

Recurrent hypertrophic laryngeal lesions in a patient with a history of pesticide exposure – a case report

Nawracające zmiany przerostowe krtani u chorego z wywiadem narażenia na pestycydy – opis przypadku

Authors' Contribution:

A – Study Design
B – Data Collection
C – Statistical Analysis
D – Manuscript Preparation
E – Literature Search
F – Funds Collection

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Article history: Received: 10.01.2020 Accepted: 18.02.2020 Published: 21.02.2020

ABSTRACT:

Chronic irritation of the laryngeal mucosa by external factors can lead to the development of dysphonia: hoarseness, change of the voice tone or weakening of its strength. Patients who additionally report alarming symptoms, such as dyspnea, dysphagia, or odynophagia require urgent diagnosis and treatment. Long-term exposure to irritants may lead to the development of numerous recurrent hypertrophic laryngeal lesions requiring continuous otorhinolaryngological care and multiple surgical procedures, as it was in the presented case.

KEYWORDS:

dysphonia, hoarseness, larynx, pachydermia, pesticides

STRESZCZENIE:

Przewlekłe drażnienie błony śluzowej krtani przez czynniki zewnętrzne może prowadzić do rozwoju dyfonii o charakterze: chrypki, zmiany barwy głosu lub osłabienia jego siły. Chorzy zgłaszający dodatkowo objawy alarmowe, takie jak: duszność, dysfagia lub odynofagia, wymagają pilnej diagnostyki i leczenia. Wieloletnie narażenie na czynniki drażniące może prowadzić do rozwoju licznych, nawracających zmian przerostowych krtani, wymagających stałej opieki otorynolaryngologicznej oraz wielokrotnych zabiegów operacyjnych, tak jak to miało miejsce w prezentowanym przypadku.

SŁOWA KLUCZOWE:

chrypka, dysfonia, krtań, pachydermia, pestycydy

ABBREVIATIONS

NBI – Narrow Band Imaging

INTRODUCTION

Disruptive, relentless hoarseness persisting over 4 weeks is an indication for urgent otorhinolaryngological or phoniatic consultation for morphological and physiological evaluation of the larynx.

Hypertrophic lesions of the larynx are some of the most common organic changes leading to dysphonia. They often coexist with the history of chronic exposure to agents that irritate laryngeal mucosa as a result of, i.e. smoking, untreated pharyngolaryngeal reflux or environmental exposure [1].

Diagnostics should be based on necessary tests enabling assessment of the appearance and function of various anatomical structures of the larynx and potential qualification to diagnostic and therapeutic procedures. In selected cases, it is advisable to conduct a number of imaging studies to allow analysis of the scope of observed changes [2].

CASE REPORT

A 59-year-old man presented acutely at the Department of Otorhinolaryngology, Head and Neck Surgery of the Medical University of Warsaw, due to dyspnea accompanied by hoarseness and weakening of voice that have been gradually increasing over the past few months.

Medical history included hypertension (well controlled) and spinal osteoarthritis. For about 40 years he had been exposed to oc-



Fig. 1. Picture of the larynx in nasofiberoptic examination – numerous exophytic lesions, pachydermia, in the area of posterior laryngeal commissure and leukoplakia on both sides on vestibular folds.

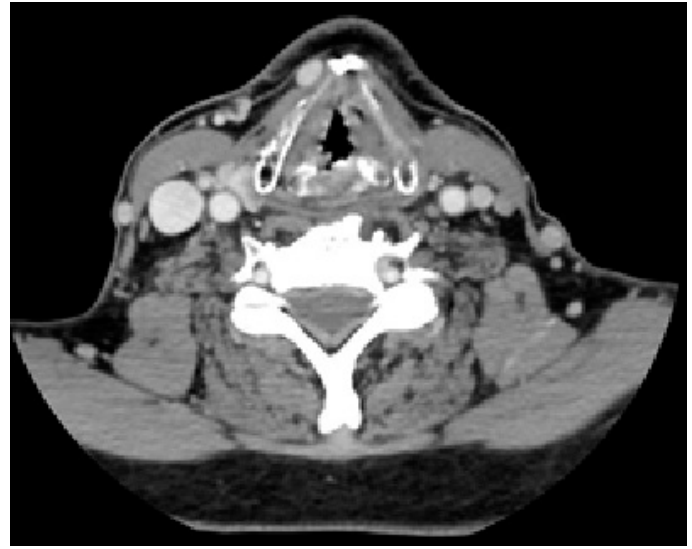
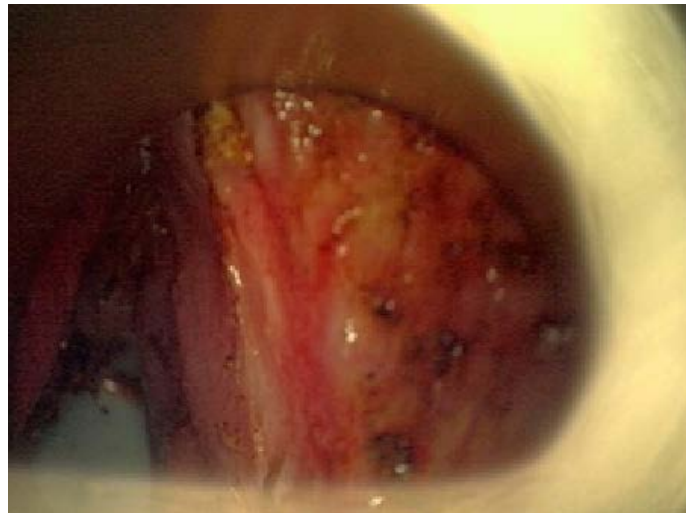


Fig. 2. Computed tomography image of the neck, frontal scan, examination after contrast administration. Apparent irregular outline at the level of vocal folds and lesions protruding into the lumen of the glottis.



Fig. 3. and 4. Intraoperative pictures during laser microsurgery of the larynx. In photo no. 3 the area of posterior laryngeal commissure with pachydermia before resection and after removing the lesions with CO₂ laser.



cupational contact with pesticides and chemical plant protection products. Moreover, he reported a long-term history of smoking – about 35 pack-years.

No significant pathologies were found in clinical examination during otoscopy, anterior rhinoscopy or during assessment of oral and nasal parts of the throat. Evaluation of the larynx and lower throat revealed numerous exophytic lesions encompassing vestibular folds and the edges of true vocal folds. Nasofiberoptic examination was performed for a more thorough assessment of the larynx, exposing bilateral pachydermia of the epiglottic area and glottis. Mobility of the vocal folds was symmetrically preserved. The space between vocal folds edges for breathing was 3 mm (Fig. 1.).

Inflammatory markers (WBC $6.77 \times 10^9/L$; CRP $< 5 \text{ mg/dL}$) on admission were not elevated and there were no abnormalities in routine chest X-ray. Urgent computed tomography of the neck with

contrast showed no features of pathological contrast enhancement, destruction of cartilaginous structures of the larynx, or enlarged lymph nodes (Fig. 2.).

Since the patient remained in good general condition and his saturation was stable within the normal limits, a decision was made to implement conservative treatment with anti-edematous drugs in combination with intravenous proton pump inhibitor (methylprednisolone 500 mg and omeprazole 40 mg), empirical antibiotic therapy i.v. (cefazolin 1000 mg every 8 h) and observation in a hospital setting.

Gradual attenuation of dyspnea was observed following implementation of parenteral treatment. In order to treat the underlying cause, patient was referred for microsurgery of the larynx, during which, lesions resembling leukoplakia were removed from the supraglottic area using CO₂ laser (vestibular folds, laryngeal surface of the epiglottis).

Tab. I. The most common causes of dysphonia [17].

MILD LESIONS	HYPERPLASIA AND PRECANCEROUS	THE MOST COMMON CAUSES OF DYSPHONIA					
		NEUROLOGICAL REASONS	SYSTEMIC	TRAUMATIC	INFECTIVE	ABNORMALITIES IN ANATOMICAL STRUCTURE	OTHER
Nodules and other fibrous lesions	Leukoplakia	Paralysis of vocal folds	Granulomatosis with vasculitis	Blunt trauma	Papilloma	Vascular malformations	Laryngeal hypersensitivity
Polyps	Erytroleukolakia	Parkinson's disease	Syphilis	Chemical injuries	Bacterial laryngitis	Laryngocele	
Varicose veins/vascular lesions	Pachydermia	Post-polio syndrome	Tuberculosis		Fungal laryngitis		
Cysts	Squamous cell carcinoma	Myasthenia gravis	Amyloidosis		Viral laryngitis		
Hematomas	Mesenchymal or neurogenic tumors		Sarcoidosis				
Reinke's edema			Rheumatoid larynx lesions				
Granuloma							

Type II cordectomy was performed to remove hypertrophic lesions of the vocal folds. Keratinized masses resembling pachydermia were removed from the posterior laryngeal commissure (on one side, to the midline keratinized masses were removed together with the mucosa, while on the other side their size was only reduced, for fear of synechia in the posterior commissure with extensive resection) (Fig. 3. and 4.). In the postoperative period, shortness of breath was not observed, and the patient reported subjective improvement in the quality of the voice. Lesions excised from the vocal folds, posterior commissure and vestibular folds were sent for histopathological examination, which demonstrated keratinized stratified squamous epithelium with local foci of high-grade dysplasia and characteristics of mixed inflammation.

Due to good general condition, patient was discharged home on the 2nd day after surgery under regular care of hospital's ENT outpatient clinic and speech therapists. Considering past medical history of gastroesophageal and laryngo-pharyngeal reflux, he was put on treatment with proton pump inhibitors (omeprazole 40 mg/day); anti-reflux diet and further gastroenterological care were recommended. Therapy of concomitant diseases remained unchanged.

Two months after microsurgery, patient was referred for the second stage of surgical treatment of the larynx using the CO₂ laser (Fig. 5.). Lesions were removed from the second vocal fold and the other part of the posterior commissure.

Despite these two procedures, the recurrence was observed in a 1-year follow-up: relapse of hypertrophic lesions, leukoplakia and keratinized masses in the posterior commissure, which no longer caused shortness of breath, but due to the foci of high-grade dysplasia in previously removed laryngeal tissues, laser microsurgery was repeated twice. In subsequent histopathological examinations, low-grade dysplasia was identified in the excised material. Patient remains under continuous care of the ENT and phoniatic clinics, where he reports for regular monthly checks, and has been referred to speech therapy services for voice emission rehabilitation.



Fig. 5. Endoscopic examination of the larynx using NBI imaging: visible extensive hypertrophic lesions of the larynx with the appearance of leukoplakia and pachydermia, that prevent assessment of mucosa vascularization.

DISCUSSION

Propagation of information regarding harmfulness and toxicity of pesticides and other agents used to protect plants from pests has a strong impact on rising public awareness [3]. A number of studies have been conducted showing a direct link between exposure to pesticides and development of cancer, particularly in people exposed to long-term contact with these substances, such as agricultural workers [3, 4, 5]. The list of plant protection agents authorized for sale and use in Poland is published by the Ministry of Agriculture and Rural Development, together with warnings and recommendations regarding their use. Unfortunately, not everyone takes the risks of exposure to harmful compounds seriously and adequately applies the recommended protection measures.

One of the first seemingly harmless symptoms that patients exposed to long-term contact with these preparations may report to the ENT specialist is dysphonia. It manifests in various ways: as hoarseness, change in voice tone or reduced strength. Other accompanying symptoms that may occur in this group of patients, and doctors should pay particular attention to, include dysphagia

or odynophagia, which constitute an indication for urgent laryngological or phoniatic evaluation to exclude the presence of hypertrophic lesions within the upper respiratory tract and/or gastrointestinal tract [6]. The above symptoms depend on the size and location of the lesions.

Sometimes, enlargement of regional lymph nodes may be noted on palpation, which is an absolute indication for the diagnosis including imaging (ultrasound, computed tomography, magnetic resonance), in order to assess their size and character.

Patients with a history of occupational exposure to pesticides and dysphonia require detailed physical examination and medical history taking, including indirect laryngoscopy and endoscopic examination of the upper respiratory tract. Patients with pathological lesions in the larynx and laryngopharynx should undergo imaging to determine the extent of the disease.

Observed pathological changes in the larynx should be evaluated during indirect laryngoscopy using a surgical microscope and ultimately verified in a histopathological examination. In case of small lesions, same-time complete removal using microtools or CO₂ laser beam can be performed during the diagnostic procedure. In case of numerous or extensive changes, the scope of the procedure depends on careful clinical evaluation, results of imaging studies and histological type of the lesion. It should be remembered that extensive, single-step resection of lesions in the posterior and anterior commissures can lead to development of adhesions and worsening of dyspnea and hoarseness. When planning the extent of the resection of hypertrophic lesions in the larynx it is necessary to take into account: the result of histopathological examination, the course of the disease and patients' expectations. Unfortunately, in case of recurrent lesions, especially with confirmed high-grade dysplasia, as in the presented case, repeated microsurgical procedures may be necessary.

Leukoplakia, pachydermia and chronic hypertrophic laryngitis are some of the most common pathological lesions of the upper respiratory tract mucosa diagnosed during laryngological examination and indirect laryngoscopy. They are considered clinically precancerous lesions and require diagnostics. Over the years, many studies have been conducted to establish a link between the occurrence of leukoplakia and the risk of developing squamous cell carcinoma of the larynx [7]. The study by Kosteva et al. from 2018 found that 11% of patients developed laryngeal cancer within 6 months of leukoplakia diagnosis. In each age range, the risk of laryngeal cancer increased, reaching as much as 31.3% in the age group above 65 years. An additional feature predisposing to the development of malignancy was male sex [8].

A factor that may also affect the development and recurrent nature of lesions resembling pachydermia may be pharyngeal reflux, which is associated with chronic exposure to the low, acidic content of the stomach. Such a chronic irritation leads to inflammation of the mucosal membrane, primarily the area of posterior commissure of the larynx. In the study by Ozturk et al. coexistence of pachydermia was identified in 79.1% of patients who were diagnosed with pharyngolaryngeal reflux [9]. However, the presence

of laryngeal pachydermia is not an independent criterion for the diagnosis of this disease [10]. In patients with pharyngolaryngeal reflux pharmacotherapy and dietary recommendations should be implemented in addition to surgical treatment. Leukoplakia as well as pachydermia are not histopathological diagnoses, but merely a clinical term for lesions visualized endoscopically or in direct examination. According to the WHO definition leukoplakia means a white plaque or a patch of an undeterminate nature, appearing on the mucosa, while pachydermia is a white-grayish exophytic formation, most often located at the posterior laryngeal commissure.

The first scientific reports describing pachydermia in the larynx appeared at the turn of the 19th and 20th century [11, 12]. Pachydermia is one of the lesion classified as precancerous. Morphologically, excessive keratosis of the superficial layer of the laryngeal epithelium is observed and there are usually single keratinized cells in deeper tissues. In case of massive keratosis and bulging of the epithelium into the lumen of the larynx, there may be disruption of vibration and even impaired mobility of the vocal folds resulting in dysphonia. Shortness of breath requiring urgent surgical treatment may be observed in patients with large areas of pachydermia obstructing the lumen of the upper respiratory tract and larynx.

Narrow band imaging (NBI) is increasingly often used for the diagnosis of patients with laryngeal hyperplasia. It uses the classification proposed by Ni et al. to assess the vascular pattern within observed changes. It is also important to take into account phoniatic examination evaluated in videolaryngostroboscopy. Numerous studies have confirmed the value of the NBI technique in preliminary evaluation of the nature of observed lesions in the laryngeal mucosa, although the final diagnosis is still determined on the basis of a histopathological examination [13]. Unfortunately, in case of extensive hypertrophy with excessive keratosis, the usefulness of the NBI method in determining the diagnosis is very limited due to the inability to visualize vessels under keratinized epithelium [14].

In patients with hypertrophic lesions of the larynx we should first seek to eliminate all suspected causative factors, tobacco smoke in particular. In the past, alternative methods of treating hypertrophic lesions of the larynx less invasive than surgery and utilizing local retinoid administration were used. The effectiveness of treatment of precancerous lesions varies from 10 to 85% depending on the agent and duration of therapy. Unfortunately, the use of retinoids is associated with general toxicity, and relapses of lesions are common [15]. Photodynamic therapy is another method recently used in the therapy of cancerous and precancerous lesions, especially of the skin and mucous membranes. It works well for small, well-demarcated, superficial lesions and allows for a complete remission of changes in 89.1% of cases [16].

Currently, surgical resection using the CO₂ laser is still the optimal treatment for hypertrophic lesions of the larynx. Hypertrophic lesions of the larynx most often lead to development of dysphonia due to segmental restriction of vocal fold vibration. The principle of phonosurgical procedures is to remove exophytic lesions of the vocal folds, which allows to restore proper vibration during phonation and improve voice quality [10]. Unfortunately, resection of extensive, especially recurrent, potentially dysplastic

lesions of vocal fold mucosa, usually leads to formation of scars and permanent deterioration of voice quality. In this group of patients, intensive physiotherapy of voice emission supervised by a phoniater and a speech therapist after healing of the vocal fold epithelium, can significantly improve function of the glottis.

CONCLUSIONS

Patients with persistent voice disorders, such as hoarseness or change in tone, require urgent laryngological and/or pho-

niatric consultation to assess morphology and function of the larynx. Organic changes found in indirect laryngoscopy or endoscopic examination should be verified by histopathological examination of samples obtained during a biopsy carried out using surgical microscope or of entire lesion removed during endoscopic surgery.

Patients with relapsing lesions should remain under constant otorhinolaryngological and phoniatic care even after excluding malignancy due to the need for periodic evaluation of laryngeal structures and qualification for voice therapy.

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Word count: 2760 Tables: 1 Figures: 5 References: 17


Access the article online: DOI: 10.5604/01.3001.0013.8518


Table of content: <https://otorhinolaryngologypl.com/issue/12511>

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Competing interests: The authors declare that they have no competing interests.

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Cite this article as: Kloc M., Krawczyk P., Rzepakowska A., Niemczyk K.: Recurrent hypertrophic laryngeal lesions in a patient with a history of pesticide exposure – a case report; Pol Otorhino Rev 2020; 9 (1): 39-44
