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Endoscopic approach to hyperplastic laryngeal lesions: a literature review and personal experience

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Abstract

Background Presently, there is a lot of confusion in the identification and classification and no consensus regarding the management of hyperplastic laryngeal lesions (HLL). Conventional transoral microsurgery has some drawbacks and is not always possible. The purpose of the study was to identify criteria for preoperative detection of HLL with high malignant potential and to assess the effectiveness of flexible endoscopic surgery (FES) in the management of HLL.

Methods A review of relevant English literature and a retrospective review of medical records of 37 patients with HLL, treated by FES, was performed.

Results Endoscopic and histologic features of HLL are discussed. An endoscopic classification of HLL is proposed: chronic hyperplastic laryngitis (CHL), chronic hyperplastic laryngitis with keratosis (CHLK), leukoplakia, pachydermia, and verrucous neoplasia. The role of FES using different tools in the diagnosis and management of HLL is presented.

We applied flexible endoscopic laryngeal surgery (FELS) for 37 patients (ages, from 20 to 77 years, men 34, women 3) with the following types of HLL: CHLK 5, leukoplakia 18, pachydermia 12, verrucous neoplasia 2. Tracheostomy was offered in 1 case of obstructive verrucous neoplasia with subsequent decanulation after successful endoscopic management.

According to the data from the literature and our own observations, the following criteria seem to point to a HLL with high malignant potential: verrucous neoplasia, pachydermia, a lesion affecting more than a half of the vocal fold, mucosal hyperemia, high-grade dysplasia in biopsy samples.

The expected result (total eradication of the visible lesion) was obtained in all of our cases (mean follow-up period 76 months). Invasive carcinoma developed subsequently in 2 patients that continued to smoke after surgery. All the patients that could be followed-up stated an improvement of their voice after surgery.

Conclusion The following criteria can be used for preoperative detection of HLL with high malignant potential: verrucous neoplasia, pachydermia, a lesion affecting more than a half of the vocal fold, mucosal hyperemia, high-grade dysplasia in biopsy samples. Flexible endoscopic surgery, preceded by large flexible forceps biopsy, is a good alternative for HLL management. Diathermy snare is a useful tool for the diagnosis and first-line treatment in selected patients.

Keywords Hyperplastic laryngeal lesions, Endoscopy, Office-based laryngeal surgery

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Background

There is a lot of confusion in the identification and clinicopathological classification of hyperplastic laryngeal lesions (HLL) [1–4]. The variety of classifications of squamous intraepithelial lesions (SIL) reflects discrepancies among laryngologists and pathologists concerning classification, clinical and pathologic diagnosis, prognosis, and management of these lesions. An appropriate classification and unified terminology that would permit reproducible interpretation of HLL, would reflect biological behavior of SIL, and would divide lesions of high malignant potential from those of low malignant potential, seems to be desirable, because it would result in a rational management of the disease. It is important to identify some endoscopic criteria that would guide the clinician in preoperative detection of lesions of high malignant potential. This would contribute to the selection of a rational strategy of treatment and monitoring of the patients with HLL.

Materials and methods

A review of relevant English literature, based on the search in PubMed, Hinari, and Google Scholar databases, was made, using such search terms as hyperplastic laryngeal lesions, precancerous laryngeal lesions, premalignant laryngeal lesions, laryngeal leukoplakia, laryngeal dysplasia, verrucous lesions of the larynx, larynx endoscopy, office-based laryngeal surgery, endoscopic laser surgery of the larynx, and laser ablation of glottic neoplasms.

Additionally, our experience from performing more than 10 000 diagnostic flexible laryngoscopy procedures was used in this manuscript, and a retrospective review of medical records of the patients with HLL, treated by a single surgeon between 1993 and 2022, was performed.

Flexible endoscopic laryngeal surgery (FELS) was applied for 37 patients (ages, from 20 to 77 years, men 34, women 3) with HLL. Written informed consent was obtained from the patients. Thirty-three out of 37 patients (89.2%) underwent surgery under topical anesthesia and 4 patients—under general anesthesia with superimposed high frequency jet ventilation (SHFJV). Twenty-two patients (59.5%) were operated on in an outpatient setting. The desire to be operated on under topical anesthesia and ability to tolerate the procedure were the main criteria for patients selection for unsedated procedures. Tracheostomy was offered in 1 case of obstructive lesion with subsequent decanulation after successful endoscopic management. A flexible therapeutic bronchoscope with a large working channel (2.8 mm), inserted transnasally, was used to perform unsedated procedures. The necessary accessories (biopsy forceps, diathermy snare, flexible laser guide) were brought to the lesion, being introduced via the working channel of the endoscope. For interventions performed under general anesthesia, the flexible bronchoscope together with accessories was introduced through the rigid suspended jet laryngoscope. The following types of interventions were used: cold eradication by large/jumbo biopsy forceps (7.3 mm cup opening)—1 case, Nd:YAG laser (1064 nm) ablation—33, laser vaporization preceded by diathermy snare resection—3.

Diagnostic flexible laryngoscopy (FLS) is performed under topical anesthesia. Upright sitting position of the patient is preferred. After topical anesthesia of the nasal cavity and the pharynx with 10% Lidocaine spray, the flexible bronchoscope is introduced transnasally close to the larynx. After that, 2% Lidocaine solution (10–15 ml) is instilled onto the larynx during phonation, producing laryngeal gargle, by a catheter placed through the working channel of the bronchoscope. After thorough visual examination of the larynx, the biopsy of the visible lesion is taken using flexible biopsy forceps that is introduced through the working channel of the endoscope. Sometimes, in the presence of a prominent exophytic component, a diathermy snare resection in cutting mode is performed for obtaining of a large biopsy specimen.

FELS is always preceded by diagnostic FLS. Good cooperation with the patient is essential during awake FELS. The grade of patient compliance is estimated during diagnostic FLS procedure. The same technique of topical anesthesia as for diagnostic FLS is used. Small lesions (1–4 mm) can be eradicated by a cold manner using biopsy forceps. The Nd:YAG laser (1064 nm) is used as a main tool for flexible endoscopic surgery (FES) of HLL. Laser coagulation or/and vaporization of the visible lesion is performed in a targeted manner using continuous non-contact irradiation mode, the power being set from 20 W up to 40 W. When prominent exophytic component of a lesion is present, we prefer to resect it by diathermy snare in cutting mode and to use the laser as a second-line tool. This technique allows faster debulking, shortens the operation time and reduces collateral thermal damage to adjacent tissues. Immediately after snare resection of the lesion, the patient is called to cough it out for subsequent histologic examination. In case of accidental aspiration of resected specimen into the tracheobronchial tree it could be easily extracted using flexible bronchoscope, forceps and aspiration force. In cases of extensive and obstructing lesions we recommend general anesthesia, provided there are no contraindications for general anesthesia and transoral surgery.

Etiology of HLL

Smoking, especially, being associated with chronic alcohol abuse, is considered the most important factor in the

occurrence of epithelial abnormalities in premalignant and malignant laryngeal lesions. A direct correlation between cancer development risk and smoking duration was revealed: every 5 years of smoking increases the risk of cancer by 23%, and additional daily alcohol consumption increases the risk of cancer by 17% [5]. Gastroesophageal reflux disease (GERD) is also considered a risk factor in laryngeal carcinogenesis [5]. Some industrial harmful agents (wood and metal dust etc.), vocal abuse and nutrition deficiency of vitamins are mentioned as risk factors [6]. The role of human papillomavirus (HPV) in etiology of SIL is not proven [7].

Pathologic epithelial changes in HLL

Clinical and histopathological terminology in characterization of SIL will be discussed separately, because there is not a predictable correlation between them. Identification of some endoscopic criteria that would guide the clinician in preoperative detection of lesions of high malignant potential would be very useful.

Clinical/endoscopic features

There is a lot of ambiguity in the description, interpretation and classification of some laryngeal epithelial lesions with malignant potential. Uloza mentions chronic hyperplastic laryngitis with keratosis and papilloma of the adults as mandatory precancerous conditions [1]. Some authors use the term "pachydermia" to describe a pebbled keratosis of the posterior glottis [2]. Gallo et al. [3] suggest limitation of the clinical appearance of premalignant laryngeal lesions to three types: (1) leukoplakia (synonym of keratosis)—a white/whitish keratotic area; erythroplakia—red/reddish musosal area; (3) erythrokeratosis—a mixed lesion (alternating of leukoplakia and erythroplakia zones). The term of leukoplakia implies epithelium thickening and the term of erythroplakia implies thinning of the epithelium. Ferlito et al. mention the following terminology for characterizing proliferative epithelial lesions: leukoplakia (any white lesion on the mucosa that cannot be wiped off or ascribed to a specific condition (e.g., Candidal infection); erythroplakia (any reddish plaque on the mucosa, invasive carcinoma being present in a substantial number of biopsies); erythroleukoplakia (mixed lesions that combine zones of leukoplakia and erythroplakia); pachydermia (indicates extensive thickening of the mucosa) [4]. Chen et al. proposed the classification of leukoplakia, based on the macroscopic appearance, into three types: (1) flat and smooth, (2) elevated and smooth, and (3) rough type (elevated lesion with wrinkled surface). Analyzing the correlation of endoscopic appearance and histologic appearance in a group of 375 patients with leukoplakia who underwent CO2 laser excision of the lesion, the authors stated the absence of dysplasia in those 3 macroscopic types, respectively, in 68%, 13%, and 1%, and the presence of carcinoma—in 0%, 5.2% and 30.6% [8]. Li et al. proposed a similar classification of leukoplakia: (1) smooth flat, (2) smooth hypertrophic, and (3) rough lesions (irregular, grained or verrucous appearance). The authors specify that no patients (0%) with smooth flat lesions manifested high-grade dysplasia; in smooth hypertrophy group severe dysplasia and carcinoma were found in 28.1%; and 87.8% of rough lesions were represented morphologically as severe dysplasia or carcinoma [9]. Some authors state that the term "keratosis" is purely histological [10]. We agree with the experts who use this term in clinical interpretations. Based on personal experience, we can state that, if the clinician performs a biopsy from a white flat or elevated laryngeal lesion, it is very unlikely to not obtain keratosis in histological response.

Analyzing the macroscopic appearance of HLL, we use and propose the following endoscopic/clinical classification that we consider relevant:

1. Chronic hyperplastic laryngitis (CHL): vocal folds are thickened, the mucosa is hypertrophied, the surface is irregular or plicated, the exposure of laryngeal ventricles is reduced. Mucosal hypertrophy can involve also laryngeal ventricles (being manifested as focal prolapse of ventricular mucosa into the lumen), interarytenoid space and vestibular folds. In case of pronounced hypertrophy of vocal and vestibular folds, laryngeal lumen may become narrowed, leading to stridor. It is important to mention the diffuse and symmetric character of epithelial changes that uniformly affect both hemilarynxes;
2. Chronic hyperplastic laryngitis with keratosis (CHLK): flake-like whitish semitransparent focal deposits with indistinct contour that adhere to hypertrophied mucosa (Fig. 1);
3. Leukoplakia: a flat lesion with white membranous patch appearance, with smooth or irregular surface and well-defined or indistinct contour. The lesion can be solitary or multifocal (several separate or confluent foci) (Fig. 2);
4. Pachydermia: an elevated lesion with well-defined white plaque appearance, with smooth, irregular, granular, or rugous surface and hard consistence (Fig. 3);
5. Verrucous neoplasia: an exophytic tumor-like white lesion with a broad base, tuberous or papillary/warty surface with villiform projections and hard consistence. Endoscopic appearance frequently resembles sheep fur (Fig. 4).

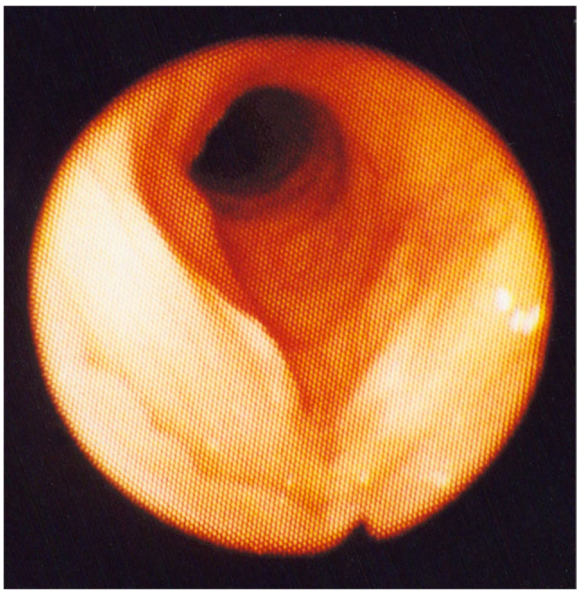

Fig. 1 CHLK: In the anterior third of both vocal folds there are flake-like whitish semitransparent focal deposits with indistinct contour that adhere to hypertrophied mucosa

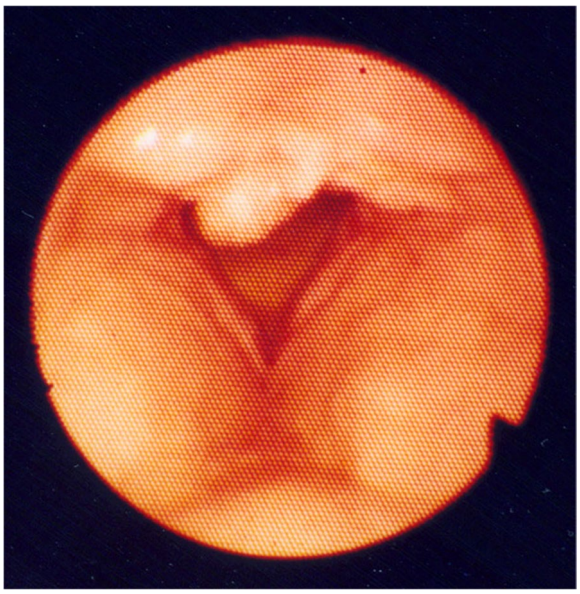

Fig. 3 Pachydermia of the interarytenoid space: an elevated lesion with well-defined white plaque appearance affects the interarytenoid area of the larynx

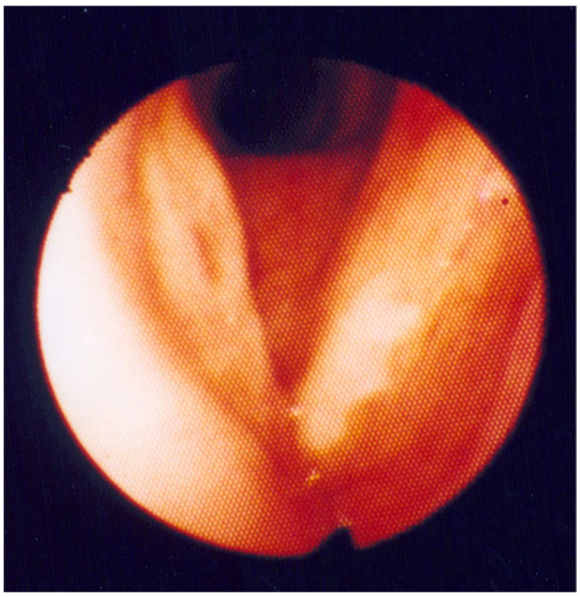

Fig. 2 Glottic leukoplakia: a flat lesion with white membranous patch appearance affects the anterior third of the left vocal fold

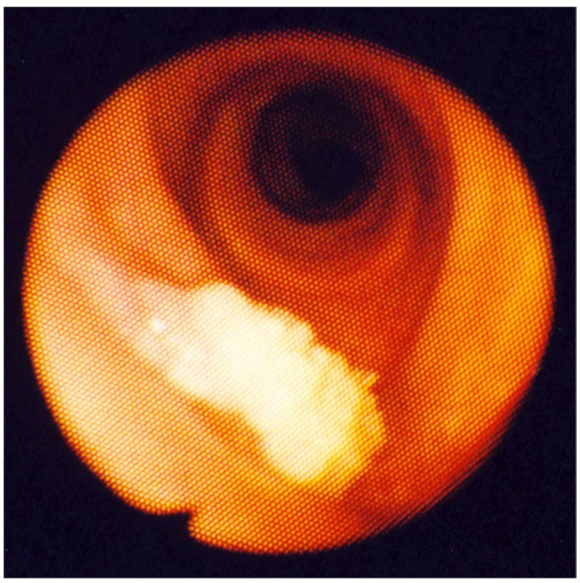

Fig. 4 Verrucous neoplasia: an exophytic tumor-like white lesion with a broad base, warty surface with villiform projections affects anterior two thirds of the right vocal fold

Summarizing shortly the above-mentioned classification of HLL, we would focus on the following main features: CHL-barely symmetric diffuse hypertrophy; CHLK—flake-like focal white deposits; leukoplakia—a flat well-defined white lesion; pachydermia—an elevated white lesion; verrucous neoplasia—a tumor-like warty white lesion.

The discrepancies that appear in clinical classifications can be explained by the fact that the same lesion may be perceived, interpreted and named differently by different specialists. Analyzing the data from literature, we conclude that "leukoplakia" in our interpretation, corresponds to "flat and smooth leukoplakia" described by Chen et al. [8], "pachydermia" in our interpretation, is similar to "elevated and smooth type of leukoplakia" and "rough type of leukoplakia" according to Chen et al. [8] and "verrucous neoplasia" in our interpretation, corresponds to "keratinizing/hyperkeratotic papilloma" described by Uloza [1] and partially to "rough leukoplakic lesion" described by Li et al. [9]. We believe that behind such terms as "hyperkeratosis", "rough type of leukoplakia", "hyperkeratotic papilloma", "white papilloma", in a substantial proportion of cases could be, actually, verrucous carcinoma that is difficult to diagnose due to a massive layer of keratin on the lesion surface and a high degree of tumor cells differentiation. As a result, a conventional biopsy by forceps, as a rule, is not informative, being followed by an inconclusive histologic response [11]. We promote the mentioned presumption based on the fact that papilloma of the adults is considered a mandatory precancerous condition by some authors with up to 25% malignization rate [1], whereas more recent data demonstrate that the rate of malignant transformation of laryngeal papilloma is up to 4% [12]. For this reason, in our opinion, the term "verrucous neoplasia" is more appropriate for this type of lesion. The benign or malignant nature of this type of lesion can be established only histologically after a thorough examination of the whole lesion or, at least, of a large enough fragment of it, so that the pathologist could examine not only the epithelium, but the stromal component of the lesion as well.

After performing more than 10 000 flexible laryngoscopy procedures, we have never considered acceptable to interpret a lesion as "erythroplakia" or "erythroleukoplakia". After analyzing the interpretation of these lesions in selective literature, we found a confusion: some authors interpret erythroplakia as a sign of epithelium thinning [3], whereas others present it as a hyperplastic lesion with reddish plaque appearance [4]. Taking into consideration mentioning the substantial proportion of invasive carcinoma presence in biopsy specimens, obtained from these lesions [4], most probably, we described these red mucosal areas as hyperemia and defined these lesions as carcinomas in our endoscopic reports.

Gale et al. state that precancerous lesions have no specific macroscopic appearance and none of laryngoscopic features can be considered as reliably diagnostic of precancerous lesions [13]. However, according to the data presented by Chen et al. [8] and Li et al.[9], the presence of dysplasia and carcinoma in a white lesion increases in proportion as the lesion becomes more elevated and its surface becomes more irregular. Li et al. state a high correlation between the macroscopic appearance of the lesion and its degree of dysplasia [9]. A close correlation between the presence of vocal fold hyperemia and high-risk leukoplakia was stated by Fang et al. [14] and Li et al. [15]. The authors consider that mucosal hyperemia/redness predicts malignant potential of vocal fold leukoplakia. Taking into account the mentioned data, we consider that biopsy, performed during flexible laryngoscopy by large/jumbo biopsy forceps, is an adequate approach when dealing with leukoplakia (flat lesion), but in case of pachydermia (elevated lesion) or verrucous neoplasia (exophytic tumor-like lesion), a biopsy by total or subtotal excision of the lesion, that would result in a conclusive histologic response, is preferable. We performed endoscopic ablation in 26 cases of verrucous neoplasia, from which in 24 cases (92%) verrucous carcinoma was established (these cases are not discussed in detail within present publication), and in 2 cases the malignant nature of the lesion was not confirmed histologically. In 22 of 24 cases (92%) of verrucous carcinoma histologic confirmation of the diagnosis was possible only after partial diathermy snare excision of the lesion. We admit the possibility of verrucous carcinoma presence also in the cases when malignancy was not confirmed, because lesion ablation in those cases was performed after biopsy of the lesion by forceps. Presently, we perform the eradication of the verrucous neoplasia only after receiving a conclusive histologic response as a result of obtaining large enough tissue fragments by diathermy snare in order to not omit carcinoma. Hence, based on our experience, the endoscopic appearance of verrucous neoplasia raises a high suspicion for malignancy.

Histopathologic features

After biopsy or resection of a laryngeal lesion, one can come across several phenomena in histological reports: hyperplasia, akanthosis, keratosis, parakeratosis, dyskeratosis, atypia, dysplasia, carcinoma in situ, invasive carcinoma, etc. There are more than 20 classifications of SIL of the larynx [4]. In 1923, Jackson introduced the concept of premalignant laryngeal lesion and presented a case series of larynx carcinoma in association with keratosis [16]. In 1963, Kleinsasser proposed the first classification for premalignant laryngeal lesions: (1) simple squamous cell hyperplasia, (2) hyperplasia with atypia, and (3) carcinoma in situ (CIS) [17]. Friedman introduced the term "laryngeal intraepithelial neoplasia" (LIN), considering different stages of dysplastic progression within the epithelium [18]. Gallo et al. classify keratosis into four groups: (1) keratosis without dysplasia, (2) keratosis with mild dysplasia

(LIN1), (3) keratosis with moderate dysplasia (LIN2), and (4) keratosis with severe dysplasia or CIS (LIN3) [3]. Ferlito et al. (2012) mention three grades of dysplasia: (1) mild dysplasia (LIN1), (2) moderate dysplasia (LIN2), (3) severe dysplasia and CIS LIN3) [4]. The Ljubljana classification of hyperplastic laryngeal lesions accepts four categories of lesions: (1) simple hyperplasia; (2) abnormal hyperplasia; (3) atypical hyperplasia; (4) carcinoma in situ. First two categories are considered benign, third category—potentially malignant and fourth category—actually malignant [13]. The World Health Organization (WHO) 2005 classification includes three grading systems: (1) the dysplasia system, (2) the squamous intraepithelial neoplasia (SIN) system, and (3) the Ljubljana classification [19]. The experts recognized the presence of a subjectivism element in grading of laryngeal dysplasia by pathologists that generates discrepancies in diagnosis of laryngeal dysplasia, even using the same classification system. Different grades of dysplasia can be attributed by different pathologists in the evaluation of the same case. Also, there is a possibility to evaluate differently the same intricate case by the same pathologist after a period of time [20]. Discouraging results of appreciating the variability of histological interpretations according to the WHO 2005 classification, that were declared by many groups of experts, led to development of unified morphological criteria of SIL, that are reflected in the new WHO 2017 classification of SIL [21], that divides SIL into two or three categories: (1) low-grade dysplasia/SIL (includes, according to previous classification, squamous hyperplasia and mild dysplasia), has low malignant potential, the spectrum of morphological changes ranging from squamous hyperplasia to an augmentation of basal/parabasal cells, occupying up to the middle of the epithelial thickness, upper part being unchanged; (2) high-grade dysplasia/SIL (includes, according to previous classification, moderate and severe dysplasia, and carcinoma in situ), has high malignant potential, the spectrum of atypical epithelial cells, occupying at least lower epithelial half up to the whole epithelial thickness; (3) carcinoma in situ, distinguished from high-grade dysplasia if three-tier system is used—showing features of conventional carcinoma, e.g., structural and cellular abnormalities but without invasion. The last WHO 2017 classification of SIL, that defines lesions with low malignant potential and lesions with high malignant potential, seems to be more practical and relevant than previous ones, with better inter-observer agreement, this being confirmed by Gale et al. [7], offering laryngologists a more clear guidance for the choice of rational management strategy.

Evolution of HLL

Gallo et al. [3] suppose that transformation of laryngeal keratosis to carcinoma happens through a chain of consecutive progressive changes of the normal epithelium, initially into keratosis without dysplasia, then into increasing grades of dysplasia, then into carcinoma in situ and, finally, into invasive carcinoma. Isenberg et al. in a review article state that about half of the patients (53.6%) with laryngeal leukoplakia do not have dysplasia at the time of diagnosis, mention malignant transformation rate of leukoplakia of 8.2%, underlining that even in the absence of dysplasia in initial biopsy specimen, the chance of transformation of leukoplakia into invasive carcinoma in the future is about 3.8% [22]. Weller et al. mention that the average period of malignant transformation for a dysplastic laryngeal lesion is about 5.8 years with an overall malignant transformation rate of 14%. Malignant transformation rate was bigger for severe dysplasia (30.4%), than for low/moderate grade dysplasia (10.6%) [23]. Lee et al., indicating a statistically significant correlation, suggest that the extent of the lesion (more than half of the vocal fold) and the degree of dysplasia are predictive factors for the malignant transformation of leukoplakia [24].

Diagnosis of HLL

The most frequent symptom of HLL is dysphonia that imposes the need for a focused examination. Usually the diagnostic process begins with indirect mirror laryngoscopy, then it is followed by 70° rigid laryngoscopy or flexible laryngoscopy and, finally, by direct transoral microlaryngoscopy. Stroboscopic findings cannot reliably predict the presence of malignancy [25]. New imaging techniques, such as narrow band imaging (NBI), contact endoscopy, seem to have a potential in targeting areas of biopsy [25], but cannot replace a biopsy for the diagnosis. Direct transoral microlaryngoscopy, performed under general anesthesia, is considered too invasive to be used just for laryngeal biopsy [26]. Some authors state that office biopsy often understages the severity of lesions, demonstrating a false-negative rate of 33% and mentioning as reasons poor depth of biopsy and small tissue specimens [25]. Other authors demonstrated that awake laryngeal biopsy and tumour staging is as effective as staging in the operating room [27]. We consider flexible laryngoscopy with biopsy, performed under topical anesthesia, as the method of choice for the diagnosis of SIL that can be successfully practiced in an outpatient basis. For the biopsy of flat lesions (leukoplakia) and some elevated lesions (pachydermia) we use large/jumbo biopsy forceps and often perform staged in depth biopsies, the forceps being withdrawn together with the endoscope so

that not to lose tissue fragments in the working channel. For some elevated lesions and, especially, for verrucous lesions we perform the biopsy by diathermy snare excision that allows obtaining large enough tissue samples for a conclusive histologic response. Direct rigid laryngoscopy under general anesthesia is reserved for rare cases when the patient cannot tolerate unsedated flexible laryngoscopy and in a compromised airway.

Management

There is no consensus among specialists related to the management of SIL. There is a variety of proposed treatment approaches: only observation and conservative therapy, radiotherapy, vocal fold stripping, phonomicrosurgical cold excision, laser excision, laser ablation. The choice of treatment modality for HLL is highly dependent on physician preference, experience and available equipment. Some specialists consider that, due to scarring effect, vocal fold stripping has no role in modern laryngology [28, 29]. Gale et al. report that radiotherapy is never used in Slovenia as the treatment for high-grade SIL and is reserved only for carcinoma management [30]. Taking into account potential complications and side effects, and the fact that typically only a single course of radiotherapy can be applied to a patient, it makes little sense to exhaust its potential for treating a premalignant lesion instead of reserving it for a carcinoma [25]. On the one hand, laryngologists are concerned that insufficient measures could result in progression towards invasive carcinoma, on the other hand, a too aggressive approach to SIL that will not progress could lead to vocal fold scarring and voice impairment. However, the oncological approach, considering the malignant potential of SIL to matter more than voice quality, seems to be more reasonable [30]. The following recommendations were included in a consensus statement by otorhinolaryngologists and pathologists at a meeting on the diagnosis and treatment of laryngeal dysplasia in 2010: in most cases resection of the lesion provides both histological diagnosis and initial management of the disease; the overall appearance of the lesion is considered to be the most important factor in determining management; single and multiple foci should be completely excised; in the presence of widespread, confluent leukoplakia, multiple biopsies should be initially performed, followed by staged resection; transoral microsurgery with cold steel or CO2 laser resection is recommended [31]. Li et al. select a therapeutic modality for leukoplakia based on the endoscopic appearance of the lesion. "Smooth flat" and "smooth hypertrophy" lesions are initially treated conservatively. Cure rates of, respectively, 77.8% and 67.7%, are reported. Surgical treatment is applied in cases of unsuccessful conservative therapy and as initial treatment for "rough" lesions [9].

Traditional transoral microsurgery is not always possible due to contraindications for general anesthesia or anatomic difficulties (inadequate glottis exposure, temporomandibular joint ankylosis, etc.). Office-based unsedated laryngeal surgery (OBULS) has become one of the emerging trends in modern laryngology, mainly, due to the development of flexible endoscopy and flexible fiber-based laser technology. This approach is successfully used nowadays for the treatment of premalignant laryngeal diseases, because of its indubitable advantages: avoiding of general anesthesia risks, economic efficiency, and time economy [32, 33]. Surgery in an office-based setting seems to be preferred also by patients. Rees et al. mention that 87% of patients that underwent both, traditional operating room surgery and OBULS, gave preference to the last one [34]. Sung, using angiolytic lasers (PDL and KTP laser) in office-based setting, underlines that patients with suspicion for dysplasia are primarily treated in the operating room by traditional surgery to exclude carcinoma [33]. Transitioning patients with recurrent disease to the office for photoangiolytic treatment after initial operating room surgery is mentioned as a trend by Karatayli-Ozgursoy et al. [28]. Zeitels et al., analyzing treatment results with KTP laser through flexible endoscope for 29 patients with glottic dysplasia, report 75–100% lesion regression rate in 62% of cases [35]. Koufman et al. report that 20 of 25 patients (80%) with laryngeal leukoplakia who underwent office-based laser surgery with PDL did not require further treatment [36]. Hu et al. report that 9 of 11 patients (82%) with leukoplakia who received their entire treatment in the office with fiber delivery CO2 laser showed complete resolution [37]. Wellenstein et al. report the results of SIL treatment with flexible guide-based CO2 laser in office-based setting, mentioning that in 10 from 16 patients (63%) with leukoplakia and hyperkeratosis there was no residual or recurrent lesion after the treatment [38].

We applied flexible endoscopic laryngeal surgery (FELS) for 37 patients with the following types of HLL: CHLK 5, leukoplakia 18, pachydermia 12, verrucous neoplasia 2. In the majority of cases (35/37), the glottic portion of the larynx was affected, in 2 cases the pachydermia of the interarytenoid space was detected. Histologically, according to WHO Classification (2017), high-grade dysplasia was detected in 1 case and low-grade dysplasia was revealed in the rest of the cases. Actually, altogether we performed FELS in 26 patients with verrucous neoplasia, from which in 24 cases (92%) verrucous carcinoma was revealed. These carcinoma cases are not included in the group of HLL and are not discussed within this publication, dedicated to premalignant lesions, but are discussed in another article. The expected result (total eradication of the visible lesion) was obtained in all the

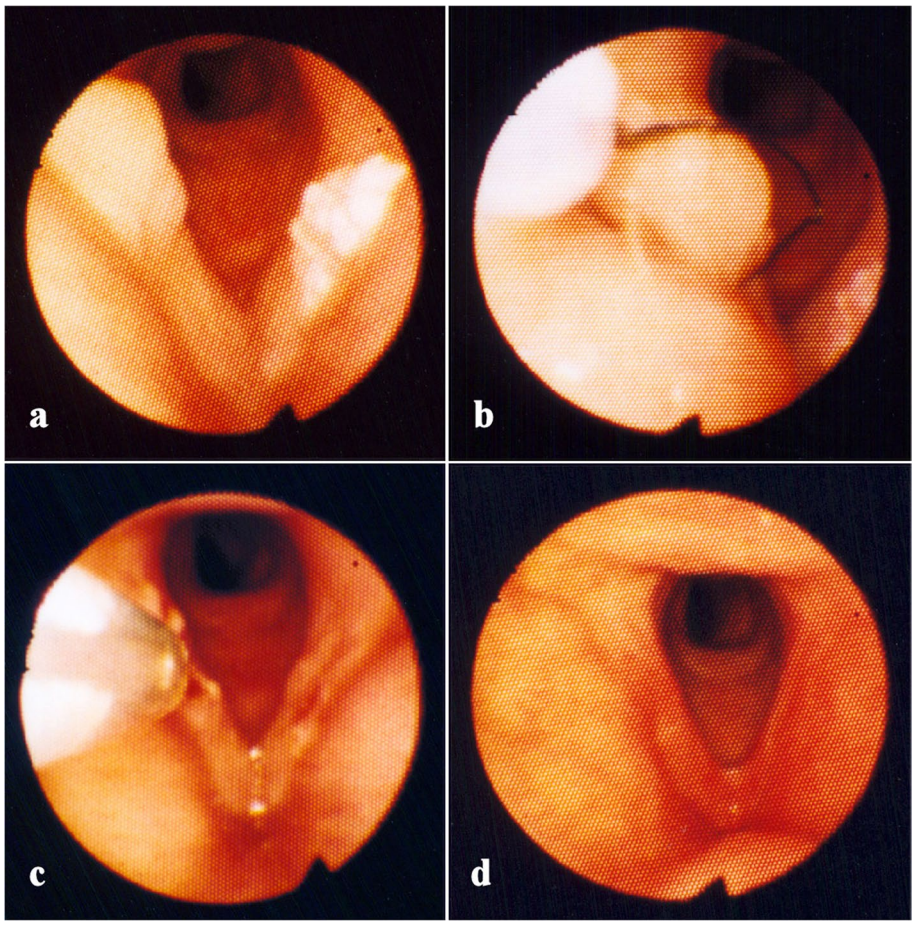

Fig. 5 **a** Pachydermia of vocal folds: elevated lesions with well-defined white plaque appearance affect the posterior third of the right vocal fold and the middle third of the left vocal fold. **b** The moment of diathermy snare excision of the lesion of the right vocal fold. **c** The moment of Nd:YAG laser ablation of the residual lesion of the right vocal fold. **d** Twelve months after laser ablation of glottic pachydermia: no visible lesions

cases (Fig. 5). In one case of leukoplakia, a recurrent lesion was detected in 93 months after surgery that was repeatedly ablated by laser. Invasive carcinoma developed in 2 patients that continued to smoke after surgery (one patient with CHLK—in 22 months and one patient with pachydermia—in 103 months after endoscopic surgery). The follow-up period after surgery varied from 1 to 206 months (average 76 months). Three patients could not be monitored over time. All the patients that could be followed-up stated an improvement of their voice after surgery (21 patients assessed their voice as satisfactory, 9 patients had mild dysphonia and 2 patients had severe dysphonia). The voice quality largely depended on lesion size and location. Anterior commissure involvement and diffuse bilateral process worsen voice quality prognosis.

In selection of treatment methods for HLL both oncological efficacy and preserving of voice function are important. It is always a trade-off, and priorities should be set after determining the malignant potential of the lesion. In low-risk lesions it seems reasonable to focus on preserving the voice function, and in high-risk lesions the oncological approach seems to be a priority. Authors of some publications, dedicated to comparison of CO2 laser resection and laser ablation by angiolytic lasers (mainly, KTP laser) for glottic neoplasms, mention superior voice outcome after laser ablation [39, 40], but it is still unclear, which factor is responsible for better voice quality, laser type, or surgical technique [39]. There is no consensus regarding types of lasers that should be used for HLL management and the advantage of one type of laser over another. Rosen et al., in a review article, comparing different types of lasers in office-based treatment (PDL, KTP laser, CO2 laser, thulium laser, Nd:YAG laser), state that the choice of laser is largely theoretical. Claims of superiority of one type of laser over others are not supported by thorough comparative studies on laryngeal tissues due to, partricularly, a big number of variables, beside the wavelength, involved in laser-tissue interactions [27]. Wellenstein et al., in another review on office-based

laryngoscopic procedures, state a lack of comparative studies concerning effectiveness of different laser types for specific lesions [41]. Parker, also in a review publication on vocal fold leukoplakia, concludes that different lasers are simply different tools for achieving the same goal of disease eradication [29]. Yan et al. state that treatment efficacy with all lasers is highly dependent on surgical technique and surgeon's skills [42].

Taking into account that even leukoplakia without dysplasia can progress to malignancy, a close follow-up on patients with HLL is recommended, regardless of the initial histologic response [10, 25]. We recommend follow-up visits after surgery at least once every 3 months over a period of 2 years and, at least, once a year later on.

Conclusion

According to the data from the literature and our own observations, using the proposed classification of HLL (chronic hyperplastic laryngitis, chronic hyperplastic laryngitis with keratosis, leukoplakia, pachydermia, and verrucous neoplasia), the following criteria are suggested for preoperative detection of HLL with high malignant potential: verrucous neoplasia, pachydermia, a lesion affecting more than a half of the vocal fold, mucosal hyperemia, high-grade dysplasia in biopsy samples.

Flexible endoscopic surgery, preceded by large flexible forceps biopsy, is a good alternative for HLL management, taking into account: possibility to avoid general anesthesia related risks, applicability to patients with risks or contraindications to general anesthesia and transoral microsurgery, beneficial cost-efficiency ratio and time economy. This approach is attractive for recurrent lesions management, allowing to avoid repeated general anesthesia. Diathermy snare is a useful tool for diagnosis and first-line treatment in selected patients.

Abbreviations

CHL	Chronic hyperplastic laryngitis
CHLK	Chronic hyperplastic laryngitis with keratosis
CIS	Carcinoma in situ
FELS	Flexible endoscopic laryngeal surgery
FES	Flexible endoscopic surgery
FLS	Flexible laryngoscopy
GERD	Gastroesophageal reflux disease
HLL	Hyperplastic laryngeal lesions
HPV	Human papillomavirus
LIN	Laryngeal intraepithelial neoplasia
NBI	Narrow band imaging
OBULS	Office-based unsedated laryngeal surgery
SHFJV	Superimposed high frequency jet ventilation
SIL	Squamous intraepithelial lesions
SIN	Squamous intraepithelial neoplasia
WHO	World Health Organization

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Author's contributions
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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study has been granted an exemption from requiring ethics approval by Institutional Ethics Committee of „Timofei Moșneaga" Republican Clinical Hospital in view of the retrospective nature of the study and all the procedures being performed were part of routine care. The research was conducted ethically, with all study procedures performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki. This study has been granted an exemption from requiring written informed consent from participants in the study by Institutional Ethics Committee of "Timofei Moșneaga" Republican Clinical Hospital.

Consent for publication
Written informed consent for publication was obtained from the paticipants whose images are included in the manuscript.

Competing interests
The author declares no competing interests.

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