



Vocal cord paralysis: What matters between idiopathic and non-idiopathic cases?

Ses teli felci: İdiyopatik ve idiyopatik olmayan olgular arasında önemli olan nedir?

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ABSTRACT

Objectives: This study aims to evaluate the demographic and clinical characteristics of patients with idiopathic and non-idiopathic vocal cord paralysis (VCP).

Patients and Methods: This retrospective cohort was performed on data extracted from medical files of 92 consecutive patients (43 males, 49 females; median age 52.1±23.1 years; min. 1 - max. 87) with VCP diagnosed in the otorhinolaryngology department between April 2012 and December 2015. Diagnoses associated with VCP, side of involvement (right, left or bilateral) and previous medical histories were noted and compared between patients with idiopathic and non-idiopathic VCP.

Results: Vocal cord paralysis occurred on the left side (n=56, 60.9%), right side (n=28, 30.4%) or bilaterally (n=8, 8.7%). A clinical entity related with VCP was identified in 63 patients (68.5%), while 29 (31.5%) patients had idiopathic VCP. Most common etiologies for VCP were thyroid surgery (n=32, 34.8%), cardiovascular surgery (n=9, 9.8%), lung cancer (n=6, 6.5%) and cardiac anomalies (n=4, 4.3%), respectively. Patients with idiopathic VCP were significantly older (p<0.001), while gender distribution (p=0.121) and side of involvement (p=0.340) did not differ between two groups.

Conclusion: Vocal cord paralysis is a relatively common clinical entity with substantial rate of morbidity. Identification of the underlying etiology and awareness on the clinical characteristics are keystones for foreseeing complications and determining the appropriate therapeutic modality.

Keywords: Etiology; idiopathic; paralysis; vocal cord.

ÖZ

Amaç: Bu çalışmada idiyopatik ve idiyopatik olmayan ses teli felci (STF) olan hastaların demografik ve klinik özellikleri değerlendirildi.

Hastalar ve Yöntemler: Bu geriye dönük kohort çalışması, Nisan 2012 - Aralık 2015 tarihleri arasında kulak burun boğaz kliniğinde STF tanısı konmuş 92 ardışık hastanın (43 erkek, 49 kadın; medyan yaş 52.1±23.1 yıl; dağılım 1-87 yıl) tıbbi dosyalarından alınan verilere göre yapıldı. İdiyopatik ve idiyopatik olmayan STF hastalarının STF ile ilgili tanıları, tutulum tarafı (sağ, sol veya iki tarafı) ve önceki tıbbi geçmişleri kaydedildi ve karşılaştırıldı.

Bulgular: Ses teli felci sol tarafta (n=56, %60.9), sağ tarafta (n=28, %30.4) ya da iki taraflı (n=8, %8.7) meydana geldi. Altmış üç hastada (%68.5) STF ile ilgili klinik birer tablo tanımlanırken, 29 (%31.5) hastada idiyopatik STF vardı. Ses teli felci için en yaygın etyolojiler sırasıyla tiroid ameliyatı (n=32, %34.8), kalp ve damar cerrahisi (n=9, %9.8), akciğer kanseri (n=6, %6.5) ve kardiyak anomalileri (n=4, %4.3) idi. İdiyopatik STF hastaları önemli ölçüde daha yaşlıyken (p<0.001), cinsiyet dağılımı (p=0.121) ve tutulum tarafı (p=0.340) iki grup arasında farklılık göstermedi.

Sonuç: Ses teli felci azımsanmayacak morbidite oranı ile oldukça yaygın bir klinik tablodur. Altta yatan nedenlerin tanımlanması ve klinik özellikler hakkında farkındalık, komplikasyonları öngörmek ve uygun tedavi yaklaşımı belirlemek için temel yapı taşı niteliğindedir.

Anahtar Sözcükler: Etiyoloji; idiyopatik; felç; ses teli.



Vocal cord paralysis (VCP) can occur as a consequence of processes that interfere with the normal function of the vagal nerves or recurrent laryngeal nerves. Vocal cord paralysis can be the first sign of extensive and severe pathology. Clinicians and radiologists should know the tracts of the vagal and recurrent laryngeal nerves and be able to recognize clinical characteristics and radiological findings (anteromedial displacement of the ipsilateral arytenoid cartilage with medial displacement of the posterior vocal cord margin, dilatation of the ipsilateral piriform sinus and laryngeal ventricle) consistent with VCP.^[1,2]

Vocal cord paralysis can be attributed to any lesion along the course of the vagal nerves above the branching of the recurrent laryngeal nerves, or of the recurrent laryngeal nerves themselves. A lesion in the brainstem or skull base often leads to multiple cranial nerve deficits since the vagal nerve is closely related with other cranial nerves at this level. Pathologies that involve the recurrent laryngeal nerves and/or the extracranial vagal nerves may give rise to isolated laryngeal symptoms. Vocal cord paralysis usually affects one side and many pathologic processes such as malignancy, trauma, infection and inflammation can present as VCP owing to the long anatomical course of the vagal and recurrent laryngeal nerves.^[1,3] Almost 75% of the cases are unilateral with just 10% of the pathologies in the central nervous system.

Iatrogenic injury linked with mediastinal and neck surgery has been reported as the most important cause of VCP.^[3] Surgical injury is responsible for approximately 40% of unilateral VCP and 50% of bilateral VCP. Bilateral VCP is more often caused by thyroid surgery, while unilateral VCP occurs frequently due to other surgical interventions such as carotid endarterectomy, anterior approaches to the cervical spine and cardiovascular surgery.^[3] Bilateral VCP is indicative of a central cause in the medulla oblongata. Acute onset of symptoms also points toward a central cause. Unilateral VCP is idiopathic in 20% of cases (second most common) and extralaryngeal malignancy is the third most common cause of unilateral VCP. Traumatic injury associated with intubation is another important cause of unilateral VCPs.^[3] Central nervous system

disease, infection, inflammation, radiation therapy, and aortic aneurysm are less common causes of VCP.^[4]

A detailed history, clinical examination and laboratory evaluation must be made carefully for diagnosis. Chief complaints are dyspnea, dysphonia, shortness of breath, hoarseness and vocal fatigue. Moreover, aspiration during swallowing may lead to compromise of the normal protective function on the vocal cords. If reflexive coughing mechanism is weak, life-threatening pneumonia may develop.^[5]

If any cause could not be identified as an etiology of VCP, the condition is considered as idiopathic. However, the term "idiopathic" indicates that VCP is of unknown origin, rather than signifying that there is no cause. In other words, idiopathic VCP means that no causes could have been identified to elucidate the clinical picture. The rate of idiopathic cases in unilateral VCP ranges between 2% to 41%.^[6] In idiopathic VCP, further examinations, such as MRI could show a cancer, so it must be kept in mind that cancer rates are higher in idiopathic cases.^[7,8] On the contrary, bilateral idiopathic VCP is a relatively rare entity with a prevalence ranging from 3 to 13%.^[6] In the majority of patients with idiopathic VCP, the disease has been associated with viral infections including herpes simplex, influenza and pathogens affecting the upper respiratory tract.^[6]

This wide spectrum of etiologic factors call for a meticulous and detailed diagnostic study in the evaluation of patients with idiopathic VCP. Since the natural course of disease is vague, the actual rate of recovery remains unclear in many cases with VCP. If spontaneous resolution is to be expected, it is more likely to occur within 12 months after the onset.^[4,9] If no etiologic factor can be determined, implementation of subsequent therapeutic approach can be a challenge. Moreover, prognostic outcomes can be favorable without any intervention. Hence, clinicians must be aware of the differences in characteristics of patients with idiopathic and non-idiopathic VCP. Accordingly, knowledge on the medical backgrounds and clinical features of the patients is critical for tailoring the convenient policy for every VCP case.

The aim of this report is to retrospectively assess and compare the demographic and clinical

features of patients with idiopathic and non-idiopathic VCP.

PATIENTS AND METHODS

This retrospective study was carried out in the Baskent University Otorhinolaryngology Department between April 2012 and December 2015. Medical files of 92 consecutive patients (43 males, 49 females; median age 52.1±23.1 years; min. 1 - max. 87) diagnosed with VCP were investigated for descriptive and clinical features. Patients with idiopathic and non-idiopathic VCP were both included.

The study protocol was approved by the Başkent University Ethics Committee. A written informed consent was obtained from each patient or from patient parents. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Data points under investigation were age, gender, side of involvement (right, left or bilateral), presence of medical conditions and surgical procedures related with VCP, radiological imaging modalities and etiology (whether VCP is idiopathic or non-idiopathic). Patients were grouped into two categories with respect to the etiologic status and idiopathic cases were compared to non-idiopathic VCP in terms of aforementioned variables.

Statistical analysis

Analysis of data was performed via IBM SPSS Statistics 20.0 software (IBM Corporation, Armonk, NY, USA). The normal distribution of

Table 1. Baseline characteristics of vocal cord paralysis patients

	n	%	Mean±SD	Min.- Max.
Age (years)			52.1±23.1	1-87
Sex				
Female	49	53.3		
Male	43	46.7		
Diagnosis				
Idiopathic	29	31.5		
Non-idiopathic	63	68.5		
Side of involvement				
Right	28	30.4		
Left	56	60.9		
Bilateral	8	8.7		

SD: Standard deviation.

variables was tested with Kolmogorov-Smirnov test and non-parametric tests were used for variables that do not display normal distribution. Two independent groups were compared with Mann-Whitney U test, while Pearson chi-square test was utilized for categorical variables. Quantitative variables under investigation were expressed as mean, standard deviation or median, interquartile range (IQR), minimum and maximum values. Confidence interval was set at 95% and results with a chance probability <0.05 were considered as statistically significant.

RESULTS

Baseline characteristics of VCP patients including age, gender, side of involvement and etiology are shown in Table 1. Females had a slight predominance (53.3% vs. 46.7%) over males in this series. In a majority of cases (56, 68.5%), an underlying cause for VCP could be identified; whereas almost one third of patients (29, 31.5%) were termed as idiopathic. Left, right and bilateral vocal cords were paralytic in 56 (60.9%), 28 (30.4%) and eight (8.7%) patients, respectively. The most common causes of VCP were thyroid surgery (32, 34.8%), cardiovascular surgery (carotid endarterectomy, arterial switch, cardiac bypass) (13, 14.1%), lung cancer (adenocarcinoma, small cell carcinoma) (6, 6.5%) and cardiovascular malformations (patent ductus arteriosus, great artery transposition) (4, 4.3%) (Table 2). All the bilateral VCP were due to thyroid surgery.

Table 2. The etiology of vocal cord paralysis in our series

Etiology	n	%
Idiopathic	29	31.5
Surgery		
Thyroid	32	34.8
Cardiovascular	13	14.1
Pulmonary	1	1.1
Tumor		
Malignant		
Lung	6	6.5
Breast	1	1.1
Benign		
Posterior fossa tumor	1	1.1
Glomus tumor	1	1.1
Cardiac disease or malformation	6	7.5
Head and neck trauma	1	1.1
Cerebrovascular occlusion	1	1.1

Table 3. Comparison of descriptive characteristics in patients with idiopathic and non-idiopathic vocal cord paralysis

Parameter	Etiology for VCP				p
	Idiopathic		Non-idiopathic		
	n	IQR	n	IQR	
Age (year)		67.0-22.5		55.0-22.0	<0.001*
Gender distribution					0.121
Female	12		37		
Male	17		26		
Side of involvement					0.340
Left	17		39		
Right	11		17		
Bilateral	1		7		

VCP: Vocal cord paralysis; IQR: Interquartile range; * Statistically significant.

In most of the thyroid and cardiac surgeries the left vocal cord was involved due to its anatomy. In idiopathic cases both of the vocal cords were involved.

Patients with idiopathic VCP were significantly at a more advanced age than patients with non-idiopathic VCP (67.0-22.5 vs. 55.0-22.0; $p < 0.001$). Nevertheless, there was no difference between the two groups of VCP with respect to gender distribution ($p = 0.121$) and side of involvement ($p = 0.340$) (Table 3).

Imaging modalities consisted of computed tomography (CT) scan (neck, thoracic, cranial, larynx) and magnetic resonance imaging (MRI) (neck, thoracic, larynx, cranial). Data derived from radiologic methods are shown in Table 4. CT scan revealed mucosal thickening ($n = 4$), cardiomegaly ($n = 2$), lung metastasis ($n = 1$), emphysema ($n = 1$); while MRI revealed neck mass lesion ($n = 6$), cranial mass lesion ($n = 1$), and laryngeal mass lesion ($n = 6$). The rest of the patients CT scan and MRI findings were normal.

DISCUSSION

The current study was performed to evaluate and compare the clinical characteristics of idiopathic VCP and non-idiopathic VCP. Our data revealed that VCP was more frequent in men, left vocal cord was more commonly involved and an underlying cause could be identified in about two third of the patients. Patients with idiopathic VCP were significantly older and surgical trauma constituted a remarkable etiologic factor.

The incidence, clinical presentation and significance of VCP are still under debate. In spite of an intact pathophysiological basis, many aspects of this entity necessitate clarification. History and laryngoscopic examination do not reliably discriminate each laryngeal asymmetry from immobility attributed to paralysis. Employment of all steps properly can improve the diagnostic accuracy that is critical in elucidation of causes. Consequently, documentation of prevalence and achievement of

Table 4. Imaging methods used in patients with vocal cord paralysis

Imaging method	Diagnosis	n
Computed tomography		
Neck ($n = 6$)	Mucosal thickening	4
	Normal	2
Thoracic ($n = 16$)	Normal	12
	Cardiomegaly	2
	Metastasis	1
	Emphysema	1
Larynx ($n = 1$)	Mass lesion	1
Cranial ($n = 7$)	Normal	5
	Asymmetry	2
Magnetic resonance		
Neck ($n = 11$)	Mass lesion	6
	Normal	5
Cranial ($n = 9$)	Normal	8
	Mass lesion	1
Larynx ($n = 6$)	Mass lesion	6
Thoracic ($n = 3$)	Normal	3

better outcomes owing to increased compliance with the therapeutic algorithm may be possible.^[9]

Females had a slight predominance (53.3% vs. 46.7%) over males in this series, similar to the literature.^[10] Similar to the findings of Chen et al.,^[10] malignancy was the most common cause for vocal cord paralysis in males, while the most common in females was surgery (thyroidectomy). Among idiopathic causes, males (n=17) had a slight predominance over females. In our series median age was 52.1±23.1, which is similar to the literature.

Koufman et al.^[11] reported that most VCP cases in their series were idiopathic (68%). However, similar to the results of Heman-Ackah and Barr,^[12] we were able to detect a cause in more than half of the patients. Surgery was a leading cause in the present series and this may be partially attributed to the fact that our hospital is a referral center for complicated diseases. Interestingly, unilateral VCP was more common in the current study, similar to the findings of Koufman et al.^[11] who found unilateral vocal cord immobility more common (50%) in his series. On the other hand, Heman-Ackah and Barr^[12] reported that bilateral paralysis was more common (53%). The number of patients as well as regional, environmental and institutional factors may explain the variability among these studies. Misdiagnosis of VCP can cause delay, unnecessary additional evaluation and inappropriate management. Hence, increased awareness of the features of VCP is important for recognition and differential diagnosis.^[13]

Malignant infiltration must be considered as a potential cause of immobilization or thickening of the vocal cord. Laryngoscopy is particularly useful for the focal lesions of the vocal cord which can be distinguished from VCP.^[3] To investigate any pathology along the course of the vagus and recurrent laryngeal nerves, contrast-enhanced CT can be utilized from the midbrain to the aortic arch.^[14]

Bilateral VCP and acute onset of symptoms may be consistent with a central cause.^[15] The medullary nuclei of the vagal nerve can be assessed with MRI.^[16] Frequent pathologies that cause extracranial vagal or recurrent laryngeal nerve palsy are lung cancer with mediastinal lymph node metastases and squamous cell carcinoma of the neck as well as infectious

processes, benign masses or malignancies of other structures in the neck and upper mediastinum.^[17]

Computed tomography must be performed after the diagnosis of idiopathic VCP, since 81% of these patients were found to have malignancies.^[18] If the initial CT scan was normal, further scanning is unwarranted. Patients with a diagnosis of idiopathic paresis (not paralysis) may not call for a CT work-up.^[19]

Results of the current study demonstrated that a complete diagnostic study with appropriate imaging measures is mandatory in the evaluation of VCP. No consensus exists on the optimal diagnostic modality and we observed that laryngeal MRI yielded some potentially malignant lesions that were not detected during physical examination. Therefore, we suggest that use of laryngeal MRI can provide important clues to diagnose hidden premalignant or malignant lesions within larynx. The likelihood of detection of a cause for VCP may decrease with advancing age. This may be deterioration of neurological functions, increased possibility for laryngeal or extralaryngeal malignancies or diminution of immune function leading to viral infections manifesting as VCP. Another notable point was that despite technologic improvements and increased experience, surgical trauma was still an important cause. Efforts must be spent to improve the surgical technique and to minimize injury to the laryngeal nerve. Further trials must target sophistication and increased safety of surgical procedures that may predispose to lead to VCP. The decision for surgical intervention, selection of imaging modality and assessment of outcomes can be difficult due to the variability in etiology, symptoms and limited patient population.

Restrictions of the current report are the retrospective design and small sample size. Furthermore, impacts of social, environmental and ethnic factors involved in the etiology, presentation and detectability of VCPs must be taken into account during extrapolation of our results to larger populations.

However, we hope that our results may yield important clues or tips and pearls for diagnosis and follow-up of VCP patients. Development of more sophisticated surgical techniques and increased experience are important to avoid iatrogenic injury during surgery.

In conclusion, VCP is a relatively common clinical entity with a substantial rate of morbidity. Identification of the underlying etiology and awareness of the clinical characteristics are keystones for foreseeing complications and determining the appropriate therapeutic modality.

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REFERENCES

1. Stager SV. Vocal fold paresis: etiology, clinical diagnosis and clinical management. *Curr Opin Otolaryngol Head Neck Surg* 2014;22:444-9.
2. Simpson DM, Sternman D, Graves-Wright J, Sanders I. Vocal cord paralysis: clinical and electrophysiologic features. *Muscle Nerve* 1993;16:952-7.
3. Dankbaar JW, Pameijer FA. Vocal cord paralysis: anatomy, imaging and pathology. *Insights Imaging* 2014;5:743-51.
4. Dworkin JP, Treadway C. Idiopathic vocal fold paralysis: clinical course and outcomes. *J Neurol Sci* 2009;284:56-62.
5. Brunner E, Friedrich G, Kiesler K, Chibidziura-Priesching J, Gugatschka M. Subjective breathing impairment in unilateral vocal fold paralysis. *Folia Phoniatr Logop* 2011;63:142-6.
6. Rosenthal LH, Benninger MS, Deeb RH. Vocal fold immobility: a longitudinal analysis of etiology over 20 years. *Laryngoscope* 2007;117:1864-70.
7. Misono S, Merati AL. Evidence-based practice: evaluation and management of unilateral vocal fold paralysis. *Otolaryngol Clin North Am* 2012;45:1083-108.
8. Ward PH, Berci G. Observations on so-called idiopathic vocal cord paralysis. *Ann Otol Rhinol Laryngol* 1982;91:558-63.
9. Sulica L, Blitzer A. Vocal fold paresis: evidence and controversies. *Curr Opin Otolaryngol Head Neck Surg* 2007;15:159-62.
10. Chen HC, Jen YM, Wang CH, Lee JC, Lin YS. Etiology of vocal cord paralysis. *ORL J Otorhinolaryngol Relat Spec* 2007;69:167-71.
11. Koufman JA, Postma GN, Cummins MM, Blalock PD. Vocal fold paresis. *Otolaryngol Head Neck Surg* 2000;122:537-41.
12. Heman-Ackah YD, Barr A. Mild vocal fold paresis: understanding clinical presentation and electromyographic findings. *J Voice* 2006;20:269-81.
13. Hillel AD, Benninger M, Blitzer A, Crumley R, Flint P, Kashima HK, et al. Evaluation and management of bilateral vocal cord immobility. *Otolaryngol Head Neck Surg* 1999;121:760-5.
14. Chin SC, Edelstein S, Chen CY, Som PM. Using CT to localize side and level of vocal cord paralysis. *AJR Am J Roentgenol* 2003;180:1165-70.
15. Dankbaar JW, Pameijer FA. Vocal cord paralysis: anatomy, imaging and pathology. *Insights Imaging* 2014;5:743-51.
16. Stimpson P, Patel R, Vaz F, Xie C, Rattan J, Beale T, et al. Imaging strategies for investigating unilateral vocal cord palsy: how we do it. *Clin Otolaryngol* 2011;36:266-71.
17. Yumoto E, Minoda R, Hyodo M, Yamagata T. Causes of recurrent laryngeal nerve paralysis. *Auris Nasus Larynx* 2002;29:41-5.
18. Tsikoudas A, Paleri V, El-Badawey MR, Zammit-Maempel I. Recommendations on follow-up strategies for idiopathic vocal fold paralysis: evidence-based review. *J Laryngol Otol* 2012;126:570-3.
19. Badia PI, Hillel AT, Shah MD, Johns MM 3rd, Klein AM. Computed tomography has low yield in the evaluation of idiopathic unilateral true vocal fold paresis. *Laryngoscope* 2013;123:204-7.