Reply to J. Dulski and J. Slawek's "Fibrodysplasia ossificans progressiva as a form of pseudodystonia"

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We thank Dr Dulski and Dr Slawek for sharing their fascinating case of pseudodystonia due to fibrodysplasia ossificans progressiva (FOP), a connective tissue disorder characterised by heterotopic ossification in muscles, tendons and ligaments. The patient presented with abnormal neck postures suggestive of cervical dystonia and further developed abnormal trunk and limb postures. Considering imaging evidence of inflammation in the sternocleidomastoid muscles, the abnormal postures were characterised within the spectrum of pseudodystonia rather than dystonia. Surprisingly, botulinum toxin (BT) injections improved the abnormal postures in this patient, possibly by local anti-inflammatory or antinociceptive effect of BT [1]. While we agree this is a probable interpretation, we would like to draw attention to two other possible mechanisms of BT injections responsive abnormal postures in musculoskeletal disorders.

Firstly, there is evidence to suggest that muscle afferents may have a role in producing dystonic movements, as exemplified by work of Kaji et al., who showed that tonic vibration reflex induces dystonic postures in patients with writer's cramp, while local injections of lidocaine into muscles abort dystonia [2]. There is also evidence that changes of afferent input by experimental intervention may affect cortical organisation and excitability [3]. Hence, abnormal afferent input from the muscles affected by a disease or injury may favour aberrant sensorimotor reorganisation in susceptible patients, eventually resulting in dystonia. We have previously described a patient with facioscapulohumeral muscular dystrophy and cervical dystonia responsive to BT injections. We speculated that dystonia could be related to aberrant sensorimotor reorganisation driven by abnormal afferents from the weak muscle rather than the direct consequence of weak muscles and related contractures, thus representing "true" dystonia and not pseudodystonia [4]. Similar mechanism may be involved in some cases of dystonia induced by peripheral trauma, where injury of sensory afferents may trigger changes in the brain network postulated in isolated dystonia.

Secondly, there is now increasing recognition of central nervous system (CNS) involvement in otherwise classical muscle or connective tissue diseases. It was suggested that FOP is not purely a musculoskeletal disorder, but a multisystemic disease that also affects the CNS. This is based on a range of imaging abnormalities observed in some patients, such as demyelination and dentate nucleus hyperintensity [5]. More than half of patients with FOP report chronical neurological symptoms, which could be related to the effects of dysregulated bone morphogenetic protein (BMP) signalling on the nervous system [5].We note that the patient of Dulski and Slawek had a normal brain magnetic resonance imaging scan. However, a contribution of CNS pathology to dystonic manifestations cannot be completely ruled out.

Irrespective of the exact mechanism, the overlap between clinical features and presumed mechanisms of dystonia and pseudodystonia may provide a rationale for expanding our arsenal of therapeutic options in these two groups of disorders.

Conflict of interest

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References

[1] J. Dulski, J. Slawek, Fibrodysplasia ossificans progressiva as a form of pseudodystonia, Park. Relat. Disord. In press (2020).

[2] R. Kaji, J.C. Rothwell, M. Katayama, T. Ikeda, T. Kubori, N. Kohara, T. Mezaki, H.

Shibasaki, J. Kimura, Tonic vibration reflex and muscle afferent block in writer's cramp., Ann. Neurol. 38 (1995) 155–62.

[3] J.P. Brasil-Neto, L.G. Cohen, A. Pascual-Leone, F.K. Jabir, R.T. Wall, M. Hallett, Rapid reversible modulation of human motor outputs after transient deafferentation of the forearm: A study with transcranial magnetic stimulation, Neurology. 42 (1992) 1302–1306.

[4] I. Pareés, M. Kojovic, L. V. Prasad Korlipara, K.P. Bhatia, Cervical dystonia associated with facioscapulohumeral dystrophy: Expanding the clinical spectrum?, Mov. Disord. 26 (2011) 765–766.

[5] J.A. Kitterman, J.B. Strober, L. Kan, D.M. Rocke, A. Cali, J. Peeper, J. Snow, P.L.R. Delai, R. Morhart, R.J. Pignolo, E.M. Shore, F.S. Kaplan, Neurological symptoms in individuals with fibrodysplasia ossificans progressiva, J. Neurol. 259 (2012) 2636–2643.