Received: 31 August 2023 | Revised: 27 September 2023 | Accepted: 27 September 2023

DOI: 10.1002/cia2.12334

Journal of Cutaneous Immunology and Allergy

WILEY

CASE STUDY

Early improvement of nailfold videocapillaroscopy abnormalities in dermatomyositis patients with anti-NXP-2 antibody

Naoki Mugii PhD[1] | Yasuhito Hamaguchi MD, PhD[2] | Natsumi Fushida MD[2] | Motoki Horii MD, PhD[2] | Tasuku Kitano MD[2] | Ko Fujii MD[2] | Kaori Sawada MD, PhD[2] | Kyosuke Oishi MD, PhD[2] | Shintaro Maeda MD, PhD[2] | Takashi Matsushita MD, PhD[2]

[1]Department of Rehabilitation, Kanazawa University Hospital, Kanazawa, Japan

[2]Department of Dermatology, Faculty of Medicine, Institute of Medical, Pharmaceutical, and Health Sciences, Kanazawa University, Kanazawa, Japan

Correspondence
Yasuhito Hamaguchi, Department of Dermatology, Faculty of Medicine, Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University, 13-1 Takaramachi, Kanazawa, Ishikawa 920-8641, Japan.
Email: yasuhito@med.kanazawa-u.ac.jp

Abstract

This study aimed to evaluate long-term changes in nailfold videocapillaroscopy (NVC) findings in dermatomyositis patients with antinuclear matrix protein 2 (NXP-2) antibody (Ab). All four patients with anti-NXP-2 Ab presented irregularly enlarged and reduced capillaries and hemorrhages at the initial assessment. After disease stabilization, irregularly enlarged capillaries and hemorrhages disappeared within the mean observation period of 6 months. These early improvements were not observed in patients with anti-TIF1 Ab. The results of this study show that long-term changes in NVC findings should be assessed using myositis-specific Ab information.

KEYWORDS
anti-NXP-2 Ab, dermatomyositis, nailfold capillary changes

1 | INTRODUCTION

Nailfold videocapillaroscopy (NVC) abnormalities are one hallmark of microangiopathy in idiopathic inflammatory myopathy (IIM), including dermatomyositis (DM). The clinical utility of NVC has been established through examination of the correlation between NVC findings and disease status in systemic sclerosis.[1] Based on these findings, NVC has recently been employed in IIM.[2,3]

Various myositis-specific autoantibodies (MSAs) are detected in patients with IIM, and each MSA is closely linked to characteristic clinical presentation.[4] NVC findings for IIM were initially evaluated as one group of IIM.[2] However, subsequent studies investigated NVC findings for each MSA and demonstrated that NVC findings differed by MSA. We reported that the longitudinal changes in NVC findings varied among patients with anti-ARS, anti-TIF1, and anti-MDA5 Abs.[5]

Anti-NXP2 Ab was first reported as anti-MJ Ab associated with juvenile DM.[6] In juvenile DM, around 20% of cases are positive for anti-NXP2 Ab, whereas, in adult DM, the prevalence is only 1.6%. Adult-onset DM cases with anti-NXP-2 Ab are characterized by muscle weakness and skin eruptions. Additionally, 29% of patients in adult-onset developed malignant tumors within 3 years of diagnosis and most progressed.[7] Clinical characteristics of anti-NXP-2 Ab are similar to those of anti-TIF1 Ab. However, NVC findings and long-term changes to NVC findings for anti-NXP-2 Ab have yet to be elucidated.

2 | CASE REPORT

Four Japanese DM patients with anti-NXP-2 Ab (three females and one male, with a median age of 49 years [range 24–65 years]) were

included in the present study. Anti-NXP-2 Ab was detected by immunoprecipitation (IP)-Western assay.[8] The baseline characteristics of the four DM patients in the present study are summarized in Table 1. The mean observation period was 6 months [range 5–9 months]. Although only one patient had a heliotrope rash, all four had facial erythema other than heliotrope rash. Three patients had Gottron's sign/papules; all four had periungual erythema and nailfold bleeding. None of the four patients had flagellate erythema, skin ulcers, or cutaneous calcifications. Fever, ILD, and malignancy were seen in a single case each. None of the patients had Raynaud's phenomenon. Creatine kinase (CK) levels were greater than 1000 IU/L in three patients, and aldolase levels were elevated by over 10 IU/L in all four patients. Lactate dehydrogenase (LDH) was elevated in all four patients, but KL-6 (Krebs von den Lungen-6) levels were normal. All four patients received immunosuppressive therapy, including prednisolone, tacrolimus, azathioprine, and/or intravenous immunoglobulin. All four patients had a favorable outcome.

We evaluated each NVC finding at the initial visit for all four patients using the video capillaroscopy systems: CP-1000 (Chunichi Denshi, Nagoya, Japan) and/or GOKO Bscan/Bscan-Z (GOKO Imaging Devices, Kawasaki, Japan).[2,5] We evaluated seven findings: irregularly enlarged capillaries; reduced number of capillaries (reduced capillaries); more than two punctate hemorrhages per finger or confluent hemorrhage areas (hemorrhages); tortuous, crossed, and/or ramified capillaries (capillary ramification); disorganization of normal capillary distribution (disorganization of the vascular array); moderate or extensive capillary loss (loss of capillary); and giant capillaries. To assess long-term changes in NVC findings, we evaluated NVC findings at the initial visit and after disease stabilization. The NVC score was calculated by adding the positive items of the above seven findings (maximum score = 7).[9] All four patients presented irregularly enlarged and reduced capillaries and hemorrhages (Table 2). In contrast, none of the four patients had capillary ramifications, disorganization of the vascular array, or giant capillaries. Loss of capillary was observed in only one patient. After disease stabilization with immunosuppressive treatment, reduced capillaries remained in two patients, while irregularly enlarged capillaries and hemorrhages disappeared in all four. None of the four patients had capillary ramifications, disorganization of the vascular array, giant capillaries, or loss of capillary after disease stabilization. The NVC

TABLE 1 Clinical characteristics of four dermatomyositis patients with anti-NXP-2 antibody.

	Patient 1	Patient 2	Patient 3	Patient 4
Age, years	24	51	65	47
Gender	Male	Female	Female	Female
Observation period, months	9	7	5	8
Skin eruptions				
Heliotrope rash	−	−	+	−
Facial erythema other than heliotrope rash	+	+	+	+
Gottron's sign/papules	+	+	−	+
Periungual erythema	+	+	+	+
Nailfold bleeding	+	+	+	+
Flagellate erythema	−	−	−	−
Skin ulcers	−	−	−	−
Cutaneous calcification	−	−	−	−
Clinical features				
Fever	−	−	+	−
Raynaud's phenomenon	−	−	−	−
Interstitial lung disease	+	−	−	−
Malignancy	−	+	−	−
Laboratory findings				
CK, IU/L	2503	1834	1130	316
Aldolase, IU/L	22	15	10	10
LDH, IU/L	396	542	588	457
KL-6, U/mL	209	210	405	172
Treatment	PSL, Tac, IVIG	PSL, AZA, IVIG	PSL, Tac, IVIG	PSL
Outcome	Alive	Alive	Alive	Alive

Note: CK, LDH, and KL-6 levels indicated as the maximum values during the clinical course.

Abbreviations: AZA, azathioprine; CK, creatine kinase; IVIG, intravenous immunoglobulin; KL-6, Krebs von den Lungen-6; LDH, lactate dehydrogenase; PSL, prednisolone; Tac, tacrolimus.

TABLE 2 Nailfold videocapillary findings between at the initial visit and after stabilization in patients with anti-NXP-2 and anti-TIF1 antibodies.

	At the initial visit			After stabilization		
	NXP-2 ($n=4$)	TIF1[5] ($n=24$)	p	NXP-2 ($n=4$)	TIF1[5] ($n=24$)	p
Irregularly enlarged capillaries	4 (100%)	21 (88%)	.454	0 (0%)	24 (100%)	<.0001
Reduced capillaries	4 (100%)	23 (96%)	.678	2 (50%)	21 (88%)	.070
Hemorrhages	4 (100%)	22 (92%)	.549	0 (0%)	7 (29%)	.409
Capillary ramifications	0 (0%)	1 (4%)	.678	0 (0%)	4 (17%)	.378
Disorganization of the vascular array	0 (0%)	3 (13%)	.454	0 (0%)	4 (17%)	.378
Loss of capillary	1 (25%)	0 (0%)	.013	0 (0%)	0 (0%)	–
Giant capillaries	0 (0%)	0 (0%)	–	0 (0%)	1 (4%)	.678
NVC score	3.5 (3–4)	2.9 (2–4)	.019	0.5 (0–1)	2.4 (1–3)	<.0001

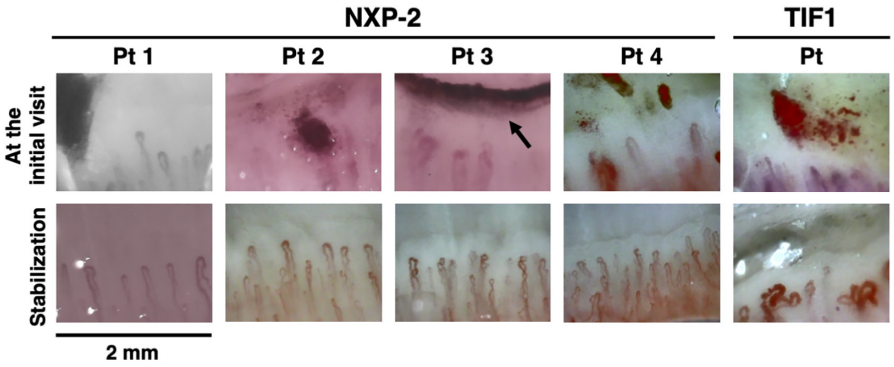

FIGURE 1 Representative images of nailfold videocapillaroscopy findings in patients with anti-NXP-2 and anti-TIF1 antibodies at the initial visit and after stabilization. Pt 3 at the initial visit showed a giant linear hemorrhage in the upper part of the image (arrow).

score was also significantly improved after disease stabilization (3.5 [range 3–4] vs. 0.5 [range 0–1], $p<.0001$).

Next, we compared the longitudinal changes in NVC findings between patients with anti-NXP-2 Ab and those with anti-TIF1 Ab (Table 2). The data for anti-TIF1 Ab were referred from a previous study.[5] The mean observation period for anti-TIF1 Ab was 11.5 months [range 2–87 months].[5] NVC findings at the initial visit were similar between anti-NXP-2 and anti-TIF1 Abs. The NVC score was significantly higher for anti-NXP-2 Ab (3.5 [range 3–4]) than for anti-TIF1 Ab (2.9 [range 2–4]) ($p=.019$). After disease stabilization, the frequency of irregularly enlarged capillaries was significantly lower in patients with anti-NXP-2 Ab than those with anti-TIF1 Ab ($p<.0001$). The NVC score was also significantly lower for anti-NXP-2 Ab (0.5 [range 0–1]) than for anti-TIF1 Ab (2.4 [range 1–3]) ($p<.0001$). These data demonstrate that, although the mean observation period was shorter in patients with anti-NXP-2 Ab than in those with anti-TIF1 Ab, NVC findings improved significantly in patients with anti-NXP-2 Ab.

Representative images showing NVC changes before and after treatment for anti-NXP-2 and anti-TIF1 Abs are shown in Figure 1. The first panels show images from all four patients with anti-NXP-2 Ab and a representative patient with anti-TIF1 Ab. Irregularly enlarged and reduced capillaries and multiple hemorrhages were present prior to treatment (at the initial visit). Patient 3 (Pt 3) had a giant linear hemorrhage. However, after treatment (stabilization), irregularly enlarged capillaries were restored to normal conditions, and hemorrhages disappeared (Figure 1). Reduced capillaries remained in Patients 1 and 2. In contrast, although hemorrhages disappeared, irregularly enlarged and reduced capillaries were still present after treatment in a patient with anti-TIF1 Ab.

3 | DISCUSSION

This is the first study to evaluate long-term changes to NVC findings in DM patients with anti-NXP-2 Ab from the initial visit to disease stabilization after treatment. At the initial visit, all four patients with anti-NXP-2 Ab had NVC abnormalities, including irregularly enlarged and reduced capillaries and hemorrhages. However, these NVC findings improved significantly after treatment with a shorter period. These short-term improvements in NVC findings in anti-NXP-2 Ab differed from those with anti-TIF1 Ab. Therefore, when evaluating NVC findings over time in patients with IIM, it is crucial to remember that long-term changes in NVC findings differ by each MSA.

The clinical utility of NVC findings in IIM is becoming an attractive field. A study examining longitudinal changes in NVC findings among patients with anti-MDA5, anti-TIF1, and anti-ARS Abs showed that both enlarged and reduced capillaries improved after stabilization by treatment in patients with anti-MDA5 Ab. However, these improvements were not observed in patients with anti-TIF1 and anti-ARS Abs. On the contrary, a significant reduction in hemorrhages was observed in all three groups.[5] Therefore,

when evaluating NVC findings in patients with IIM, it is necessary to consider them based on the MSA subtypes.

The clinical characteristics of anti-NXP-2 and anti-TIF1 Abs are similar. Both are representative MSAs of juvenile DM and are associated with malignancy in adults, but ILD is less common.[7,10] Therefore, long-term changes in NVC findings were expected to be similar, but this study showed that long-term changes in NVC findings were different. In patients with anti-TIF1 Ab, although hemorrhages disappeared by treatment, irregularly enlarged and reduced capillaries did not improve after about 1 year of disease stabilization. In contrast, abnormalities of NVC findings improved within a shorter medical course in patients with anti-NXP-2 Ab. Thus, although the clinical features are similar between these two groups, mechanisms and contributions against vascular abnormalities may differ between anti-NXP-2 and anti-TIF1 Abs.

This study has several limitations. First, this study was performed retrospectively; therefore, a prospective study is needed to confirm the study results. In addition, this study included only four patients, which limits the generalizability of the findings. Further studies, including a larger number of patients and different ethnicities, are needed to confirm the results of the present study.

In conclusion, long-term follow-up of NVC findings in patients with IIM should be conducted based on the information from MSA.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

ETHICS STATEMENT

Approval of the research protocol: The study protocol was approved by Kanazawa University Hospital.

Informed Consent: All study participants provided written informed consent.

Registry and the Registration No.: No. 963.

Animal Studies: N/A.

ORCID

Yasuhito Hamaguchi https://orcid.org/0000-0001-5305-7770

Shintaro Maeda https://orcid.org/0000-0001-7824-7060

REFERENCES

1. Cutolo M, Herrick AL, Distler O, Becker MO, Beltran E, Carpentier P, et al. Nailfold videocapillaroscopic features and other clinical risk factors for digital ulcers in systemic sclerosis: a multicenter, prospective cohort study. Arthritis Rheumatol. 2016;68:2527–39.
2. Mugii N, Hasegawa M, Matsushita T, Hamaguchi Y, Horie S, Yahata T, et al. Association between nail-fold capillary findings and disease activity in dermatomyositis. Rheumatology (Oxford). 2011;50:1091–8.
3. Manfredi A, Sebastiani M, Campomori F, Pipitone N, Giuggioli D, Colaci M, et al. Nailfold videocapillaroscopy alterations in dermatomyositis and systemic sclerosis: toward identification of a specific pattern. J Rheumatol. 2016;43:1575–80.
4. Lundberg IE, Fujimoto M, Vencovsky J, Aggarwal R, Holmqvist M, Christopher-Stine L, et al. Idiopathic inflammatory myopathies. Nat Rev Dis Primers. 2021;7:86.
5. Mugii N, Hamaguchi Y, Horii M, Fushida N, Ikeda T, Oishi K, et al. Longitudinal changes in nailfold video capillaroscopy findings differ by myositis-specific autoantibody in idiopathic inflammatory myopathy. Rheumatology (Oxford). 2023;62:1326–34.
6. Oddis CV, Fertig N, Goel A, Espada G, Gregorian M, Cocco J, et al. Clinical and serological characterization of the anti-MJ antibody in childhood myositis [abstract]. Arthritis Rheum. 1997;40:S139.
7. Ichimura Y, Matsushita T, Hamaguchi Y, Kaji K, Hasegawa M, Tanino Y, et al. Anti-NXP2 autoantibodies in adult patients with idiopathic inflammatory myopathies: possible association with malignancy. Ann Rheum Dis. 2012;71:710–3.
8. Kang EH, Kuwana M, Okazaki Y, Lee EY, Lee YJ, Lee EB, et al. Comparison of radioimmunoprecipitation versus antigen-specific assays for identification of myositis-specific autoantibodies in dermatomyositis patients. Mod Rheumatol. 2014;24:945–8.
9. Hamaguchi Y, Mugii N, Matsushita T, Takehara K. Long-term changes in nail fold capillary abnormalities and serum fibroblast growth factor 23 levels in dermatomyositis patients with anti-melanoma differentiating antigen 5 antibody. J Dermatol. 2021;48:106–9.
10. Kaji K, Fujimoto M, Hasegawa M, Kondo M, Saito Y, Komura K, et al. Identification of a novel autoantibody reactive with 155 and 140 kDa nuclear proteins in patients with dermatomyositis: an association with malignancy. Rheumatology (Oxford). 2007;46:25–8.

How to cite this article: Mugii N, Hamaguchi Y, Fushida N, Horii M, Kitano T, Fujii Ko, et al. Early improvement of nailfold videocapillaroscopy abnormalities in dermatomyositis patients with anti-NXP-2 antibody. J Cutan Immunol Allergy. 2023;6:245–248. https://doi.org/10.1002/cia2.12334