JCN Open Access LETTER TO THE EDITOR

pISSN 1738-6586 / eISSN 2005-5013 / J Clin Neurol 2020;16(3):510-512 / https://doi.org/10.3988/jcn.2020.16.3.510

Rimmed Vacuoles in Myositis Associated with Antimitochondrial Antibody

Rui Shimazaki[a]
Akinori Uruha[a,b]
Hideki Kimura[a]
Utako Nagaoka[a]
Tomoya Kawazoe[a]
Satoshi Yamashita[c]
Takashi Komori[d]
Kazuhito Miyamoto[a]
Shiro Matsubara[a]
Keizo Sugaya[a]
Masahiro Nagao[a]
Eiji Isozaki[a]

[a]Departments of Neurology and [d]Laboratory Medicine and Pathology (Neuropathology), Tokyo Metropolitan Neurological Hospital, Tokyo, Japan
[b]Department of Neuropathology, Charité-Universitätsmedizin, Berlin, Germany
[c]Department of Neurology, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan

Dear Editor,

Myositis associated with antimitochondrial antibodies (AMAs) is characterized by proximal and axial muscle weakness and cardiac involvement.[1-4] The muscle pathology most commonly manifests as necrotizing myopathy with a variable extent of inflammatory cell infiltrates. Granulomatous inflammation has been observed in 25% of myositis patients.[1] However, the underlying pathomechanism remains poorly understood. Here we describe a patient with myositis associated with AMA characterized by the presence of rimmed vacuoles (RV) in the biopsied muscle, suggesting the involvement of a degenerative process.

A 73-year-old Japanese male presented with a 1-year history of gradual progressive dropped head. The initial examination revealed atrophic cervical paraspinal muscles and that the patient could not lift his head. Manual muscle testing revealed weaknesses of Medical Research Council grades 2 and 4– in the neck extensor muscle and proximal upper-limbs muscles, respectively. Laboratory testing revealed that the serum creatine kinase level was elevated to 1,075 U/L (normal range 30–150 U/L). A fluorescent antibody method revealed positivity for AMA-M2, but negativity for other myositis-specific/associated autoantibodies including antisynthetase, anti-Mi-2, antisignal recognition particle, anti-3-hydroxy-3-methylglutaryl-CoA reductase, anti-PM/Scl, and anti-Ku antibodies. The patient was also negative for anticytosolic 5'-nucleotidase 1A antibodies, which are detected in some patients with inclusion-body myositis.[5] Magnetic resonance imaging revealed edematous changes in his left biceps brachii and cervical paraspinal muscles as well as fat replacement in the soleus muscles and semimembranosus muscles. Electromyography showed myopathic changes with abundant fibrillation and positive sharp waves, while electrocardiography and echocardiography did not reveal any abnormalities.

A histological examination of the left deltoid muscle showed abnormal variations in the myofiber diameters (Fig. 1), with some necrotic and many regenerating fibers. Mononuclear cell infiltration was seen in the endomysium and perimysium, predominantly comprising CD68-positive cells and without CD8-positive cells surrounding or invading nonnecrotic fibers. Granulomatous lesions were not observed. There was no overexpression of major histocompatibility complex class 1 in myofibers or sarcolemmal deposition of membrane attack complex (C5b-9 complements). Several fibers with RV were observed. TDP-43-positive granular aggregates were present in the sarcoplasm of some myofibers, although p62-positive aggregates were not clearly evident.

The patient was started on treatment with intravenous methylprednisolone at 1,000 mg per day for 3 days, followed by the oral intake of prednisolone at 30 mg per day (0.5 mg/kg body weight). This treatment improved the muscle strength in the four limbs to almost normal, and eventually the head drop disappeared. The serum creatine kinase level also normalized. Tapering of corticosteroid was successful to date, with the patient taking 15 mg of prednisolone daily at 6 months after discharge without any sign of recurrence.

Received April 14, 2020
Revised May 6, 2020
Accepted May 8, 2020

Correspondence
Rui Shimazaki, MD
Department of Neurology, Tokyo Metropolitan Neurological Hospital, 2-6-1 Musashidai, Fuchu, Tokyo 183-0042, Japan
Tel +81-42 323 5110
Fax +81-42 322 6219
E-mail rui_shimazaki@tmhp.jp

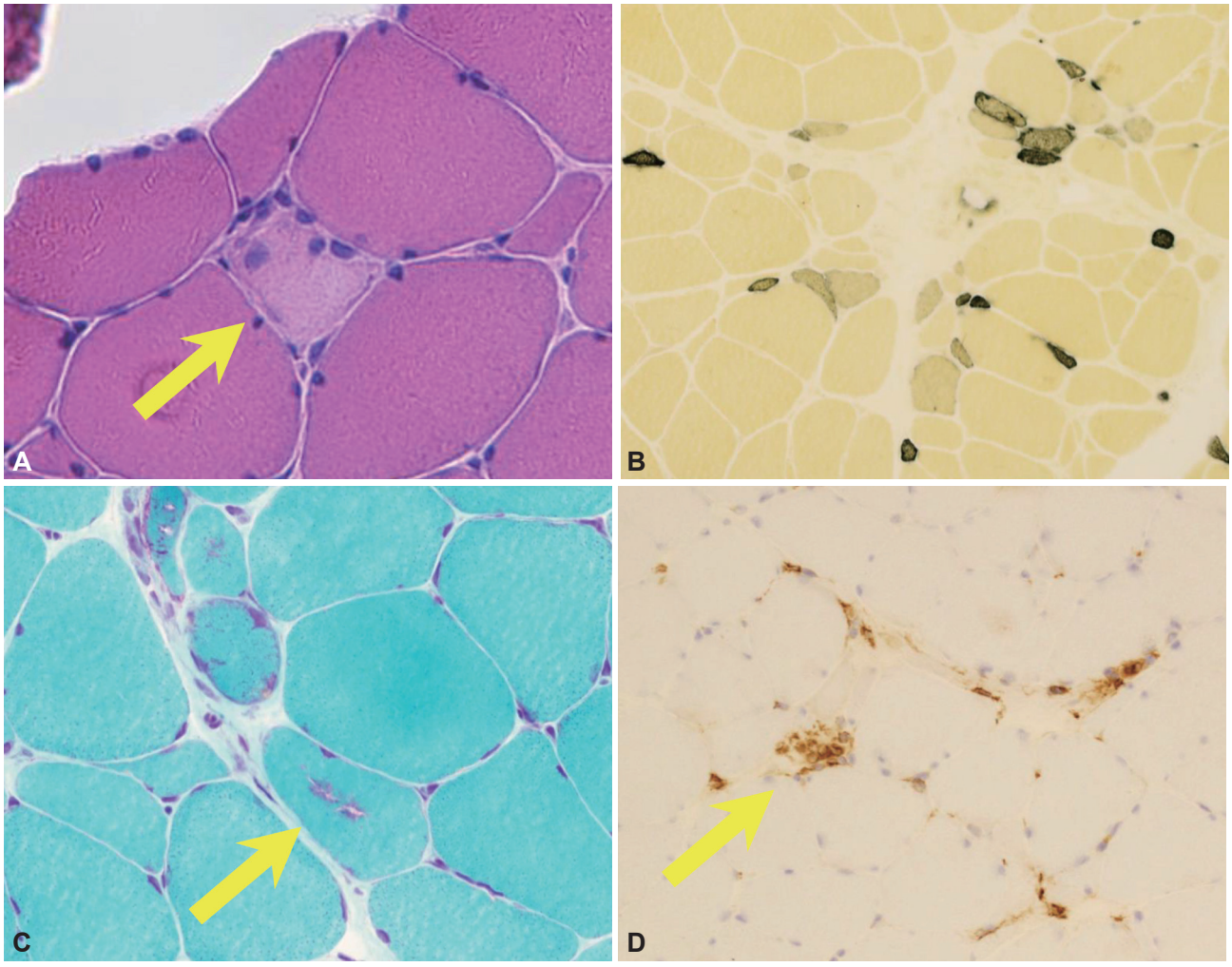

Fig. 1. Pathological findings in a left deltoid muscle biopsy. A: A necrotic fiber with hematoxylin and eosin staining (arrow). B: Numerous myofibers with elevated alkaline phosphatase activity, which is suggestive of the early stage of regeneration. Alkaline phosphatase staining. C: Rimmed vacuoles in myofibers with modified Gömöri trichrome staining (arrow). D: CD68-positive cells are scattered in the endomysium. The arrow indicates myophagocytosis. Immunohistochemistry for CD68. Original magnification: ×200 in A, B, and D and ×400 in C.

The muscle pathology in this patient featured the presence of RV. Previous studies of myositis associated with AMA have not revealed RV or other related findings.[1-4] Among idiopathic inflammatory myopathies, inclusion-body myositis commonly shows RV, but several other features in the present patient made this diagnosis less likely, including the lack of the characteristic distribution of muscle involvement (finger flexor and quadriceps muscles), no endomysial inflammatory cell infiltration surrounding or invading nonnecrotic muscle fibers, and the clearly favorable response to corticosteroid therapy. The pathogenesis of RV has been considered to be associated with the disruption of autophagy and the ubiquitin-proteasome system.[6-8] The presence of the vacuolar change suggests that myositis associated with AMA has not only autoimmune but also degenerative features. Further studies are needed to confirm the involvement of degenerative processes, which will lead to a better understanding of the underlying pathomechanism.

Author Contributions

Conceptualization: Rui Shimazaki, Akinori Uruha. Investigation: Rui Shimazaki, Akinori Uruha, Hideki Kimura, Utako Nagaoka, Tomoya Kawazoe, Satoshi Yamashita, Kazuhito Miyamoto, Shiro Matsubara. Supervision: Kazuhito Miyamoto, Shiro Matsubara, Takashi Komori, Keizo Sugaya, Masahiro Nagao, Eiji Isozaki. Visualization: Rui Shimazaki, Akinori Uruha. Writing—original draft: Rui Shimazaki, Akinori Uruha. Writing—review & editing: Hideki Kimura, Utako Nagaoka, Tomoya Kawazoe, Satoshi Yamashita, Takashi Komori, Kazuhito Miyamoto, Shiro Matsubara, Keizo Sugaya, Masahiro Nagao, Eiji Isozaki.

ORCID iDs

Rui Shimazaki https://orcid.org/0000-0001-6870-2840
Akinori Uruha https://orcid.org/0000-0002-4758-183X
Hideki Kimura https://orcid.org/0000-0002-3158-6265
Utako Nagaoka https://orcid.org/0000-0001-9296-4779

Tomoya Kawazoe https://orcid.org/0000-0002-0227-2566
Satoshi Yamashita https://orcid.org/0000-0001-9315-3492
Takashi Komori https://orcid.org/0000-0002-6812-2149
Shiro Matsubara https://orcid.org/0000-0002-1003-0540
Keizo Sugaya https://orcid.org/0000-0002-6334-1289
Masahiro Nagao https://orcid.org/0000-0001-6379-0554
Eiji Isozaki https://orcid.org/0000-0003-0166-2041

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Acknowledgements

The authors thank Mina Hiraishi in Tokyo Metropolitan Neurological Hospital for her excellent technical assistance.

REFERENCES

1. Maeda MH, Tsuji S, Shimizu J. Inflammatory myopathies associated with anti-mitochondrial antibodies. *Brain* 2012;135:1767-1777.
2. Uenaka T, Kowa H, Ohtsuka Y, Seki T, Sekiguchi K, Kanda F, et al. Less limb muscle involvement in myositis patients with anti-mitochondrial antibodies. *Eur Neurol* 2017;78:290-295.
3. Hou Y, Liu M, Luo YB, Sun Y, Shao K, Dai T, et al. Idiopathic inflammatory myopathies with anti-mitochondrial antibodies: clinical features and treatment outcomes in a Chinese cohort. *Neuromuscul Disord* 2019;29:5-13.
4. Tanboon J, Nishino I. Classification of idiopathic inflammatory myopathies: pathology perspectives. *Curr Opin Neurol* 2019;32:704-714.
5. Yamashita S, Tawara N. Determination of cN1A autoantibodies by cell-based immunofluorescence cytochemistry. *Methods Mol Biol* 2019;1901:89-94.
6. Badadani M, Nalbandian A, Watts GD, Vesa J, Kitazawa M, Su H, et al. VCP associated inclusion body myopathy and paget disease of bone knock-in mouse model exhibits tissue pathology typical of human disease. *PLoS One* 2010;5:e13183.
7. Nogalska A, D'Agostino C, Terracciano C, Engel WK, Askanas V. Impaired autophagy in sporadic inclusion-body myositis and in endoplasmic reticulum stress-provoked cultured human muscle fibers. *Am J Pathol* 2010;177:1377-1387.
8. Murata-Shinozaki Y, Takahashi T, Matsubara T, Maruyama H, Izumi Y, Matsumoto M. The origins of rimmed vacuoles and granulovacuolar degeneration bodies are associated with the Wnt signaling pathway. *Neurosci Lett* 2017;638:55-59.