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Histopathologic Study and Expression of TGF-β1 of Choanal Polyp

Byung Hoon Ahn

Department of Otolaryngology, College of Medicine, Keimyung University, Daegu 700–712, Korea

The pathogenesis of the nasal polyp is multifactorial and choanal polyps can be defined by its origin of genesis: antrochoanal (maxillochoanal), ethmochoanal and sphenochoanal polyp. Transforming growth factor-β (TGF-β) has various biologic activities, including the regulation of epithelial proliferation, the promotion of extracellular matrix formation and the induction of angiogenesis, hence closely related to pathogenesis of nasal polyp. Twenty cases of choanal polyps (13 antrochoanal, 4 ethmochoanal and 3 sphenochoanal polyps) were included in this study. Each polyp was subdivided into its origin, pedicle and choanal part. Hematoxylin and eosin stain for routine histopathology and immunohistochemistry were employed to detect expression of TGF-β1. According to polyp type, edematous type is common at origin part and fibrous type at choanal part, and showed no difference at pedicle part in frequency. In ethmochoanal and sphenochoanal polyps, glandulocystic and edematous type is more common than fibrous type. TGF-β1 was expressed in epithelial cells, endothelial cells, eosinophils and lymphocytes. There was no different expression of TGF-β1 in each kind of choanal polyps and separate parts in each polyp. But histologic finding of choanal polyp is different between origin, pedicle and choanal part. Also infiltration of inflammatory cells including eosinophils has no difference between origin site. The expression of TGF-β1 was observed at all the choanal polyps and no difference between origin site and each portions was noted.

Key Words: Choanal polyp, TGF-β1, Histopathology

INTRODUCTION

Choanal polyp accounts for 3–6% of all polyps which originate from sinonasal mucosa and can be differentiated according to their clinical entity and pathogenesis. Choanal polyp arise from mucosa of paranasal sinus and protrude into nasal cavity up to choana, posterior end of nasal cavity. Origin of choanal polyp is mostly maxillary sinus antrum and can be seen at anterior ethmoid sinus and sphenoid sinus infrequently (Lee et al, 1994; Sohn & Chae, 1996; Lopatin et al, 1997; Chung, 2000). Transforming growth factor-β (TGF-β) is a multipotential cytokine and closely related to the pathogenesis of nasal polyp due to its ability: epithelial proliferation, angiogenesis and increasing extracellular matrix (Kim et al, 1996; Wang et al, 1997; Coste et al, 1998; Min et al, 1998).

Author classified the choanal polyps into antrochoanal, ethmochoanal and sphenochoanal polyp according to their origin site and studied their histopathology and expression of TGF-β1 in each polyp, and subdivided them into their origin, pedicle and choanal part.

Corresponding to: Byung Hoon Ahn, Department of Otolaryngology, College of Medicine, Keimyung University, 194 Dongsan-dong, Jung-gu, Daegu 700-712, Korea. (Tel) +82-53-250-7718, (Fax) +82-53-256-0325, (E-mail) bhahn@dsmc.or.kr

METHODS

From July 1997 to Jun 1998, twenty cases of choanal polyp (13 cases of antrochoanal polyp, 4 cases of ethmochoanal polyp and 3 cases of sphenochoanal polyp) were included in this study and all polyps were removed under nasal endoscopy by same surgeon.

Hematoxylin and eosin stain was done for light microscopic exam and immunohistologic stain was

performed for identification of expression of TGF-β1. Each choanal polyp was subdivided into their origin part, pedicle and choanal part, and processed separately.

Under low power field of light microscopy, each polyp was classified as edematous, glandulocystic and fibrous type. Also each polyp was examined under high power field (HPF) for counting the inflammatory cells (eosinophils, plasmacyte and lymphocyte). Each slide was counted at 3 different fields and the average count of each cells were classified as few: less than 3 cells/HPF, moderate: 4 to 10 cells/HPF, abundant: more than 10 cells/HPF.

For immunohistologic stain for TGF-β1, 4 μm thickness of paraffin section was attached to slide glass and stored 60°C for one hour. Xylene and serial alcohol were used for deparaffinization and hydration. Methanol and 30% hydrogen peroxide were added for blockage of endogenous peroxidase activity for 15 min and washed with phosphate buffered saline (PBS, pH 7.2). To enhance antigenity of tissue, tissues were emulsed in zinc sulfate solution and heated for 15 min with microwave oven. After storage in room temperature for 20 min, normal horse serum was applied for 30 min. Primary antibody, anti-mouse monoclonal IgG (TB21, Serotec, UK), was used as 1 : 100 diluted form for 2 h and at 37°C, washed with PBS, anti-mouse IgG (Dako, Carpitenia, USA), secondary antibody, was added and washed with PBS for 15 min. Peroxidase-conjugated streptavidin (Dako, Carpitenia, USA) 1 : 500 diluted solution was applied at 37°C for 15 min, washed with PBS. DAB (3,3'-diaminobenzidine tetrahydrochloride) was added for 10 min at room temperature and Mayer's hematoxylin was used for counterstain.

RESULTS

Histologic classification of choanal polyps

In antrochoanal polyp, edematous type was dominant (50%) and followed by glandulocystic type (35%), fibrous type (15%) (Fig. 1). Ethmochoanal polyp revealed edematous type (40%), glandulocystic type (40%), fibrous type (20%). In cases of sphenochoanal polyp, edematous type was dominant (50%) and followed by glandulocystic type (35%), fibrous type (15%). According to subsection of each type of polyp, origin part mostly had edematous type (70%) followed by glandulocystic type (20%), fibrous type (10%). At the area of pedicle, glandulocystic type and fibrous type (35%) were more common than edematous type (25%). At the choanal part, fibrous type was predominant (50%) and followed by edematous type (25%) and glandulocystic type (35%) (Fig. 2).

Distribution of inflammatory cells such as eosinophils, plasmacytes and lymphocytes showed no dif-

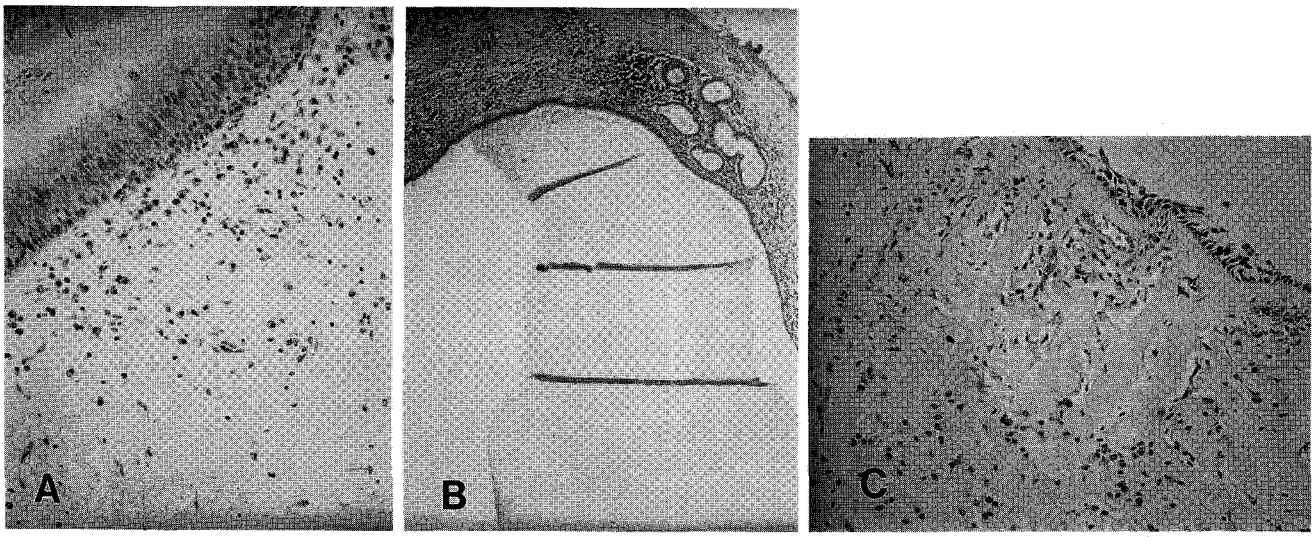

Fig. 1. Light microscopic finding (Hematoxylin and eosin stain, ×100) shows edematous type (A), glandulo-cystic type (B) and fibrous type (C) of choanal polyps, also shows scattered stromal eosinophils (arrows) and other inflammatory cells.

ference according to their origin site (Fig. 3).

Expression of TGF-β1

TGF-β1 was uniformly expressed in epithelial cells of polyps, endothelial cells, partly eosinophils and lymphocytes (Fig. 4). There was no difference of expression according to each type of polyp.

In addition there was no difference of expression at each subsites (origin, pedicle and choanal part) of polyp.

DISCUSSION

Choanal polyps are usually presented as unilateral nasal mass and occur at children and young adolescent (Lee et al, 1994; Min et al, 1995; Chung, 2000). Sexual predilection is usually onto male group as ratio of 1.3～3 times (Lee et al, 1994; Lee & Lee, 1996; Chung, 2000).

Most frequent origin site of antrochoanal polyp is posterior and inferior wall of maxillary sinus antrum (Lee et al, 1994; Min et al, 1995) In contrast Lee et al (1999) mentioned natural ostium of maxillary sinus as most frequent site of origin. Author observed that

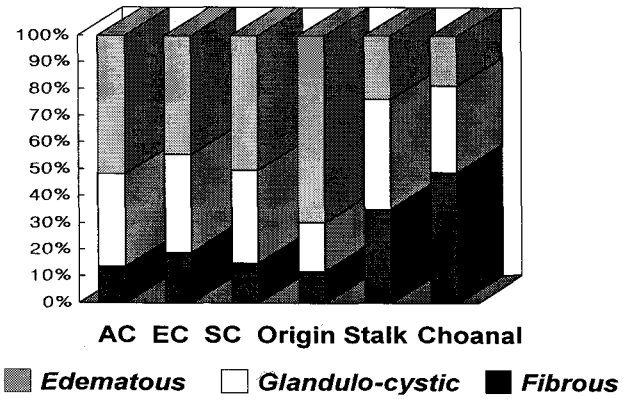

Fig. 2. Pathologic classification of polyp according to its origin and each subdivided part. AC: Antrochoanal, EC: Ethmochoanal, SC: Sphenochoanal

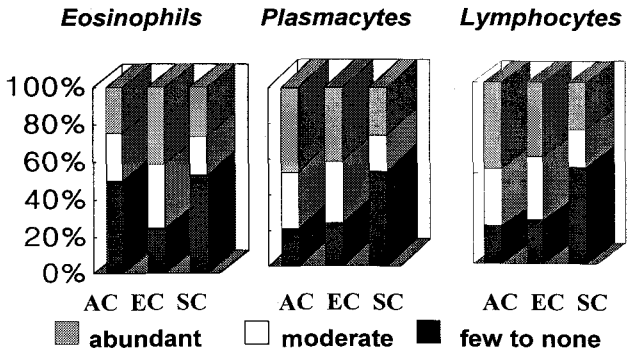

Fig. 3. Distribution of inflammatory cells in each type of choanal polyp. AC: Antrochoanal, EC: Ethmochoanal, SC: Sphenochoanal

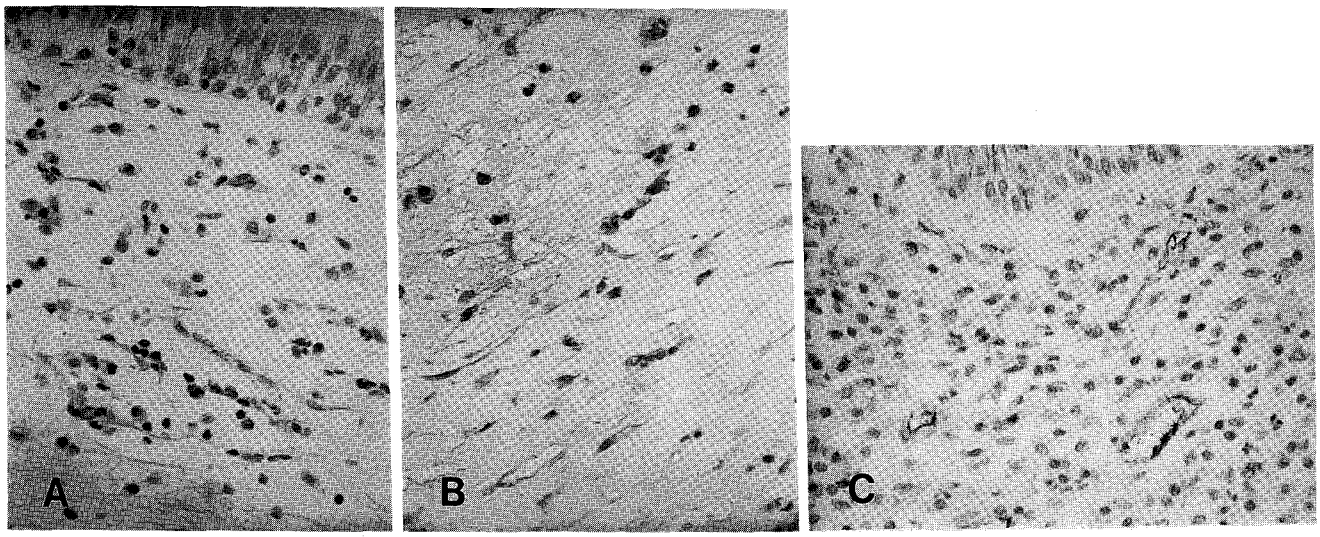

Fig. 4. Immunohistochemical staining for TGF-β1 shows positive brownish deposit of epithelial layers and stromal endothelial cell (arrowhead), and inflammatory cells (arrows): eosinophils, plasma cells and lymphocytes at origin part (A), pedicle (B) and choanal part (C).

maxillary sinus floor was most frequent site of antrochoanal polyp. During endoscopic widening of maxillary sinus ostium, it is sometimes crucial step to reduce the size of antral part of polyp first and identify the exact site of origin of choanal polyp (Lopatin et al, 1997; Kim et al, 1998; Kwon et al, 2000).

Histologically nasal polyp is covered with respiratory epithelium and edematous type is most frequent form which infiltrated with eosinophils and plasmacytes (Bernstein, 1997; Larsen et al, 1998). Typical microscopic findings of nasal polyp are proliferation of epithelium, glandular hyperplasia, basement membrane thickening and stromal edema (Kang et al, 1993; Min et al, 1995; Coste et al, 1998). But in cases of choanal polyp, infiltration of eosinophils is uncommon and partly fibrotic due to continuous stimulation by nasal air current (Min et al, 1995; Bernstein, 1997).

Histologic features of antral part of choanal polyp shows that edematous type 50% and fibrous type 30% (Min et al, 1995), Sohn & Chae (1996) stated edematous type (63%) and fibrous type (88%) is common in antral and choanal part respectively. In contrast, Lee et al (1994) pointed out that pathogenesis of antrochoanal polyp presumably related to transformation of retention cyst of maxillary sinus due to more fibrotic change of choanal part and more infiltrated with inflammatory cells, but antral part is thin and mostly edematous type. Our data showed similar result but there were no correlation about histologic type and origin site. When comparing with allergic and non-allergic nasal polyp, there is less eosinophilic infiltration and submucosal gland and more neutrophilic infiltration in antrochoanal polyp. Edematous hyperplasia of respiratory epithelium is more related to the pathogenesis of antrochoanal polyp than glandular hyperplasia or hypertrophy (Min et al, 1995; Jordana & Dolovich, 1997). Larsen et al (1998) reported topographic distribution of inflammatory cells and more abundant eosinophils, evenly distributed plasmacytes and neutrophils at the origin site. But author found no correlation of inflammatory cells distribution between each type of choanal polyps. It might be explained by different histologic features between common nasal polyp and choanal polyp, also less eosinophils infiltration in choanal polyp.

Eosinophils are main source of cytokines such as TGF-α and TGF-β which regulate the epithelial proliferation, promote the formation of extracellular matrix and induce the angiogenesis (Jordana & Dolovich, 1997; Wang et al, 1997; Coste et al, 1998). In the model of cultured nasal epithelial cells, TGF-β uniformly inhibited the growth of epithelial cells, but stimulated proliferation of the fibroblast (Min et al, 1998). Especially TGF-β1 is a chemoattractant of fibroblast and monocytes, and mucopolysaccharides (MPS) are produced by mainly by fibroblasts (Jordana & Dolovich, 1997; Wang et al, 1997). Glycosaminoglycan is main constituent of MPS and capable of retaining 1,000 times of fluid that induce the intracellular edema, the main pathology of formation and growth of the nasal polyp (Wang et al, 1997). Increased expression of the TGF-β1 in nasal polyp tissues is general result of many experiments (Kim et al, 1996; Jordana & Dolovich, 1997; Yun et al, 1997; Coste et al, 1998). Especially Yun et al (1997) stated the gradual decreased expression of TGF-β in regenerating mucosa after endoscopic sinus surgery. Wang et al (1997) stressed the importance of TGF-β and α-smooth muscle actin in the formation of nasal polyp in the topographic expression. Author expected gradual increment of TGF-β1 expression toward choanal part but, could not find any topographic difference of expression of TGF-β1 and correlation between pathologic type and expression. It might be supposed that TGF-β1 contributes the formation, fibrotic change and further growth of choanal polyp. In the future study, quantitative analysis will be helpful for understanding the genesis and growth of choanal polyp.

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