

Enhancement of IgE Production in B Cells by Neutrophils via Galectin-3 in IgE-Associated Atopic Eczema/Dermatitis Syndrome

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Key Words

Atopic eczema/dermatitis syndrome · Galectin-3 · IgE production · Neutrophils

Abstract

Spontaneous IgE production by B cells from patients with IgE-associated atopic eczema/dermatitis syndrome (AEDS) is enhanced by polymorphonuclear leukocytes (PMN) from patients with AEDS, but not by PMN from non-atopic controls. The enhancement is abolished by preincubation of PMN with lactose, but not with glucose. Anti-galectin-3 serum, but not control rabbit serum, blocked the enhancement. These results indicate that AEDS PMN can enhance IgE production via galectin-3.

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B cells from IgE-associated atopic eczema/dermatitis syndrome (AEDS) contain surface IgE-positive (sIgE+) B cells which spontaneously produce IgE upon in vitro culture, while B cells from non-atopic controls fail to do so [1]. Polymorphonuclear leukocytes (PMN) express galectin-3 which can bind IgE, and thereby IgE induces these cells to undergo a respiratory burst [2]. I studied the effect of PMN on spontaneous IgE production by B cells from subjects with AEDS. After obtaining informed consent, blood was obtained from 15 patients with AEDS (mean age 33 years, range 19–54 years, 8 men and 7 women) and 15 age-matched non-atopic controls (mean age 32 years, range 20–52 years, 8 men and 7 women). B cells were isolated from the blood [1]. Purified B cells contained <1% CD3+ T cells, <1% CD14+ monocytes and <1% CD16+ NK cells [1]. None of them took any medication for 1 week before the study. In patients with AEDS, sIgE+ and surface IgE-negative (sIgE–) B cells were also obtained as previously reported [1]. PMN from patients with AEDS or controls were separated by dextran sedimentation, followed by centrifugation through Ficoll-Hypaque as reported [2]. Whole B cells ($1 \times 10^5/0.2$ ml/well), sIgE+ or sIgE– B cells ($2 \times 10^4/0.2$ ml/well) were cultured with medium alone or with PMN (1×10^5) in the presence or absence of rabbit anti-galectin-3 serum (Cosmo Bio, Tokyo, Japan; 1:100 dilution) or normal rabbit serum (1:100; n = 15). IgE production from these sIgE+ B cells

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1018–2438/02/1282–0168\$18.50/0

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Table 1. Involvement of galectin-3 in enhanced IgE production by AEDS PMN

Factors	IgE production, ng/ml			
	AEDS			control
	whole B cells	sIgE+ B cells	sIgE- B cells	whole B cells
Medium	1.4 ± 0.1	4.1 ± 0.2	<0.3	<0.3
Control PMN	1.3 ± 0.1	3.9 ± 0.2	<0.3	<0.3
AEDS PMN	3.1 ± 0.2*	10.3 ± 0.3*	<0.3	<0.3
AEDS PMN preincubation				
With lactose	1.5 ± 0.1	4.0 ± 0.2	<0.3	<0.3
With glucose	2.9 ± 0.2*	10.1 ± 0.3*	<0.3	<0.3
AEDS PMN +				
Anti-galectin-3 serum	1.2 ± 0.1	3.8 ± 0.2	<0.3	<0.3
Normal rabbit serum	3.0 ± 0.2*	10.0 ± 0.3*	<0.3	<0.3

Values are means ± SEM (n = 15). * p < 0.01 vs. medium. AEDS B cells from each subject (n = 15) were cultured with autologous or control PMN.

was inhibited by anti-IgE antibodies as previously reported [3]. In some cases, AEDS PMN were preincubated with lactose (25 mM) or glucose (25 mM). After 14 days of culture, IgE production was determined by ELISA [1].

As shown in table 1, AEDS whole B cells or sIgE+ B cells produced IgE spontaneously, and this production was enhanced by addition of AEDS PMN, but not by control PMN. Production of IgG1, IgG2, IgG3, IgG4, IgM, IgA1 or IgA2 was unaltered by the presence of AEDS or control PMN (data not shown). This is not surprising, since even IL-10, which enhances IgG4 production in some culture systems, failed to affect IgG4 production in others [1]. Cell surface galectin-3 can be detached by lactose, but not by glucose [4]. Thus, preincubation of PMN with lactose, but not with glucose, abolished the enhancement of IgE production by PMN. Moreover, rabbit anti-galectin-3 serum, but not normal rabbit serum, blocked the enhancement. In contrast, neither AEDS sIgE- B cells nor control whole B cells spontaneously produced IgE (<0.3 ng/ml), nor did addition of AEDS PMN induce IgE production from these cells. Staining of PMN with anti-galectin-3 mAb revealed that mean fluorescence intensities for AEDS PMN and control PMN were 61 and 18, respectively (n = 6). Thus it is possible that failure of control PMN to enhance IgE production may be due to insufficient amount of galectin-3. Indeed, addition of galectin-3 (20 µg/ml) to cultures of AEDS B cells with control PMN enhanced IgE production, although there are no phenotypic differences between normal and AEDS PMN. Moreover, stimulation of control or AEDS PMN with myeloma IgE-PS (10 µg/ml) induced similar levels of chemiluminescence [manuscript in prep.]. Furthermore,

the addition of soluble CD40 fusion protein did not inhibit AEDS-PMN-induced enhancement of IgE production, indicating that CD40-CD40L interactions were not involved. Taken together, these results indicate that AEDS PMN can enhance IgE production by B cells already committed to IgE production via galectin-3. In addition, only 5.2% of unstimulated AEDS T cells expressed galectin-3, but 35.7% of T cells expressed it upon activation by solid-phase anti-CD3 mAb (n = 4). When AEDS B cells were cultured, activated T cells enhanced spontaneous IgE production by sIgE+ B cells 3.8-fold, while unstimulated T cells enhanced it only 2.7-fold (n = 4).

It has been reported that activated PMN, but not resting PMN, produced various cytokines and chemokines including IL-10 and macrophage inflammatory protein 1α (MIP-1α) [5, 6], both of which enhance IgE production in sIgE+ B cells [1]. I have previously reported that IL-10 directly enhance IgE production in B cells stimulated with IL-4+ hydrocortisone or with IL-13+ hydrocortisone [7]. It is tempting to speculate that AEDS PMN, but not control PMN, are activated in such a way in vivo via IgE interaction that they can specifically enhance IgE production from sIgE+ B cells via production of IL-10 and/or MIP-1α or other factors. Indeed, intracytoplasmic staining of AEDS PMN revealed positive staining of IL-8, IL-10, IFN-γ, and MIP-1α, while in culture supernatants only IL-10 and MIP-1α were found. Moreover, addition of anti-IL-10 mAb and anti-MIP-1α mAb reduced AEDS-PMN-mediated enhancement of IgE production [manuscript in prep.]. Detailed analysis is currently under investigation.

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