Clinical Neurophysiology 130 (2019) 1407–1408

Contents lists available at ScienceDirect

Clinical Neurophysiology

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

Editorial

A new diagnostic tool for the detection of steroid myopathy

See Article, pages 1460–1464

Corticosteroid-induced myopathy (hereafter steroid myopathy) is the most common drug-induced myopathy and is a common accompaniment of diseases where corticosteroids are the mainstay of treatment. Steroid myopathy is typically an insidious process that causes proximal muscle weakness, most commonly manifest in the hip girdle musculature. The incidence of steroid myopathy is particularly high in patients receiving prolonged high-dose corticosteroid treatment (greater than the equivalent of 30 mg prednisone per day). Steroid myopathy affects more than 60 % of patients regularly taking 40 mg of prednisone per day (Bowyer et al., 1985). It is more common in patients receiving fluorinated corticosteroids such as dexamethasone, than non-fluorinated corticosteroids such as prednisone. Besides the typical presentation described above, an acute form of steroid myopathy has been reported, with features overlapping critical illness myopathy (Haran et al., 2018).

In terms of pathology, muscle biopsy in steroid myopathy demonstrates type II muscle fiber atrophy, in particular involving fast twitch muscle fibers (type IIB). Typically absent are muscle inflammatory changes and muscle fiber necrosis or regeneration (Danon and Schliselfeld, 2007). The histological changes appear driven by muscle protein catabolism induced by the corticosteroid.

Steroid myopathy typically lacks positive findings on objective investigations. Serum creatine kinase is usually normal. Electromyography (EMG) is commonly performed to assess for typical myopathic motor unit changes. However, motor unit morphology analysis is performed on the earliest recruited motor units, which are typically composed of slow twitch type I muscle fibers. Fast twitch type II muscle fibers form the end of the motor unit recruitment curve (Henneman, 1957; Henneman et al., 1974). As such, EMG is usually normal in patients with steroid myopathy. Indeed, the presence of EMG abnormalities such as fibrillations and myopathic motor unit morphology is more likely to be reflective of an underlying muscle disease than steroid myopathy.

A paper published in this issue of *Clinical Neurophysiology* addresses the lack of diagnostic tests in steroid myopathy (Martucci et al., 2019). Martucci and colleagues evaluated quantitative muscle ultrasound in patients receiving dexamethasone for brain tumors. They identified increased echogenicity (the brightness of muscle in the ultrasound image) in patients receiving dexamethasone relative to healthy control subjects, which correlated with the duration of dexamethasone treatment. Of interest, the maximal change in muscle echogenicity was seen in tibialis anterior, despite this muscle containing a relatively lower proportion of type II fibers than other studied muscles (Johnson et al., 1973). While a specific explanation was not offered, another recent study using quantitative muscle ultrasound in patients with Cushing's Disease identified tibialis anterior as one of three lower limb muscles with the maximal increase in echogenicity (Minetto et al., 2018), suggesting a susceptibility of tibialis anterior to corticosteroid-induced effects beyond the predominant muscle fiber type. In clinical terms, while hip more than shoulder girdle weakness is most common, significant ankle dorsiflexion weakness may be observed in patients with steroid myopathy.

Quantitative muscle ultrasound therefore has the potential to be a useful diagnostic tool for steroid myopathy. However, further study is required to confirm the value of muscle ultrasound in this setting. Specifically, the study by Martucci and colleagues apportioned the observed muscle ultrasound changes to the administration of corticosteroid but did not exclude the confounding influence of neurological weakness. Of relevance, there is increased echogenicity in muscles affected by post-stroke spasticity (Gao et al., 2018), and this may be relevant in patients with brain tumors.

Beyond spasticity, immobility is associated with disuse atrophy of muscles, associated with both type I and II muscle fiber atrophy. Muscle ultrasound in immobilized patients (for example following major trauma) may identify reduced bulk and increased echogenicity (Annetta et al., 2017). Accordingly, a comparison group controlling for confounds of spasticity and immobility should be considered in future studies of muscle ultrasound in steroid myopathy.

Another practical issue is dealing with the patient with inflammatory myopathy being treated with corticosteroid. Worsening proximal muscle weakness in patients receiving high dose corticosteroid for autoimmune inflammatory diseases that may be associated with inflammatory myositis, such as connective tissue disease, are often diagnostic dilemmas. In these situations it may be difficult to distinguish activity of the underlying disease process versus the emergence of drug-induced muscle weakness. Inflammatory myopathy is also associated with increased muscle echogenicity (Reimers et al., 1993). As such, quantitative muscle ultrasound may be more limited in this setting. Comparison of the ultrasound findings in patients with active myositis versus those on high dose steroid treatment is needed to clarify the role of muscle ultrasound in this scenario.

https://doi.org/10.1016/j.clinph.2019.05.019
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Beyond muscle echogenicity, novel ultrasound techniques such as shear-wave elastography (SWE) may provide further clinically relevant information in patients with steroid myopathy. Muscle echogenicity is less reliable than other ultrasound morphometric measurements such as muscle thickness and cross-sectional area due to the variations in echo intensity that occur with small changes in the angle of the ultrasound transducer (Simon et al., 2015). SWE assesses the stiffness of tissues, which is altered by histopathological changes that occur in muscle disease. While not immune to technical issues, muscle SWE demonstrates good reproducibility (Cortez et al., 2016). As such, there may be the potential for SWE to dissect different histopathological muscle changes in myositis and steroid myopathy.

The ability to monitor patients being treated with corticosteroids may enable clinicians to detect evolving changes of steroid myopathy prior to clinically significant weakness. Serial quantitative muscle ultrasound in patients before and during treatment with corticosteroid may provide an opportunity to adjust treatment regimens, such as increasing steroid-sparing immunomodulatory agents to minimize corticosteroid exposure. Such active monitoring is likely to enhance patient care and reduce the complications associated with the use of corticosteroids.

Declaration of Competing Interest

Dr Simon reports no conflicts of interest.

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Accepted 23 May 2019

Available online 30 May 2019