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*CORRESPONDENCE

Takeshi Fukumoto,
✉ fukumoto@koto.kpu-m.ac.jp

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A case of anti-laminin 332-type mucous membrane pemphigoid with ocular symptoms successfully treated with mycophenolate mofetil and prednisolone in an elderly man

Shoko Fukumitsu¹, Takashi Hashimoto², Yukari Matsumoto¹, Takayuki Nagai³, Keisuke Iritani⁴, Yoshiaki Hirako⁵, Akiharu Kubo¹ and Takeshi Fukumoto^{1,6*}

¹Division of Dermatology, Department of Internal Related, Kobe University Graduate School of Medicine, Kobe, Japan, ²Department of Dermatology, Graduate School of Medicine, Osaka Metropolitan University, Osaka, Japan, ³Department of Ophthalmology, Kobe University Graduate School of Medicine, Kobe, Japan, ⁴Department of Otolaryngology-Head and Neck Surgery, Kobe University Graduate School of Medicine, Kobe, Japan, ⁵Division of Biological Science, Graduate School of Science, Nagoya University, Nagoya, Japan, ⁶Department of Dermatology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan

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Dear Editors,

Mucous membrane pemphigoid (MMP) is a rare autoimmune blistering disease affecting the mucous membranes, sometimes causing blindness or potentially life-threatening nasopharyngeal and esophageal obstruction [1–3]. Based on the disease severity and involved sites, patients with MMP are classified as low-risk patients, with only oral mucosal lesions; and high-risk patients, with severe and rapidly progressive lesions in the ocular, genital, nasopharyngeal, esophageal, and laryngeal mucosa [1, 2]. Currently, prednisolone in combination with cyclophosphamide or azathioprine is recommended for high-risk patients [1, 2]. MMP patients have autoantibodies to several basement membrane zone (BMZ) proteins, including BP180, laminin 332 and integrin β 4. Approximately 25% of patients with MMP express autoantibodies against laminin 332 [1, 2]. Further, because some patients with anti-laminin 332-type MMP may have an underlying malignancy, differentiation from other types of MMPs is critical [1]. Herein, we report an elderly non-paraneoplastic case of anti-laminin 332-type MMP that was successfully treated with mycophenolate mofetil and prednisolone.

A 73-year-old male presented with gradually worsening erosions of the nasopharyngeal and ocular mucosae (Figures 1A–D). Three months following development of the initial symptoms, vesicles with erythema appeared on the trunk (Figure 1E) and limbs. Histopathological examination of the abdominal skin lesion revealed a subepidermal bulla with eosinophil, lymphocyte, and histiocyte infiltration (Figure 1F). Histopathological examination of a nasal septal biopsy specimen revealed granulation with extensive inflammation (Figure 1G). Direct immunofluorescence revealed linear deposition of IgG and C3 in the BMZ (Figures 1H,I). Indirect immunofluorescence using normal human skin showed IgG anti-BMZ antibodies, which reacted with the dermal side of the 1M NaCl-split normal human skin (Figures 1J,K).

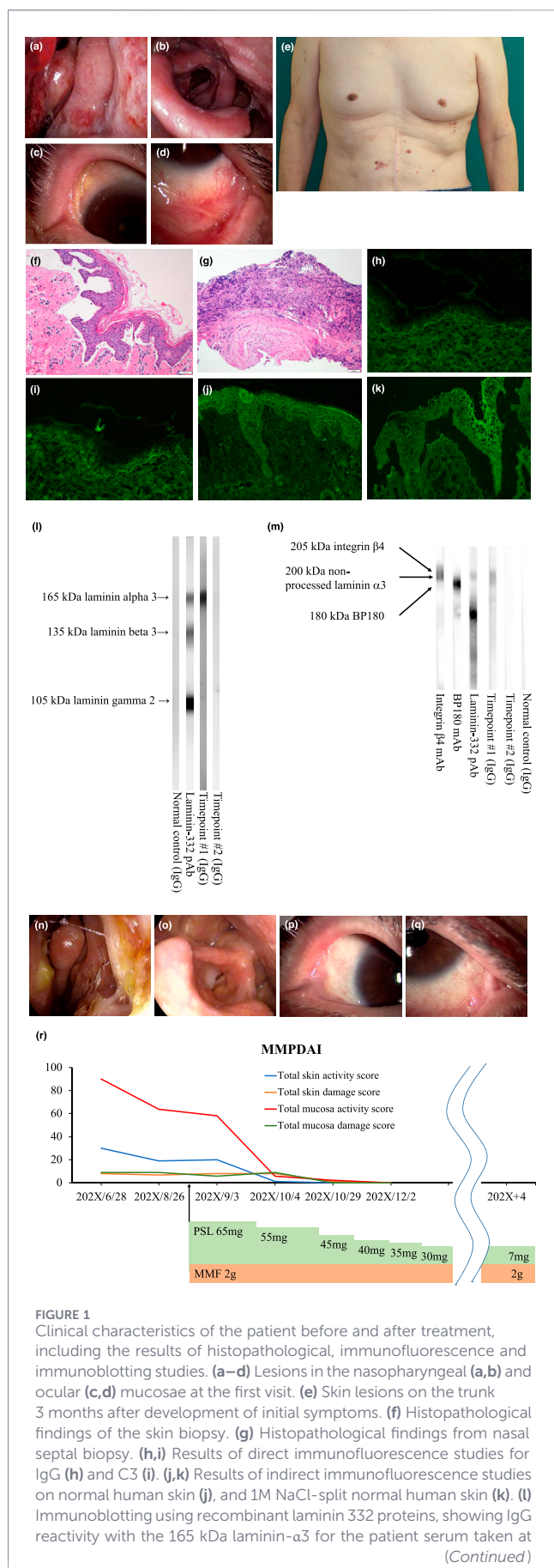


FIGURE 1 (Continued)

timepoint #1 (before treatments), which disappeared at timepoint #2 (5 months after treatments). (m) Immunoblotting using hemidesmosome-rich fraction showing IgG reactivity with the 200 kDa unprocessed laminin-α3, but not to the 205 kDa integrin β4 for the patient serum taken at timepoint #1 (before treatments). Reactivity with laminin-α3 became negative at timepoint #2 (5 months post-treatment). (n–q) lesions in the nasopharyngeal (n,o) and ocular (p,q) mucosae disappeared after treatment. (r) Longitudinal changes in disease activity assessed by the Mucous Membrane Pemphigoid Disease Area Index (MMPDAI). Total skin activity score, total skin damage score, total mucosal activity score, and total mucosal damage score over time. Prednisolone (PSL) was started at 65 mg/day and tapered during the observation period, and mycophenolate mofetil (MMF) was started at 2 g/day.

Chemiluminescent enzyme immunoassays for BP180 and desmogleins 1 and 3, as well as enzyme-linked immunosorbent assays for BP230 and type VII collagen, were all negative. Immunoblotting with recombinant laminin 332 proteins revealed the presence of IgG antibodies against the 165 kDa laminin α3 (Figure 1L). Immunoblotting with a hemidesmosome-rich fraction revealed IgG antibodies against the 200 kDa laminin α3 but not against the 205 kDa integrin β4 (Figure 1M).

The patient was diagnosed with anti-laminin 332-type MMP. Computed tomography (CT) and upper and lower endoscopies revealed no malignancies. The initial mucous membrane pemphigoid disease area index (MMPDAI) scores for total activity and total damage were 130 (skin; 30, scalp; 10, mucosa; 90) and 18 (skin; 8, scalp; 1, mucosa; 9) respectively. Within 4 months of treatment with mycophenolate mofetil (MMF) at 2000 mg/day and oral prednisolone at 1.0 mg/kg/day, all mucocutaneous lesions had resolved (Figures 1N–Q), and the MMPDAI scores became negative (Figure 1R). Immunoblotting analyses of the patient's IgG reactivity with recombinant laminin 332 proteins and the hemidesmosome-rich fraction were negative 5 months later (Figures 1L,M).

In the present study, immunoblotting with hemidesmosome-rich fraction detected laminin α3, but not integrin β4, leading to a diagnosis of anti-laminin 332-type MMP. The patient was successfully treated with mycophenolate mofetil and prednisolone. MMF may be more effective in combination with prednisolone in patients with anti-laminin 332-type MMP, particularly in cases with ocular involvement, with fewer side effects than other treatments, such as other immunosuppressants [4, 5]. Although such conditions are rare, and specific information regarding the use of MMF in elderly patients is lacking, MMF may be employed safely and effectively in elderly patients with ocular involvement.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by the Medical Ethics Committee of Kobe University. The studies were conducted

in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

SF and TF conceptualized and designed the study. SF, TH, and YM performed the experiments and collected the data. TN, KI, YH, and AK contributed to data analysis and interpretation. SF drafted the manuscript. TF supervised the study and critically revised the manuscript for important intellectual content. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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