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Allergy and Benign Lesions of the Vocal Cord Mucosa

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1. Introduction

Hoarseness is a result of the vocal cords not working properly and it can be detected by hearing. Basic and higher harmonic tones are associated with severe hoarseness, as well as noises replacing the harmonic noise. Hoarseness can also appear as a result of organic changes of the vocal cords (also caused by allergic mucosal changes) or functional disorders.

The most common organic changes of the vocal cords are polyps, nodules and Reinke's oedema (1). Under a microscope they share many common characteristics of mucosal changes and indicate pathological changes in the superficial layer of the lamina propria, in the so-called Reinke's space (2). The main changes include: fluid oedema, elevated interstitial and exudative proteins, dilated or hypertrophic vein walls. The aetiology of the benign changes is, however, slightly different although the changes in the lamina propria are quite similar. The most common cause is trauma (phonotrauma), exposure to unfavourable microclimate conditions, smoking, voice overuse or incorrect vocal technique, hormonal changes, and allergy (3).

Reinke's oedema is a swelling of vocal cords that mostly occurs bilaterally. It is a chronic benign condition. On examination a transparent, sometimes a pink swelling is seen along the length and on the upper side of the vocal cord. As long as the swelling remains small, the vocal cords can vibrate normally. However, as the oedema grows and therefore changes the biomechanics of the larynx, the functional impairment of the phonation appears, vocal cords do not vibrate appropriately and the voice becomes low-pitched and hoarse.

Histologically, the mucosa is covered by a layer of normal and hyperplastic epithelium. By enlargement of the swelling, it may become atrophic. Persisting etiologic factors can cause the epithelium to thicken or become hypertrophic. Simple hyperplasia is the most common form of the epithelial changes due to hypertrophy (1).

A polyp is a mucosal thickness usually found at the front midpoint of the vocal cord. It is most commonly thought to be caused by vocal overuse or incorrect vocal technique. It is very similar to the Reinke's oedema, except that the polyp is localised.

Of all the benign oedematous vocal cord lesions, nodules are the smallest and by aetiology similar to polyps. The oedema is modified as in Reinke's oedema or polyps.

2. Allergy and Reinke's edema

There is a lack of research on aetiological factors such as allergies, allergic inflammation, and hormonal changes. We became suspicious of their influence over oedematous changes of the mucosa only on the basis of our clinical experience. Pathohistological examination did not reveal any pathognomonic changes of the mucosa neither during an allergy nor during hormonal changes. The changes of the lamina propria in Reinke's oedema, polyps and nodules are nearly the same: oedema with interstitial proteins (collagen, elastane), fibroblasts, intercellular substance (glycoproteins and proteoglycans), dilated vessels, thickened basal membrane. The number of inflammatory cells in the lamina propria in the tissue samples of patients with and without allergy was the same: individual monocytes are visible (4).

Reinke's oedema patients are not more allergy-prone compared to normal population. A study carried out among ENT outpatient clinic patients with Reinke's oedema showed that the frequency of allergy was 20%, which complies with the number of allergies among normal population (5).

3. Hypersensitivity skin tests and Reinke's edema

On the basis of history we determined how many patients with Reinke's edema (N=80) suspected on possible hypersensitiveness. Only in five cases patients noticed changes in their voice in contact with a certain substance or in certain circumstances. In the study group there were 16 patients with clinical signs of allergy and positive allergy skin tests, and in the control group (N=80) there were 19 subjects with proven allergy type I; this did not present a statistically significant difference ($\chi_c = 0,59$; $p = 0,57$). 16 subjects were hypersensitive to inhalatory allergens, three among them also to food allergens (flour, eggs, fruit). Hypersensitivity to mite was the most frequently established.

4. Allergic rhinitis ena Reinke's edema

Among the patients with Reinke's edema on vocal folds (N=80) there were 28 subjects with chronic hyperplastic rhinitis (35,0%). In 11 patients with Reinke's edema and hyperplastic rhinitis allergy was proven by skin tests. In the control group there were 9 such patients with allergic rhinitis and positive skin tests. The difference in the prevalence of allergic hyperplastic rhinitis between the groups was not statistically significant ($\chi_c = 0,06$, $p = 0,863$).

We also compared the prevalence of allergy between the patients with RE and rhinitis, and the patients with Reinke's edema without rhinitis. Allergy skin tests were positive in the group with rhinitis and RE in 11 cases, and in the group with Reinke's edema without rhinitis in 5 subjects, what presented a statistically significant difference ($\chi_c = 13,29$, $p = 0,001$).

5. Thyroid disease and Reinke's edema

In the study group there were 13 patients who claimed thyroid diseases in the history: 9 subjects had enlarged thyroid gland in euthyroid state, and 4 subjects had hypothyroidism. In the control group two subjects had difficulties with the thyroid gland (one hypothyroidism, the other hyperthyroidism).

The prevalence of other risk factors for the occurrence of Reinke's edema in the study and control groups is represented in Table 1.

Etiological factor	Study group n=80	Control group n=80	P
Smoking	69	10	0.001
Thyroid diseases	13	2	0.003
Gastroesophageal reflux	38	20	0.003
Microclimate conditions	25	12	0.015
Unsuitable speaking and voice technique	21	7	0.04

Table 1. Prevalence of some risk factors for the occurrence of RE on vocal folds in the study and control groups

6. Discussion

According to the results of our study we suppose that allergy is one of the factors contributing to the occurrence of RE on vocal cords, but it is by no means a crucial one. We have established that other risk factors (smoking, unsuitable speaking habits and vocal load at work, gastroesophageal reflux, thyroid diseases) are much more frequent (5).

Allergy type I was confirmed on the basis of history, clinical examination and skin tests in 20% of patients from the study group with RE and in 23.8% of subjects from the control group; this is similar to the prevalence of allergy in general. Among general population the prevalence of allergy type I is about 20% (6). In the case that allergy type I is an important factor in the etiology of RE, an infiltration of eosinophils in the vocal cord mucosa is expected. Actually, there were no eosinophils found in the removed vocal fold mucosa in any of 10 patients who had previous surgery on vocal folds because of RE. Similar data were also reported by Hočevnar-Boltežar et al. who on the basis of history and clinical data presumed the allergy as an etiologic factor in the patients with RE and other epithelial hyperplastic lesions on vocal cords, however histopathological picture of vocal cord mucosa did not confirm it (7).

In studying allergy as an etiological factor for the occurrence of epithelial hyperplastic lesions on vocal cords, we suppose that immediate hypersensitivity type I, according to Gel and Coombs, does not play a significant role, because there are other types of hypersensitivity that are much more important. Immediate hypersensitivity is easier to study because the tests are fast, easy and reliable tests for determining it. However, medical literature describes that the most notable type of allergy causing laryngeal mucosa lesions is allergy type III but this one is difficult to prove. Sometimes we can rely only on anamnestic data which present the basis for the performance of a tolerance test - a patient is exposed to a particular allergen.

It is possible that allergy type I is relevant for the occurrence of RE only in connection with the other risk factors. Despite the fact that allergy is not more frequent in the patients with RE than in the population in general, we have to consider it and decide for allergy skin tests if there is anamnestic and clinically set suspicion to allergy. This is important primarily

in the patients with RE and hyperplastic rhinitis. Regarding the results of our study, allergy was the cause of rhinitis almost in 40% of patients with RE and hyperplastic rhinitis. On the basis of test results the patient will find out which allergens should be avoided.

In the patients with RE, we have found a relatively frequent occurrence of hyperplastic rhinitis (35% of the study group). It is possible that apart from allergy type I there are also other factors – above all unfavourable microclimate conditions in workplace – affecting the occurrence of rhinitis.

All authors investigating the etiology of RE agree that smoking is the main risk factor for the occurrence of RE (3). In our study, there were significantly more smokers in the study group than in the control group. Smoking was the only risk factor merely in 8 patients with RE on vocal folds, in all the others it was one of two or more simultaneously acting factors. There were also some previous researches emphasizing the importance of simultaneous acting of several risk factors (8).

In the study group we expected a greater percentage of those who incorrectly or excessively strain vocal folds while speaking. This factor was only on the fourth place among the most important etiologic causes for RE. Voice strain or incorrect speaking technique is performed by abnormal activity of the muscles participating in speaking. The fluid accumulates in the RS because of microtraumas of vocal folds' vessels, caused by greater mechanical forces during vocal folds' vibration. The mechanical stress makes the vessels more permeable because their walls degenerate faster. At indirect laryngoscopy, adduction of ventricular folds during phonation is often noticed. Their contraction pushes interstitial fluid down into the vocal fold and enlarges the edema in RS (9). Learning correct speaking and voice technique is the most important step in the treatment of RE, besides giving up smoking. It is especially important after the vocal folds' surgery for RE..

Due to limited technical possibilities in our study, we determined GER on the basis of history, and estimation of typical changes in the larynx and pharynx at indirect laryngoscopy performed with the rigid laryngoscope. The findings of the esophagogastroscope which was carried out in less than one quarter of the patients before the inclusion in the study confirmed the diagnosis. In our study GER was significantly more often present in the study group than in the control group. Therefore, we presume that GER is an important factor in the etiology of RE on vocal folds but not the only one and not a crucial one. GER has never occurred as the only etiologic factor. It was always accompanied by at least one more risk factor for the occurrence of RE. GER causes inflammation of laryngeal mucosa, so the vessels become more fragile. Thick mucus accumulated in the posterior part of the larynx forces patients to clear their throats. Coughing represents a huge mechanical strain of vocal folds and results in their damage.

Until now, not much has been determined about the role of thyroid hormones in the occurrence of RE. The main cause for RE is most probably hypothyroidism. In 1992, Benfary performed a thorough study on assessing the thyroid function by measuring seven different parameters after indirectly stimulating the thyroid gland with TRH (thyrotropin-releasing hormone). As much as 78% of patients had pathological tests which indicated subclinical hypothyroidism (10). In our study we stated statistically significant difference between the study group and the control group regarding thyroid gland problems. The majority of subjects with thyroid gland problems had normal serum levels of TSH and thyroid hormones. During the research period only 3 subjects had increased level of TSH. According

to the findings of the endocrinologist two subjects needed treatment. Our scarce experience with the relation between hypothyroidism and RE indicate that a wider spectrum of tests (for example, thyroid stimulation test, determination of thyroid antibodies) is necessary in the estimation of thyroid function.

Laryngeal lesions in subjects working in unfavourable microclimate conditions in chemical industry were studied. Some chronic inflammatory changes on laryngeal mucosa were found also in the workers without any subjective laryngeal problems. It was supposed that the damages of the laryngeal mucosa occurred because of the irritation of chemicals or harmful concentration of inhaled dust (11). More recent studies presumed that the possible cause of laryngeal inflammation could also be an allergic reaction to chemicals and dust (12). Therefore, the laryngeal inflammation can be the consequence of immunological and non-immunological reaction to the unfavourable microclimate at work. In our study we determined only how unpleasant microclimate in workplace influences the occurrence of vocal fold swelling without getting in details. The results have shown that the subjects from the study group were significantly more often exposed to unfavourable microclimate conditions than the subjects from the control group. Patients stated constant flow of cold air in workplace as the most frequent unpleasant factor. This factor has not been stated by studies already mentioned; they even very rarely mentioned temperature changes in workplace. According to the frequency of appearance, the unpleasant microclimate factors are arranged in the following order: dust, industrial chemicals, detergents, cold air due to refrigerating chamber or air-conditioning systems, welding gases, lathe dust, cement dust, hair-dressing chemicals, and hot water steam. On the basis of our research we claim that microclimate conditions in workplace have a significant influence on the occurrence of the vocal fold swelling. The inflammation that occurs as a consequence of their irritating effect, changes vessel walls in vocal folds. The changed vessels get more permeable after the action of mechanical forces occurring during phonation. Because almost one third of the patients with RE from our study was exposed to harmful substances or abnormal temperature in workplace, it would be useful to expand the research with the cooperation of other experts from this field. Patients with the recurrence of RE on vocal folds were also significantly more frequently exposed to unfavourable microclimate than the patients who had the first occurrence of RE.

7. Conclusion

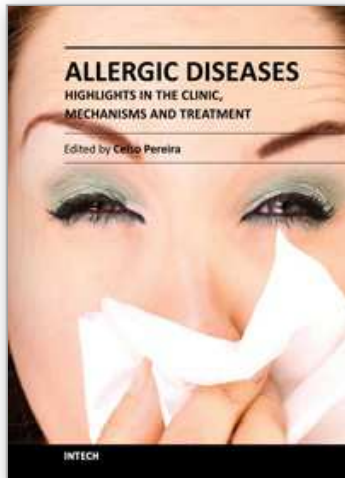
On the basis of the results of the study we have found out that in the majority of patients with RE at least two risk factors were present simultaneously, sometimes even more. Every otorhinolaryngologist treating a patient with RE has to be aware of the interconnectedness of all the factors. He/she should think about all six factors described and exclude or confirm them with selected diagnostic procedures. The treatment has to be etiological, otherwise vocal fold swelling can also reoccur after the surgical treatment. We wish to stress that in all patients with the recurrence of RE we found at least two risk factors which undoubtedly brought up the recurrence of the disease.

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