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## Introduction

The gold standard for diagnosing allergic contact dermatitis (ACD) is patch testing interpreted by a dermatologist with expertise in ACD. Achieving this is often limited by access and expense but is consequential for the appropriate management of skin disease. With difficult rashes, histopathologic evaluation of lesional skin is frequently performed and is used to guide appropriate management. However, the histologic differential diagnosis of ACD, which shares similar or identical clinical and histopathologic features with other eczematous lesions, is challenging. Previously published efforts have yielded inconsistent and sometimes controversial findings, and long-standing dermatopathology dogma dictates that the presence of eosinophils favors ACD. Herein we report a comprehensive histopathologic evaluation on our ACD cohort that, to our knowledge, represents the largest number of patch test-confirmed ACD cases to date.

## Methods

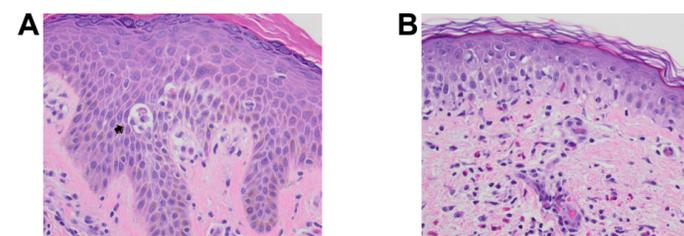
IRB approval was obtained for examination of biopsies of patch-test eligible patients at an academic tertiary referral center. Patients were seen for patch testing by a Board-certified dermatologist and nationally recognized expert in patch testing. The selected histopathologic features (Table 1) were reviewed by an experienced Board-certified dermatopathologist and resident physician in pathology in a blinded fashion and included the most significant histopathologic features reported in the largest published ACD studies from Europe and North America.<sup>1-3</sup> Statistical analyses were performed with Stata®.

## Results

109 cases were examined, of which 69 were patch test-confirmed ACD. The predominant presence of Langerhans cell collections within spongiotic vesicles, but not dermal eosinophilic infiltration, was significantly positively associated with ACD ( $p=0.008$ , Table 2, Figure 1A). In contrast, heavy dermal eosinophilic infiltration showed a significant association with non ACD cases ( $p=0.004$ , Table 3, Figure 1B). Similarly, epidermal eosinophilic spongiosis also had a negative association with ACD ( $p=0.023$ , Table 4). Other features including multinucleated dermal dendritic cells, papillary dermal edema and hypogranulosis, were not statistically significantly associated with diagnosis of ACD.

**Table 1. Pre-defined grading system for histopathologic features of ACD**

Histopathologic Features		Grading
Epidermal Spongiosis		0-3
Follicular Spongiosis		0-3
Spongiotic Vesicle	Langerhans cells	0-2
	Eosinophils	0-2
	Neutrophils	0-2
	Lymphocytes	0-2
Eosinophilic Spongiosis		0-1
Lesional Stage	Acute	0-1
	Subacute	0-1
	Chronic	0-1
Papillary Dermal Edema + Hypogranulosis		0-1
Dermal Perivascular Infiltrate	Superficial	0-1
	Mid	0-1
	Deep	0-1
Dermal Eosinophils		Count
Dermal Neutrophils		Count
Dermal Multinucleated Dendritic Cells		0-1



**Figure 1. Histopathologic features evaluated. A.** Langerhans cell collection within spongiotic vesicles (arrow). **B.** Heavy dermal eosinophilic infiltration. Refer to the text for more details. (H&E, 400x).

**Table 2. Langerhans cell collections within spongiotic vesicles in ACD**

	Spongiotic Vesicles		
	Absent	Present-Other Type	Present-Langerhans Cell Predominated
Patch -	31	4	5
Patch +	50	0	19
Chi <sup>2</sup> p	0.008		

**Table 3. Heavy dermal eosinophilic infiltration (defined as >100 eosinophils/5 HPFs\*) in ACD**

	Dermal Eosinophilic Infiltration (counts/5 HPFs)	
	<100	100-1199
Patch -	30	10
Patch +	65	4
Chi <sup>2</sup> p	0.004	

\* HPF, high power field

**Table 4. The relation of epidermal eosinophilic spongiosis and ACD**

	Epidermal Eosinophilic Spongiosis	
	Absent	Present
Patch -	27	13
Patch +	56	9
Chi <sup>2</sup> p	0.023	

## Discussion

Our analysis supported the previous observation that the presence of dermal eosinophilic infiltration is not a reliable clue for the diagnosis of ACD.<sup>2</sup> Whereas heavy dermal eosinophilic infiltration and epidermal eosinophilic spongiosis were associated with a non-ACD diagnosis (Table 3 and 4), presence of Langerhans cell collections was consistent with ACD (Table 2). These results challenge the long-standing dogma of eosinophils associated with a diagnosis of ACD but support the experience that Langerhans cell collections are consistent with ACD.

## References

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