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# Association of eosinophil major basic protein with intraocular lens dislocation in atopic dermatitis

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The study aimed to investigate whether eosinophil major basic protein (MBP), which is linked to cataract formation due to lens epithelial cell (LEC) damage in atopic dermatitis (AD), is associated with intraocular lens (IOL) dislocation. This retrospective observational study was conducted at a Medical University Hospital and included 22 eyes (10 AD, 12 non-AD [NAD]) that underwent IOL explantation and fixation. Surgeries were conducted to extract the intraocular lens capsule for morphological evaluations. Quantitative analysis of the MBP staining was conducted using the staining area ratio (SAR) gap. MBP staining was negative in all cases for both the lens capsule and LEC. The SAR gap in Soemmering's ring was significantly higher in the AD group ( $14.3 \pm 8.7\%$ ) than in the NAD group ( $1.1 \pm 1.1\%$ ) ( $p = 0.0037$ ). In contrast, the SAR gap for fibrous metaplasia showed no significant difference between the AD ( $8.3 \pm 13.2\%$ ) and NAD ( $6.5 \pm 12.3\%$ ) groups ( $p = 0.75$ ). Six cases of fibrous metaplasia, including those in the NAD group, showed SAR gaps equal to or greater than those in the positive control group, with five classified as low-density fibrosis (LDF). While Soemmering's rings in AD cases demonstrated greater MBP immunoreactivity than NAD controls, both groups exhibited MBP-positive fibrous metaplasia specimens.

**Keywords** Atopic dermatitis, Eosinophil major basic protein, Intraocular lens dislocation, Lens epithelial cell, Soemmering's rings

Intraocular lens (IOL) dislocation can occur months to years after cataract surgery. The annual incidence of IOL dislocation is less than 0.05%, and the cumulative incidence over 10–25 years is approximately 0.1–3%<sup>1</sup>. Advances in cataract surgery have enabled IOL insertion into the capsular bag, even in cases where the zonule is weak, which was previously considered challenging<sup>2</sup>. Consequently, the number of IOL dislocation cases may increase in the future. The risk factors for IOL dislocation include cataract surgery in patients with a history of ocular trauma, vitrectomy, pseudoexfoliation syndrome, retinitis pigmentosa, high myopia, uveitis, and atopic dermatitis (AD)<sup>1</sup>. The prevalence of AD in developed countries has increased two- to threefold in recent decades<sup>3</sup>. AD can cause various ocular complications, such as cataracts, retinal detachment, glaucoma, conjunctivitis, and keratoconus, which significantly impair vision, particularly in younger individuals<sup>4,5</sup>. Notably, IOL dislocation in patients with AD can result not only from capsular bag dislocation (CBD) caused by zonular rupture due to scratching and rubbing associated with ocular itching, but also from dead bag syndrome (DBS), due to a very clear bag many years postoperatively, without fibrotic changes or proliferative material within the bag<sup>6,7</sup>. The reasons for these differences in the dislocation form remain unclear.

We observed morphological abnormalities in lens epithelial cells (LECs) and insufficient fibrosis of the lens capsule in patients with AD-associated IOL dislocations. Furthermore, we reported a high incidence of capsular splitting, a pathological feature characteristic of DBS, regardless of the dislocation type in AD cases<sup>8</sup>, suggesting that AD may be a contributing factor to previously unexplained DBS<sup>9</sup>. LEC damage caused by eosinophil major basic protein (MBP), which is present in high concentration in the aqueous humor of patients with AD, has been implicated as a cause of cataracts in patients with AD<sup>10,11</sup>. We investigated whether MBP is associated with the pathological features of AD-related IOL dislocation.

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To test this hypothesis, we conducted MBP immunostaining on the extracted capsular bags in cases of IOL dislocation in AD and non-AD (NAD) cases and examined the involvement of MBP in AD-associated IOL dislocation.

## Results

The AD group comprised 10 patients (10 eyes) (Male,  $n=9$ ; mean age,  $47.0 \pm 10.3$  years). One eye had a history of trauma, two eyes had a history of vitrectomy, and one eye had a history of uveitis. The IOL dislocation types included seven eyes with CBD and three eyes with DBS. The mean duration until IOL dislocation was  $11.5 \pm 5.6$  years, and the mean axial length was  $25.5 \pm 1.4$  mm (Table 1).

Twelve patients (12 eyes) were assigned to the NAD group (male,  $n=10$ ; mean age,  $64.0 \pm 13.8$  years). Six eyes had a history of trauma, five eyes had a history of vitrectomy, and the cause was unknown in three eyes. All patients in the NAD group had CBD. The mean duration until IOL dislocation was  $10.2 \pm 5.7$  years, and the mean axial length was  $25.6 \pm 1.5$  mm (Table 2).

In MBP immunostaining, the SAR gap for the positive control was 12.7%. The SAR gap was  $14.3 \pm 8.7\%$  in the AD group and  $1.1 \pm 1.1\%$  in the NAD group, with the AD group showing a significantly higher SAR gap than that in the positive control group ( $p$ -value = 0.0037) (Fig. 1). For example, in the DBS case in the AD group (Case 2), MBP staining in the Soemmering's ring was higher than that in the negative control (Fig. 2). Similarly, in the CBD case of the AD group (Case 9), the same trend was observed (Fig. 3). In contrast, in the CBD case of the NAD group (Case 12), MBP staining and the negative control showed similar staining levels (Fig. 4a, b).

The SAR gap in fibrous metaplasia was  $8.3 \pm 13.2\%$  in the AD group and  $6.5 \pm 12.3\%$  in the NAD group, with both groups showing SAR gaps below that of the positive control; no significant difference was observed ( $p$ -value = 0.75) (Figs. 4c and d and 5). However, six cases of fibrous metaplasia, including those in the NAD group, showed an SAR gap  $\geq 10\%$ , equivalent to that of the positive control. Of these cases, five were classified as LDF (Tables 1 and 2).

Furthermore, the lens capsule and LEC were negative in all cases in both groups (Tables 1 and 2; Fig. 6).

## Discussion

This study provides novel insights into the pathological characteristics of the lens capsule complex and its relationship with MBP in patients with AD-associated IOL dislocations. The AD group showed a significantly higher SAR gap in the Soemmering's ring than the NAD group, confirming the MBP staining. These results suggest that, in the AD group, MBP may continue to contribute to the weakening of the lens capsule complex even after cataract surgery.

Several studies have reported the involvement of MBP toxicity in the development of AD-associated cataracts. Yokoi et al. measured MBP immunostaining in the lens capsule and LEC, as well as aqueous MBP concentrations in AD-associated cataracts and age-related cataracts. Several cases of AD-associated cataracts showed MBP adhesion to LEC and elevated aqueous MBP concentrations, while no such findings were observed in the age-related cataracts<sup>12</sup>. In contrast, Yamamoto et al. demonstrated in vivo that MBP detected in the aqueous humor of AD-associated cataracts originated from the patient's plasma and established in vitro that MBP damages human LEC, proposing the hypothesis that MBP-induced LEC damage contributes to the mechanism of AD-associated cataracts<sup>10</sup>. Furthermore, MBP toxicity is suggested to be involved in the development of AD-related ocular complications other than cataracts. Matsuda et al. detected MBP in the aqueous humor of approximately half of the cases of AD-associated retinal detachment, while no MBP was detected in non-AD-associated retinal detachment, proposing the involvement of MBP in the development of AD-associated retinal detachment<sup>13</sup>. The involvement of MBP in AD-associated keratoconjunctivitis has also been reported<sup>14</sup>.

Based on these findings, we propose that LEC dysfunction due to LEC damage caused by MBP toxicity, termed "Lens Epitheliopathy," may weaken the lens capsule, which normally forms the basement membrane produced by LEC. The LEC dysfunction may also result in inadequate fibrosis formation through epithelial-mesenchymal transition (EMT) post-cataract surgery, contributing to the fragility of the lens capsule complex and IOL dislocation in patients with AD. In our initial report, we investigated the pathology of the lens capsule complex in cases of AD-associated IOL dislocation, reporting the fragility of the lens capsule, including capsular splitting and inadequate fibrosis formation<sup>8</sup>. Moreover, in IOL dislocation cases caused by DBS, where LECs are believed to be deficient or significantly reduced, immunostaining of the lens capsule complex revealed positive staining for fibrous components, such as type I collagen and fibronectin, which are produced during EMT, suggesting that even a small number of LECs may have remained post-cataract surgery and secreted fibrous components before disappearing<sup>15</sup>. These results suggest that LEC damage may continue after cataract surgery, which is consistent with MBP-related toxic damage.

This study identified the differences in MBP staining patterns across various ocular tissues. The AD group showed a higher SAR gap in the Soemmering's ring and some fibrous metaplasia than the positive control, possibly because of cell density difference. High cell density inhibits antibody penetration, leading to reduced staining<sup>16</sup>. Soemmering's ring has lower cell density compared to fibrous metaplasia, making it more permeable to MBP in cases where aqueous MBP concentration is elevated in AD.

In contrast, no MBP staining was observed in the Soemmering's ring in any of the patients with NAD. However, three cases (Cases 16, 20, and 21) showed an SAR gap in fibrous metaplasia equivalent to that in the positive control, with histories of trauma and unknown etiology. Additionally, two of the three cases exhibited LDF, a characteristic feature of AD<sup>8</sup>. Although AD was classified based on patient self-reporting in this study, these two cases were likely predisposed to AD. Future studies should use biomarkers and clinical diagnoses to confirm the presence of AD.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Average ± SD or Total n (%)
Classification of IOL dislocation	DBS	DBS	DBS	CBD	CBD	CBD	CBD	CBD	CBD	CBD	
Explanting surgeon	YM	YM	YM	IN	KK	SO	TW	YM	YM	KK	
Age at explantation (years)	55	39	46	46	47	59	47	26	62	43	47.0 ± 10.3
Sex	M	M	M	M	M	F	M	M	M	M	
Eye	L	R	L	L	R	R	R	L	R	L	
Length of implantation (years)	17	14	3	5	22	13	12	8	10	11	11.5 ± 5.6
Axial length (mm)	25	25.5	24.3	26.3	25.5	24.2	27	23.1	27.6	26.4	25.5 ± 1.4
Causes of IOL dislocation	AD, Trauma	AD	AD	AD	AD	AD, Behcet's disease	AD, Vitrectomy	AD	AD	AD, Vitrectomy	
History of Ophthalmic Surgical Treatments	In-the-bag IOL	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	10 (100%)
	Vitrectomy	(-)	(-)	(-)	(-)	(-)	(+)	(-)	(-)	(+)	2 (20%)
LEC degeneration or loss	High-density fibrosis	(+)	(+)	(-)	(+)	(+)	(+)	(+)	(+)	(+)	9 (90%)
	Low-density fibrosis	(-)	(-)	(-)	(-)	(+)	(-)	(-)	(-)	(+)	3 (30%)
Fibrous metaplasia	High-density fibrosis	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	10 (100%)
	Low-density fibrosis	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	0 (0%)
MBP Immunostaining	Soemmering's ring SAR gap (%)	12.2	27.1	18.0	0.6	21.6	NA	10.9	NA	9.5	14.3 ± 8.7*
	Fibrous metaplasia SAR gap (%)	2.7	11.6	27.9	0.0	1.6	36.6	0.1	1.0	1.3	8.3 ± 13.2
	Lens capsule	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	0 (0%)
	LEC	(-)	(-)	(-)	NA	(-)	(-)	NA	(-)	NA	0 (0%)

**Table 1.** Atopic dermatitis case characteristics. AD = atopic dermatitis; CBD = capsular bag dislocation; DBS = dead bag syndrome; IOL = intraocular lens; L = left; LEC = lens epithelial cells; M = male; MBP = eosinophil major basic protein; NA = not applicable; R = right; SAR = staining area ratio; SD = standard deviation. \*Cases deemed “not applicable” were excluded from the mean value calculation.

Additionally, no MBP was detected in the lens capsule. The lens is an avascular tissue, and nutrients are supplied to the LEC through the anterior capsule. The anterior capsule facilitates passive transport, which is influenced by the molecular size of the product. Larger molecules, such as dextran, composed of the polysaccharide glucose (500 kDa), do not pass through the anterior capsule, but MBP, with a molecular weight of 13.8 kDa, is small enough to pass through<sup>10</sup>, suggesting that MBP may not have been detected because of the sensitivity limitations of the immunostaining method. While MBP in the lens capsule may exist at the protein level, more sensitive methods, such as immunoelectron microscopy, are needed for detection.

LECs in AD-associated cataracts have been reported to be positive for MBP<sup>10</sup>. However, in this study, LECs in AD-associated IOL dislocation cases were negative for MBP. The anterior capsule was extensively removed during the initial cataract surgery, which significantly reduced the number of LECs. It is plausible that the remaining LECs in the open capsule were further exposed to MBP due to aqueous inflow, leading to accelerated cell degeneration or reduction, which may explain the lower staining observed in this study<sup>8</sup>.

Patients with AD have elevated serum MBP levels, and when the blood-aqueous barrier is compromised, aqueous MBP concentration increases, leading to LEC damage and development of specific types of cataracts at a young age<sup>17</sup>. Since the severity of AD varies from case to case, the risk and pathology of IOL dislocation may differ individually. Depending on the aqueous MBP concentration and the extent of mechanical irritation from rubbing, either zonular weakening or capsular fragility at the zonular attachment site may dominate, resulting in CBD, or overall capsular fragility may lead to DBS<sup>8,18</sup>. Future investigations are needed to examine whether differences in MBP concentrations in the blood, aqueous humor, and vitreous humor of patients with AD are related to the mechanism of IOL dislocation. In the future, MBP biomarkers may help identify patients at high risk of IOL dislocation, enabling interventions such as controlling MBP levels in the blood and aqueous humor with medication or surgical operation that avoids IOL insertion into the capsule during initial cataract surgery, potentially preventing IOL dislocation in patients with AD.

This study has several limitations. First, our small sample—particularly sparse DBS cases—limits generalizability. Second, while we standardized IHC protocols, the absence of aqueous MBP levels leaves open questions about systemic vs. local protein dynamics. Third, the cross-sectional design cannot establish whether MBP deposition precedes or results from dislocation.

To the best of our knowledge, this study provides novel insights into the pathological characteristics of the lens capsule in AD-associated IOL dislocation and its relationship with MBP. Compared with the NAD group, the AD group showed a higher incidence of MBP positivity in the Soemmering's ring. These findings suggest that MBP may potentially contribute to the unique fragility of the lens capsule, even after cataract surgery, in patients with AD.

## Methods

### Ethical approval

This case series was approved by the Institutional Review Board of Jikei University School of Medicine and conducted in accordance with the principles of the Declaration of Helsinki (approval number: 35-057[11680]). This study did not involve any invasive or interventional procedures and used only existing samples and information.

### Patient consent statement

Informed consent was obtained from the participants using an opt-out method, in accordance with the Ethical Guidelines for Medical and Health Research Involving Human Subjects (Japanese Ministry of Health, Labour, and Welfare). Documents approved by the Institutional Review Board of Jikei University School of Medicine were posted on the university's website, and the information for this research was announced on the hospital's bulletin board. All participants had the right to refuse participation at any time (opt-out method).

### Study setting and data sources

This study was conducted between November 2022 and June 2023 in the Department of Ophthalmology, Jikei Medical University Hospital, Tokyo. The study participants corresponded to cases previously reported in a peer-reviewed journal, where we described findings based only on hematoxylin & eosin and Masson's trichrome staining<sup>8</sup>.

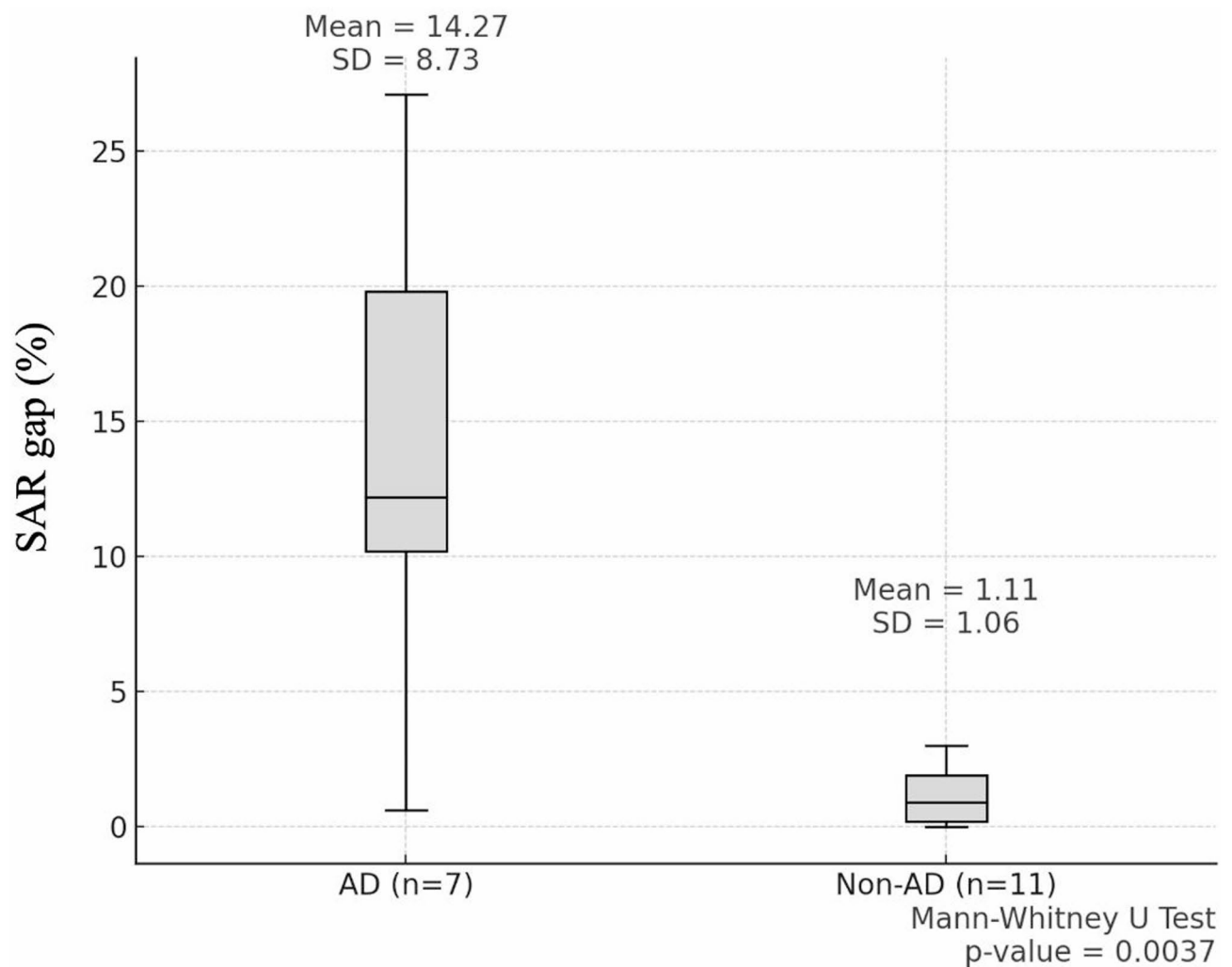
This study included patients with IOL dislocation who underwent IOL extraction. In particular, only the cases in which the extracted lens bag was appropriately processed as a specimen were included. Based on the slit-lamp examination and intraoperative findings, IOL dislocations were classified as CBD or DBS. Specifically, dislocations in which the IOL remained within the capsular bag and formed a complex with the capsule were classified as CBD. Cases in which the crystalline lens capsule was intact at the time of the initial cataract surgery, but subsequently ruptured, leading to IOL dislocation without an accompanying capsular bag, were classified as DBS. Patient data on age, sex, history of prior intraocular surgery, eye axial length, AD, history of trauma, pseudoexfoliation syndrome, uveitis, and the presence or absence of retinitis pigmentosa were extracted from the medical records. The participants were divided into an AD group with 10 eyes (10 patients) and a non-AD group with 12 eyes (12 patients).

### Surgical technique<sup>8</sup>

Surgeries were performed by seven surgeons (three authors of this study). To extract the acrylic IOL, a small incision was made, and the IOL was either removed as a whole using IOL extraction forceps or fragmented using an IOL cutter<sup>19</sup>. An L-shaped scleral tunnel incision was made to remove the polymethyl methacrylate IOL<sup>20</sup>. In CBD cases, the lens bag was extracted simultaneously with the IOL. In DBS cases, after IOL extraction, the zonules were incised using a vitreous cutter and extracted.

	Case 11	Case 12	Case 13	Case 14	Case 15	Case 16	Case 17	Case 18	Case 19	Case 20	Case 21	Case 22	Average ± SD or Total n(%)
Classification of IOL dislocation	CBD	CBD	CBD	CBD	CBD	CBD	CBD	CBD	CBD	CBD	CBD	CBD	
Explanting surgeon	KK	IN	KKon/AW	YM	TW	IN	KKon/AW	SO	YM	KK	IN	KKon/TW	
Age at explantation (years)	57	67	78	66	67	33	51	55	63	76	70	85	64.0 ± 13.8
Sex	M	M	M	M	M	M	M	M	M	M	F	F	
Eye	R	L	R	R	L	L	L	L	L	L	R	L	
Length of implantation (years)	12	8	10	19	8	13	23	6	6	6	7	4	10.2 ± 5.7
Axial length (mm)	24.5	25	24.2	25.5	28.2	26.7	24.3	26.6	25.9	27.9	24.8	23.9	25.6 ± 1.5
Causes of IOL dislocation	Trauma, Vitrectomy	Trauma, Vitrectomy	Vitrectomy	unknown	Trauma	Trauma	Trauma	Vitrectomy	Trauma	unknown	unknown	Vitrectomy	
History of Ophthalmic Surgical Treatments	In-the-bag IOL	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	12 (100%)
	Vitrectomy	(+)	(+)	(-)	(-)	(-)	(-)	(+)	(-)	(-)	(-)	(+)	5 (41.6%)
LEC degeneration or loss		(+)	(+)	(-)	(-)	(-)	(+)	(-)	(+)	(+)	(-)	(+)	6 (50%)
		(+)	(+)	(-)	(-)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	11 (91.6%)
Fibrous metaplasia	High-density fibrosis	(+)	(+)	(-)	(+)	(+)	(-)	(+)	(-)	(+)	(-)	(-)	3 (25%)
	Low-density fibrosis	(-)	(-)	(-)	(+)	(-)	(-)	(-)	(-)	(+)	(-)	(-)	1.1 ± 1.1
Soemmering's ring SAR gap (%)		0.0	1.8	2.4	0.4	0.2	2.0	1.3	NA	0.0	0.9	3.0	1.1 ± 1.1
MBP Immunostaining	Fibrous metaplasia SAR gap (%)	4.8	0.4	0.8	NA	0.0	0.0	1.1	0.2	41.1	10.4	0.3	6.5 ± 12.3
	Lens capsule	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	0 (0%)
	LEC	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	0 (0%)

**Table 2.** Non-Atopic dermatitis case characteristics. CBD = capsular bag dislocation; F = female; IOL = intraocular lens, L = left; LEC = lens epithelial cells; M = male; MBP = eosinophil major basic protein; NA = not applicable; R = right; SAR = staining area ratio; SD = standard deviation.



**Fig. 1.** MBP evaluation in Soemmering's ring. Comparison of mean SAR gaps between the Atopic Dermatitis group and the Non-Atopic Dermatitis group. (Cases deemed "not applicable" were excluded from the mean value calculation.) MBP = major basic protein; SAR = staining area ratio.

### Pathology specimen Preparation<sup>8</sup>

The lens capsule extracted during surgery was fixed in 10% neutral-buffered formalin. After dehydration, it was embedded in paraffin, sectioned into 3- $\mu$ m thick slices, and then stained with hematoxylin & eosin and Masson's trichrome. The pathological evaluations were conducted by two ophthalmologists (two authors) and two pathologists (two authors). Morphological evaluations of the lens capsule, LEC, Soemmering's ring, and fibrous metaplasia (distinguishing between high- and low-density fibrosis [LDF]) were also conducted. Additionally, MBP immunostaining was performed on these structures.

### Immunohistochemical staining Method<sup>10</sup>

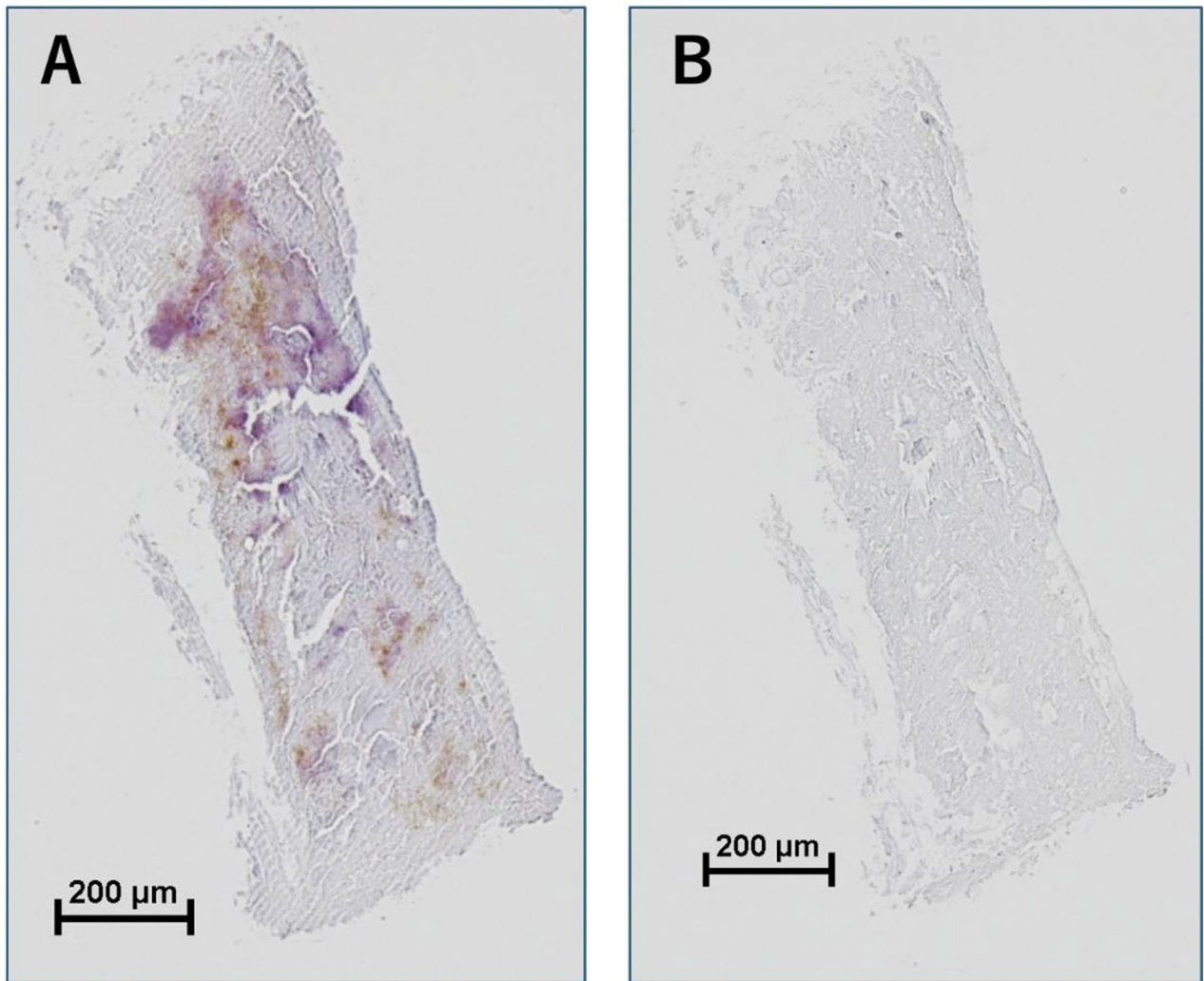
Formalin-fixed, paraffin-embedded lens capsule specimens were sectioned and blocked with endogenous peroxidase, followed by enzyme digestion using Proteinase K (S3020, Agilent Technologies, Santa Clara, CA). After washing with PBS, blocking was performed using goat serum (426041; NICHIREI, Tokyo, Japan). The primary antibody used was a mouse anti-human eosinophil MBP antibody (1:200, BMK13, Bio-Rad, Oxford, UK), and the secondary antibody was Histofine Simple Stain MAX-PO-Multi (NICHIREI, Tokyo, Japan). For color development, 3,3'-Diaminobenzidine (DAB, 343-00901, Dojindo Laboratory, Kumamoto, Japan) was used.

For each specimen, mouse IgG1k monoclonal antibody (ab170190, Abcam, Cambridge, UK) was used as an isotype control (negative control). An isotype control was used instead of the primary antibody and processed using the same protocol.

### Immunohistochemical staining evaluation

Digital pathology images captured by the microscope slide scanner Aperio AT2 (Leica Biosystems) were magnified 40 x, and image regions were set at 300  $\times$  300 pixels (Supplementary Fig. 1a). Quantitative evaluation



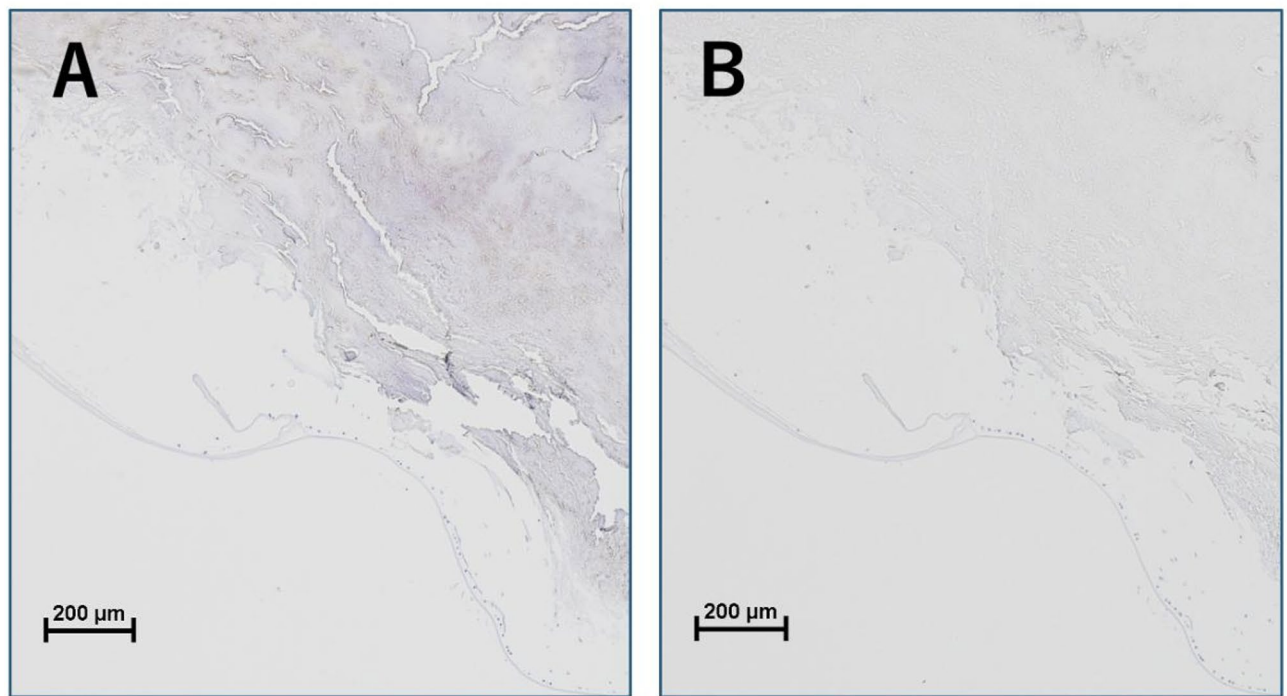


**Fig. 2.** Dead bag syndrome case in the Atopic Dermatitis group (Case 2). MBP staining of Soemmering's ring (a) and the negative control in the same area (b). Compared to (b), a shows stronger staining. MBP = major basic protein.

of MBP immunostaining was performed using image analysis software ImageJ2 (version 2.14.0), based on methods from previous studies that employ RGB channel separation and red-channel thresholding, with reference to negative control slides<sup>21–23</sup>. To detect brown DAB coloration, the MBP-stained images were split into RGB (red-green-blue) channels, and the red channel was used to detect the stained areas, which were then highlighted in red (Supplementary Fig. 1b). Thresholds corresponding to specific staining areas were set, and the MBP staining area ratio (SAR) was measured. The same process was applied to the negative control images of the same regions, and the SAR of the negative control was measured (Supplementary Fig. 1c, d). Based on these results, the difference in SAR between the MBP and negative control was defined as the SAR gap and was compared between the two groups. Tissues from patients with eosinophilic esophagitis were used as a positive control, and the SAR gap was calculated under the same conditions (Supplementary Fig. 2). Due to sample size limitations, a quantitative evaluation of the lens capsule and LEC could not be performed. Instead, a qualitative assessment was performed by an ophthalmologist (one author) and pathologist (one author), who were blinded to the patients' clinical history.

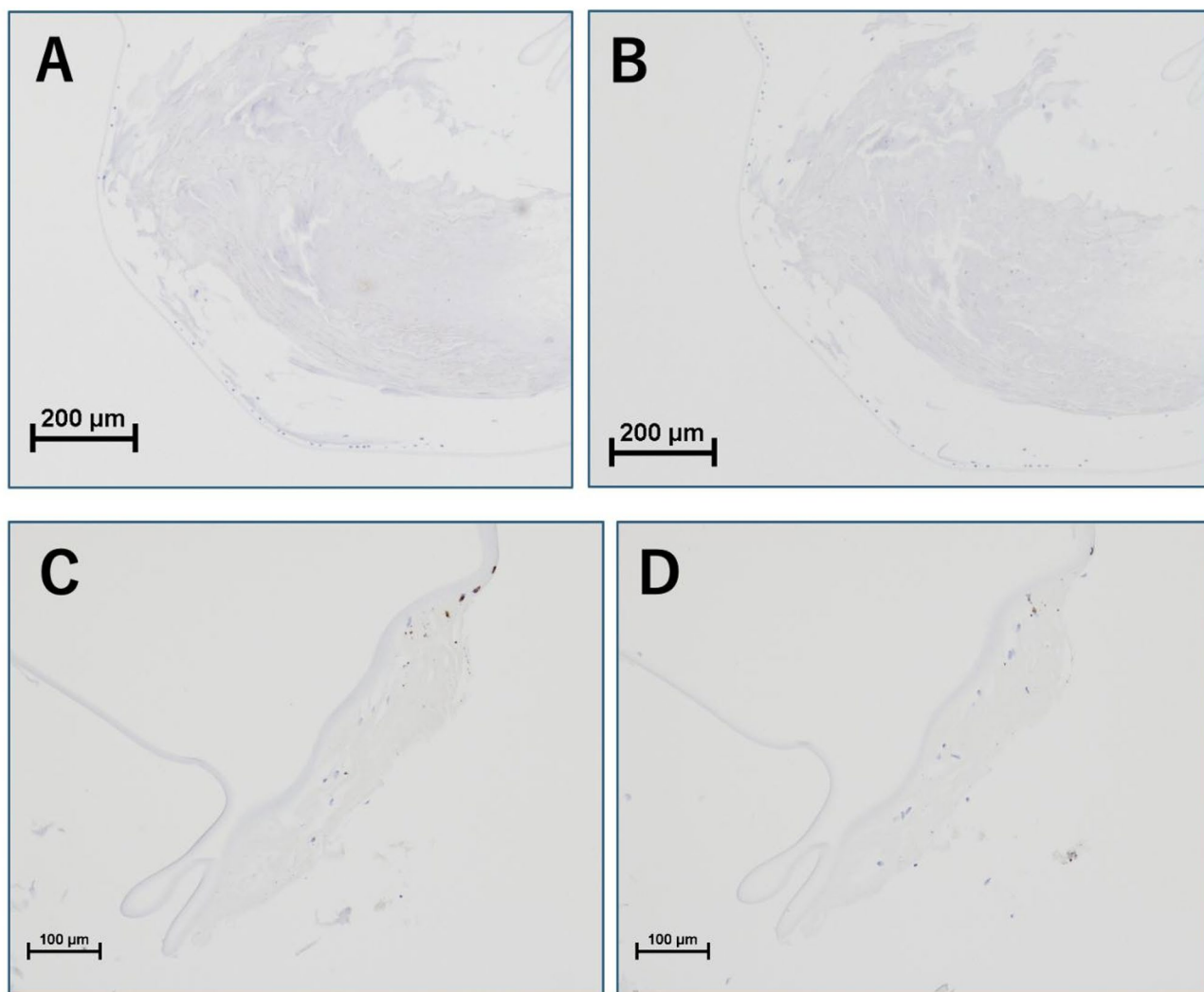
#### Statistical analysis for MBP immunostaining quantification

To quantify MBP immunostaining, statistical analysis was conducted using the SciPy library version 1.9.1 in the Python programming language. The Mann–Whitney U test was used to compare the SAR gap between the AD and NAD groups. The results are visualized using boxplots displaying the median, interquartile range, and range of data. Additionally, the mean  $\pm$  standard deviation of each group is included in the boxplots. Statistical significance was set at  $p < 0.05$ . The data were visualized using Matplotlib version 3.5.1.

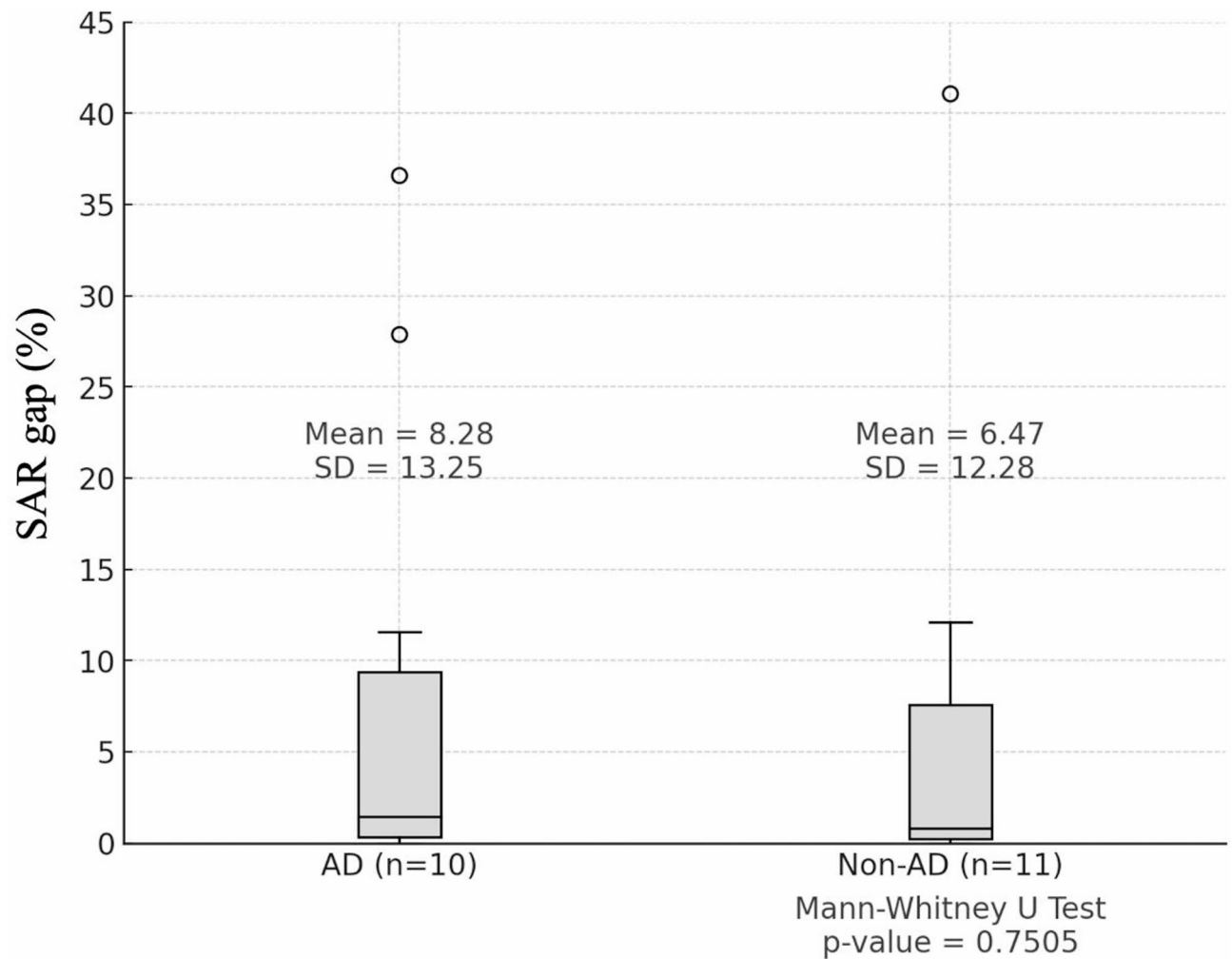


**Fig. 3.** Capsular bag dislocation case in the Atopic Dermatitis group (Case 9). MBP staining of Soemmering's ring (**a**) and the negative control in the same area (**b**). Compared to (**b**, **a**) shows stronger staining. MBP = major basic protein.

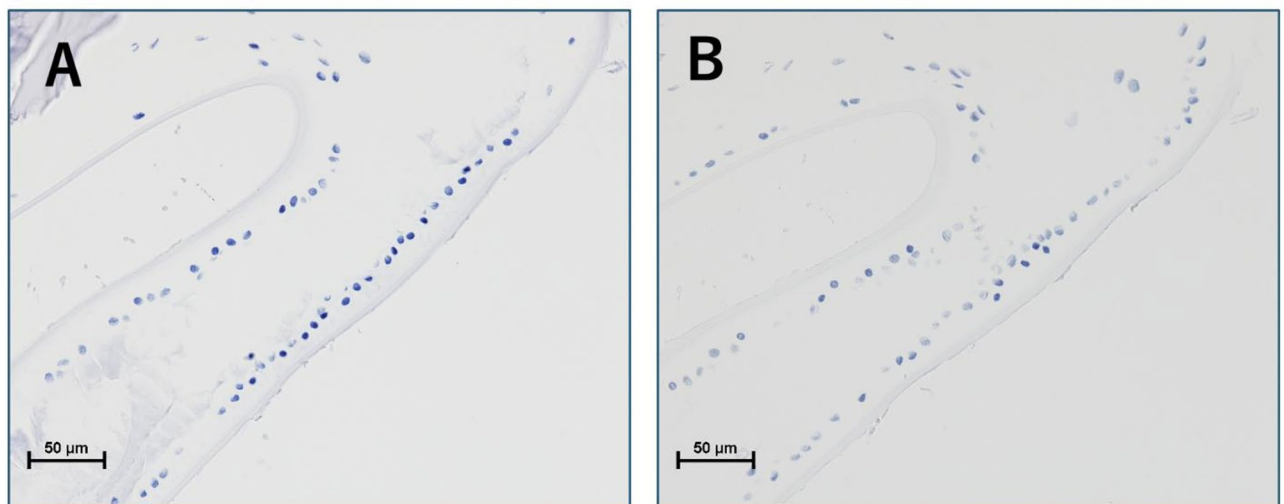




**Fig. 4.** Capsular bag dislocation case in the Non-Atopic Dermatitis group (Case 12). MBP staining of Soemmering's ring (**a**) and the negative control in the same area (**b**). (**a** and **b**) show similar staining intensity. MBP staining of fibrous metaplasia (**c**) and the negative control in the same area (**d**). Compared to (**d**, **c**) shows similar staining intensity. MBP = major basic protein.



**Fig. 5.** MBP evaluation of fibrous metaplasia. Comparison of mean SAR gaps between the Atopic and Non-Atopic Dermatitis groups. MBP = major basic protein; SAR = staining area ratio.



**Fig. 6.** MBP staining of the lens capsule and lens epithelial cells (A) and the negative control in the same area (B). Compared to (B, A) shows similar staining intensity. MBP = major basic protein.

## Data availability

The data are available from the corresponding author upon reasonable request. E-mail: ymasuda@jikei.ac.jp  
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## Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors criteria for authorship. Conception and design: K.K. and Y.M. Acquisition of data: K.K., Y.M., M.I., and K.I. Data analysis and interpretation of data: K.K., Y.M., H.K., A.I., E.N., and N.Y. Writing and revision of the manuscript: K.K., Y.M., H.K., A.I., E.N., and N.Y. Additionally, all authors have reviewed the manuscript.

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## Declarations

## Competing interests

The authors declare no competing interests.

## Additional information

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