From the Université Paris VII, Assistance Publique-Hôpitaux de Paris, Service de dermatologie hôpital Bichat Claude-Bernard, Paris, France[a]; and the Sorbonne Université, Faculté de Médecine Sorbonne Université, Service de Dermatologie et Allergologie, Hôpital Tenon, Paris, France.[b]

Drs Salle and Chasset are cofirst authors.

Funding sources: None.

Conflicts of interest: None disclosed.

IRB approval status: Not applicable.

Reprints not available from the authors.

Correspondence to: François Chasset, MD, Assistance Publique-Hôpitaux de Paris, Service de Dermatologie et d'Allergologie, Université Pierre et Marie Curie, Hôpital Tenon, 4 rue de la Chine 75970, Paris CEDEX 20, France

E-mail: francois.chasset@aphp.fr

REFERENCES

1. Manzi S, Sánchez-Guerrero J, Merrill JT, et al. Effects of belimumab, a B lymphocyte stimulator-specific inhibitor, on disease activity across multiple organ domains in patients with systemic lupus erythematosus: combined results from two phase III trials. *Ann Rheum Dis*. 2012;71:1833-1838.
2. Vashisht P, Borghoff K, O'Dell JR, Hearth-Holmes M. Belimumab for the treatment of recalcitrant cutaneous lupus. *Lupus*. 2017;26:857-864.
3. Iaccarino L, Bettio S, Reggia R, et al. Effects of belimumab on flare rate and expected damage progression in patients with active systemic lupus erythematosus. *Arthritis Care Res (Hoboken)*. 2017;69:115-123.
4. Klein R, Moghadam-Kia S, LoMonico J, et al. Development of the CLASI as a tool to measure disease severity and responsiveness to therapy in cutaneous lupus erythematosus. *Arch Dermatol*. 2011;147:203-208.
5. Wenzel J, Landmann A, Vorwerk G, Kuhn A. High expression of B lymphocyte stimulator in lesional keratinocytes of patients with cutaneous lupus erythematosus. *Exp Dermatol*. 2018;27:95-97.

https://doi.org/10.1016/j.jaad.2020.05.058

Eosinophil cationic protein is a potential surrogate marker of allergic contact dermatitis: A single-center, retrospective study of 216 patients

To the Editor: Although patch testing is the gold standard diagnostic test for allergic contact dermatitis, assessing the clinical relevance and differentiating between allergic and irritant contact dermatitis or another intrinsic eczema can be challenging[1] because of a lack of reliable diagnostic tools and disease-specific biomarkers to support the diagnosis.

Table I. Comparison of patient characteristics and serum allergy markers between allergic and nonallergic contact dermatitis groups

	ACD group (n = 169)	Non-ACD group (n = 47)	*P* value
MOAHLFA index, No. (%)			
Men	46 (27.2)	20 (42.6)	.07*
Occupational†	16 (9.5)	3 (6.4)	.77*
Atopic dermatitis‡	0	0	NA
Hand dermatitis	26 (15.4)	6 (12.8)	.83*
Leg dermatitis	18 (10.7)	6 (12.8)	.88*
Face dermatitis§	59 (34.9)	18 (38.3)	.80*
Age ≥40 y	103 (60.9)	26 (55.3)	.60*
Disease duration, mo	20.0 (12.5—41.5)	17.0 (8.0—37.0)	.10‖
BSA involvement (%)	3.0 (1.5—6.8)	4.5 (1.8—10.2)	.19‖
Serum allergy marker			
ECP, μg/L	20.6 (12.9—31.3)	13.3 (6.7—18.3)	<.001‖
Eosinophil count, cells/μL	140 (70—215)	110 (70—170)	.19‖
Total IgE, IU/mL	60.6 (22.3—142)	36.3 (15.5—96)	.07‖

Nonparametric continuous variables are presented as median (P25-P75).
ACD, Allergic contact dermatitis; *BSA*, body surface area; *ECP*, eosinophil cationic protein; *IgE*, immunoglobulin E; *NA*, not available.
*χ^2 Test (with Yates continuity correction) or Fisher's exact test; $P < .05$ statistically significant.
†Excludes uncertain.
‡Patients with atopic dermatitis were excluded, according to the study design.
§Primary sites of lips, nose, eyes, and eyelids are all included.
‖Mann-Whitney *U* test.

Eosinophil cationic protein is a sensitive marker of allergic inflammation that has diagnostic and prognostic roles in eosinophil-related diseases such as asthma and atopic dermatitis.[2] However, a role for serum eosinophil cationic protein has not been previously evaluated in allergic contact dermatitis, to our knowledge. Therefore, we analyzed the relationship between serum eosinophil cationic protein levels and the clinical and laboratory findings in allergic contact dermatitis.

We retrospectively reviewed the 216 patients with suspected allergic contact dermatitis and categorized them into allergic contact dermatitis and nonallergic contact dermatitis groups; patients with relevant

Table II. Logistic regression analysis of positive patch-test reactions to clinical independent variables and serum markers in allergic contact dermatitis

	Odds ratio (95% confidence interval) of independent variables							
Positive patch-test result*	**Female sex**	**≥40 years**	**Face**	**Hand**	**Leg**	**ECP†**	**Eosinophil count‡**	**Total IgE‡**
Nickel (II) sulfate hexahydrate	2.23 (1.16−4.68)§	0.63 (0.34−1.17)	1.03 (0.55−1.94)	1.09 (0.47−2.52)	1.97 (0.70−5.53)	0.96 (0.82−1.14)	0.93 (0.76−1.15)	1.10 (0.94−1.31)
Cobalt (II) chloride hexahydrate	1.11 (0.56−2.21)	1.29 (0.69−2.42)	0.77 (0.40−1.46)	0.79 (0.34−1.87)	1.06 (0.40−2.83)	0.93 (0.78−1.11)	1.02 (0.83−1.25)	1.07 (0.91−2.41)
Myroxylon pereirae resin (balsam Peru)	0.90 (0.38−2.12)	1.43 (0.63−3.28)	1.22 (0.55−2.73)	0.15 (0.02−1.16)	2.52 (0.87−7.35)	0.84 (0.63−1.10)	0.95 (0.72−1.27)	0.92 (0.71−1.26)
Thimerosal	1.79 (0.63−5.04)	0.31 (0.13−0.73)§	1.94 (0.84−4.46)	0.95 (0.30−3.01)	1.59 (0.48−5.26)	0.89 (0.68−1.16)	0.61 (0.37−1.00)	1.03 (0.84−1.26)
Potassium dichromate	1.08 (0.42−2.76)	0.77 (0.33−1.76)	0.48 (0.18−1.26)	0.95 (0.30−3.01)	2.26 (0.73−6.96)	1.02 (0.82−1.27)	1.04 (0.80−1.35)	0.95 (0.74−1.22)
Fragrance mix I	0.57 (0.23−1.41)	1.33 (0.54−3.32)	1.14 (0.47−2.79)	0.46 (0.10−2.08)	1.24 (0.33−4.65)	0.90 (0.68−1.19)	0.66 (0.40−1.07)	0.89 (0.65−1.21)
p-Phenylenediamine	1.14 (0.39−3.33)	4.15 (1.17−14.78)§	1.00 (0.38−2.67)	0.26 (0.03−2.04)	1.58 (0.41−6.01)	0.93 (0.70−1.24)	0.99 (0.71−1.37)	1.13 (0.93−5.01)
Formaldehyde	0.81 (0.26−2.46)	1.08 (0.37−3.11)	0.83 (0.28−2.52)	1.99 (0.59−6.71)	0.53 (0.07−4.30)	1.59 (1.24−2.04)§	1.51 (1.15−2.00)§	0.96 (0.72−1.27)
Captan	0.44 (0.15−1.26)	1.08 (0.37−3.11)	1.13 (0.39−3.29)	0.77 (0.16−3.60)	0.53 (0.07−4.30)	1.25 (1.01−1.54)§	1.49 (1.13−1.96)§	1.09 (0.88−1.34)
Polysensitization‖	0.77 (0.39−1.55)	0.88 (0.47−1.66)	0.45 (0.23−0.89)§	3.62 (1.50−8.72)§	0.99 (0.36−2.70)	1.09 (0.92−1.29)	0.96 (0.77−1.19)	1.08 (0.92−1.28)

Patch testing with the Korean standard series (KOR-1000, Chemotechnique Diagnostics, Vellinge, Sweden) was performed.

ECP, Eosinophil cationic protein; *IgE*, immunoglobulin E.

*Contact allergens presenting less than 10% of total cases (n = 17) on the patch test were excluded from the analysis for statistical accuracy.

†Serum levels of ECP were divided by 10 from the original value.

‡Serum eosinophil counts and total IgE were divided by 100 from the original value.

§Significant effects.

‖Polysensitization is defined as contact allergy to greater than or equal to 3 allergens in patch testing.

positive patch-test results were assigned to the allergic contact dermatitis group (n = 169); those with negative or irrelevant patch-test results, to the nonallergic contact dermatitis group (n = 47). Demographic data, clinical characteristics, patch-testing results, serum eosinophil cationic protein level, eosinophil count, and total immunoglobulin E levels were assessed.

Differences in clinical characteristics between the 2 groups were not statistically significant (Table I). The serum eosinophil cationic protein level in the allergic contact dermatitis group was 20.6 μg/L, which was significantly higher ($P < .001$) than in the nonallergic contact dermatitis group (13.3 μg/L). The blood eosinophil counts and total immunoglobulin E levels were also higher in the allergic contact dermatitis group than in the nonallergic contact dermatitis one, but neither was statistically significant. The optimal cutoff value of eosinophil cationic protein level to differentiate allergic from nonallergic contact dermatitis with a receiver operating characteristic analysis was 16.95 μg/L, with a sensitivity of 66.9% and a specificity of 63.8%. Univariate logistic regression analyses (Table II) indicated that patients with higher eosinophil cationic protein and eosinophil levels had higher sensitization risk to the formaldehyde and captan. Multivariate analysis adjusted for age, sex, and serum allergy markers revealed that increasing serum eosinophil cationic protein level posed a significant sensitization risk to formaldehyde only (odds ratio 1.48; 95% confidence interval 1.11-1.96).

Our study showed that serum eosinophil cationic protein levels are significantly higher in patients with allergic contact dermatitis than in those with nonallergic contact dermatitis who had dermatosis that mimicked allergic contact dermatitis. Thus, elevated serum eosinophil cationic protein level strengthens the relevance of a positive patch-test result in patients with allergic contact dermatitis. Still, we believe that detailed history taking and clinical response to allergen avoidance are essential to assess the current relevance in allergic contact dermatitis,[1] and elevated serum eosinophil cationic protein level should be interpreted along with patch testing and clinical contexts.

General eosinophil activation and recruitment by mast cells in the signaling cascades of allergic contact dermatitis[3] and underlying allergen-specific T-helper cell type 2–mediated pathways might be explanations for elevated serum eosinophil cationic protein levels.[4] Formaldehyde especially has been known to be involved in airborne contact dermatitis,[5] which may cause systemic eosinophilic inflammation and subsequent eosinophil cationic protein level elevation. Retrospective design at a tertiary referral center, statistical limitations caused by small sample size, lack of follow-up assessment of the serum allergy markers after allergen avoidance, and exclusion of atopic patients are limitations.

In summary, serum eosinophil cationic protein is a sensitive marker of allergic inflammation whose level is elevated in patients with allergic contact dermatitis. The protein can be used as a supportive test for the diagnosis of allergic contact dermatitis and is especially useful in assessing the clinical relevance of a positive patch-test result.

Jemin Kim, MD,[a] Sumin Kim, MD,[a] Young In Lee, MD,[a] Jihee Kim, MD,[a] Ju Hee Lee, MD, PhD,[a] and Chang Ook Park, MD, PhD[a,b]

From the Department of Dermatology and Cutaneous Biology Research Institute[a] and Institute of Allergy,[b] Severance Hospital, Yonsei University College of Medicine, Seoul, Korea.

Funding sources: Supported by a National Research Foundation of Korea grant funded by the Korean government (Ministry of Science and ICT) (NRF-2017R1A2B4009568), and by grants from the Korean Health Technology R&D Project, Ministry of Health, Welfare and Family Affairs, Republic of Korea (HI14C1324).

Conflicts of interest: None disclosed.

Correspondence to: Chang Ook Park, MD, PhD, Department of Dermatology and Cutaneous Biology Research Institute, Yonsei University College of Medicine, 50-1 Yonsei Ro, Seodaemun-gu, Seoul 03722, Korea

E-mail: copark@yuhs.ac

REFERENCES

1. Watts TJ, Watts S, Thursfield D, Haque R. A patch testing initiative for the investigation of allergic contact dermatitis in a UK allergy practice: a retrospective study. *J Allergy Clin Immunol Pract*. 2019;7:89-95.
2. Park SY, Oh S, Kim EJ, et al. Utility of eosinophil cationic protein levels in the diagnosis of intrinsic atopic dermatitis. *Acta Derm Venereol*. 2014;94:333-334.
3. Galdiero MR, Varricchi G, Seaf M, Marone G, Levi-Schaffer F, Marone G. Bidirectional mast cell-eosinophil interactions in inflammatory disorders and cancer. *Front Med (Lausanne)*. 2017;4:103.
4. Dhingra N, Shemer A, Correa da Rosa J, et al. Molecular profiling of contact dermatitis skin identifies allergen-dependent differences in immune response. *J Allergy Clin Immunol*. 2014;134:362-372.
5. Swinnen I, Goossens A. An update on airborne contact dermatitis: 2007-2011. *Contact Dermatitis*. 2013;68:232-238.

https://doi.org/10.1016/j.jaad.2020.05.070