



Research Article

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The Importance of Nasal Cytological Examination in Determining The Etiology and Treatment of Idiopathic Recurrent Epistaxis In Children



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Abstract

Background and aim : It was aimed to clarify the etiology of recurrent idiopathic epistaxis (RIE) by evaluating the results of the nasal cytological examination (NCE) and to evaluate their responses to treatment prepared according to nasal cytological findings.

Materials and methods: Pre and post-treatment the results of NCE, 78 children who applied to the ENT clinic for RIE and 40 healthy children were evaluated. In the majority of cases with RIE, the main cell type was determined to be neutrophils (70%) followed by eosinophils (20%). The treatments of the children were tailored by their nasal cytology findings. According to the results of NCE, 25 / 3.6 mg/kg of amoxicillin /clavulanate was administered orally twice a day for 7 days to children with high neutrophil counts. Children with high eosinophil count were given 5 ml of desloratadine orally once a day for 15 days. These treatments were administered together and at the same doses to children with high neutrophil and eosinophil counts.

Results : Clinical evaluation and NCE was performed at the end of the first month. Families reported that epistaxis did not occur in children after treatment. As a result of the re-performed NCE, 74 (94.8%) of the patients responded to the treatment. In children with recurrent epistaxis due to inflammation caused by neutrophils and eosinophils, the dominance of cells decreased after treatment and no epistaxis was observed. The relationship between the dominance of inflammatory cells in the nasal mucosa and epistaxis was found to be statistically significant ($p<0.05$).

Conclusion : NCE, which is used in the differential diagnosis and follow-up of rhinological diseases, can help us to clarify the etiology of RIE in children. According to the results of the nasal cytological examination, anti-inflammatory treatment with a high response to treatment can be planned in these children.

Keywords: Nasal cytological examination, idiopathic recurrent epistaxis, etiology, treatment, children

Introduction

Epistaxis is a common problem in the pediatric population. Thirty percent of children younger than 5 years old, 56% of children 6 to 10 years old, and 64% of 11 to 15 years olds have had at least one epistaxis episode. Although epistaxis in children is usually mild, it can cause significant parental concerns. Most cases are self-limited and managed with simple first aid measures [1].¹ The etiological factors of epistaxis in children can be classified as primary or secondary. Primary epistaxis is defined as idiopathic hemorrhages without identifiable accelerating factors, whereas bleeding known to be associated with a clear and definite cause is classified as secondary epistaxis. The most common cause of nosebleeds in children is idiopathic. Recurrent idiopathic epistaxis (RIE) is self-limiting nasal bleeding of which no specific

cause can be determined. There is no consensus on the frequency, severity, etiology and treatment of relapses. Up to 9% of children may have recurrent epistaxis, usually caused by the anterior septum where the vessels anastomose to form the Kiesselbach plexus. The vessels in the nasal septum are located very close to the bone and cartilage, very weak mucosa covers it. Changes in the mucosa due to local inflammation disrupt the ciliary function, increase vascularization and cause mucosal fragility. This situation facilitates the occurrence of epistaxis [2-4]. In pediatric patients with idiopathic epistaxis, determining the etiology, planning treatment, and follow-up is very important. Today, there is still no method that determines the etiology of this disease. Therefore, its treatment is not known.

The nasal cytological examination (NCE) technique allows physicians to detect cellular modifications in the nasal mucosa caused by exposure to physical or chemical, acute or chronic irritation. It also makes it easy to evaluate different types of inflammation (viral, bacterial, fungal, or parasitic) [5-6]. The nasal mucosa consists of a ciliated pseudo-stratified epithelium composed of striated and basal ciliated mucosa-secreting cells. It is seen that epithelial cells are predominant in a cytological examination of the normal nasal mucosa. The presence of eosinophils, neutrophils, mast cells, bacteria, spores, and fungi should be considered a clear sign of nasal pathology. Cellular changes that occur cause mucosal inflammation and damage. A large number of papers have been published on the cytological changing of nasal pathologies, particularly on allergic and non-allergic rhinitis. NCE contributed to the understanding of some pathophysiological mechanisms of allergic rhinitis and the identification of new disorders such as non-allergic rhinitis with eosinophils (NARES), non-allergic rhinitis with mast cells (NARMA) and non-allergic rhinitis with neutrophils (NARNE) and non-allergic rhinitis with eosinophils and mast cells (NARESMA) [7-9].

In our study, we aimed to clarify the etiology of recurrent idiopathic epistaxis by evaluating the results of the NCE and to evaluate their responses to treatment prepared according to nasal cytological findings.

Material and Method

Ethics Committee Approval for this study was obtained from the Kavaklıdere Umut Hospital Ethics Committee (Approval Date/No:16 December 2015/2). Our study was prepared according to the principles of Helsinki, and informed consent was obtained from the parents of all patients to participate in this study.

In this prospective study conducted in 2016-2019, the NCE results of 78 (3-14 years old) children who applied to the ENT clinic with the complaint of recurrent epistaxis and diagnosed with RIE as a result of the examination and hematological tests were evaluated. As the control group, 40 (5-12 years old) healthy children were also included in the study.

Children with chronic, systemic, hematological disease, malignancy, acute respiratory tract infection, using local or systemic antibiotics, anti-inflammatory drugs (eg, antihistamine, corticosteroid) and family history of epistaxis were not included

in the study.

The children were examined by the same ENT specialist. NCE was made by the same microbiologist. After the nasal swab was dried on a slide, it was stained with Giemsa and 100 cells were counted in each area at 40-100 magnification under the light microscope.

The treatments of the children were shaped according to the nasal cytology findings. According to the results of the NCE, 25 / 3.6 mg/kg of amoxicillin /clavulanate was administered orally twice a day for 7 days to children with high neutrophil counts. Children with high eosinophil count were given 5 ml of desloratadine orally once a day for 15 days. These treatments were administered together and at the same doses to children with high neutrophil and eosinophil counts. At the end of the first month, clinical evaluation and repeat NCE were performed on the patients.

The results of the study were evaluated using statistical analysis program (Statistical Package for the Social Sciences (SPSS) version 22.0, SPSS Inc. Chicago, IL, USA). Chi-Square test was used to assess the differences between groups. Statistical significance level accepted as $p < 0.05$.

Results

Of the 78 children with RIE included in the study, 44 (56.4%) were male and 34 (43.6%) were female, 40 healthy children participating in the control group, 26 (65%) were male and 14 (35%) were female. In healthy children, epithelial cells were dominant as a result of the NCE, neutrophil and eosinophil cell dominance was not detected.

The distribution of the percentage of neutrophils, eosinophils and epithelial cells in the pre-treatment NCE result of children with epistaxis is shown in Table 1. In the majority of cases, the main cell type was determined to be neutrophils (70%) followed by eosinophils (20%). Neutrophils were predominant in 43 children, eosinophils in 19 children, and 16 children had similar amounts of both neutrophils and eosinophils. In the control performed in the first month after the treatment, the families of the children reported that there was no epistaxis. It was observed that 74 (94.8%) of the patients responded to the treatment after NCE re-performed in the 1st month. Neutrophils were predominant in 2 children and eosinophils in 1 child, and similar amounts of both neutrophils and eosinophils were detected in 1 child (Table 2).

Table 1: The distribution of percentage of neutrophils, eosinophils and epithelial cells in nasal smear.

	Mean±SD	Median	Min-Max
Neutrophils (%)	66.58±32.05	70	0-100
Eosinophils (%)	31.15±30.53	20	0-100
Epithelial cells (%)	2.51±15.69	0	0-98

In children with recurrent epistaxis due to inflammation caused by neutrophils and eosinophils, the dominance of cells decreased after treatment and no bleeding was observed. The

relationship between the dominance of inflammatory cells in the nasal mucosa and epistaxis was found to be statistically significant ($p < 0.05$).

Table 2: Distribution of patients regarding nasal smear findings and response to the treatment.

Nasal smear cells in children with Epistaxis (n)	Neutrophils dominant	Eosinophils dominant	Both neutrophils and eosinophils
Treatment	Amoxicillin/clavulanate	Desloratadine	Amoxicillin/clavulanate and Desloratadine
No of patients with epistaxis before the treatment (n)	43(55%)	19 (24%)	16 (21%)
No of patients with epistaxis after the treatment (n)	2 (0.026%)	1 (0.012%)	1 (0.012%)

Discussion

The diagnosis and treatment of recurrent idiopathic epistaxis in children pose a major problem for ENT specialists and pediatricians. In this study, we think that nasal NCE can be a valuable diagnostic method in determining the etiology in these patients and its treatment with antibiotics and antihistamine is successful according to the results.

We determined that neutrophils that play a role in infection in children with recurrent epistaxis are the main cell type of nasal smear and eosinophils that play a role in allergic rhinitis are the second dominant cell type. According to the results of NCE, it was thought that the most common cause of idiopathic recurrent epistaxis in children was non-allergic rhinitis with neutrophils (NARNE), allergic rhinitis and non-allergic rhinitis with eosinophils (NARES) was the second causes. However, clinical and laboratory studies are needed to support this study.

After the antibiotic and antihistamine treatment, we found that there was no epistaxis due to the decrease in neutrophil and eosinophil cells causing inflammation in the nasal mucosa. Although mild in children, recurrent epistaxis can significantly increase their parents' anxiety levels. It may also lead to recurrent urgent applications and increased healthcare costs [10,11]. In this respect, it is essential to define the etiology and an appropriate treatment method for recurrent epistaxis in children. Eyer mann, in 1927, detected the presence of eosinophils in the nasal secretions of allergic patients and found their importance in diagnosing the disease. This discovery, a great value was attributed to the identification of specific cellular subsets related to different nasal pathologies, and this consideration opened the way to the routine use of nasal cytology in the study of allergic and non-allergic, infectious and inflammatory rhinitis. After the 2000s, NCE more systematically found its role in the nasal diagnosis algorithm [12,13].

NCE is a very attractive, simple, safe, non-invasive, inexpensive tool used in clinical practice and can be easily repeated in the same patient. Despite these important features of nasal cytology, sufficient information and number of studies on its use in children is scarce. Studies are mostly related to allergic rhinitis, non-allergic rhinitis and rhinosinusitis. To our knowledge, this is the first study in the literature to evaluate nasal cytological changes in children with recurrent epistaxis. In 1988, Sala et al. reported a decrease in the ciliary component and an increase in goblet cells as a result of nasal mucosal cytological changes in children with chronic allergic rhinitis [14]. In 2007, the role of cytology in the diagnosis of rhinosinusitis in children was re-evaluated [15]. Recently, the histopathology of chronic rhinosinusitis in children has been analyzed based on different techniques including nasal biopsies. It has been revealed that nasal biopsies are not very applicable as a routine method to detect inflammatory cells in the nose, while cytology is the optimal method to evaluate this aspect [16,17]. In the study by Murray et al. 557 children with allergic rhinitis were evaluated. Prick test positivity and recurrent epistaxis were found in 20.2% of these children. According to the study, it is stated that the cause of nasal bleeding in allergic rhinitis is inflammation of the nasal mucosa and resulting mucosal damage [18].

We can recommend NCE to determine the etiology in children with recurrent epistaxis. The treatment can be tailored according to the etiology and the response to the treatment and the follow-up of the disease can be re-evaluated with the NCE.

Conclusion

NCE, which is used in the differential diagnosis and follow-up of inflammatory and non-inflammatory rhinologic diseases, can help us to clarify the etiology of recurrent idiopathic epistaxis in children. More prospective studies are needed to define the role of this method in the diagnosis, treatment, and follow-up of children with recurrent epistaxis. According to the results of the NCE, anti-

inflammatory treatment with a high response to treatment can be planned in these children.

Ethical approval: This prospective study was approved by the hospital ethics committee.

Informed Consent: Informed consent was obtained from the parents of the children participating in the study.

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