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Terminology, diagnostics and therapy of laryngopharyngeal reflux – A glimpse into the past

Terminologija, dijagnostika i terapija laringofarinksnog refluksa – pogled u prošlost

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Introduction

Laryngopharyngeal reflux (LPR) is the presence of refluxed gastric contents in the laryngopharyngeal space, where it is in close contact with the tissues of upper aerodigestive tract. Some authors consider it an entity, while others as extraesophageal manifestation of gastroesophageal reflux. However, it is considered that its pathophysiology and symptoms are different from gastroesophageal reflux. Main symptoms are: throat clearing, hoarseness, chronic cough, postnasal drip, halitosis, dysphagia, sense of foreign body in pharynx. As a confirmation of suspected LPR, indirect laryngoscopy shows: mucous edema, redness, ventricular obliteration, pseudoulcer, hypertrophy of posterior laryngeal region and laryngeal granulomas. It is believed that the presence of gastric contents in larynx and hypopharynx plays a role in the development of cancer lesions of this region. Today, an influence of pepsin and hydrochlorid acid on many other disorders in otorhinolaryngological region are being considered [1].

At the level of assumptions

Although in the middle of XIX century the only possible way to visualize larynx was *post mortem*, negative impact of numerous factors on different laryngeal functions, predominantly phonation, were known. Singing teacher in Paris, Manuel Garcia [2], wrote "Studies about human voice" in 1840, where he stated: "Gourmet dishes, oils from certain herbs, spirits, it all has negative impact on our apparatus." Thus, he pointed out a possible influence of reflux on larynx, without actually being able to prove it. Guided by a wish to show larynx, in 1854 Garcia performed the first "autolaryngoscopy", and managed to visualize this organ for the first time. By the end of the XIX century, changes of posterior part of larynx were confirmed histopathologically, which caused a series of researches on gastric contents reflux as an etiology factor in many laryngeal disorders in the XX century.

In 1880, Rudolf Virchow wrote a descriptive term "pachydermia verrucosa laryngis" for changes on arytenoid mucosa, which he associated with vocal abuse. In his original paper, Virchow described it as a state different from laryngeal leucoplacia and keratosis [3]. In the same year, Morell Mackenzie [4] identified the changes of arytenoid cartilage based on the presence of ulceration. Journal of the Royal Society of Medicine in 1908 published the abstract of W. Jobson Horne's [5] presentation, in which he confirms that pachydermia is a consequence of hyperplasia due to persistent laryngitis, but he identified rather different causes. In the cuts of a 37-year old patient's vocal cords, besides hyperplasia, he found excrescence with sulcus in front of and behind it.

In 1928, Chevalier Jackson [6] observed 217 patients during a 4-year period, and named changes he found on arytenoids "contact ulcer". It was almost 50 years after Mackenzie's description. Jackson [6] emphasized that this term refers strictly to nontuberculous lesions, but that any of them can turn into cancer. He associated these lesion to excessive vocal use, occurring frequently among salesman, doctors who gave lectures, priests, with the significant influence of alcohol and tobacco use. In his work about laryngeal keratosis in 1946, Clerf [7] also said that pachydermia occurred more

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often at alcoholics or excessive vocal use, as in street sellers, for example.

From posterior laryngitis to "silent" gastroesophageal reflux

The advance in understanding the posterior laryngeal changes happened in 1968, when first reports on posterior laryngitis caused by gastroesophageal reflux occurred. That year Delahunty and Cherry [8] concluded on animal model that described changes on posterior larynx were caused by gastroesophageal reflux, while Cherry and Margulies [9] treated three patients with posterior laryngitis, and changes disappeared in six months. In 1970, Delahunty and Ardran [10] tried to explain globus hystericus as a possible manifestation of reflux esophagitis. In 1972, Delahunty climbed one floor above larynx, and in "Journal of Laryngology" published the paper titled "Acid laryngitis" [11]. In it, he stated as a postulate that "patients with reflux esophagitis can regurgitate acid contents even more, especially during the night, which causes inflammatory reaction of posterior larynx".

Searching PubMed data base showed a lack of papers until 1984, when a research of otorhinolaryngologists from Ljubljana, Vinko Kambič and Zora Radšel [12], "Acid posterior laryngitis" was published in the same journal in which Delahunty published the results of his researches. They published the histological results of biopsy of mucosa in 44 patients with chronic posterior laryngitis caused by acid. From phoniatric point of view, Živko Majdevac [13], student of Czech phoniatric school and founder of Phoniatric Department of Otorhinolaryngology Clinic in Novi Sad, was also interested in these changes. At the VIII Congress of UEP (Union of European Phoniatrics) in 1979 in Köszeg (Hungary), he presented his "Classification of dysphonia regarding primary etiological factor", and in the first group of disorders – functional disorders, described "contact hyperplastic dysphonia" as a condition which occurs in men whose voice is in range of baritone or bas, and more often at military commanders and teachers. During phonation, posterior thirds of vocal cords are overcontracted, which causes the appearance of circumscriptive yellowish thickening. At the time, he associated the mentioned changes on vocal processes of arytenoid cartilage with gastric hyperacidity, considering it a significant cofactor.

In 1986, Benjamin [14] published a paper on extraesophageal complications of gastroesophageal reflux, stating that gastric contents can get from esophagus into hypopharynx and lungs. In 1989, Wilson et al. [15] published a paper based on a 23-hour long ambulatory measurement of pH and biopsy of posterior larynx in patients with hoarseness, throat burn and globus sensation.

In 1991, Olson [16] mentioned laryngopharyngeal manifestations of gastroesophageal disease. In the same year, James A. Koufman [17] published a paper on otolaryngeal manifestations of gastroesophageal disease in 225 patients, which was the highest number of patients up to the time. At that moment, he did not refer to the disorder as LPR yet, but called it "occult (silent) gastroeophageal reflux disease". A paper on measuring pH on children with gastroesophageal reflux was published in 1992 by Contencin et al. [18].

Gastroesophageal *vs* laryngopharyngeal reflux

In 1996 in the Journal of Voice, Koufman, Sataloff and Toohil [19] published a report from consensus conference on LPR, and that was the first paper to refer to the term laryngopharyngeal reflux. In 1992, Kamel et al. [20] published the results of prospective study on the use of omeprazole in the therapy of reflux laryngitis, while Shaw et al. [21] in 1996 published a paper with the special emphasis on laryngoscopic findings before and after the therapy with omeprazole. In 1997, Wo et al. [22] published a work on empiric use of high doses of omeprazole in patients with posterior laryngitis, while Habermann et al. [23] published a study on *ex iuvantibus* therapy with pantoprazole in patients with posterior laryngitis in 1999. In 1999, Koufman [24] made a report about the treatment of LPR (for the first time with this name) on I International Symposium about human pepsin, held at the University of York (England). The term of laryngeal reflux in children was first mentioned in 2000 by Zalzal and Tran [25] in the paper titled "Pediatric gastroesophageal reflux and laryngopharyngeal reflux". The term LPR was not yet used in that year, but "laryngitis gastrica" was used instead.

In 2000, Koufman et al. [26] found that reflux is observed in 50% of their examined patients with laryngeal and vocal problems. In June 2001, Belafsky, Postma and Koufman [27] published a paper in the Laryngoscope Journal, in which they explain their scoring system of reflux findings [*Reflux Finding Score* – (RFS)], questionnaire about the LPR symptoms named Reflux Simptom Index (RSI) and support the term LPR. In August of the same year, in the same journal, they explained the validity and usefulness of RFS in detail [28]. A year later, the same team [29], (joined by Amin) made a detailed evaluation of RSI usefulness, while Koufman [30] definitively explained that LPR is different from classic gastroesophageal reflux disease.

Nissen's fundoplication as a method for the treatment of extraesophageal manifestations of gastroesophageal reflux disease was promoted in the study by Lindstrom et al. [31] in 2002. In 2003 Siupsinskiene and Adamonis [32] published a paper on *ex iuvantibus* diagnosis by administration of omeprazole and monitoring the response. In the same year, Galli et al. [33] published a study based on the hypothesis that biliary reflux, as well as gastric reflux, has an influence on inflammatory, precancerous and neoplastic changes of larynx. The first paper on the quality of life in patients with LPR was published in 2007 [34].

In April 2011, during 132nd annual meeting of American Laryngology Association (ALA), Jamie A. Koufman [35] was awarded for extraordinary contribution to the research and medical references in laryngology. It was a reward for a lifelong work on explaining etiology, pathophysiology, clinical findings, diagnostics, therapy and prevention of laryngopharyngeal reflux. In order to grasp the importance of her contribution, it should be mentioned that among the scien-

tists who got this award were Chevalier Jackson and John Kirchner.

Conclusion

Researches on the influence of laryngopharyngeal reflux on the organs of otorhinolaryngology region keep on, especially after understanding that this disorder can be a stand-alone factor or cofactor in etiology of secretory otitis, chronic rhinitis, nose-sinus polyposis and cancer of aerodigestive ways. However, without looking back in the past and paying tribute to everyone who explained the term and nature of laryngopharyngeal reflux, no new researches would have the full sense.

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