Letter to the Editor

Laryngopharyngeal reflux and idiopathic vocal fold scars

Reflusso laringofaringeo e cicatrici idiopatiche delle corde vocali

Giovanna Cantarella[1,2], Jerome F. Lechien[3-5], Lorenzo Pignataro[1,2], Mirko Aldè[1,6], Ludovica Battilocchi[1], Maria Rosaria Barillari[7]

[1] University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [2] Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Department of Specialist Surgical Sciences, Otolaryngology Unit, Milan, Italy; [3] Polyclinic of Poitiers, Elsan Hospital, Poitiers, France; [4] Department of Anatomy and Experimental Oncology, Mons School of Medicine, UMONS Research Institute for Health Sciences and Technology, University of Mons (UMons), Mons, Belgium; [5] Department of Otolaryngology-Head and Neck Surgery, EpiCURA Hospital, Baudour, Belgium; [6] Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Department of Specialist Surgical Sciences, Audiology Unit, Milan, Italy; [7] Department of Mental and Physical Health and Preventive Medicine, "L. Vanvitelli" University, Naples, Italy

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Dear Editor,

Scarring of the vocal folds (SVF) is a relevant issue that is associated with definitive impairment of the viscoelastic properties of the lamina propria of the vocal folds and related long-term deterioration of the vibratory function. The voice quality of patients with SVF may be severely impaired with negative social and professional consequences in daily life. In spite of advancement in comprehension of the vocal fold microarchitecture and of the physiology of glottic sound production, the currently available micro-phonosurgical and rehabilitative procedures are still not able to guarantee successful restoration of voice quality in all SVF cases [1]. Regenerative and tissue engineering procedures are currently being proposed for the treatment of severe fibrosis of the lamina propria, and represent a relevant therapeutic advancement [2]. Nevertheless, better understanding of the causes of extensive fibrosis of the lamina propria is needed to improve the prevention and treatment of SVF.

For some patients, the clinical history of previous laryngeal surgery or trauma clarifies the pathogenesis of SVF, but the development of SVF appears unpredictable. In other words, some patients do not develop SVF while others do. Moreover, some patients may develop SVF without history of phonosurgery or trauma. In these cases, the pathogenesis of scars remains a diagnostic dilemma, especially if there is no clear clinical evidence of professional or social vocal abuse [3].

In the present commentary, the case of a young female patient with idiopathic SVF is discussed. Figure 1 shows an example of idiopathic diffuse bilateral scars in a 36-year-old woman with chronic dysphonia and voice fatigue lasting two years in the absence of any previous intubations or vocal fold surgery. Our patient reported previous episodes of typical gastro-oesophageal reflux disease (GERD) that was treated with proton pump inhibitors, alginates and anti-reflux diet with complete resolution of the clinical picture. At the time of laryngological evaluation, she did not have any typical symptoms of GERD (regurgitation

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Correspondence
Mirko Aldè
Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Department of Specialist Surgical Sciences, Audiology Unit, via Pace 9, 20122 Milan, Italy
Tel. +39 02 55033936. Fax +39 02 50320754
E-mail: mirko.alde@unimi.it

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and heartburn), but general ear-nose-throat assessment, completed by videolaryngoscopy and by administration of the Reflux Symptom Index (RSI) and the Reflux Finding Score (RFS), showed significance for laryngopharyngeal reflux (LPR) with RSI > 13 and RFS > 7, in the absence of other medical conditions that could mimic (clinically and objectively) LPR, such as active seasonal allergies or asthma, alcohol abuse, current smoking and/or history of upper respiratory tract infection within the previous month [4,5].

Due to the hypothesis of LPR-related dysphonia she was prescribed proton pump inhibitors (PPI), magnesium alginate, and dietary and lifestyle changes for the two months prior to surgery without significant improvement. She underwent microlaryngoscopy and extensive bilateral fibrosis of the lamina propria was observed during the procedure, which was more pronounced on the left side. The operation included bilateral cordotomy, freeing of the adherences and ablation of part of the scar tissue from both vocal folds, mainly from the left side (Fig. 2). PPI and alginate treatment was also prescribed after surgery. The patient experienced voice quality improvement and normalisation of vocal fold mucosal wave, with total glottal closure during vocalisation seen at videostroboscopy (Fig. 3): results were stable at 12 months follow-up after surgery.

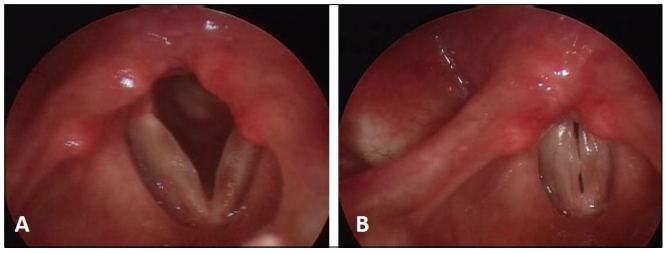

Figure 1. (**A, B**) Pre-operative video-stroboscopy demonstrates reduction of mucosal wave amplitude in both vocal folds and hourglass defective glottic closure.

The case described is just a single example of "idiopathic" impairment of the viscoelastic properties of the lamina propria resulting in reduced or absent mucosal wave. The patient's clinical history and videolaryngoscopic findings suggest a role of LPR in this clinical condition; for other patients without typical symptoms and suggestive scores, a more specific instrumental assessment such pH-impedance study should be mandatory [6]. For several reasons, not all patients with suspicion of VFS will undergo phonosurgery, mainly because improvement in voice quality may not be guaranteed; therefore, a diagnosis of fibrosis in the lamina propria layer may not be definitely demonstrated in these cases.

We hypothesise that LPR could be a causative factor for VFS, especially if no other causes are found. It has been shown that LPR can delay healing after phonosurgery and influence the re-epithelisation process [7]. The role of LPR has been demonstrated for multiple vocal pathologies for several decades and pepsin has been isolated in benign vocal fold lesions and in dysplasia [8,9]. For the present case, the search for pepsin in the removed tissue was not feasible in our institution; in addition, the tissue sample for histology was very limited and fibrous tissue removed from the Reinke's space appeared as a stabilised consequence of previous reiterated chemical and physical insult to the vocal fold microstructure. The clinical history of the patient was the main reason for hypothesising that her idiopathic scarring might be related to LPR.

We hypothesise that the chronic inflammatory stimulus caused by reiterated episodes of LPR might be a contributing or major factor in the pathogenesis of fibrosis in the lamina propria, and in particular in Reinke's space whose integrity is crucial for the traveling mucosal wave. Refluxed pepsin into the larynx might impair healing of phonatory micro-traumas on the free edge of the vocal folds, thus favouring the process of fibrosis. Adhesion of the epithelium

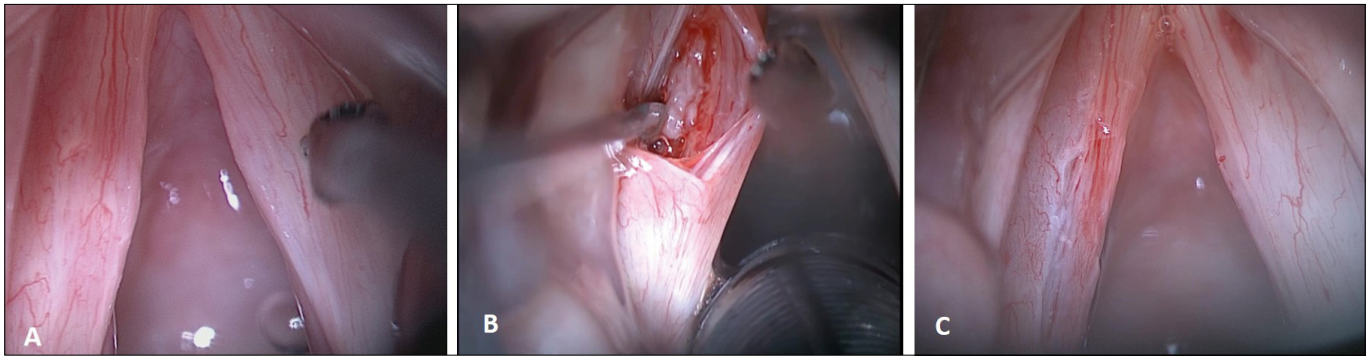

Figure 2. (**A**) Aspect of the vocal folds at microlaryngoscopy; (**B**) After left cordotomy, extensive scarring in the lamina propria layer was found, and the scar tissue was dissected and removed; (**C**) End of the procedure; cordotomy and release of adherences in Reinke's space were also performed on the right vocal fold.

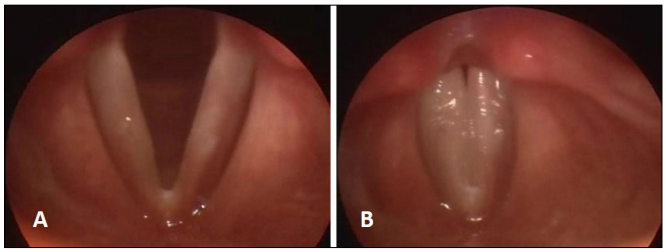

Figure 3. (**A, B**) Videostroboscopy performed 12 months after surgery demonstrated long term improvement in mucosal wave amplitude and achievement of total glottic closure during vocalisation.

to the fibrotic superficial lamina propria would hinder the mucosal wave, altering the superficial gliding tissue of the vocal fold.

The role of LPR has not been investigated to date in the pathogenesis of vocal fold scars, whose treatment is a well-recognised challenge for the phonosurgeon. Demonstrating a role of LPR might shed light on the pathogenetic process leading to Reinke's space fibrosis and might also confirm a preventive role of post-operative anti-reflux treatment in reducing the risk of recurrence. Prospective studies on a large number of patients are needed to demonstrate our hypothesis.

Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

GC: substantial contributions to the conception, design, acquisition, interpretation of data for the work; drafting the work; final approval of the version to be published; agreement to be accountable for all aspects of the work. JL: revising the work critically for important intellectual content; giving final approval of the version to be published; agreement to be accountable for all aspects of the work. LP: revising the work critically for important intellectual content; giving final approval of the version to be published; agreement to be accountable for all aspects of the work. MA: revising the work critically for important intellectual content; giving final approval of the version to be published; agreement to be accountable for all aspects of the work. LB: revising the work critically for important intellectual content; giving final approval of the version to be published; agreement to be accountable for all aspects of the work. MRB: revising the work critically for important intellectual content; giving final approval of the version to be published; agreement to be accountable for all aspects of the work.

Ethical consideration

The present study was conducted according to the World Medical Association's Declaration of Helsinki and was approved by the local Ethics Committee. Written informed consent was obtained from each participant for study participation and data publication.

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