Review

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Ortner's syndrome: A systematic review of presentation, diagnosis and management

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SUMMARY Ortner's syndrome (OS), also called cardiovocal syndrome, is a rare condition hallmarked by left recurrent laryngeal nerve palsy due to underlying cardiopulmonary disease. The purpose of this review is to systemically analyze the existing literature for cases of OS to outline typical presentation, methods of diagnosis, and management of these patients. Case reports, case series, and cohort studies describing OS between 1955 and 2021 were identified. Individual manuscripts were reviewed for clinical features, presentation, and management. A total of 117 patient cases were gathered from 92 published articles. Common symptoms included hoarseness, dyspnea, cough, and dysphagia. The most common associated comorbidity was aortic aneurysm (41%), followed by pulmonary hypertension (35%), mitral stenosis (17%), and hypertension (12%). Among those who were managed *via* surgical intervention, 85.4% reported improvement in their hoarseness. While historically OS was associated with mitral stenosis, in recent decades, aortic aneurysms and dilation of the pulmonary artery from pulmonary hypertension have emerged as primary etiologies of OS. Therefore, OS should be considered in any patient presenting with hoarseness and history of cardiopulmonary disease. Surgical intervention in appropriate candidates resolves OS in most cases.

Keywords Ortner's syndrome, cardiovocal syndrome, hoarseness

1. Introduction

Vocal cord paralysis presenting as hoarseness due to an underlying cardiovascular pathology is a rare clinical entity known as Ortner's syndrome (OS) or cardiovocal syndrome. The syndrome was first described by Norbert Ortner in 1897 in a review of three patients with severe mitral stenosis (*1*). It was postulated that left atrial enlargement in these patients was responsible for left vocal cord paralysis and subsequent dysphonia.

The pathophysiology of OS is related to the anatomy of the recurrent laryngeal nerve (RLN). The RLN is a branch of the vagus nerve (cranial nerve X) that innervates all the intrinsic muscles of larynx except for the cricothyroid muscle. These muscles act to open, close, and adjust tension on the vocal cords bilaterally. The RLN is also responsible for the sensory supply to the larynx below the vocal cords and the upper part of the trachea. The pathways for the RLN on both sides of the neck are asymmetrical. The right recurrent laryngeal nerve branches off the right vagus nerve, loops around right subclavian artery and tracks superiorly between the trachea and esophagus. On the other hand, the left recurrent laryngeal nerve branches off the left vagus nerve, loops around the ligamentum arteriosum and tracks superiorly between the trachea and the esophagus (Figure 1). In general, injury to left recurrent laryngeal nerve (*i.e.* impingement, stretching, or compression) is more common than injury to the right recurrent laryngeal nerve, likely due to its proximity to the aortopulmonary window and other intrathoracic structures (*2*).

OS is specific for left recurrent laryngeal nerve injury due to underlying cardiac disease. Although it is commonly associated with severe mitral stenosis (as initially described by Ortner), there are many causes of OS including compression from other vascular (*i.e.* aortic aneurysms, aortic dissections, pulmonary hypertension) or mediastinal (*i.e.* neoplasms) structures (*3-5*). Similarly, although the classic symptom associated with OS is dysphonia/hoarseness, there have been several other

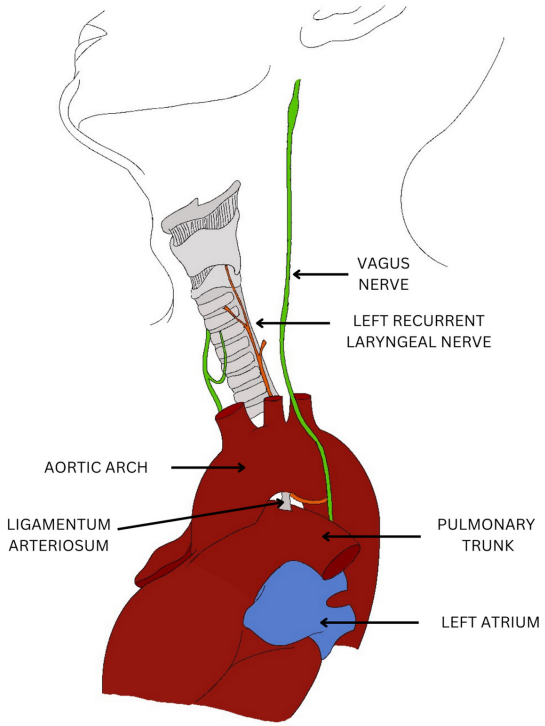

Figure 1. Anatomic pathway of the left recurrent laryngeal nerve.

manifestations of the syndrome described in the literature including aspiration, dysphagia, and shortness of breath (*6*).

As OS is a rare clinical entity, there is a paucity of literature comprehensively describing the spectrum of clinical manifestations as well as etiologies of the syndrome. As such, the purpose of this manuscript is to systemically review the existing literature for cases of OS to outline the syndrome's various etiologies, symptomatology, methods of diagnosis, and management strategies.

2. Systematic review

This systematic review was conducted in line with the PRISMA 2020 guidelines. As this is a review of existing literature, institutional ethics approval was not required by our institutional review board. A PubMed search was performed by two authors (SV, SK) to find articles published between 1955 and 2021 using the keywords "Ortner's syndrome" or "cardiovocal syndrome". Case reports, case series, and cohort studies were included. The references lists of articles were also reviewed to find additional relevant literature. Only English language literature was included in the analysis. Manuscripts were excluded if they described right recurrent laryngeal nerve palsy or if they described idiopathic left recurrent laryngeal nerve palsy. Full text review was subsequently conducted of all remaining studies for completeness of information. Any disagreements were resolved by a third reviewer (AT). Literature that met inclusion criteria was reviewed for patient clinicodemographic data, disease presentation, diagnosis, and management.

3. Main findings

Figure 2 is a PRISMA diagram depicting the literature search process. After omitting duplicate literature, a total of 188 records were included in our initial search. Of these publications, only 92 ultimately fulfilled inclusion criteria (Supplemental Table 1, *http://www.irdrjournal.com/action/getSupplementalData.php?ID=166*), encompassing a total of 117 patient cases (*1,3,6-95*). Most patients were older than 50 years of age (n = 67, 57%) (Table 1). The mean age was 53.3 years ± 34.6 years, with a range of 1.4 years to 89 years of age. Of note, the age of one patient was not presented and two patients were described as toddlers (without a specific age). There were 66 males (56%) and 50 females (44%), with one patient of unknown sex.

3.1. Clinical presentation

The most common clinical presentation in OS was hoarseness of voice, which was found in 101 patients (86.3%). Hoarseness varied in severity, with the onset described as either gradual or sudden. Other common symptoms on initial presentation were dyspnea (n = 47, 40.1%), cough (n = 15, 12.8%), and dysphagia (n = 15, 28.8%). Less common presenting symptoms are further described in Table 2. On examination, 40 patients (34.2%) had audible murmurs. The most common comorbidity described was aortic aneurysm (n = 48, 41%), followed by pulmonary hypertension (n = 41, 35%), mitral stenosis (n = 20, 17%), and hypertension (n = 14, 12%). Less common comorbidities are tabulated in Table 3.

3.2. Diagnostic workup

There were several modalities reported in the workup of OS. The most common modality was laryngoscopy to visualize vocal cord dysfunction (n = 90, 77%). In other patients, cardiovascular and mediastinal abnormalities were noted on CT scan (n = 72, 62%), chest x-ray (n = 63, 59%), and echocardiography (n = 39, 33%). Among all patients, the most common mediastinal abnormalities were thoracic aortic aneurysm (n = 48, 41%), pulmonary artery dilatation (n = 36, 31%), cardiomegaly (n = 31, 26%) and left atrial enlargement (n = 30, 27%) (Table 4). Interestingly, 38 patients (32.4%) had abnormal EKGs on initial evaluation.

3.3. Management

In total, 41 patients (35.0%) received some form of surgical intervention. Another 44 patients (37.6%) received conservative treatment, including non-surgical therapies. It was unknown whether the final 32 patients

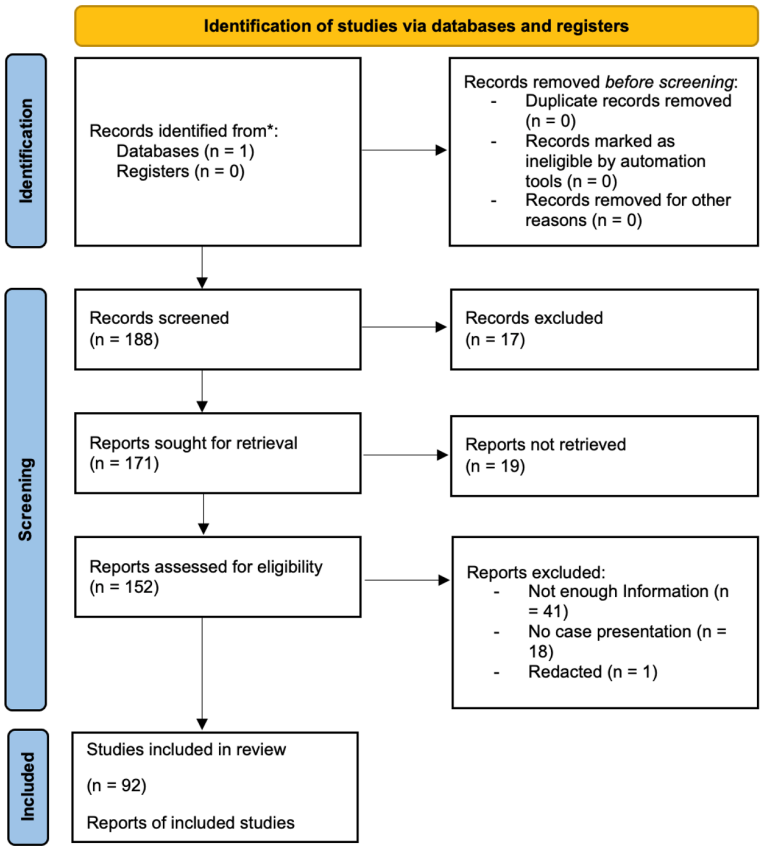

Figure 2. PRISMA flow diagram for article selection.

Table 1. Demographic characteristics of included patients

Characteristic	Number of patients	Percentage of patients
Sex[a]		
Male	66	56.90%
Female	50	43.10%
Age (years)[b]		
<10	2	1.75%
11-19	7	6.14%
20-29	13	11.40%
30-39	15	13.16%
40-49	10	8.77%
50-59	13	11.40%
60-69	18	15.79%
70-79	21	18.42%
80-89	15	13.16%

[a]: the sex of one patient was not reported; [b]: the ages of three patients were not reported.

Table 2. Clinical findings for patients with Ortner's syndrome

Clinical symptom	Number of patients	Percentage of patients
Hoarseness of voice	101	86.32%
Dyspnea	46	39.32%
Murmur	40	34.19%
Cough	15	12.82%
Dysphagia	14	11.97%
Edema	11	9.40%
Dysphonia	10	8.55%
Chest Pain	6	5.13%
Hemoptysis	6	5.13%

Table 3. Past medical history of included patients

Comorbidities	Number of patients	Percentage of patients
Pulmonary hypertension	41	35.04%
Mitral stenosis	20	17.09%
Hypertension	14	11.97%
Congenital heart disease	13	11.11%
Connective tissue disease	5	4.27%
COPD	5	4.27%

Table 4. Radiologic findings of included patients

Finding	Number of patients	Percentage of patients
Aortic aneurysm	48	41.03%
Cardiomegaly	31	26.50%
PA dilation	36	30.77%
LA enlargement	30	25.64%

(27.4%) received surgical treatment or not. The type of surgical intervention was wide-ranging and considered based on the underlying comorbidity. In cases where an aneurysm was determined to be a cause of OS, open aortic repair or thoracic endovascular aortic repair (TEVAR) were the most common treatment options considered. In patients with congenital heart disease, such as atrial septal defect (ASD) or ventricular septal defect (VSD), surgical closure of these aberrations was performed. Some other procedures were reported as well such as medialization of vocal cords, thyroplasty and angioplasty. Ultimately, 35 patients out of the 41 who were operated on reported improvement in their hoarseness after surgical treatment (85.4%).

4. Discussion and evaluation

Left recurrent laryngeal nerve injury can lead to unilateral vocal cord paralysis and hoarseness of voice. The differential diagnosis of this condition is far and wide. When this occurs due to underlying cardiovascular pathology, it is known as Ortner's syndrome or cardiovocal syndrome. Though first described in 1897 by Nobert Ortner, only a handful of cases have been reported on in the literature over the last half-century. The present analysis is a conglomeration of the reported cases in the literature and elucidates several key characteristics surrounding the diagnosis and management of Ortner's syndrome.

Most saliently, this review shows that OS can occur in patients of all ages and in patients with many different cardiovascular pathologies. Early on, mitral stenosis was thought to be the primary cause of OS (*7*). In fact, our analysis found that the most common cause of OS in the literature between 1955 and 1990 was mitral stenosis. However, from the 1990s onwards, vascular lesions (particularly thoracic aortic aneurysms) were the most common cause of OS among the cases included in this analysis. This epidemiological shift may be due to improved early detection and treatment of mitral stenosis.

Taking all patients into consideration, we found that the most common etiology of OS in the literature is thoracic aortic aneurysm (41%) as opposed to left atrial enlargement (26%). This is in line with Yuan SM's work which reported that left atrial enlargement accounts for approximately 8% of all reported cases of OS (*96*). In general aortic aneurysm related to any etiology (traumatic (*97*), mycotic (*98*), dissecting aneurysm (*99*), infection (*100*) have all been related with this condition. Thus, it is important for senior surgeons to suspect aortic aneurysm in cases of de novo hoarseness.

Interestingly, cardiovascular pathologies affecting the great vessels aside from the left heart and aorta can also lead to OS. For example, the present review includes several cases of OS in patients with pulmonary artery dilation, in the setting of either primary pulmonary hypertension (*54*) or secondary pulmonary hypertension associated with chronic thromboembolism (*58,101*). In these patients, OS manifests when the dilated pulmonary artery compresses the recurrent laryngeal nerve against the aorta. We also found 13 cases of OS that were associated with congenital heart disease. These conditions included ASD, VSD, Ebstein's anomaly, patent ductus arteriosus with or without associated aneurysm (*25*), and double outlet right ventricle associated with aortopulmonary window. It is possible that these patients developed Eisenmenger syndrome resulting in compression of the left recurrent laryngeal nerve against the aorta.

Given the rarity of OS, it is generally not part of the initial differential diagnosis of hoarseness of voice. Therefore, to confirm a diagnosis of OS, one must have a high index of suspicion, and, at times, multiple diagnostic imaging modalities are required. In patients presenting with hoarseness, a chest x-ray is usually the primary imaging study ordered which can emphasize any underlying condition such as a lung mass or cardiomegaly. Besides an x-ray, symptoms of hoarseness should also propagate a referral to specialist for laryngoscopy, which most of the patients in our analysis received. Laryngoscopy confirms the presence of vocal cord dysfunction although VC palsy can also be seen on the CT of the neck (*102*). Echocardiography is one of the most routine procedures done in to evaluate structural integrity of cardiovascular system, and is an important consideration given that cardiovascular abnormalities seem to be the most common etiology of OS. Regardless, a prompt diagnosis is critical because the underlying condition can be a risk factor for other complications such as dysphagia and/or airway obstruction.

Treatment of OS entails direct management of the underlying condition. Since hoarseness is the main presenting symptom, the prospect of recovery from hoarseness is dependent on its duration and severity (*45*). The decision to intervene is also dependent on other factors such co-morbidities, surgical risk, and patient's readiness. Indeed, 27% of our patients opted for non-surgical management, indicating how important it is for providers to assess each patient's case. In this group, patients were managed with conservative management or no treatment at all. Still, among the patients who pursued treatment, 35 (85%) had improvement in symptomatology, indicating that OS is a potentially reversible syndrome.

In conclusion, OS is a rare condition and can remain undiagnosed for a long period of time. Hoarseness is its landmark presenting symptom. It can present in any age group, but suspicion should be high if a patient has history of pulmonary hypertension or cardiac pathology. From a historical perspective, mitral stenosis was considered a primary cause of the syndrome. However, in the last two decades, aortic arch aneurysms and dilation of the pulmonary artery from pulmonary hypertension

have emerged as a primary etiology. In either case, heart murmur is the most common physical exam sign and the decision to intervene depends on many factors, such as age, comorbidity, and patient willingness. Notably, surgical intervention resolves OS in most cases.

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