Letters to the Editors

Utility of lower extremity magnetic resonance imaging followed by muscle biopsy for myeloperoxidase-antineutrophil cytoplasmic antibodies positive antineutrophil cytoplasmic antibody-associated vasculitis: a single-centre study

Sirs,

Early diagnosis of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is important because, without prompt treatment, it can often be life-threatening or result in permanent organ damage. Histopathological confirmation of vasculitis is required to diagnose systemic vasculitis with confidence. However, a renal biopsy is not indicated for patients with certain conditions, such as bleeding diathesis. By contrast, a muscle biopsy is a relatively simple and safe procedure. Previous reports showed variable sensitivity (50–70%) of a muscle biopsy for vasculitis diagnosis (1, 2).

We conducted a retrospective chart review of all incident inpatient cases of myeloperoxidase (MPO)-ANCA-positive AAV from 2013 to 2021 at Saiseikai Nakatsu Hospital. The diagnosis of MPO-ANCA-positive AAV was made by a rheumatologist according to the 2012 International Chapel Hill Consensus Conference nomenclature (3). A positive Magnetic resonance imaging (MRI) finding was defined by the presence of increased signal in non-contrast short tau inversion recovery sequences within all muscle groups of the thighs and calves. Muscle biopsy samples were obtained from the area of increased signal in MRI. A positive muscle biopsy was defined by the presence of necrotising vasculitis or non-necrotising vasculitis in haematoxylin and eosin stain. Sensitivity of muscle biopsy was calculated by the number of patients who had positive muscle biopsies divided by the number of patients who were diagnosed with MPO-ANCA-positive AAV. The institutional review board of Saiseikai Nakatsu hospital approved this analysis (2021-66).

There were 50 individual patients who were diagnosed with MPO-ANCA-positive AAV. Thirty-nine of the 50 total patients (78%) underwent lower extremity (LE) MRI, and 33 (66%) underwent muscle biopsy. There were 32 patients (64%) who underwent both LE MRI and muscle biopsy (Table I). Patients in the negative biopsy were older (p=0.05) and had lower serum CRP (p=0.04) than those in the positive biopsy. Of 32 patients, the muscle biopsy demonstrated vasculitis in 28 patients, with 87.5% sensitivity (28/32; 95% confidence interval 71–96).

In this single centre analysis, the muscle biopsy demonstrated high sensitivity for MPO-ANCA-positive AAV. Our results suggest LE MRI may be considered in patients with suspected MPO-ANCA-positive AAV to indicate muscle biopsy for those whose MRI is abnormal. The reason for better sensitivity of the muscle biopsy compared with previous reports may be due to the fact that majority of our patients who underwent LE MRI had abnormal MRI findings, suggesting muscle involvements were relatively common in our patients.

Previous reports described muscle symptoms without other organ system involvement as a relatively rare presentation in AAV, leading to a significant delay in the diagnosis (4, 5). However, in this cohort, a significant number of patients had abnormal MRI findings suggestive of muscle oedema, with vasculitis confirmed by biopsy, indicating muscle involvement is not uncommon in MPO-ANCA-positive AAV. If patients have nonspecific symptoms such as fever and malaise as well as possible early signs of organ damage along with positive MPO-ANCA, muscle involvement due to vasculitis may be considered. A LE MRI scan early in the course of disease may be considered for cases without involvement of other organs, as well as for targeting muscle biopsy when required.

Most patients underwent LE MRI prior to a muscle biopsy, and the majority of the patients had abnormal MRI findings suggestive of muscle oedema. Therefore, our sensitivity result for muscle biopsy may not be applicable for those who did not undergo LE MRI or whose MRI results were normal. In conclusion, LE MRI followed by the muscle biopsy demonstrated high sensitivity for MPO-ANCA-positive AAV. Our results suggest lower extremity MRI may be considered in patients with suspected MPO-ANCA-positive AAV to indicate muscle biopsy for those whose MRI is abnormal.

Table I. Baseline demographic and clinical characteristics of 32 patients who underwent both LE MRI and muscle biopsy.

Characteristic	Positive biopsy (n=28)	Negative biopsy (n=4)	p-value
Age, average years (IQR)	73 (67-80)	82 (76-88)	0.05
Female sex, n (%)	20 (71%)	3 (75%)	1.00
MPO-ANCA positive	28 (100%)	4 (100%)	1.00
Myalgia or muscle weakness	12 (43%)	1 (25%)	0.63
Muscle tenderness on exam	18 (64%)	3 (75%)	1.00
Constitutional symptoms with no clear focus	6 (21%)	2 (50%)	0.25
Nephritis	7 (25%)	1 (25%)	1.00
Lung involvement	7 (25%)	0 (0%)	0.55
Peripheral neuropathy	13 (46%)	1 (25%)	0.61
*Other organ involvements	12 (43%)	1 (25%)	0.63
Muscle biopsy performed	28 (100%)	4 (100%)	1.00
Kidney biopsy performed	1 (4%)	0 (0%)	1.00
Skin biopsy performed	2 (7%)	0 (0%)	1.00
Positive MRI findings	25 (89%)	4 (100%)	1.00
Serum CRP (mg/dL), median (IQR)	12.3 (9.7-16.7)	7.2 (5.5-9.5)	0.04
Serum creatinine kinase (U/L), median (IQR)	22 (13-34)	29 (16-62)	0.53

*Other organ involvements in the positive biopsy group included skin (n=3), ear, nose, and throat (n=2), joint (n=3), brain (n=2), and sclera (n=1).
Positive muscle biopsy is defined as presence of necrotising vasculitis or non-necrotising vasculitis. Positive MRI findings are defined as presence of muscle oedema.
ANCA: antineutrophil cytoplasmic antibody; CRP: C-reactive protein; LE: lower extremity; MPO: myeloperoxidase; MRI: magnetic resonance imaging.

S. Jinno[1,2], *MD, MSc*
P.A. Monach[3], *MD, PhD*
T. Nakazawa[1], *MD, PhD*

[1]Department of Rheumatology, Osaka Saiseikai Nakatsu Hospital, Osaka; [2]Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe, Japan; [3]VA Boston Healthcare System, Boston, MA, USA.

Please address correspondence to:
Sadao Jinno
Department of Rheumatology, Osaka Saiseikai Nakatsu Hospital, 2-10-39 Shibata, Kita-ku, Osaka 530-0012, Japan.
E-mail: sadaoj@gmail.com

Competing interests: none declared.

References

1. HERVIER B, DURANT C, MASSEAU A, PONGE T, HAMIDOU M, MUSSINI JM: Use of muscle biopsies for diagnosis of systemic vasculitides. *J Rheumatol* 2011; 38: 470-4. https://doi.org/10.3899/jrheum.100390
2. NUNOKAWA T, YOKOGAWA N, SHIMADA K, ENATSU K, SUGII S: The use of muscle biopsy in the diagnosis of systemic vasculitis affecting small to medium-sized vessels: a prospective evaluation in Japan. *Scand J Rheumatol* 2016; 45: 210-4. https://doi.org/10.3109/03009742.2015.1086431
3. JENNETTE JC, FALK RJ, BACON PA *et al*.: 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum* 2013; 65: 1-11. https://doi.org/10.1002/art.37715
4. NAGIAH S, SARANAPALA DMM: Severe proximal muscle weakness with normal CK as a presenting feature of ANCA-associated vasculitis. *BMJ Case Rep* 2020; 13: 10.1136/bcr-2019. https://doi.org/10.1136/bcr-2019-232854
5. OJIMA Y, SAWADA K, FUJII H *et al*.: Anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV) restricted to the limbs. *Intern Med* 2018; 57: 1301-8. https://doi.org/10.2169/internalmedicine.9848-17