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Vascular endothelial growth factor and children featuring nasal polyps

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Summary

Background: The aim of this study is to explore the expression of vascular endothelial growth factor within nasal polyps, and the implication of such expression as regards the development of nasal polyps amongst children.
Material and methods: Sixty children suffering from chronic rhinosinusitis were enrolled in this study. Amongst them, 30 patients featured rhinosinusitis with associated nasal polyps. A biopsy specimen was taken from the stalk or the base of the nasal polyp for nasal-polyp sufferers, and the ethmoid sinus for study participants who featured no nasal polyps. The primary lesions biopsied were immunohistochemically stained with a specific endothelial-cell marker and also stained for the presence of vascular endothelial growth factor. The specific level of vascular endothelial growth factor and the mean number of blood vessels present in a visual microscopic (biopsied-specimen) field were calculated under light microscopy ($\times$400).
Results: The number of vascular endothelial growth factor-expressing cells for the nasal-polyp group and for the sinusitis group was, respectively, 20.8 ± 4.0 and 11.5 ± 3.4 per visual field. Correspondingly, the mean intra-polyp blood-vessel density for the nasal-polyp group and that for the control group was, respectively, 10.5 ± 2.6 and 5.0 ± 1.9 per visual field. The mean intra-polyp blood-vessel density and the number of vascular endothelial growth factor-expressing cells proved to be significantly greater amongst individuals from the nasal-polyp group than was the case for their analogs from the sinusitis group ($P < 0.01$, for both). The presence of vascular endothelial growth factor was found to be distributed predominantly within

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the vascular endothelium and the mast cells of polyp tissue. In addition, the level of vascular endothelial growth-factor expression and the mean blood-vessel count per field correlated significantly for nasal-polyp tissue ($P < 0.001$). Furthermore, the relative size of nasal polyps correlated significantly with the number of (intra-polyp) vascular endothelial-cell growth factor-expressing cells and the mean blood-vessel density ($P < 0.05$, for both).
Conclusion: The level of expression of vascular endothelial-cell growth factor (VEGF) and the mean blood-vessel density were shown to be significantly greater within nasal polyps than within corresponding sinusitis mucosa. Clinically, the expression of both of these parameters correlated well with the relative size of nasal polyps. Vascular endothelial growth factor participates in the formation of nasal polyps amongst children suffering from chronic rhinosinusitis (CRS).

1. Introduction

Chronic rhinosinusitis (CRS) is a common disorder amongst children [1]. The condition may be associated with the formation of nasal polyps, although nasal polyps are not so frequently found amongst children as amongst adults [2]. To the best of our knowledge, the exact etiological mechanism leading to the formation of nasal polyps appears to have remained largely obscure, however nasal polyps are believed, by many, to be a multifactorial disease [3,4]. The histomorphological findings associated with nasal polyps typically include submucosal fibrosis with remarkable edema [2]. It would appear that developing a good understanding of the pathomechanisms of inflammation underlying the development of nasal polyps would seem to be crucial for further success as regards the treatment of such disease.

In recent years, several studies have drawn attention to the potential role for certain growth factors as regards the development of nasal polyps [5—7]. Vascular endothelial-cell growth factor (VEGF) appears to participate in a number of inflammatory processes by inducing plasma extravasation and angiogenesis [8]. The development of edema within nasal polyps is suggested, by some, to be caused by chronic and persistent inflammatory stimuli, thus it would appear imperative to determine the role VEGF plays as regards the development of CRS featuring nasal polyps versus CRS without nasal polyps.

The aim of this study is to demonstrate, immunohistochemically, the presence of VEGF within nasal polyps, and to compare the level of activity of VEGF for CRS patients featuring nasal polyps versus those CRS patients who do not suffer from nasal polyps.

2. Materials and methods

From January 1999 to December 2004 inclusively, 60 children (31 boys) afflicted with chronic rhinosinusitis were enrolled to receive endoscopic sinus surgery as part of this study. Thirty of the 60 children revealed CRS associated with nasal polyps and the other 30 children suffered from CRS with no evidence of nasal polyps, these latter individuals acting as study controls. Patient ages ranged from 11 to 16 years inclusively (mean, 13.6 years). All patients exhibited signs and symptoms of chronic paranasal sinusitis such as yellowish rhinorrhea, nasal obstruction, and postnasal drip, symptoms that had been present, reportedly, for between 8 and 25 months (mean, 12.1 months), and that had not responded to antibiotic treatment for at least three months. All study-participating patients underwent sinus computed tomography (CT) for image confirmation of their condition. Nasal polyps were confirmed by nasoendoscopy. None of the patients reported any prior history of sinus or nasal surgery. Cystic fibrosis was excluded in children with nasal polyps by the traditional diagnostic criteria include sweat test, pulmonary and gastrointestinal disease, pancreatic dysfunction, and a family history of cystic fibrosis [9]. Ten specimens were obtained from children with no history of chronic rhinosinusitis or inhalant allergies (six boys, four girls, median age: 12.4 years), who underwent turbinate surgery to improve nasal breathing. These ten specimens were used as healthy controls. The study was approved by the Bioethical committee of the hospital.

A biopsy specimen was taken from the stalk or the base of the nasal polyp for nasal-polyp sufferers, and the ethmoid sinus for study participants who featured no nasal polyps. Immunohistochemical staining was performed using a streptavidin-biotin immunoperoxidase technique as previously described [10]. Briefly, 6 μm tissue sections were dried at 60 °C to melt the paraffin in xylene and rehydrated in decreasing concentrations of ethanol to water. They were then washed with 3% H_2O_2 in methanol in order to remove endogenous peroxidase activity. For immunostaining with anti-VEGF polyclonal antibody and JC-70A monoclonal antibody, sections were pretreated with