SHORT COMMUNICATION

Diagnostic value of additional histopathological fascia examination in idiopathic inflammatory myopathies

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Background and purpose: Correct diagnosis of idiopathic inflammatory myopathies (IIM) may prevent harm from both lack of treatment in IIM patients and unnecessary treatment in non-IIM patients. However, it is unknown whether additional histopathological fascia examination may contribute to diagnosing IIM.

Methods: Thirty-two magnetic resonance imaging guided *en bloc* biopsies from patients diagnosed with IIM (except inclusion body myositis) from 2010 to 2017 were reviewed: dermatomyositis (DM) (n = 6), non-specific/overlap myositis (NM/OM) (n = 11), immune-mediated necrotizing myopathy (n = 12) and anti-synthetase syndrome (n = 3). Muscle biopsy specimens were examined according to the 2004 European Neuromuscular Centre (ENMC) criteria. Fascia was subsequently examined for the presence of lymphocytic infiltrates. Isolated fascia involvement was defined as the presence of lymphocytic infiltrates in the fascia/epimysium on histopathology in the absence of any ENMC muscle histopathology/immunohistochemistry criteria.

Results: One patient with DM (17%) and one patient with NM/OM (9%) had isolated fascia involvement. One patient with immune-mediated necrotizing myopathy (8%) and one patient with anti-synthetase syndrome (33%) had fascia involvement, albeit in combination with muscle involvement.

Conclusion: Histopathological fascia examination may contribute to early diagnosis of DM and NM/OM in a small proportion of patients.

Introduction

Correct diagnosis of idiopathic inflammatory myopathy (IIM) may prevent harm from both lack of treatment in IIM patients and unnecessary treatment in non-IIM patients. [1]. However, correctly diagnosing a patient with IIM can be complicated and, except for patients with dermatomyositis (DM) with classic skin features, a multimodality diagnostic evaluation is needed. Muscle biopsy is still considered as the gold standard in these cases [2]. However, muscle biopsy can be falsely negative in 10%–20%, even when using muscle imaging to guide the biopsy [3,4]. Recent reports have suggested that fascia imaging has additional value in the early diagnosis of DM [5,6]. However, it is unknown whether histopathological fascia examination might contribute to the diagnosis of IIM. Therefore, this explorative retrospective analysis was conducted to assess whether histopathological fascia examination increases sensitivity of *en bloc* biopsy in patients with IIM except inclusion body myositis.

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Patients and methods

Thirty-two consecutive muscle *en bloc* biopsies (skin, fascia and muscle) from patients diagnosed with IIM (except inclusion body myositis) in a single neuromuscular referral centre from 2010 to 2017 based on the

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2004 European Neuromuscular Centre (ENMC) criteria were retrospectively reviewed [7]. Tissue was obtained and used in accordance with the Declaration of Helsinki and the Academic Medical Centre (AMC) Research Code provided by the AMC Medical Ethics Committee and AMC Pathology Biobank.

Muscle involvement was defined in accordance with the 2004 ENMC criteria [7] and fascia involvement was defined as the presence of lymphocytic infiltrates in the fascia and/or epimysium. Isolated fascia was defined as the presence of lymphocytic infiltrates in the fascia and/or epimysium in the absence of any ENMC muscle biopsy criteria. Results were analysed using simple descriptive statistics.

Results

Patients were diagnosed with DM (n = 6), non-specific myositis/overlap myositis (NM/OM) (n = 11), immune-mediated necrotizing myopathy (IMNM) (n = 12) and anti-synthetase syndrome (ASS) (n = 3). Three patients underwent *en bloc* biopsy after already being treated with either low dose corticosteroids or other immunosuppressants because of concomitant connective tissue disease (n = 2) or a previously suspected diagnosis of polymyalgia rheumatica (n = 1).

Fascia involvement was seen in three patients with DM (50%), five patients with NM/OM (45%), one patient with IMNM (8%) and one patient with ASS (33%) (Table 1). One patient (13%) with DM (patient A; Fig. 1) and one patient (9%) with NM/OM (patient B) had isolated fascia involvement. Both patients were treatment naïve at the time of magnetic resonance imaging (MRI) guided muscle biopsy and had muscle biopsy specimens of good quality in which minor abnormalities on histopathology/immunohistochemistry, i.e. muscle fibre size variation and focal muscle fibre necrosis, focal major histocompatibility complex class 1 overexpression, focal sarcolemmal complement deposition, not specific for IIM were found (Table 1; Fig. 1). However, on additional electron microscopy in the patient with DM and isolated fasciitis, tubulo-reticular inclusions were seen. None of the patients with IMNM or ASS had isolated fascia involvement.

Table 1 Muscle and fascia involvement in 54 patients diagnosed with idiopathic inflammatory myopathies

	Fascia involvement	Muscle involvement	Isolated fascia involvement
DM (n = 6)	3 (50%)	5 (83%)	1 (17%)
NM/OM (n = 11)	5 (45%)	15 (91%)	1 (9%)
IMNM (n = 12)	1 (8%)	12 (100%)	0 (0%)
ASS (n = 3)	1 (33%)	3 (100%)	0 (0%)

Numbers of cases are shown with percentages in parentheses. Isolated fascia was defined as the presence of cellular infiltrates in the fascia and/or epimysium in the absence of any 2004 European Neuromuscular Centre muscle biopsy criteria.

ASS, anti-synthetase syndrome; DM, dermatomyositis; IMNM, immune-mediated necrotizing myopathy; NM/OM, non-specific myositis/overlap myositis.

Discussion

The presence of isolated histopathological fascia involvement in 32 MRI guided *en bloc* biopsies was explored and isolated fascia involvement was found on histopathology/immunohistochemistry in single cases with DM and NM/OM but not in patients with IMNM and ASS.

Our findings support previous reports that fascia examination may have additional value in (early) diagnosis of DM [5,6]. Furthermore, case B suggests that fascia examination has additional value in the diagnosis of NM/OM too. Previous studies reported comparable histopathological features such as

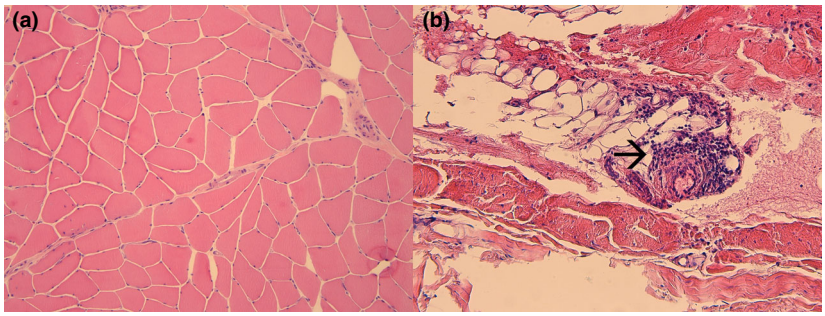

Figure 1 Haematoxylin and eosin stain of the muscle (a) and fascia (b) of patient A. No specific signs of disease involvement are seen on histopathological (a) or immunohistochemistry (data not shown) examination of the quadriceps femoris muscle of a patient with dermatomyositis. In contrast, lymphocytic cellular infiltrates – consistent with fasciitis – are seen on histopathological examination of the fascia ((b), black arrow). [Colour figure can be viewed at wileyonlinelibrary.com]

perivascular/perimysial cellular infiltrates on muscle biopsy in patients with DM and NM/OM [8]. These findings stress the importance of additional histopathological characterization of NM/OM, which may provide insight to possible overlap and/or differences between DM and NM/OM.

Currently, muscle biopsy remains the gold standard for diagnosing myositis except for patients with DM with classic skin features. Needle muscle biopsy is widely used for acquiring biopsy specimens as its diagnostic accuracy seems comparable to that of the more invasive *en bloc* biopsy [3]. However, *en bloc* biopsy allows for additional histopathological examination of the fascia. As such, *en bloc* biopsy may have additional value in patients with suspected IIM and a negative needle muscle biopsy.

The main limitations of our study are the small numbers of different subtypes of IIM, and the retrospective nature of the study. A small proportion of patients were not treatment naïve, which could have influenced fascia and muscle involvement at examination. In conclusion, our findings indicate that histopathological fascia examination may contribute to reaching a diagnosis in a small subset of patients with DM and NM/OM. Future multicentre studies should preferably focus on the additional value of *en bloc* biopsy in patients with negative needle biopsy.

Disclosure of conflict of interest

Dr J. Lim, Dr J. Raaphorst and Dr E. Aronica have nothing to disclose. Dr F. Eftimov has no disclosures related to myositis or to this work. Dr Anneke J. van der Kooi reports grants from CSL Behring, outside the submitted work.

Approval

Approval from our institutional Review Board was not required in accordance with the local research code provided by the ethics committee and national legislation: namely, (1) the research subject is not physically involved in the research, (2) the data being researched are also not being gathered for the sake of the research, (3) the research subjects do not have to change their behaviour for the sake of the research.

Consent

Informed consent from the patients was not required in accordance with the local research code provided by the ethics committee and national legislation, namely the data were not gathered for the sake of the research (also see our comment with regard to confirmation of study approval).

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