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CORRESPONDENCE

Magnetic resonance imaging characteristics of injection site reactions after long-term subcutaneous delivery of drisapersen

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To the Editor,

We read with interest the report of Hilhorst et al. [1] describing prolonged injection site reactions following subcutaneous injection of drisapersen, an antisense oligonucleotide tested in a number of clinical trials in Duchenne muscular dystrophy (DMD). As part of a large natural history study, ImagingDMD, we have acquired MR images of these areas of sclerosis and lipoatrophy over time and wish to share the progressive subcutaneous changes in signal intensity we observed using several magnetic resonance imaging methods.

MR imaging revealed several attributes of pathology in these images. Chemical shift-encoded imaging, sometimes called Dixon imaging, reveals numerous aspects of pathology (Fig. 1a, b), capturing the lipoatrophy (seen as decreased subcutaneous fat thickness) and fluid accumulation (seen as increased signal on Dixon water maps) as well as markedly decreased fat content within the affected region (seen as areas of decreased signal on Dixon fat maps). This area likely includes both sclerosis and fluid changes. Notably, all these characteristics persist or worsen over time, even several years after cessation of drisapersen administration (Fig. 1c). In keeping with the report of Hilhorst et al., lipoatrophy is particularly striking in the upper extremity (Fig. 1d). Additionally, T_2-weighted MR imaging revealed areas of clear hyperintensity within the subcutaneous fat, which indicate fluid accumulation consistent with inflammation and associated edema (Fig. 1e).

These images provide additional insight into the characteristics of the persistent injection site reactions following drisapersen treatment and demonstrate the ability of MRI to capture multiple aspects of this pathological process. We hope that by sharing them with the community, we can assist in the discussion of the management of this phenomenon and prevention of this effect in future trials of antisense oligonucleotides.

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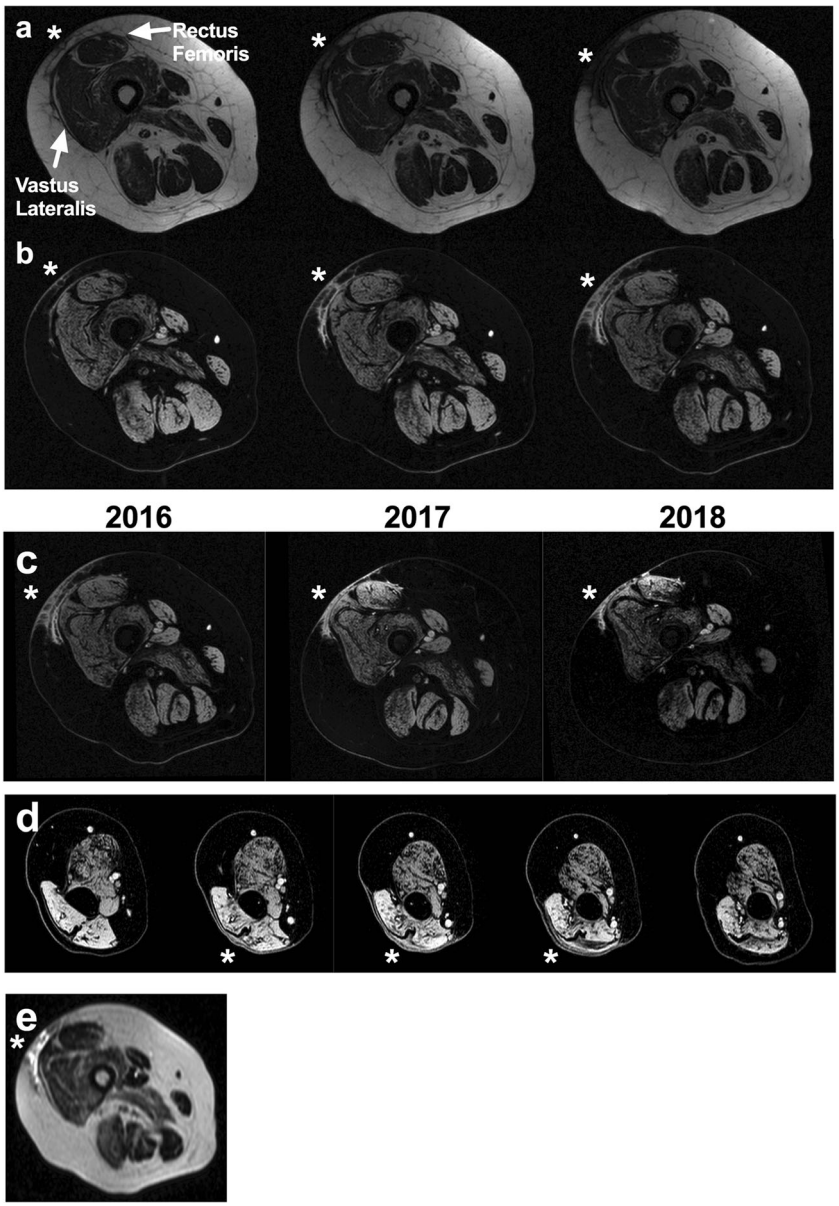

Fig. 1 MR characteristics of lesions in subcutaneous fat. **a** Chemical shift-based fat maps of the thigh (three axial slices separated by ~ 12 mm) showing areas of hypointensity (indicated with an asterisk next to the affected area) in the subcutaneous fat adjacent to the vastus lateralis and rectus femoris muscles, which may be the result of edema, inflammation, or fibrosis. **b** Chemical shift-based water maps from the same locations as **a**, showing marked hyperintensity in the area of the lesion in subcutaneous fat (*). **c** Over time, the inflammation or edema in the subcutaneous fat persists, while the lipoatrophy (*) progresses. Note that drisapersen administration was halted between the first and second visit, but the lesion continues to worsen over time. **d** Axial chemical shift-based water maps covering ~ 5.5 cm of the upper arm of a treated patient ~ 2.5 years after cessation of treatment and showing the pronounced lipoatrophy (*) over the triceps brachii muscle affecting an area 5–7 cm in diameter. **e** T_2 changes in the subcutaneous fat indicative of inflammation or edema can be easily seen using T_2-weighted imaging (indicated with an asterisk next to the affected area). This image was taken prior to the cessation of administration of drisapersen

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Abbreviations DMD, Duchenne muscular dystrophy

Reference

1. Hilhorst N, Spanoudi-Kitrimi I, Goemans N, Morren MA (2018) Injection site reactions after long-term subcutaneous delivery of drisapersen: a retrospective study. Eur J Pediatr