An update on the etiology of acquired vocal cord palsy- A single institutional study from south India

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Abstract

Background: Etiology of acquired vocal cord palsy is variable with time, place and side. Updating the etiology and awareness of the most probable to the rarest diagnosis can help in the management.5Aim: To study the current etiological profile of acquired unilateral and bilateral vocal cord palsy and to compare the results with existing literature. Materials and methods: A retrospective chart review of 167 patients with vocal cord palsy from 2011-2016 was conducted in a tertiary care center in South India. All patients were evaluated by meticulous history, physical examination and relevant blood tests. Endoscopy of the aerodigestive tract was conducted if required. CT, MRI were done when etiology remained elusive after preliminary evaluation .Results: Of 167 cases, 127 (76%) were unilateral and 40 (24%) bilateral. Left side predominated with 92 (72.4%) cases. The incidence of vocal cord palsy (UVCP) was highest in the seventh and eighth decades. Malignancy (28.3%) was the commonest etiology for UVCP. Amongst them thyroid cancer was found in 36% followed by lung cancer (25%) and metastases(25%). Surgery (42.5%) was the predominant cause for BVCP with thyroidectomy at fault in 35% .Conclusion: Etiology of vocal cord palsy is diverse. Barring 15-20% of cases a cause can be identified in all. A broader perspective and a comprehensive workup should be adopted so that no system is overlooked

Key words: vocal cord palsy, unilateral vocal cord palsy, bilateral vocal cord palsy.

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DOI: https://doi.org/10.26611/10161117

Access this article online			
Quick Response Code:	Website: www.medpulse.in		
	Accessed Date: 18 July 2019		

INTRODUCTION

Etiology of vocal cord palsy (VCP) has always been a subject of research since it is variable with time, laterality, ethnicity and geographic location.¹. VCP can occur in intracranial disease or by involvement of the vagus or its recurrent laryngeal nerve (RLN) branch anywhere between the jugular foramen and its entry into the larynx .VCP maybe congenital or acquired. The

causes of acquired vocal cord palsy are neoplasms, surgical, intubation or external trauma, neurological, infectious or inflammatory conditions, miscellaneous or idiopathic. Syphilitic aneurysm of arch of aorta and pulmonary tuberculosis were the common diagnoses for unilateral vocal cord palsy (UVCP) in 1930s.² In the latter half of century, the focus shifted towards malignancy. By 21st century surgery had emerged as the major etiology in a number of studies.^{3,4} Longitudinal analysis in the same institution had shown variability in etiology.³ In comparison the etiology of bilateral vocal cord palsy (BVCP) show little variation over time.³By and large thyroid surgery is attributed to be the commonest cause for BVCP.^{2,3} Intubation trauma ,esophageal cancer etc are also frequently encountered in BVCP¹. Updating the etiology and awareness of the most probable to the rarest diagnosis can help in the management.5

How to cite this article: Jayanthy Pavithran, Pradeep R K A. An update on the etiology of acquired vocal cord palsy- A single institutional study from south India. *MedPulse International Journal of ENT*. July 2019; 11(1): 25-29. https://www.medpulse.in/ENT/

AIMS AND OBJECTIVES

To study the current etiological profile of acquired unilateral and bilateral VCP and compare with the existing literature.

MATERIALS AND METHODS

We retrospectively reviewed 167 case records of VCP from 2011-2016, retrieved from electronic data base of a tertiary care center in South India. Cases were inhouse referrals or seen in the outpatient services of ENT, with complaints of dysphonia or aspiration .A complete clinical evaluation was done which included meticulous history, systemic examination, head and neck examination with indirect/flexible laryngoscopy and specialty referrals where required. Hematology, liver and renal function tests, urine analysis, Mantoux, chest X-ray and serology were routinely performed. Bronchoscopy and/or esophagoscopy were done if symptomatic. If after preliminary evaluation the etiology remained elusive a CT or MRI scan with intravenous contrast was considered mandatory to search for occult disease in the brain, skull base, neck and mediastinum before the case was labeled idiopathic. **Inclusion Criteria**

All consecutive cases with primary or secondary diagnosis of acquired VCP with probable vagal, RLN or intracranial involvement were included. Both unilateral and bilateral VCP were studied.

Exclusion Criteria

Cases with incomplete data/evaluation, laryngeal and hypopharyngeal malignancy with contiguous involvement of vocal cord musculature and congenital palsy were excluded.

RESULTS

167 cases of VCP were finally found acceptable after exclusion. Of these 127 cases (76%) were unilateral and 40 (24%) were bilateral . 35(27.6%) had right sided and 92 (72.4%) had left sided palsy. Age ranged from 0-89 years for UVCP and 0-81 years for BVCP with a mean age of 52.21 years and 51 years respectively.

Male:female ratio was 1.4:1 in UVCP and 0.9:1 in BVCP. Etiology of unilateral, bilateral, right and left VCP were categorized as malignancy, surgery, benign lesions ,intubation, central , idiopathic, nonsurgical trauma, and miscellaneous. [Table 1]The results are compared with other studies from last two decades. [Table 2.5] Nonthyroid surgery responsible for UVCP were excision of paraganglioma (3) and schwannoma(3) in the neck and thoracic procedures such as CABG+sac repair(1), oesophagectomy(2), PTCA stenting(2),PDA ligation (2), PDA device closure(1) and juxta aortic arch mass excision. A case of foramen magnum decompression also resulted in UVCP. The nonthyroid surgery (7.5%)resulting in BVCP were tracheoesophageal fistula repair(2 cases) and Tetrology of Fallot (one case) correction.Preoperative and postoperative causes of thyroid related VCP were noted.[Table 3,4]. Malignancy arising in the thorax were Hodgkins lymphoma(1), lung malignancy (9), bronchogenic carcinoma (2), mediastinal lymphoma(2) and metastases (2). Mediastinal secondaries were from carcinoma of rectum and an unknown primary. Malignant causes in the neck were papillary thyroid carcinoma (9),follicular carcinoma(2), anaplastic carcinoma and lymphoma of thyroid (1), thyroid lymphoma (1) and metastases (7) from carcinoma of rectum(1),neuroblastoma(1),carcinoma of cervical oesophagus (2), lung adenocarcinoma (1) and unknown primary(2).Benign tumours causing preoperative UVCP included colloid goiter (4) ,benign follicular neoplasm(1)and vagal schwannoma (1).Infective/inflammatory causes were pulmonary tuberculosis (2), lung abcess(1) bronchopulmonary aspergillosis with hilar/mediastinal nodes(1), R upper lobe consolidation (1) and sarcoidosis with cervical deposits (1). Two cases of EBRT with mediastinal irradiation for carcinoma breast and metastases from carcinoma rectum induced left sided VCP .One case of UVCP was presumed to develop secondary to methotrexate toxicity.

Table 1: Etiolo	gy of acquired unita	iteral and bilateral v	ocal cord palsy	
Category	UVCP* (76.1%)	BVCP **(23.9%)	R VCP	L VCP
Surgery	33 (25.9%)	17(42.5%)	10 (28.5%)	23 (25%)
thyroid	15(11.8%)	14(35%)	7	8
other neck surgery	6	-	2	5
thoracic	10	3	1	9
neurosurgery	1	-	-	1
Benign lesions	12 (9.4%)	-	4 (11.4%)	8 (8.6%)
Benign tumors	6	-	2	4
Infectious/inflammatory	6	-	2	4
Malignancy	36 (28.3%)	2(5%)	14(40%)	22(23.9%)
Ortners syndrome	7 (5.5%)	-	-	7

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	Intubation	3 (2	.3%)	1(2.5%)	-	3	
Ex	ternal trauma	trauma 5 (3.9%) 4		4(10%)	2	3	
	Idiopathic	diopathic $22(17.3\%)$		9(22.5%)	3 (8.5%)	19(20.6	5%)
	Neurologic	7 (5	.5%)	7(17.5%)	1	6	
[Drug induced	1 (0 7%)		-	1	-	
-	Radiation	2 (1	5%)	-	-	2	
	Total	2 (1	.570) 27	40	25	92	
	*UVCP-ur	nilateral vocal	cord nalsy	** BV/CP_bilate	ral vocal cord nal	SV SV	
	0101 01		sol a paisy	DVCI DIlatei		sy	
		Table 2: Ind	cidence of	UVCP * and BV	CP **.		
		Study		UVCP (%)	BVCP(%)		
		Rosenthal et a	al(2005) ³	83.5	16.5		
		Gupta <i>et al</i> (2009) ¹	98.21	6.67		
	Тс		al (2014) ⁷	93.18	6.82		
		Present study	(2016)	76	24		
	*UVCP-ur	nilateral vocal	cord palsy	** BVCP-bilate	ral vocal cord pal	sy	
		T 0 T				5	
			roldectom	y and vocal cor	d paisy	-	
		Туре		UVCP (n=15)	BVCP (n=14)	-	
	То	tal thyroidecto	omy	6	10		
	Subtotal th		tomy	2	2		
	Completion th		ectomy	3	2		
R hemithyroi		emithyroidect	omy	1	-		
	L h	emithyroidect	omy	3	-	_	
		Table 4: Thyro	oid patholo	ogy and vocal co	ord palsy		
Pr	reoperative caus	ses		Pos	stoperative HPE		
	UVCP	BVCP	l	JVCP		BVCP	
20	(15.7%)	1 - 17	15	(11.8%)	14	4 (35%)	
Maligna	ancy-12 (60%)		Malignar	ncy -4(26.6%)	Maligna	ncy-2 (14.3°	%)
Ũ	y		ů.			,	
Papillary	v carcinoma (8)	/ - /	Papillary	carcinoma (4)		2	
Follicula	r carcinoma (2)		Benign	-11(73.4%)	Benigr	-12 (85.7%))
Lvm	phoma (1)	- /	Nodular	colloid (10)	5	12	
Âna	aplastic (1)		Ade	noma (1)		-	
Beni	an -8 (40%)	_		(1)			
	<u>g</u>						
		Table	• 5: UVCP *	over the years			
Study	Benninger ⁵	Rosenthal ³	Nerurkar	6 Gupta ¹	Pavithran ²	Gandhi	Present
Year	1998	2005	2006	2009	2010	2014	2016
Males %	58%	42%	-	69.67	72 3	2011	58 33
1110105 /0		1 - 70		07.07	, 2.0		70.00
Left /right %	68/32	61/39		69 6/30 4	61/39		124/214
Left /right % Malignancy%	68/32 40	61/39 13 5	14 1 2	69.6/30.4 34 82	61/39	12 9	/2.4/2/.4 28 3
Left /right % Malignancy%	68/32 40 35	61/39 13.5 46 3	14.12 44.27	69.6/30.4 34.82 10.71	61/39 6.6	12.9 21.6	72.4/27.4 28.3 25 0
Left /right % Malignancy% Surgery % Trauma%	68/32 40 35	61/39 13.5 46.3	14.12 44.27 11 76	69.6/30.4 34.82 10.71	61/39 6.6 22.3	12.9 21.6 3 7	72.4/27.4 28.3 25.9 3.0
Left /right % Malignancy% Surgery % Trauma%	68/32 40 35 1	61/39 13.5 46.3 2.2 3	14.12 44.27 11.76	69.6/30.4 34.82 10.71 9.82 15.17	61/39 6.6 22.3 6.6	12.9 21.6 3.7 6.1	72.4727.4 28.3 25.9 3.9 5.5
Left /right % Malignancy% Surgery % Trauma% Central % Idiopathic %	68/32 40 35 1 2	61/39 13.5 46.3 2.2 3 17.6	14.12 44.27 11.76 4.71 16.47	69.6/30.4 34.82 10.71 9.82 15.17 12.20	61/39 6.6 22.3 6.6 12.4	12.9 21.6 3.7 6.1	72.4/27.4 28.3 25.9 3.9 5.5 17.2

*UVCP-unilateral vocalcordpalsy

		Table 6: Ortners syndrome.
Age	Sex	Pathology
68	М	Saccular aneurysm of aortic arch
80	Μ	Saccular aneurysm of aortic arch
62	Μ	Saccular aneurysm of aortic arch
63	Μ	Left ventricular aneurysm
64	F	Ectatic aorta
70	Μ	Left ventricular dilatation with dilated cardiomyopathy
68	F	Bilateral pulmonary thromboembolism

DISCUSSION

UVCP predominated with 127 (76%) cases. J. Gupta et al and several others have provided comparative figures.^{1,7,8,9} The relatively high number of BVCP in our study maybe ascribed to the endemicity of thyroid disease in Kerala (South India). The predominance of left side (69.7%) is justified by the longer course of left RLN rendering it more vulnerable compared to the right. There was a male preponderance in UVCP in similarity with other studies ^{1,2,6}. Rosenthal reported female preponderance in UVCP.³ The majority of unilateral cases was found in the seventh decade. Increased life expectancy and growing number of malignancy is the possible explanation. Other studies from Northern states of India reported majority of UVCP in younger age.^{1,9} Similar to UVCP in the present series, BVCP occurred at a higher frequency in seventh and eighth decades.Malignancy (28.3%) accounted for the majority of UVCP: which agrees with Gupta et al and Ahamed et al from North India (34.82%) and 29.09% respectively).^{1,10}. Malignancy was the commonest etiology in a recent series from South India (Varghese et al 2017). Nerurkar et al and Gandhi et al reported lesser incidence of malignancy.^{5,9} This diversity in the same country may be explained by the referral bias. The most common malignancy causing UVCP in our series was thyroid cancer (36%) followed by lung cancer (25%) and metastases(25%). Hodgkins and Non Hodgkins lymphoma gave rise to 5 cases of UVCP in the neck and mediastinum. As expected papillary carcinoma was the commonest thyroid cancer. Rosental and Gupta et al reported lung malignancy as the most common malignant pathology.^{1,3} The most common cause for BVCP was surgery (42.5%). This is in concordance with Rosenthal et al.³ One case of intracranial oligodendroglioma and cervical metastasis from carcinoma rectum caused bilateral weakness in our series. The reasons assumed for preoperative VCP are acute /longstanding compression/stretching from hemorrhage or increase in size of the nodule and/or infiltration in a malignant process.There are some interesting observations on thyroid related vocal cord palsy. Preoperative UVCP outnumbered surgically induced palsy. Though malignancy predominated, a good number (40 %) of preoperative palsy was associated with benign pathology. Thyroidectomy for benign pathology accounted for more cases of postoperative palsy, both unilateral and bilateral cases. In an earlier study by the present author from another center and Rowes-Jones et al found benign thyroid tumors causing 75% of preoperative palsy.^{2,11} It may be inferred that preoperative palsy in the presence of a thyroid nodule

may not be an absolute indicator of malignancy .¹² Kay-Rivest *et al* in his study of preoperative vocal cord palsy found malignancy in 76 % cases.¹²

Trauma:

Trauma to the nerve may be surgical, due to endotracheal intubation or external.Surgery was the single major cause (42.5%) of BVCP with thyroidectomy at fault in 35% of cases. Rosenthal *et al* found 55.6% of BVCP to be caused by surgery, 48.6% of which was thyroidectomy .The incidence of thyroidectomy related VCP as reported by J Gupta *et al* were 25% and 8.04% in bilateral and unilateral cases respectively. In UVCP nonthyroid surgeries (18/14.2%) exceeded thyroidectomy (15/11.8%). The incidence of intubation induced VCP ranges from 1.8- 25.4% ³. It is presumably due to

neuropraxia arising from compression of motor branch of RLN between the thyroid lamina and high riding cuff for long duration.¹³ The actual incidence may be more since this etiology goes unrecognized in surgeries where RLN is at risk 2.5% of the present series were secondary to intubation. Three cases with unilateral involvement in our series were left sided .One case of bilateral involvement was come across. One study reported endo-tracheal intubation as the major cause of vocal cord palsy.¹³ Rosenthal et al reported higher incidence of BVCP than UVCP following intubation^{3.} It may be difficult to differentiate between arytenoid dislocation and nerve injury without palpation under anesthesia or EMG assistance.External trauma to the neck in road traffic accidents with and without involvement of the larvnx were found to cause both UVCP and BVCP (5 and 4 cases respectively). A case of R upper lobe consolidation was seen which resulted in R vocal cord palsy. The right RLN maybe involved where it closely abuts the right apical pleura. The other benign lesions causing R VCP were sarcoid deposits, colloid goiter and benign thyroid neoplasm. Two cases of tuberculous mediastinal nodes resulted in left VCP. The paralysis may be caused by three possible mechanisms; (1) The nerve may be passing through or adjacent to a mass of caseating nodes, (2) the nerve may be trapped in the dense fibrous pleural thickening or in the chronic fibrosing mediastinitis that may occur, and (3) the nerve may be stretched due to retraction of the left upper lobe bronchus pulled towards the apex.14Hoarseness due to left RLN paralysis by an identifiable cardiovascular disease is referred to as Ortner syndrome (cardiovocal syndrome). Originally described in a case of severe mitral valve stenosis by Ortner in 1897, the term now includes other cardiovascular diseases with compression of the left RLN in the aortopulmonary window. The left recurrent

laryngeal nerve after its origin from the vagus nerve above the aortic arch courses under it through the aortopulmonary window which puts it under stress in instance of compression from the aorta, pulmonary artery or ligamentum arteriosum.9Ortner's syndrome is reported in 2.3-23 % of UVCP .It was identified in 7 (5.5 %) of our patients. Similar incidence was reported by Sebastian et al.¹³ We found 4 aortic lesions and 3 cases of pulmonary artery hypertension with left VCP (Table-6). The modest number could be because the palsy remains unidentified due to slow progression or morbidity of the primary disease. Furthermore, since we had excluded congenital UVCP we may have missed cases secondary to PDA. Gandhi S et al reported cardiac anomalies like the coarctation of the aorta, tetralogy of Fallot, right ventricular hypertrophy secondary to pulmonary hypertension, abnormal variant of azygous system in their series .917.5% of BVCP were neurological compared to 5.5% of unilateral cases .Brain stem stroke (4) was the predominant neurological disease in bilateral palsy while cortical/white matter lesions caused UVCP. Parkinsonism caused both types of palsy .Multisystem atrophy (MSA)and MSA-P caused BVCP in our series.In spite of technological advances over the years relative incidence of idiopathic vocal cord palsy remains within 10-20% .^{2,3,5,6} We could not identify a cause in 17.3% of unilateral cases. This meets the numbers reported by Rosenthal *et al* (18.5 %) and a few others from Northern states of India (Gupta et al 13.39% and Nerurkar 16.47 %).^{1,3,5} A few studies have reported a higher incidence of idiopathic cases (31.1%, 38.18%) in spite of exhaustive workup including pan-endoscopy and CT/MRI.10,15

CONCLUSION

Vocal cord palsy is not a diagnosis per se but a sign of an underlying disease. Barring 15-20% of cases a cause can be identified in all. A broader perspective and a comprehensive workup should be adopted so that no system is overlooked .Arriving at the correct diagnosis greatly influences the management.

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Source of Support: None Declared Conflict of Interest: None Declared