REINKE'S EDEMA

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Abstract
A persistent buildup of fluid in the subepithelial layer of the genuine vocal cord mucosa is known as *Reinke's edema* . Minimal intervention and superficial excision with edema evacuation and preservation of the medial margin of the vocal fold to enhance voice quality are the two key therapeutic tenets for Reinke's edema. We describe a case of a 65-year-old man who had smoked for 55 years and complained of dysphonia throughout the preceding year, which had become worse within the two weeks prior to admission. The patient additionally said that strenuous exercise or prolonged speech might cause dyspnea to occur. Tonsilalingualis hypertrophy grade 2 was seen during a nasopharyngoscopy, along with bilateral true vocal cord edema. Glottic region thickening and an isodense lesion at C5 level of the glottic area were both seen on the CT scan picture. The patient had vocal cord steroid injections in addition to microlaryngeal surgery. The connective tissue had subepithelial edema, according to histopathological analysis. The patient got postoperative care that included IV ranitidine 50 mg every 12 hours, IV paracetamol 500 mg every 8 hours, IV methylprednisolone 62.5 mg every 12 hours, and oral amlodipine 1 mg twice daily while in the hospital up to one day following surgery. The patient was released, and prescriptions for cefixime 200 mg twice, methylprednisolone 8 mg twice, and sodium diclofenac 50 mg twice were given. The patient was instructed to follow a customized *laryngopharyngeal* reflux (LPR) diet and to completely rest their voice for one week.

Keyword : Reinke's, Edema, Dysphonia, Injection, Corticosteroid

Introduction

Reinke's edema (RE) lesion is a benign exudative lesion that occurs in the superficial layers of the vocal folds. These lesions may be unilateral or bilateral, sessile, swollen with fluid on the vocal cords, and very mobile during phonation. [1–4] RE is also known as smoking polyp, polypoid laryngitis, polypoid degeneration, and chronic hypertrophic laryngitis. [1.5] It is reported that the prevalence of RE in the general population is less than 1%. No epidemiological studies have reported incidence by ethnicity or geographic location. Looking at all admission patients who underwent a suspension microlaryngoscopy procedure, the RE rate has been reported to be 16%. Most studies report a higher incidence in women, but some authors find a trend in [men]

Reinke's edema can involve either or both vocal cords. Expansion of the subepithelial space causes changes in the shape of the mucosal folds. It occurs not only due to smoking-induced transudates, vascular congestion, and venous stasis, but also due to voice abuse (voice abuse or overuse of the vocal cords) and gastroesophageal or laryngopharyngeal reflux. It's not clear whether allergies also contribute to rheumatoid arthritis. Patients with rheumatoid arthritis usually experience varying degrees of dysphonia, but some patients also report regular or periodic loss of breath, depending on the size of the lesion. [6,7]

Dysphonia, also known as vocal dysfunction, can reduce the patient's quality of life and has an economic impact on patients working with significant vocal stress. [8] The severity of RE disease varies. Despite the fact that patients experience dysphonia to varying degrees, some of them also report that they have difficulty sleeping, either regularly or periodically. Large lesions can compromise the airway in serious cases. [9] ER often narrows the glottic space. Because this condition can complicate airway control, the anesthesiologist must be aware of this. To perform intubation, the endotracheal tube may be smaller. Clashes with the vocal folds can cause glottic edema and obstruction, blocking positive pressure ventilation via the supraglottic device. This can be mistaken for laryngospasm or a malposition of the apparatus. Fiberoptic examination with tools to help identify the causative factor. Under certain conditions, such as surgery in the prone or Trendelenburg positions, and excessive fluid administration, previous RE can cause laryngeal edema to worsen. [10] Treatment trials of LPR, discontinuation of risk factors, and phonosurgery are the basis of the therapeutic recommendations. Phonosurgery mostly corrects dysphonia, but cannot restore its initial state.[7]

The purpose of this study is to increase knowledge about the treatment of *Reinke's edema.*

Case Report

A 65 year old man comes to the ENT-KL clinic with the main complaint that he has a hoarse voice. The patient has had this disease for the past year, and it has gotten worse in the last month. In addition to the symptoms of the disease, there was a lump on the upper neck that was the size of a quail egg, but had gotten smaller in the last two weeks. Consumption of food and drink according to the norm. Patients stated that they did not experience coughing and choking. Patients say they feel breathless if they engage in activities that are too strenuous or talk for too long. The patient refused to experience complaints of the nose and ears. The patient smoked from the age of ten, smoking between twelve and sixteen cigarettes per day. The patient has no history of DM and hypertension (+).

The results of the physical examination showed moderate KU, CM, BP: 137/72 mmHg, HR: 88 beats per

Y. A. Dewi et al. (eds.), *Proceedings of the 19th Otorhinolaryngology Head and Neck Surgery National Congress (PERHATIKL 2022)*,
Advances in Health Sciences Research 68,
https://doi.org/10.2991/978-94-6463-280-4_18

minute, RR: 20 beats per minute, and T: 36.5 degrees Celsius. Otoscopy examination showed right and left auris: CAE within normal limits, intact tympanic membrane (+/+), and right and left nasal cavities on anterior rhinoscopy: CAE within normal limits, T1-T1, hyperemia (-), and no palpable mass on the neck.

Nasolaryngoscopy examination showed that the nasal cavum, fallopian tubes, and nasopharynx were within normal limits; good felopharyngeal function; gramulation of the posterior online wall (+); hypopharynx is within normal limits; grade 2 tonsilalingual hypertrophy, erect epiglottis; moderate degree of partial ventricular obliteration is seen; erythema seen on bilateral arytenoids; vocal folds show edema bilaterally; the subglottis is difficult to evaluate; esophageal entreotus

According to the results of hematology laboratory tests, liver, kidney and electrolyte functions were within normal limits. Examination of the chest photo shows that the cor pulmo is normal in size and there are no signs of abnormalities. The results of the CT scan showed thickening in the glottic area and isodense lesions as high as VC 5.

Reinke's edematous tissue was sent to anatomic pathology for further examination, and this patient received microlaryngeal surgery and steroid injection of the vocal cords. The results of the anatomic pathology examination showed that the preparation consisted of fragments of connective tissue which partially formed protrusions and were covered by monomorphic complex squamous epithelium. Edematous, partially myxoid subepithelial connective tissue covered with sparse lymphocytes and histiocytes. There is no indication of malignancy. Vocal cord tissue: Histopathology consistent with Reinke's edema, also known as vocal cord polyps.

One day after the procedure, the patient was hospitalized and received injections of Ceftriaxone 1 gram every two hours, injections of Methylprednisolone 62.5 mg every two hours, injections of Inf Paracetamol 500 mg every eight hours, injections of Ranitidine 50 mg every two hours, and amlodipine 1x10 mg every day. The patient also received home medication cefixime 2x200 mg, methyl prednisolone 2x8 mg, and na diclofenac 2x50 mg every day. The patient received voice advice on total rest for one week and the LPRD diet.

Method

A patient who visited the ENT-KL poly at Dr. Sardjito General Hospital Yogyakarta in June 2022 became the subject of this study. Laryngology Polyclinic RSUP Dr. Sardjito in Yogyakarta conducted anamnesis and physical examination.

The author performs a free title and abstract search based on the selected criteria. Between July 2017 and July 2022, we conducted an electronic search for studies in English across two databases: (1) PubMed and (2) Google Scholar. The authors used keywords such as *"Reinke's edema" or "polypoid corditis", "microlaryngeal surgery", "vocal rest", and "laryngopharyngeal diet"* . Based on the titles that appeared in the electronic search, the authors selected irrelevant articles at the initial stage of the search.

Results

Reinke's edema is most common in women and is seen more frequently in smokers who lead vocally active lifestyles. The triad of *laryngopharyngeal reflux (LPR)* disease , voice abuse (voice abuse), and tobacco abuse are the main causes of this condition. Not all patients with Reinke's edema necessarily have all three etiological factors, but it is common for patients to have two of these when they develop rheumatoid edema (RE). The role of the LPR is still unclear. [4,7,13,14] In this case, the patient was a 65 year old male who had smoked 12–16 cigarettes daily for 55 years. There was no patient information, including voice overuse, history of GERD/LPR, sleep snoring, and OSA.

RE increases the mass of the vocal cords, decreasing the pitch of the voice. In addition, the phonation efficiency and stability of the voice decreases, which causes hoarseness. [4] Symptoms of hoarseness are common. The patient uses the vestibular folds to produce a low-pitched, harsh or hoarse voice. [17]

Significant bilateral lesions can cause stridor and airway obstruction, especially when accompanied by other vocal cord diseases. [1,13] In this case, the patient had a chief complaint of hoarseness for the past year, which had gotten worse in the past month. In addition, patients complain that they feel too busy if they do strenuous activities or talk too long.

The goal of therapy is to improve the symptoms of dysphonia. Removing all predisposing risk factors is the first step in treatment. Steroids are the only pharmacological option that has been investigated. [1,10] The treatment of choice should be surgery if voice improvement does not provide satisfactory results for the patient. For the treatment of ER, conventional microlaryngeal surgery is very good. It is safe to operate both vocal folds in the same session, but care is taken not to extend the incision into the anterior commissure. [19]

This patient underwent microlaryngeal surgery and steroid injection in the vocal cords. For five days, the patient received *cephalosporin antibiotic therapy, methylprednisolone, and diclofenac Na.* For patients with *laryngopharyngeal reflux disease (LPRD)* , it is recommended to do total voice rest for one week and follow a diet program.

Discussion

Due to diffuse polypoid degeneration of the vocal cords, *Reinke's edema* is a chronic benign laryngeal condition characterized by swelling caused by accumulation of fluid in the uppermost layers of *the lamina propria plica vocalis* . The Reinke's space is the uppermost layer of *the lamina propria plica vocalis* , which is composed of loosely

woven collagen and elastin fibers and has an average thickness of 0.3 mm. [5,6,9,11]

The number of cigarettes smoked daily and the duration of exposure to cigarette smoke correlate with clinical manifestations of RE disease. Long exposure to smoke causes higher histological damage. [11,12] However, research by Tavaluc et al. showed a weak correlation between the increase in cigarette use per pack and the severity of RE. Although exposure to tobacco can affect the development of RE, this study shows that more than just tobacco causes an increase in RE. [15] As shown by a study conducted by Hamdan et al., patients with obstructive sleep disorder (OSA) have higher rates of snoring and higher Epworth Sleepiness Scale scores compared to OSA patients without OSA. [12,16] It appears that women are affected more frequently than men. This may be because women's fundamental voice frequencies tend to be louder than men's. [12] Other sources say that the predominance of older women is due to their hormonal condition. [7].

Clinical presentation depends on the size of the lesion; usually bilateral, but occasionally asymmetric. Dysphonia is the most common complaint because of the burden of edema in the mucosal folds. [1] Deepening of the voice, vocal fatigue, decreased vocal range, and loss of high notes are signs of dysphonia. [12] Changes in the fundamental frequency (F0) are the source of most of the complaints. Because the decrease in F0 and the shift in the frequency range of women is more pronounced than that of men, women may be more frequently examined for their condition and seek treatment because the average F0 for women is 180 to 230 Hz, and F0 for men is <130 Hz. Although less common, patients may also experience dyspnea. The ER affects voice more frequently than respiration, which is dependent on the posterior cartilaginous vocal cords, as it is confined to the membranous vocal cords. [1]

The presence of a pocket of pale fluid adhering to the superior surface and edge of the vocal folds is usually found on examination of the larynx. On sudden inhalation, large ER can cause involuntary laryngeal stridor. Respiration produces a back-and-forth movement. Collections of polyps on polyps can be seen in severe situations. Unless the patient is instructed to vocalize on inspiration, the small ER is easily overlooked. It occurs when polypoid tissue is pulled from the upper surface of the vocal folds into the glottic opening, causing greater-than-normal convexity of the margins. [5] On swelling like a balloon in the vocal cords when the larynx is examined. Yonekawa et al. suggested a grading system based on the morphological characteristics of the RE when visualized under indirect laryngoscopy. They defined Grade 1 edema as edema on the superficial side of the vocal folds, Grade 2 as edema radiating to the posterior aspect of the vocal folds, and Grade 3 as gross edema. [2,12,18] This system uses gross perceptual assessment and acoustic measurements based on lesion size to assess voice changes; however, the anatomical description of the lesion is incomplete. In addition, the scale is limited to the possibly obstructive presentation of the lesion and has not been validated. As a result, this system is not widely accepted. Tan et al. recently proposed a new RE clinical assessment based on the percentage of airway involvement by each vocal fold with each side examination. They identified four grades, namely: Grade 1, minimally degenerating polypoid lesion of the vocal folds involving 25% or less of the glottic airway; Grade 2, widespread polypoid degenerative lesion occupying 25-50% of the glottic airway; Grade 3, widespread polypoid degenerative lesion involving 50-75% of the glottic airway; Grade 4, obstructive lesion >75% airway occupancy without neglecting lateralization. [9] According to de Vincentiis et al., the classification of RE is based on its morphological characteristics. They attempted to combine the features of the vocal folds and the characteristics of airway obstruction into a single system. Type ER in one vocal fold showing chronic edema of the lamina propria. Type ER of both vocal folds shows chronic edema of the lamina propria. Type ER in one vocal fold with polypoid lesions showing chronic edema of the lamina propria layer in one vocal fold with polypoid lesions.

On stroboscopy, the altered viscoelastic properties of the superficial layers of the lamina propria cause increased mucosal wave propagation and asymmetrically increased amplitude. [1,12] Radiological examination is not necessary to diagnose RE, because the diagnosis can be seen on laryngoscopy. However, if imaging is obtained, it is important for the radiologist to recognize this condition because the soft tissue thickening produced by the ER can easily be mistaken for tumoral infiltration of the vocal folds. [12]

The Reinke's space is filled with sheets of loose connective tissue that run parallel to the edges of the vocal folds. In RE, there is increased subepithelial vascularity due to chronic irritation, resulting in vessel dilation, endothelial thinning, and increased fenestrae, leading to increased vascular permeability (Figure 4). [1,9] This results in plasma exudation and the formation of hollow spaces called neobursae in light microscopy, and loosening of the junctions between cells in electron microscopy. The structural components have also changed. There are architectural changes in the collagen and elastin fibers that form the fibrous structure of the lamina propria. In normal subjects, collagen fibers are neatly arranged in a woven basket configuration. In the ER, collagen fibers become intertwined and fragmented. In addition, in normal specimens, the elastin fibers are arranged in thin, wavy lines parallel to the basement membrane of the epithelium. In the ER, the elastin fibers are scattered and tangled. Fibronectin, which is a structural glycoprotein precursor for collagen deposition and scar formation, was decreased in the ER, leading to the theory that its absence causes the characteristic deformability of the vocal cords in the ER. [1]

The cause of RE is multifactorial. Mechanical, pathological, chemical, genetic, smoking habits, *vocal abuse* , and gastroesophageal/laryngopharyngeal reflux have been

identified as potential risk factors. [2] Grill *et al.* identify altered pathways in plica vocalis fibroblasts isolated from ER tissue and to investigate the functional consequences of these changes. Long-term irritants and noxious agents such as smoking and heavy use of voices, gene expression in vocal cord fibroblasts in the ER is constantly changing, which may be epigenetically regulated and detectable in primary cell cultures of vocal cord fibroblasts. Altered expression of extracellular matrix components contributes to extracellular matrix reorganization and is found in vocal cord fibroblasts with ER. In addition, increased levels of factors involved in TGF-β signaling, as well as increased levels of mRNA receptors for inflammatory cytokines, suggest a differential response to cytokine stimulation in these cells. Regulation of transcription toward cell cycle arrest, and by the resulting decrease in proliferation, could be a result of these changes. [8]

The goal of therapy is to improve the symptoms of dysphonia. Removing all predisposing risk factors is the first step in treatment. Therefore, patients should be counseled on smoking cessation, voice therapy, and, if necessary, treatment of gastroesophageal or laryopharyngeal reflux. Quitting smoking can improve mild ER. Giving up smoking completely may not be able to restore the condition as before. However, it can stop progression and possibly even improve the voice and reduce the size of the lesion. [1,13] To optimize vocal behavior, short-term voice therapy may be appropriate. This alone can reduce the turgidity of the polyp, which means little improvement in vocal function. [5] To prevent disease progression, LPR therapy may include lifestyle changes and the use of pharmacotherapy. Ensuring an adequate airway for the RE with obstruction is the first goal of therapy. Treatment then concentrates on improving vocal performance after diagnosis or treatment of a patent airway. Patients who have an obstructed airway or are unsuccessful with conservative therapy should undergo surgical intervention. Special counseling should be given to patients who wish to undergo elective therapy for voice improvement regarding the risk of relapse if continued smoking, scarring of the vocal folds, and failure of voice repair. [13]

Steroids are the only pharmacological option that has been studied. The effects of inhaled steroids are not significant. Steroids given intravenously help reduce edema caused by inflammation. Objectively and subjectively, injection of triamcinolone acetonide into the Reinke space in patients with mild ER shows increased sound. [1.10]

The treatment of choice should be surgery if voice improvement is not satisfactory for the patient. After a surgical procedure for rheumatoid arthritis (RE), uncontrolled LPR causes problems with reepithelialization of the vocal cords. The two goals of surgical management of RE are: (1) reduce the degeneration of the superficial lamina propria; and (2) ensuring healthy vibrations of the epithelium and lamina propria. However, it is important to remember that surgical intervention is the first line of therapy for patients with dyspnea, airway problems, or breathing problems. After surgery, it is very important to restore movement of the epithelial lining over the vocal ligaments and prevent scar tissue from forming. To ensure future propagation of the mucosal wave, surgical intervention involves precise excision of the oedematous superficial lamina propria. The techniques and instruments used in surgical interventions may differ. After surgical intervention, precipitating factors such as smoking, reflux or excessive use of the voice must be eliminated. Optimal sound results require postoperative voice therapy. Cold iron or laser techniques can be used for ER surgical intervention. Potassium titanyl phosphate (KTP) lasers, carbon dioxide (CO2) lasers, and blue lasers with a wavelength of 445 nm are the most commonly used. [12]

Both vocal fold operations are safely performed in the same session as conventional microlaryngeal surgery for the treatment of ER. However, be careful not to extend the incision into the anterior commissure. [19] The cold steel technique, also known as the microflap technique, is a vertical incision parallel to the lateral edge of the vocal folds. Next, the matrix is aspirated edematous. The amount of hyperplastic tissue removed must be sufficient to ensure that the glottis has normal morphology. Tissue should be lifted from front to back without damaging the mucosa of the anterior commissure. Thereafter, excess epithelium was removed from the lesion-free margin and returned to its place. Because the incision is made far laterally from the medial surface or phonation, this method preserves the vibratory margins of the vocal folds. This method widens the glottis and reduces the mass of the vocal folds, improving the aerodynamic conditions of phonation. Because it maintains its layered functional structure, it improves the quality of vocal cord phonation movements. These changes improve the patient's quality of life score. [12]

To ensure successful airway management before surgery, preoperative evaluation of the airway by the anesthesiologist is essential. Prior to induction of anesthesia, airway management and algorithms must be determined and preparations must be completed. The extubation strategy must be planned in advance, as is the case for difficult intubations. The intubation tube used for microlaryngeal surgery should be 30 cm long, small in diameter (No. 4-6 mm), and use a standard balloon. The balloon should be low pressure and high volume, positioned between the arytenoid cartilages, with part of the glottic space visible. Patients undergoing laser surgery should use a laser-shielded intubation tube. Before the intervention, patients must wear glasses, and their subglottic area must be covered with a wet cloth. After difficult intubation, laryngeal edema, bleeding, tracheal or esophageal trauma, aspiration, and pneumothorax are potential complications. In this situation, obstructed breathing, dysphagia, and emphysema under the scalp and neck should be closely monitored. To guide future surgeries, it is very important to verbally inform the patient and family about any airway problems they are

experiencing. To reduce edema during surgery, intravenous steroid injections should be administered. Antibiotics are not needed for microlaryngeal surgery unless the area is infected or contaminated. To prevent bleeding, anticoagulant medications should be discontinued seven to ten days before laryngeal surgery. A good view of the larynx is essential for microlarynx function. With the use of the laryngoscope, several parameters, such as the interincisive gap, thyromental distance, previous history of open-neck and/or radiotherapy, modified Mallampati score, and body mass index, can indicate possible problems with laryngeal exposure. [20]

As demonstrated by a meta-analysis study performed by El-Halaby et al., there is insufficient evidence to determine whether conventional microlarynx surgery or CO2-assisted laser surgery is better. [21] As a result of a study conducted by Cohen et al., patients who underwent microlaryngeal surgery did not show a statistically significant difference between the group with vocal rest and the group without vocal rest. Sound quality and wound healing were the same in both groups. When vocal rest is not used after microlaryngeal surgery, wound healing is just as good. [22]

In a systematic review of seven studies, it was found that changes in diet, such as not fasting, avoiding food or drink about two to three hours before bedtime, consuming low-acid drinks and Mediterranean-style plant foods, reducing consumption of fat, coffee, and chocolate, may help reduce LPR symptoms. However, the study found no evidence that changes in diet can cure LPR. In one study, treatment involved the use of medication and lifestyle changes. In this study, lifestyle changes included dietary and behavioral changes, such as lowering the head of the bed and not wearing tight clothes. Thus, this reference study of dietary changes for laryngopharyngeal reflux patients is insufficient to provide advice. [23]

Men over 60 years of age can also suffer from Reinke's edema (RE), like the patients in this study. Dysphonia and, in some cases, dyspnea can be caused by this condition, especially when triggered by prolonged use of the voice or during strenuous activity. While the role of laryngopharyngeal or gastroesophageal reflux remains unclear, history of smoking and voice use are major risk factors for ER. Direct laryngoscopy and history taking are used to confirm the diagnosis of RE. Often, radiological examination is not necessary. Lifestyle changes to eliminate risk factors, such as smoking cessation, voice therapy, and LPR therapy, are the initial treatment for ER. To reduce edema, the Reinke room can receive pharmacological therapy in the form of steroid injections. Patients with dyspnea, airway obstruction, or respiratory distress may require surgical treatment if their voice improvement is not satisfactory. Conventional and laser-assisted microlaryngeal surgery (CO2, KTP, and blue) are surgical procedures. To ensure a patent airway and safe application of anesthesia, adequate knowledge of the patient's condition is required. After surgery, patients may be advised to rest their voices, but there is no evidence that this is effective.

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