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Original article

Idiopathic unilateral vocal-fold paralysis in the adult

F. Rubin , A. Villeneuve , L. Alciato , L. Slaïm , P. Bonfils , O. Laccourreye*

Service d'otorhinolaryngologie et de chirurgie cervico-faciale, hôpital Européen-Georges-Pompidou, université Paris-Descartes-Sorbonne-Paris-Cité, AP–HP, 20, rue Leblanc, 75015 Paris, France

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ABSTRACT

Goal: To analyze the characteristics of adult idiopathic unilateral vocal-fold paralysis.
Material and methods: Retrospective study of diagnostic problems, clinical data and recovery in an inception cohort of 100 adult patients with idiopathic unilateral vocal-fold paralysis (Group A) and comparison with a cohort of 211 patients with isolated non-idiopathic non-traumatic unilateral vocal-fold paralysis (Group B).
Results: Diagnostic problems were noted in 24% of cases in Group A: eight patients with concomitant common upper aerodigestive tract infection, five patients with a concomitant condition liable to induce immunodepression and 11 patients in whom a malignant tumor occurred along the path of the ipsilateral vagus and inferior laryngeal nerves or in the ipsilateral paralyzed larynx. There was no recovery of vocal-fold motion beyond 51 months after onset of paralysis. The 5-year actuarial estimate for recovery differed significantly ($P < 0.0001$): 53.2% in Group A versus 17.9% in Group B. In Group A, recovery occurred before the end of the second year following paralysis onset in 93% of cases. On univariate analysis, recovery in Group A was associated with younger age ($P = 0.0033$), shorter time to consultation ($P < 0.0001$), and absence of oncologic history ($P < 0.028$). In case of non-recovery in Group A, malignant tumor along the ipsilateral vagus or inferior laryngeal nerve was found in 17.2% of cases, 81% of which manifesting during the 30 months following the onset of vocal-fold paralysis.
Conclusion: In non-traumatic vocal-fold paralysis in adult patients, without recovery of vocal-fold motion, a minimum three years' regular follow-up is recommended.

1. Introduction

In medicine, the term "idiopathic", from the Greek ιδιοπαθεια, refers to a symptom or condition unrelated to any other disease or for which no precise cause can be identified.

In adults with unilateral vocal-fold paralysis, epidemiological studies based on cohorts with more than 500 patients report that, in the absence of any trauma (surgery, intubation, external trauma, radiation therapy), idiopathic etiology represents 29.8-65.7% of cases [1–5]. A search of the PubMed and Cochrane data-bases using the search-terms "paralysis", "immobility", "vocal fold", "recurrent", "laryngeal", "unilateral", "adult" and "idiopathic" found only two cohorts of more than 100 adult patients specifically dedicated to the study of idiopathic unilateral vocal-fold paralysis (IUVFP): Sulica's 2008 meta-analysis [6] Noel et al.'s 2016 retrospective series [7].

These figures were the impetus for the current retrospective study based on the analysis of the medical files of 311 consecutive adult patients with isolated non-traumatic unilateral vocal-fold paralysis (unrelated to surgery, intubation, radiation therapy or external trauma) seen at our ENT clinic between 1990 and 2015, 100 of whom were considered idiopathic on assessment. The study focused on difficulties arising in diagnosing IUVFP, clinical comparison between idiopathic and non-idiopathic paralysis, and recovery of vocal-fold motion in the IUVFP group. Results are discussed in the light of the literature found in the PubMed database.

2. Material and methods

Between 1990 and 2015, 311 adult patients presented at our clinic with IUVFP (no associated neurologic deficit) of less than 24 months' onset, unrelated to any trauma (surgery, intubation, external trauma or radiation therapy) affecting the central laryngeal nuclei or ipsilateral vagus or inferior laryngeal nerves. Exclusion criteria for the present retrospective analysis comprised: unilateral laryngeal immobility related to pharyngolaryngeal tumor or cricoarytenoid joint ankylosis diagnosed from the context – lack of

* Corresponding author.
E-mail address: ollivier.laccourreye@aphp.fr (O. Laccourreye).

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Table 1
Etiologies of non-idiopathic vocal-fold paralysis (Group B).

Non-idiopathic etiologies	*n*
Malignant tumor	
Esophagus, lung, thymus, thyroid, trachea.	128
Lymph nodes (colon, ENT mucosa, lymphoma, ovary, parotid, prostate, kidney, sarcoma, breast)	40
Benign tumor	
adenopathy, neurinoma, paraganglioma, parathyroid, thyroid.	39
Cardiovascular	
aneurysm, stroke, dissection, Ortner's syndrome	9
Miscellaneous	
Viral (laryngeal herpes zoster)	1
Cisplatin intoxication	1
Esophageal diverticulum	1
Neurologic (sarcoidosis, Guillain-Barré syndrome sequelae)	2

amyotrophy of the paralyzed vocal fold and presence of ipsilateral arytenoid cartilage movement when coughing (without confirmation by laryngeal electromyography) –, history of laryngeal surgery and unilateral vocal fold paralysis with other associated neurologic signs.

Work-up comprised: clinical examination with flexible endoscopy, cervicomediastinal computed tomography (CT) scan, biology (blood count, CRP, glycemia, calcemia, liver workup), serology (HIV, TPHA-VDRL, Lyme) and specific biologic analyses (anti-native DNA antibodies, antinuclear antibodies, protein electrophoresis) depending on clinical context. The unilateral vocal-fold paralysis was consequently determined as idiopathic (IUVFP: Group A) in 32.1% of cases (100/311) or related to a known etiology (Table 1) (Group B) in 67.9% (211/311).

Patients were followed up until recovery of vocal-fold motion ($n = 65$) or death ($n = 107$) in 55.3% of cases (172/311). For the other 109 patients, median follow-up was 24 months, ranging from two to 144 months. The present retrospective study of these 311 files analyzed difficulties of diagnosis in IUVFP patients (Group A), compared clinical data (time to consultation at our clinic, age, gender, comorbidities, symptomatology, paralyzed vocal fold position, rate of recovery of vocal-fold motion) between groups, and analyzed time to recovery of vocal-fold motion and associated variables in Group A. Statistical analysis used Chi^2, Student *t*, and Mann-Whitney U-tests and the Kaplan-Meier estimator with log rank test. The significance threshold was set at $P < 0.05$.

3. Results

In Group A ($n = 100$), 24% of cases presented diagnostic difficulties (Table 2), with three subgroups: eight patients with concomitant common viral infection (rhinopharyngitis, otitis media), five with a concomitant condition liable to induce immunodepression, and 11 with onset of malignant tumor along the path of the ipsilateral vagus and laryngeal nerves or in the ipsilateral larynx.

Median age in Group A was 59 years, with 47% of female patients. There was a 65% rate of severe dysphonia, 34% swallowing disorder, and 1% respiratory difficulty on effort (Table 3). Inter-group comparison found no significant difference in severity of dysphonia, swallowing or respiratory disorder, paralyzed vocal fold position or time to consultation, while three variables showed significant differences: in Group B, median age was higher ($P = 0.01$), and male gender ($P = 0.005$) and oncologic history ($P < 0.0001$) were more frequent (Table 3).

The rate of recovery of vocal-fold motion at five years on Kaplan-Meier analysis differed significantly ($P < 0.0001$): 53.2% in Group A versus 17.9% in Group B (Fig. 1). There were no cases of recovery beyond the 51st month. In group A, 93% of recoveries (39/42) occurred within 2 years of onset (Fig. 1). On univariate analysis (Table 4 and Fig. 1), recovery in Group A was significantly associated with young age ($P = 0.033$), short time to consultation ($P < 0.001$) and absence of oncologic history ($P = 0.028$). 17.2% of cases of non-recovery in Group A involved malignant tumor along the ipsilateral vagus and laryngeal nerves (Table 2), detected within 30 months of onset of IUVFP in 81% of cases.

Table 2
Diagnostic difficulties in the 100 cases of idiopathic unilateral vocal-fold paralysis.

Factors	*n*
Synchronous common ENT viral infection	8
Synchronous immunodepression	5
Treated type-2 diabetes (metformin)	1
Vitamin C deficiency	1
HIV seropositivity	1
Childbirth (24 hours before)	1
Oncologic surgery (8 days before)	1
Subsequent malignant tumor	11
Mediastino-pulmonary	4
Larynx	2
Breast	2[a]
Thyroid	1
Parotid	1[a]
Liver	1[a]

n: number of patients.
[a] Mediastinal lymph-node metastasis.

Table 3
Comparison of clinical data between Groups A and B.

Variables	Group A/Group B	*P*
Age in years (M; R)	59; 17–93/64; 25–88	0.015
Time to consultation in months (M; R)	1; 1–24/2; 1–24	0.04
Gender: female-male	47–53/64/147	0.005
Side of paralysis: right-left	41–59/65–146	0.11
Position of paralyzed fold		
Abduction-paramedian	4–96/23–188	0.051
Symptomatology of paralysis		
Dysphonia: severe-moderate-none	65–34–1/115 –90–16	0.16
Swallowing disorder: yes	25–75/68–143	0.14
Respiratory disorder: yes	2–98/8–203	0.77
Comorbidity		
Diabetes: yes-no	1–99/2–209	0.95
History of cancer: yes-no	22–78/96–115	<0.0001
HIV seropositivity: yes-no	1–99/0–210	0.99

M: median; R: range.

4. Discussion

In case of isolated unilateral vocal fold paralysis in adults, unrelated to trauma (intubation, cervical trauma, cervical radiation therapy and/or surgery), adjacent to vagus or inferior laryngeal nerves nuclei or fibers, the diagnosis of its idiopathic nature is a diagnosis by exclusion, following clinical and paraclinical assessment.

Classically, clinical features fail to distinguish idiopathic from non-idiopathic non-traumatic isolated unilateral vocal-fold paralysis. In the present study, time to consultation, severity of dysphonia and respiratory or swallowing disorder did not significantly differ between the idiopathic and non-idiopathic groups. Median age, however, was significantly greater ($P = 0.015$) and male gender ($P = 0.005$) and oncologic history ($P < 0.0001$) were significantly more frequent in the non-idiopathic group B. The most likely explanation is that malignant tumor, and notably lung cancer (Table 1), was the main etiology in this group. Clinically, concomitant common viral infection of the upper aerodigestive tract is a possible diagnostic factor for IUVFP that merits discussion. According to Ward and Berci [8], the etiology of IUVFP is viral, given the rate