Inoue et al., 2018). In two patients, the movements were "twitches" affecting the fingers of both hands and in the other two patients larger "shock-like" movements, which clinically resembled myoclonus. In all patients, the movements occur in the limb(s) most affected by MND and were brought on or exacerbated by gentle sustained contraction. Ultrasound of the affected muscles demonstrated fasciculations at rest, which became larger and more florid with gentle sustained contraction. The authors reported that these movements were due to fasciculations, which in 2 patients were of large enough amplitude to resemble myoclonus.

Classifying abnormal involuntary movements can be challenging. Myoclonus is a sudden, brief shock-like movement of a joint, the fastest and briefest of all hyperkinetic movement disorders (Blindauer, 2004; Espay and Chen, 2013). Movements are caused either by muscle contraction, or in the case of negative myoclonus, by muscle inhibition (Blindauer, 2004). Fasciculations, on the other hand cause visible twitches of a portion of an individual muscle. As opposed to myoclonus, they are too small to cause movement of a joint, although large distal fasciculations may displace a digit (Ropper et al., 2014).

Fasciculation potentials are generated from the spontaneous depolarization of a single motor axon, or its nerve terminal, with propagation to the remaining arborisation of the motor unit (Layzer, 1994). Therefore, only a small portion of the muscle contracts with any given fasciculation. In MND, hyperexcitability of upper motor neurons may also play a role in generating fasciculations (de Carvalho et al., 2017). Myoclonus involves the contraction or inhibition of a single muscle or group of muscles (Zutt et al., 2015) and can be classified by its anatomical origin into cortical, subcortical, spinal and peripheral subtypes (Blindauer, 2004).

Both myoclonus and fasciculations can be worsened by action. This is particularly seen post-hypoxic cerebral injury (Lance and Adams, 1963; Fahn, 2002), although it can be seen in other forms (Zutt et al., 2015). Fasciculations, although characteristically present at rest, may increase with muscle contraction.

Although fasciculations are a well-established feature of MND, myoclonus is not expected to occur in this condition, at least not in typical sporadic MND. However, segmental spinal myoclonus has been described in a slowly progressive familial form of MND (Alberca et al., 1981). Muscle ultrasound, combined with electrophysiological studies, may be helpful in trying to decipher myoclonus from fasciculations and other movement disorders.

On EMG, fasciculation potentials resemble motor units discharging in an irregular fashion. In myoclonus, EMG reveals short bursts of activity generally 10–50 ms duration and rarely >100 ms (Fahn, 2002; Espay and Chen, 2013). Functional movement disorders may also mimic myoclonus, and it is useful to note that bursts <50 ms are likely to be organic. Electroencephalography (EEG)-EMG back-averaging may reveal an epileptiform discharge just prior to the EMG discharge in the setting of cortical myoclonus (Fahn, 2002).

Muscle ultrasound continues to gain popularity in the neuromuscular realm with an increasing number of indications. It has been used in patients with possible MND to assess for fasciculations and is even more sensitive than EMG in this context (Misawa et al., 2011, Tsuji et al., 2017). As Inoue and colleagues have demonstrated, ultrasound has the advantage of being dynamic, able to assess muscle architecture throughout movement, so that fasciculations are detectable even in a contracted muscle, where they can otherwise be obscured by voluntary EMG activity. The two patients with movements resembling myoclonus had fasciculations in the biceps brachii at rest, which became more florid on ultrasonography with gentle sustained contraction. This finding suggests that fasciculations are likely to be causing the movements, thus distinguishing them from true myoclonus. The other two patients had finger "twitching", worse with gentle voluntary contraction, which also appeared to be associated with an increase in fasciculations from rest to finger extension on ultrasonography. Indeed other authors have noted the difficulty in clinically differentiating finger movement due to florid fasciculations from a form of distal symmetrical myoclonus – termed mini-polymyoclonus – which classically occurs in neurodegenerative disorders (Bhat et al., 2015).

Additional applications of ultrasound in the MND clinic include as an alternative to EMG for the detection of fasciculations in genioglossus, where it is not only less invasive but significantly more sensitive (Misawa et al., 2011). Ultrasound of the tongue during swallowing may indicate upper motor neuron dysfunction

https://doi.org/10.1016/j.cnp.2017.12.001

(Noto et al., 2017). Recent studies have also suggested ultrasonographic differences between MND and multifocal motor neuropathy (MMN), with nerve enlargement seen in the latter (Grimm et al., 2015). MMN can be difficult to distinguish from MND, even electrophysiologically and ultrasound is therefore, a useful adjunct. Diaphragmatic ultrasound can be useful in confirming reduced diaphragmatic movement in the context of MND and other neuromuscular disorders alone, or as an adjunct to diaphragmatic EMG (Simon and Kiernan, 2016). It is likely that in coming years more widespread use of this modality will be adopted amongst neurologists and particularly neurophysiologists as an adjunct to electrophysiology (Simon, 2015).

Overall, Inoue and colleagues remind us of the ever-challenging clinical presentations we see as neurologists and neurophysiologists. Although pattern-recognition is key in all fields of medicine, chameleons exist. These cases are an example of how two complementary methods – electrophysiology and ultrasound – can help decipher the cause of the clinical features present. EMG and related neurophysiological tools give best results when regarded in the context of an extension of the neurological examination. This is of particular importance with regard to MND which largely remains a clinical diagnosis.

Competing interests

Dr. Walker and Dr. Simon have no competing interests.

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Received 25 November 2017

Received in revised form 7 December 2017

Accepted 11 December 2017

Available online 20 December 2017