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Original Article

Role of IgE Low-Affinity Receptor (CD23) in Pathogenesis of Nasal Polyp

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Abstract

Background: Nasal polyps, a common clinical problem, are characterized by eosinophilic and mast cell inflammation. The role of allergy and IgE in pathogenesis of nasal polyps is still unclear. IgE receptors are important components of the immunological pathway in allergic and inflammatory diseases.

Objective: To determine if the low affinity IgE receptor (CD23) is presented on nasal polyp tissues as a marker of local allergy or inflammation.

Methods: Twenty patients who had undergone polypectomy enrolled into the study. Polyp tissues were stained by hematoxylin-eosin and acid-fast methods for histopathologic study. Immunohistochemical staining was performed with monoclonal antibody to leukocyte surface CD23. Polyp tissue fluid was extracted by slicing and centrifuging. Total serum IgE and tissue fluid was measured by ELISA.

Results: Thirteen of 20 polyp tissues were positive for CD23. Moderate to large number of eosinophils were observed in 5 patients. Serum IgE level was elevated (>70 IU /ml) in 13 patients and polyp IgE level was elevated in 8 patients. No significant correlation was found between CD23, serum and polyp tissue IgE, and eosinophil infiltration.

Conclusion: CD23 may act as non-IgE dependent inflammatory marker in the pathogenesis of nasal polyps.
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Keywords •Receptors, IgE • Nasal polyps • immunoglobulin E • hypersensitivity • Eosinophils

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Introduction

Nasal polyposis is believed to be a multifactorial disease.[1] It is a chronic inflammatory disorder of the mucous membranes in the nose and paranasal sinuses.[2] The disease is characterized by the presence of edematous masses of inflamed mucosa prolapsing into the nose leading to nasal obstruction, secretion, loss of sense of smell, headache and worsening life quality. Although nasal polyposis is frequently associated with asthma, aspirin sensitivity and Cystic fibrosis, its pathogenesis is still unknown.[3]

Histopathology of nasal polyps is characterized by large quantities of extracellular fluid, mast cell degranulation and infiltration of inflammatory cells. In this condition, eosinophils usually comprise more than 60% of the cell population.[3,4]

Although the eosiniphilic inflammation would suggest an allergic pathology, the existing evidences[5,6] are not conclusive. Nonetheless, some indices are suggestive of a local allergic process as the underlying etiology.[7]

IgE receptors are among the important components of immunological pathways in allergic and inflammatory reactions. As to the other immunoglobulins, so far two distinct types of receptors have been recognized for IgE. These are the high-affinity IgE receptor (Fcε RI) and the low-affinity IgE receptors (Fcε RII) . Fcε RII, also known as CD23, is expressed on activated B cells as well as many non-B cells. This cell marker is involved in antigen presentation, cellular cytotoxicity and regulation of IgE synthesis, which can be attributed to the membrane and soluble forms of CD23.[8]

In this study we tried to determine if CD23 is presented on nasal polyp tissues as a marker of local allergy or inflammation.

Patients and Methods

Fourteen male and six female patients with an age range of 23–80 years were enrolled in the study. Polyp tissues were obtained from 20 patients with unilateral or bilateral nasal polyps who had undergone polypectomy at one of the affiliated hospitals of Shiraz University of Medical Sciences. Patients with history of systemic diseases, previous nasal surgery or treatment with local or systemic corticosteroids within the last four weeks before surgery, were excluded.

Polypectomy was performed under general anesthesia in all cases and polyp tissues were immediately washed with normal saline and divided into three parts for histopathologic study, extraction of polyp fluid and immunohistochemical staining.

Tissue sections were stained with hematoxylin-eosin and acid-fast methods, and studied under light microscope for standard histomorphologic analysis. The number of cells was graded as negative (no cell), 1+ (<30% at low power field), 2+ (30%–50% at low power field), 3+ (50%–70% at low power field), and 4+ (>70% at low power field).

Total IgE concentration of serum and polyp tissue fluid was measured by a commercial ELISA kit (NMS pharmaceutical, CA, USA), in accordance with the manufacturer's instructions. Values <70 IU/ml were considered as normal. The polyp tissue fluid was extracted by slicing the tissue and microcentrifuging for 20 minutes at 14000 rpm. Straw-colored supernatants were separated and stored at -30 °C until analysis.

Polyp tissues were embedded in ornithine carbamyl transferase tissue compound and were frozen in liquid nitrogen, then stored at -70 °C. Cryostat sections of 6–8 μm were prepared for staining.

The mouse monoclonal antibody against human leukocytes CD23 (Beckton Dickenson, US) was used for histochemical staining. Cryostat sections were fixed in cold methanol (-20 °C) for 15 minutes, and incubated sequentially with the following reagents then rinsed with PBS after each incubation: 6% H_2O_2 in methanol for 5 minutes to inactivate endogenous peroxides; normal blocking sheep serum for 10 minutes at room temperature; optimal dilution of monoclonal antibody against CD23 at 37 °C for two hours; covering with the conjugate (anti-human whole Ig-peroxidase conjugate, Sigma) for one hour at room temperature; and staining for peroxidase activity with 3,3-di-amino benzidine tetra-hydrochloride (DAB, Sigma, USA). After rinsing the sections with distilled water, they were counterstained with hematoxylin for 3-10 seconds, dehydrated and mounted in Entellan.

Tonsil sections were used as positive controls for histochemical staining procedure. Nonspecific staining was controlled with incubation in PBS instead of primary antibody and all proved to be negative. The number of cells was graded as previously mentioned.

Mann-Whitney U test, Fisher's exact and Spearman's rho tests were applied for statistical analyses.

Results

Average duration of symptoms was 3.8 years. A history of asthma was elicited in two patients. Nasal allergic symptoms (itching and sneezing) were present in 7 of 20 patients. Bilateral polyp was present in 16 patients. Histologic study showed moderate to large numbers (>2+) of eosinophils in 11 and mast cells in all polyp tissues. Seventy percent of mast cells were partially degranulated.

Serum concentration of IgE was elevated in 14 patients. The IgE level of polyp tissue fluid was high in 8 patients (Table 1).

Results indicated that 13 of 20 patients had reacted to monoclonal antibody to CD23. Half of CD23 stained polyps were associated with elevated level of serum IgE and 5 patients with high grade of eosinophil infiltration.

We did not find any significant correlations between the grade of CD23 staining and the eosinophil infiltration (p=0.96), serum IgE level (p= 0.62) and polyp IgE level (p= 0.13).

Table 1: Data of Immunohistochemical (anti CD23) and histopathologic staining of polyp tissues

Patients	Bilaterality	Eosinophil[+]	Mast cell[++]	Serum IgE (IU/ml)	Tissue IgE	CD23+
1	B[*]	4[+]	P	>500	500	3[+]
2	B	4[+]	P	>500	>500	1[+]
3	B	1[+]	P	10	10	3[+]
4	LT[**]	2[+]	P	22	240	-
5	B	1[+]	C	250	160	-
6	B	4[+]	P	>500	2	2[+]
7	B	1[+]	P	17	5	-
8	B	1[+]	C	7.2	10	3[+]
9	B	4[+]	C	>500	60	3[+]
10	L[+]	2[+]	P	≥ 500	>500	-
11	B	4[+]	C	>500	>500	-
12	B	-	P	54	160	3[+]
13	L[+]	1[+]	C	110	5	3[+]
14	B	4[+]	P	>500	34	3[+]
15	B	1[+]	P	360	21	3[+]
16	B	1[+]	P	95	40	3[+]
17	B	4[+]	C	120	1.2	3[+]
18	B	1[+]	P	27	10	-
19	B	4[+]	P	>500	500	-
20	L[+]	-	P	70	13	3[+]

[+] negative (no cell), 1+ (less than 30% of low power field), 2+ (30-50% of low power field), 3+ (50-70% of low power field) and 4+ (more than 70% of low power field).
[++]P = Partially degranulated; C = Completely degranulated
* Bilateral

There was a significant correlation between the serum IgE level with either tissue IgE level ($p<0.02$, $R=0.5$) or eosinophil infiltration ($p<0.001$, $R=0.8$).

Discussion

In the present study we have demonstrated marked staining in 13 of 20 polyp tissues by anti-CD23 monoclonal antibody. The role of CD23 in allergic diseases and inflammatory processes has been studied extensively,[8,9] however, there are few reports that have investigated the presence of CD23 in nasal polyps[7,10]. It was recently reported that total IgE and soluble CD23 derived from tissue homogenates of 20 bilateral nasal polyps were significantly higher than non-polyp nasal tissue and significantly correlated with eosinophil count in histochemical study.[7]

In vitro production of IgE from nasal polyp tissue in both allergic and non-allergic subjects,[11] suggests that a local allergic process could be operative. Increased expression and production of a variety of proinflammatory cytokines and chemokines have been also reported in nasal polyps.[2]

Although we have shown a positive staining in the majority of polyp tissues by CD23, we did not find a significant correlation between the expression of CD23 and serum IgE, polyp tissue IgE and eosinophil infiltration. Therefore, no correlation could be detected between CD23 and IgE as the mainstay of the allergic reactions.

CD23 is known as an IgE receptor; however it can also be triggered through the non-IgE pathways with a number of different ligands. Expression of CD23 on polyp tissue may indicate a local inflammatory process. It has been documented that CD23 activates macrophages to produce the different proinflammatory mediators such as cytokines.[12]

The significant ($p<0.02$) correlation ($R=0.5$) of serum IgE and polyp fluid IgE in our study, is in

keeping with those reports which show that high IgE concentration in polyp tissue could be preferentially derived from the serum because of extravasation and deposition of serum proteins in polyp tissue.[7] However, allergen-induced heavy-chain switching to IgE occurs locally within the nasal mucosa of patients with seasonal allergic rhinitis. Thus, a local IgE production also seems possible in nasal polyps.[13]

Eosinophils may produce IL4 which is the most important cytokine mediating IgE synthesis,[12] therefore the significant ($p<0.001$) correlation ($R=0.8$) between serum IgE with eosinophil infiltration in polyp tissues in our study, was clearly expected.

In the present study mast cells were found in all polyp tissues and most of them (70%) were partially degranulated. It had been shown that weak and chronic stimuli rather than IgE mediated stimuli may cause partial degranulation of mast cells.[1]

Most of the patients with nasal polyps in this study showed a high expression of membrane CD23 in the polyp tissues. This may provide a new evidence to emphasize the role of inflammation in the pathogenesis of nasal polyps. However, the involvement of CD23 in the pathogenesis of nasal polyps should be the subject of further investigations. The use of local anti-inflammatory drugs such as corticosteroids as a primary or post-operative treatment could be encouraged in the management of nasal polyps.

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