Received: 15 February 2023 | Revised: 11 April 2023 | Accepted: 28 May 2023

DOI: 10.1002/cia2.12310

Journal of Cutaneous Immunology and Allergy

WILEY

CORRESPONDENCE

A case of bullous pemphigoid with correlation to serum levels of anti-BP180-NC16a antibodies and thymus and activation-regulated chemokine

Bullous pemphigoid (BP) is an autoimmune blistering disease characterized by subepidermal blisters and erosive lesions on the skin.[1] Autoantibodies against the NC16a domain of BP180 in the epidermal basement membrane zone are produced in patients with BP.[1,2] We report a case of BP with correlation to serum levels of anti-BP180-NC16a antibodies and thymus and activation-regulated chemokine (TARC/CCL17).

Case 1, an 85-year-old Japanese woman presented with a 5-month history of erythema and itching having resistance to a topical steroid treatment. She had hypertension and latent tuberculosis infection. Physical examination revealed erythema, erosions, and blisters on the body, upper arms, legs, and back (Figure 1A–D). Her BP disease area index (BPDAI) for skin blisters/erosions was 34; and BPDAI for skin uriticaria/erythema was 25. Laboratory findings were as follows (normal ranges): white blood cells count, 5570/μL (3300–8600/μL); eosinophils, 4.7% (0.4%–8.6%); lactate dehydrogenase (LD), 243 U/L (124–222 U/L); C-reactive protein (CRP), 0.08 mg/dL (0.00–0.14 mg/dL); and total immunoglobulin E (IgE), 133.0 IU/mL (0–232 IU/mL). Her serum anti-BP180-NC16a antibody titer was 159.5 U/mL (0–8.9 U/mL), TARC levels were elevated at 1031 pg/mL (0–450 pg/mL). A biopsy specimen from the right back showed subepidermal blisters (Figure 1E,F). Direct immunofluorescence showed linear deposition of IgG and C3c in the epidermal basement membrane zone (Figure 1G,H). A diagnosis of BP was made. Initiation of oral prednisolone 0.5 mg/kg/day decreased the skin symptoms. After 3 months, BPDAI was clear and the laboratory findings improved: white blood cells count, 10,920/μL; eosinophils, 0.2%; LD, 293 U/L; CRP, 0.05 mg/dL; total IgE, 14.9 IU/mL; anti-BP180-NC16a antibody titers, 4.7 U/mL; and TARC, 120 pg/mL.

To explore the correlation between anti-BP180-NC16a antibody titers and other laboratory data, we evaluated 7 patients with BP who visited Hirosaki University Hospital. Laboratory data were retrieved from medical records before oral prednisolone treatment. The patients were diagnosed with BP according to clinical, pathological, and immunofluorescence features. The study was approved by the Committee of Medical Ethics of the Hirosaki University Graduate School of Medicine approved the research study (No. 2021-025).

Among 262 patients with BP or having a possibility of BP who measured TARC and anti-BP180 antibody (NC16a), the anti-BP180 antibody (NC16a) was positive in seven patients (Figure 1I). The mean anti-BP180-NC16a antibody titers was 8990.61 U/mL, and improved after 3 months with treatments in 124.81 U/mL. The mean TARC was 4202.14 pg/mL, and improved after 3 months with treatments in 267 pg/mL. We could not show statistical significance because of the low number of cases; however, the mean of anti-BP180-NC16a antibody titers and TARC decreased after treatments.

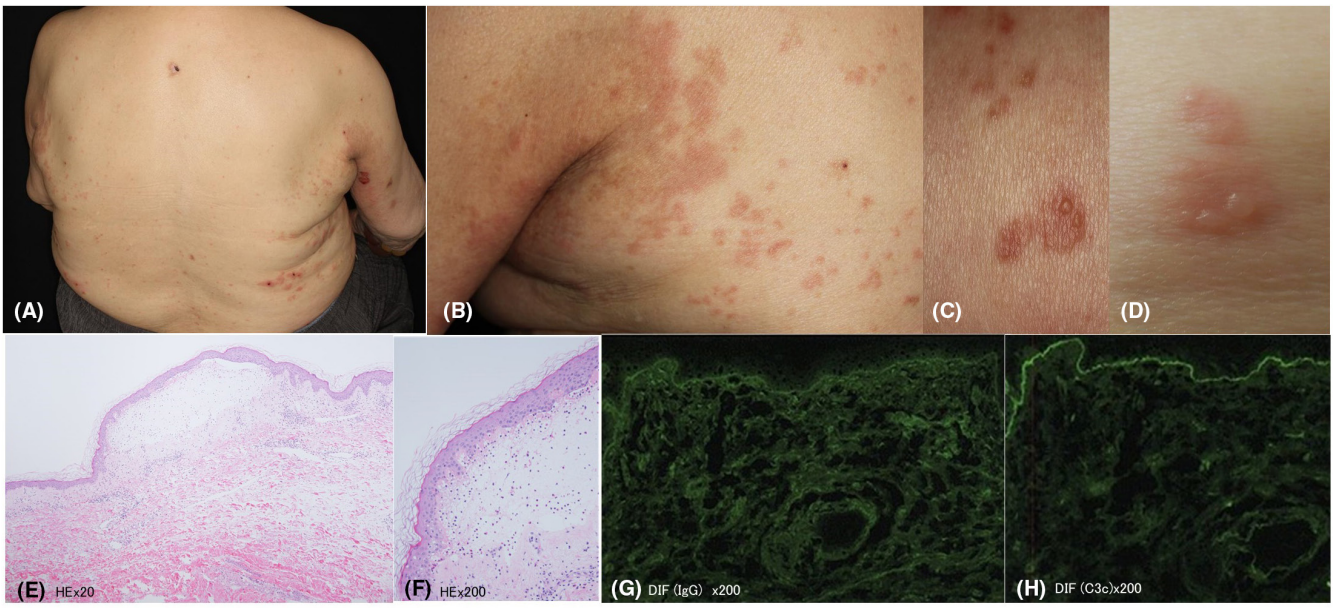
The correlation between BP disease activity and anti-BP180-NC16a antibody titers is well known. The relationship between BP and TARC has been reported.[3,4] Therefore, TARC might be an important chemokine involved in the pathogenesis of BP.[3,4] We speculate that TARC is useful for predicting the clinical condition of patients with BP, similar to anti-BP180-NC16a antibody titers.

ACKNOWLEDGMENTS

We are grateful to the patient in this manuscript for providing written informed consent for publication, and the investigators who participated in the study; Ms. Mone Mori, Hirosaki University Graduate School of Medicine, in Aomori, Japan for data analysis. This work was supported in part by a Grant-in-Aid from the Ministry of Education, Culture, Sports, Science and Technology of Japan to S. Minakawa (project 20k08684) and by the 2023 Hirosaki University Research Support System.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest. Management of the peer review process, and all editorial decision-making, for this article was undertaken by Editor in Chief, Prof. Manabu Fujimoto.



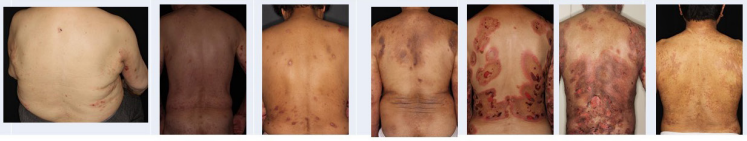
(I) Clinical features & data of 7 cases	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	The mean
Sex	Female	Male	Female	Male	Female	Male	Male	
Age (years)	85	72	76	88	74	74	73	77.4
White blood cell (μ/L)	5570	7890	6470	12580	11540	8850	22400	10,757.10
Eosinophils (%)	4.7	1.3	1.9	30	4.8	11	45	14.1
LD (U/L)	243	145	240	268	308	230	315	249.9
CRP (mg/dL)	0.08	0.064	2.247	2.41	1.492	1.138	0.733	1.166
Total IgE (IU/mL)	133	200	531	651	37	615	3920	869.57
Anti–BP180-NC16a antibody (U/mL)	159.5	2210	575.8	539	2110	49300	8040	8,990.61
Anti–BP180-NC16a antibody after 3 months	4.7	57.1	25.3	155.5	153.1	433.8	44.2	124.81
TARC (pg/mL)	1031	709	229	10956	4243	6074	6173	4202.14
TARC after 3 months	120	—	179	486	434	129	254	267
BPDAI skin Blisters/Erosions	34	20	37	69	63	76	66	52.14
BPDAI skin Uriticaria/Erythema	25	28	10	22	40	31	76	33.14
BPDAI mucosa Blisters/Erosions	0	0	0	0	0	3	0	0.43
Clinical features								

FIGURE 1 (A–D) Clinical features and direct immunofluorescence results at the time of relapse. Clinical features of the (A) body and (B) upper arms, with (C, D) blisters, erosions, and erythema on the back. (E, F) Histopathological examination of a skin biopsy specimen from the back showed subepidermal blisters (original magnification: E, ×20 and F, ×200). (G, H) Direct immunofluorescence was positive for (G) IgG and (H) C3c. (I) Clinical features and other data in seven patients with bullous pemphigoid.

ETHICS STATEMENT

Approval of the research protocol: The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution and it conforms to the provisions of the Declaration of Helsinki. The study protocol was approved by the Committee of Medical Ethics of Hirosaki University Graduate School of Medicine. Approval No. 2021-025.

Informed Consent: All informed consent was obtained from the subjects or guardians.

Registry and the Registration No.: The study outline was registered and published in the Japan Registry of Clinical Trials (trial ID no. jRCT1020210017).

Animal Studies: N/A.

Satoko Minakawa MD, PhD[1,2]
Yasushi Matsuzaki MD, PhD[1]
Atsuko Kimura MD[1]
Kageaki Taima MD, PhD[3]
Sadatomo Tasaka MD, PhD[3]
Daisuke Sawamura MD, PhD[1]

[1]*Department of Dermatology, Hirosaki University Graduate School of Medicine, Aomori, Japan*
[2]*Department of Clinical Laboratory, Hirosaki University Hospital, Aomori, Japan*
[3]*Department of Respiratory Medicine, Hirosaki University Graduate School of Medicine, Aomori, Japan*

Correspondence
Satoko Minakawa, Department of Dermatology, Hirosaki University Graduate School of Medicine, 5 Zaifu-cho, Hirosaki, Aomori 036-8562, Japan.
Email: minakawas@yahoo.co.jp

ORCID

Satoko Minakawa https://orcid.org/0000-0001-5933-3377

REFERENCES

1. Nishie W. Update on the pathogenesis of bullous pemphigoid: an autoantibody-mediated blistering disease targeting collagen XVII. J Dermatol Sci. 2014;73:179–86.
2. Nishie W, Sawamura D, Goto M, Ito K, Shibaki A, McMillan JR, et al. Humanization of autoantigen. Nat Med. 2007;13:378–83.
3. Kakinuma T, Wakugawa M, Nakamura K, Hino H, Matsushima K, Tamaki K. High level of thymus and activation-regulated chemokine in blister fluid and sera of patients with bullous pemphigoid. Br J Dermatol. 2003;148:203–10.
4. Suzuki M, Yamaguchi Y, Nakamura K, Kanaoka M, Matsukura S, Takahashi K, et al. Serum thymus and activation-regulated chemokine (TARC/CCL17) may be useful to predict the disease activity in patients with bullous pemphigoid. J Eur Acad Dermatol Venereol. 2021;35:e121–4.