Unilateral Vocal Fold Paralysis

Introduction

Unilateral Vocal Fold Paralysis is a disease often encountered by Otolaryngologists. Its causes are multifaceted, so understanding these causes is necessary for both diagnosis and treatment. While patients may be referred following a surgical complication, other cases of vocal fold paralysis present to the clinic as voice changes.

Brief Outline

In this discussion, we will begin with a brief review of anatomy and physiology of the laryngeal structures and involved neurological structures. Then,

Anatomy

Neurologically, the true vocal folds are enervated by the Recurrent Laryngeal Nerve and the Superior Laryngeal Nerve. Nerve fibers begin at Cerebral Cortex and descend through the Internal Capsule. From here, these fibers synapse at the Nucleus Ambiguus in the Medulla. The Nucleus Ambiguus manifests its actions through the cranial nerve X, the Vagus Nerve. The Vagus Nerve descends bilaterally along with the Common Carotid Artery and Internal Jugular Vein.

The Vagus Nerve gives off both the Superior Laryngeal Nerve and the Recurrent Laryngeal Nerve. Of these, the SLN branches into an internal and external branch. The Internal Branch provides sensation to the larynx above the level of the TVF while the Recurrent Laryngeal Nerve provides sensation below. The External branch of the SLN provides enervation to the Cricothyroid muscle alone. The Recurrent Laryngeal Nerve provides enervation to the Posterior Cricoarytenoids, Lateral Cricoarytenoids, Thyroarytenoids, and the Interarytenoid. It is important to note a couple reminders regarding the muscles. The Posterior Cricoarytenoids is the only abductor of the TVFs. Also, while most muscles are paired, the Interarytenoid is not paired and shares enervation from both Left and Right RLN.

With regards to anatomy, it is important to also remember the different paths of the RLN on the left and right side. On the left, the RLN travels into the mediastinum where it loops around the Arch of
the Aorta prior to penetrating the larynx thus making the left RLN more vertical at its point of penetration. The Right RLN loops around the Subclavian, and due to this shorter path, it returns and penetrates more horizontally. This difference due to embryological changes following the Right 6th arch vessel becoming the Subclavian artery while the Left 6th arch vessel becomes the Arch of the Aorta.

An anatomical anomaly may occur with regards to the recurrent laryngeal nerve. Approximately 5 out of 1000 people have a nonrecurrent laryngeal nerve on the right. A nonrecurrent laryngeal nerve occurs only on the right, except in the rare case of situs inversus. It branches from the vagus nerve at the level of the cricoid cartilage and enters the larynx directly, without looping around the subclavian artery. This anomaly occurs in conjunction with a retroesophageal right subclavian artery.

At this point, please refer to the PowerPoint presentation, as the next several slides demonstrate the muscular anatomy of the larynx. It is important to remember the penetration sites of the SLN and RLN to aid in both surgical procedures and for understanding regarding possible injuries. The internal division of the SLN penetrates the thyrohyoid membrane with the laryngeal artery and supplies sensory innervation to the larynx. The external division of the SLN provides motor innervation to the cricothyroid (CT) muscle.

At this point, our basic anatomy has been reviewed but a quick note a few terms and processes. First, defining the terms paralysis and paresis is important. Paralysis refers to complete immobility of a muscle although muscle tone may be noted secondary to re-innervation. Paresis means hypofunction or hypomobility secondary to neurologic injury.

Having mentioned re-innervation, a further explanation here is needed. The concept of re-innervation is also referred to as Synkinesis.

Paralysis first begins with axonal injury. Following this injury, there is Wallerian Degeneration, which we recall as step by step breakdown of the axon distal to the injury. Following this breakdown, there is regrowth as the proximal stump sends out nerve fibers to reconnect. However, in this step, fibers from the proximal neuron may reach any distal site, implying that adductor nerves may innervate abductors (PCA) and abductor nerve fibers may innervate adductors. While the TVF will remain paralyzed, the reinnervation helps by providing neurological stimulation in order to maintain muscle tone. At this point, the level of regeneration and subsequent strength of the abductors and adductors helps determine the final position.

On the final note regarding anatomy, there are generally 4 terms used to refer to the position of the TVF. They are the following:

- median (midline),
- abducted (lateral),
- paramedian (halfway), and
- intermediate (any position between the midline and halfway).
**Etiology of TVF Paralysis**

TVF paralysis has many causes, but five causes cover nearly 75% of cases. In order of frequency, these are Malignancy (25%), Surgical Trauma (25%), Non-surgical Trauma (11%), Intubation, (7%) and Neurological Disorders (7%). In approximately 20% of cases, the cause is technically listed as Idiopathic, although often a future cause is often discovered. Now, we will go through each of these topics with some in more complex detail.

**Malignancies**

As otolaryngologists, laryngeal and thyroid cancers are readily encountered and easily remembered as causes for TVF paralysis. However, several other cancers can cause paralysis, usually through compression from mass effect. The Left TVF is most affected due to its descent into the mediastinum as it loops around the Arch of the Aorta. Pulmonary cancers, especially bronchogenic carcinomas, which invade into the mediastinum are the most common of malignancy-related causes of TVF paralysis. Other malignancies causing paralysis include the following: Mediastinal (Thymoma, Teratoma, Lymphoma), Carotid Body Tumors, and a Paraganglioma near the skull base.

**Iatrogenic Surgical Trauma**

Surgical trauma can arise following a number of operations that occur in the neck where the RLN is at risk. The most common Otolaryngologic surgery during which trauma occurs is a Thyroidectomy. While all surgeons aim to trace the path of the nerve prior to removal of the thyroid, it is not uncommon for the route of the RLN to be altered and tortuous in the case of a large Goiter. While this injury can occur during removal of a thyroid for Thyroid cancer, anecdotal evidence tends to believe in the idea that a large goiter removal is more difficult and has an increased risk of damage to the RLN.

Typical rates of injury of the RLN in Thyroid surgery can range anywhere from 0.3% to 13.2%. This rate make Thyroidectomies the surgery with the second highest rate of damage to the RLN. Anterior Cervical Spine Surgery is currently viewed as the most common surgical cause of injury to the RLN. Rates for injury following this neurosurgical procedure range from 2% - 21.6%. Thoracic Surgery, including Aortic Arch Repair, Esophagectomy, Pulmonary Resection, and Mediastinoscopy, poses a significant risk to the RLN, although these percentages are quite low. Finally, vascular surgery in the neck, namely Carotid Endarterectomies, can also cause damage to the RLN, but again, the rate of injury in these procedures is minimal at best.

**Intubation**

Intubation can also serve as a cause for RLN injury, although this damage occurs through different means. Referring to a cross-section of the larynx, remember that the Anterior Rami of the RLN pierce the larynx in the subglottis just at the level below the TVFs. Injury through intubation is though to occur secondary to excessive cuff inflation along with placement of the cuff in this area. Further, it is likely that this compression only truly leads to damage following lengthy surgeries, those upwards of at least 1-2 hours.
Neurovascular Diseases

At this point, we will touch on a couple of neurovascular syndromes which may present as TVF paralysis in addition to other findings. At this point, refer to a picture of the brainstem. Reviewing anatomy, the Vertebral arteries proceed superiorly where they unite to form the Basilar artery. Along the way, they branch off into several vessels which supply the brainstem – the Superior Cerebellar Artery, Anterior Inferior Cerebellar Artery (which runs just inferior to the pons), and the Posterior Inferior Cerebellar Artery (which runs at the level of the medulla). These vessels being quite miniature are easily susceptible to strokes.

The most common brainstem stroke is of the Posterior Inferior Cerebellar Artery. The manifestation of the patient is known as PICA syndrome, Wallenberg’s syndrome, or Lateral Medullary Syndrome. It often presents as Vertigo, Ipsilateral Hemiataxia, Dysarthria, Ptosis, Miosis, and/or Hoarseness. These patients are often more disturbed by the Vertigo and Hemiataxia, but rarely, hoarseness can be the first symptom noted.

The second most common brainstem stroke is that of the Anterior Inferior Cerebellar Artery. This usually manifests as Vertigo, Unilateral Ipsilateral Deafness (secondary to Laryrinthine Artery Ischemia), Ipsilateral Facial Weakness and Ataxia, and hoarseness. Again, Hoarseness is not likely their first manifestation, but one should be prepared to note this syndrome can present in this way.

Neurological Diseases

A vast array of neurological disorders can present with voice changes and may cause vocal fold paresis and paralysis. While this list of diseases is extensive, in the following paragraphs, we will discuss a few of these diseases and their presentation.

Multiple Sclerosis is an autoimmune disorder which occurs secondary to a response directed against Myelin, the protein which forms the sheath around nerves. It typically affects women in their 20s-40s. While not uncommon, the disease remains a mystery with regards to several aspects. First, the exact cause is unknown, but viral, genetic, and environmental factors have been implicated. It typically presents with either vision changes or muscle weakness of the extraocular muscles. It eventually progresses to include complete loss of muscle control and function. There are two general forms, a relapsing episodic form and chronic progressive form. It is important to realize this as patients may present in between episodes or may notice some symptoms between episodes of worsening. Hoarseness is often associated and may even be the first symptom.

Amyotrophic Lateral Sclerosis, or Lou Gehrig’s Disease, is one that affects upper and lower motor neurons. As such, it causes complete atrophy of muscles due to the loss of neurological stimulation. It tends to affect breathing and swallowing functions first with several of these patients requiring a tracheotomy tube early in the disease process. Again, these patients may also present with voice changes and demonstrate paresis and paralysis of the laryngeal musculature.

Syringomyelia is a fairly rare disease which occurs secondary to the formation of a cyst in the spinal cord. While this cyst may arise at any location of the spinal cord, it has more devastating effects when located high in the cervical region or even in the brain stem. Due to mass effect, patients can develop TVF paralysis, ipsilateral tongue wasting, and ipsilateral facial sensory loss secondary to
compression of cranial nerve 5. When the cyst is located in the brainstem, it is also referred to as syringobulbia. It is typically a disease that spares proprioception, pressure, vibration, and touch intact.

Myasthenia Gravis is an autoimmune disorder occurring secondary to antibodies directed against Acetylcholine receptors at the post-synaptic junction. It often presents as fluctuating muscle weakness and fatigability. It typically affects muscles that are small and used repetitively. As such, extracocular muscle weakness is prominent and often the first sign. As with most autoimmune disorders, it is typically seen in females who present with complaints that begin to occur in the afternoon. There are five classes for MG ranging from minimal eye weakness to severe with associated limb abnormalities or bulbar abnormalities affecting the cranial nerves. Of clinical note, a thymoma, if present, should be excised as there is a strong correlation between MG improving if a thymectomy.

Guillain-Barre disease, also known as Acute Inflammatory Demyelinating Polyneuropathy, is a disease of ascending paralysis which begins in the lower extremities. It is named for Georges Guillain and Jean Alexandre Barre – two French Neurologists. Usually, the disease does not reach the facial muscles; however if cranial nerves are involved, it involves the lower cranial nerves. By attacking the disease causes demyelination. It often follows a respiratory or gastrointestinal infection with several bacteria (ex. Campylobacter) and viruses implicated. 30% of affected patients require mechanical ventilation due to loss of respiratory capacity.

Parkinson’s disease is a degenerative central nervous system disease which occurs secondary to the loss of Dopamine. It was initially presented by Dr. Parkinson in an essay on Shaking Palsy. The typical traits of Parkinson’s disease are the shuffling gait, muscle rigidity, and resting “pill-rolling” tremor. However, patients may present initially with a weak and breathy voice along with sluggish articulation. This is characterized as laryngeal bradykinesia. When performing flexible laryngoscopy, one may note weak vocal fold adduction. Further, the vocal folds may be thinned and bowed (similar to a paretic view) secondary to atrophy of the vocalis. Patients may also have strained voices similar to that seen in spasmodic dysphonia.

Patient Work-Up

The patient work-up begins as with any disease – a thorough history and physical. Due to knowledge of the aforementioned diseases, it is important to question a patient on all symptoms and complaints in order to rule out any neurological disorders. Also, patients should be questioned for having rheumatoid arthritis or gout as these can cause deposits or changes in the joints. To rule out the major cause of TVF paralysis, one should ask all patients with regards to smoking/alcohol use, past surgical history, trauma, and recent infections.

When speaking with patient, it is important to take mental note of the patient’s voice. Features that suggest neurological involvement include vocal fatigue, vocal tremor, weak or breathy voice, vocal strain, vocal stoppage, altered resonance, acquired dysarthria, and associated dysphagia.

After a thorough history, the physical exam along with flexible laryngoscopy is extremely important. While all parts of the physical exam are relevant, evaluation of the cranial nerves is particularly relevant as several of the aforementioned diseases present as a constellation of various issues. As a quick reminder, evaluating the vagus nerve can be performed by checking for palate elevation and uvular deviation – uvula will deviate away from the side of the lesion. Flexible
laryngoscopy is integral in evaluating the patient’s vocal cord function. In addition to viewing the entire larynx for obvious pathology, one should also view the movement of the vocal folds. This is done by having the patient say “ee” then having them sniff. The position of the arytenoids is also important during the exam.

Another exam which can be performed in the clinic to help in the work-up of vocal fold paralysis is the Laryngeal EMG. This test, laryngeal electromyography, aids the physical by demonstrating the level of muscle activity. Due to easier access, the thyroarytenoid muscle is often selected and tested. Three principles are important to remember when viewing the EMG. First, spontaneous activity detected is a sign of fibrillation and implies denervation. Second, recruitment is a principle of muscle with nerve innervation. Muscle that is repetitively stimulated responds with an increase in the number and rate of the motor units. This is a sign of normal functioning muscle or reinnervated muscle. Lastly, motor units on the EMG can occur in small groups but usually less than 3 in one group. If more than 3 are presents, this is a sign of an injury. The value of the Laryngeal EMG, while indicating the activity of the muscle, is to also rule out cartilage or joint dysfunction as a cause for the lack of movement of the vocal fold.

As a quick aside, we will touch on arytenoid cartilage dislocation here. This is often noted in fiberoptic laryngoscopy by viewing an anteriorly overhanging arytenoid. This is an uncommon diagnosis but does occur following neck trauma or intubations. Another thing noted on exam is the changes in the level of the vocal folds when the patient phonates. Finally, it is also noted by the absence of the “jostle” sign. The jostle sign refers to the movement of one arytenoid cartilage which occurs secondary to being “jostled” by the opposite arytenoid cartilage during closure of the TVFs. Again, this diagnosis can be ruled in or out by findings on the Laryngeal EMG.

Work-up here should also continue with a few radiological tests. An MRI of the brain, CT Neck, CT Chest, and CXR would not be unreasonable in trying to identify the cause. However, several authors suggest that a CT Neck/Chest would be adequate unless one feels that a neurological issue is present and in that case a CT Neck and MRI brain would be recommended.

**True Vocal Fold Paralysis in Children**

Following laryngomalacia, TVF paralysis is the #2 cause of stridor and #2 most common congenital anomaly in children. It is typically not bilateral, but if so, then there is often a central nervous system cause. An example of bilateral TVF paralysis is a child is Arnold Chiari malformation, where herniation of the cerebellum and brainstem can cause compression of the Vagus Nerve. Other causes of hydrocephalus in children may also cause compression of the nerve.

In children, causes are typically secondary to birth trauma, with blunt trauma, surgical injury, mediastinal masses, and iatrogenic causes also linked. Surgical causes are predominantly following cardiothoracic surgeries – especially Patent Ductus Arteriosus Ligation and Tracheo-Esophageal Fistula Repair. Children often present with stridor, breathy cry, feeding difficulties, and aspiration. Also, it has been reported that somewhere from 16 to 64% of children recover from paralysis. Therefore, watchful waiting is often the best course with possible placement of a tracheotomy if needed.
Surgical Management

First, there are several decisions to address prior to surgery. As stated, many cases of unilateral TVF paralysis resolve so a fair amount of waiting is needed prior to deciding to perform a case. While the amount of time to wait is debated, most authors suggest 12 months after injury to being an acceptable amount of time. Further, children tend to heal even after delayed periods.

The occurrence of the recovery is greater in children, and some reports say as high as 50% recover. The range for recovery in children is quite long with some case reports demonstrating recovery after 10 years. However, the mean tends to be within 12 months with another peak around 2 years if the paralysis is secondary to neurological causes. In children, injections are favored as this will give the most hope in case there is future recovery. Most injection materials last for several months – with calcium lasting the longest – up to about 1 year.

Surgical management can be broken into three main categories of procedures:

- Injection Thyroplasty
- Framework procedures
- Reinnervation procedures

Injection thyroplasty is often chosen due to the fact that it is temporary, done easily, can be repeated, and does not preclude the chance for recovery. Many materials can be used. Teflon was initially used but is no longer in use due to a granulomatous inflammatory reaction that it caused. Collage and Gelfoam have also been used but also have fallen out of favor. Fat grafts remain frequently used for several factors. Fat is easily re-absorbed in 3-4 months causing minimal trauma, and re-absorption can lead to some long-lasting effects. Also, fat is easily harvested.

Calcium Hydroxyl Apatite is a biologically inert material created by Radiesse and in use since 2003. In comparison to fat, collagen, or fascia, this substance lasts for a much greater amount of time with no studies showing negative scarring or permanent complications. A study from 2010 by Carroll and Rosen showed that in 22 patients with UVFP, approximately 0.5 mL was needed for injection and this persisted for an average of 18 months as noted by voice testing.

Hyaluronic acid gels are either animal or bacterial derived versions of naturally occurring extracellular matrix GAGs. This same material is found in the TVF lamina propria. While it is believed that it should be able to replace the lamina propria, it has shown poor results. Studies suggest that it actually worsens vocal fold vibration if placed superficially. It tends to last from an average of 6 months to even 1 year in some studies.

Carboxymethylcellulose can be used as a preview material because as an injection it only lasts for 2-3 months but can give an idea of what can be achieved by an injection. It does not cause any scarring. Also, it has no risk of biologic infection transmission. It can sometimes be coupled with calcium hydroxyl apatite.

Indications for injection thyroplasty are several. First, their temporary nature is good for patients in whom there is uncertainty regarding the state of paralysis. This is also an easy procedure that can be done in the office as an out-patient. It benefits those patients with mild glottic gap (1mm).
Finally, it requires less patient compliance. Contraindications include a posterior gap and glottic gaps greater than 3 mm. While an injection thyroplasty can help these patients, there is not as much of an effect posteriorly.

**Framework procedures** include medialization laryngoplasty and arytenoid adduction or arytenoid pexy. Medialization laryngoplasty is a procedure in which a small window in created in the thyroid cartilage. An implant of some sort – examples include GoreTex Strips, Silastic strips or blocks, or hydroxyapatite – is placed through the window to create stability and medialize the TVF. The benefits of this procedure are that it is reversible, can be “fine-tuned”, and augments the TVF in all 3 dimensions (anterior-posterior, superior-inferior, and medial-lateral). This procedure is performed under local anesthesia so fine adjustments can be made the size of a block that is inserted to increase the Gore Tex strip. There has been no differences shown as far as patient outcome with regard to use of different materials although many surgeons tend to begin the operation with a block and then use strips for adjustment.

**Arytenoid surgery** is done as an adjunct to other procedures are rarely if ever alone. Arytenoid pexy consists of the placement of a suture anchoring the muscular process of arytenoid to thyroid cartilage. This procedure achieves 3 things with respect to Vocal Process – lowers position, medializes & stabilizes the TVF, and rotates the arytenoid cartilage. It is typically recommended in patients if Maximum Phonation Time is less than 5 seconds. Again as mentioned, it is usually performed as an adjunct to Medialization Laryngoplasty.

The final type of surgery that can be performed is **re-innervation**. Re-visiting the idea of synkinesis, the surgery is founded on the concept that nerve fibers from surrounding areas will restimulate the muscles of the larynx. Re-Innervation is beneficial because muscles tend to atrophy unless they maintain innervation. Whether this is done naturally or surgically, it helps to create stability to the TVF which allows for better contact and voice. Reinnervation of the TA muscle restores tension resulting in a more normal mucosal wave. Reinnervation of the PCA and LA muscles stabilizes the arytenoids and prevents inferior displacement of the vocal process, which may occur in some patients.

Several nerves can be chosen although the ansa cervicalis, phrenic, and preganglionic sympathetic neurons are preferred. Typical connections include Ansa-RLN stumps, Hypoglossal-RLN stumps, and Ansa-Thyroarytenoid pedicle. As this procedure is definitive, 15 months waiting period is usually advised prior to surgery. Signs of reinnervation can be noted as early as 4 months post-operatively. Thyroid cancer was typically the most common cause of RLN sacrifice which led to a re-innervation procedure. The best way to measure a patient’s improvement with regards to this surgery is maximum phonation time.

In a meta-analysis, most patients were followed around 4 months after surgery. Their improvements were measured by Maximum Phonation Time which was nearly doubled in all studies. Glottic gap was also improved in all studies that reported this finding. While these findings make reinnervation a viable possibility, it is not performed alone with any frequency and not compared to injection thyroplasty or medialization. Most studies reporting on Re-innervation combine this procedure with injection or medialization procedures. Only six studies have demonstrated viable
results in humans. There has also been no direct comparison with trials comparing re-innervation with thyroplasty.

**Discussant’s Remarks 2011-02-25 Vocal Cord Paralysis by Dr. Underbrink**

That was a very good presentation Dr. Venkatesan, very thorough and included a discussion of a lot of causes for paralysis other than the most common which was nice because we tend to focus on or have tunnel vision with respect to what we see on exam and not necessarily incorporate what we see among the more unusual findings. With respect to the treatment of these, I like to think of it along the lines you did. There are temporizing procedures such as injection medialization and there’s permanent: when you’re manipulating the framework, doing an arytenoid pexy which is what you described, or arytenoid adduction which is a little bit different.

And then there’s of course re-innervation where you actually know that you’re going to sacrifice a nerve, and so you have no place to go. The thyroplasty is sort of in-between. It’s a reversible procedure. You can place a block and the patient that might recover, who’s a professional voice user who wants something more permanent doesn’t necessarily have to be removed and will recover and not lose too much function with just a block as long as you don’t manipulate the joint.

It’s also interesting that you bring up laryngeal EMG. That’s also very relevant in that as you showed some of the more subtle presentations that you’re looking at an arytenoid is sort of overhanging and the level of which you can’t really make out on a two-dimensional picture endoscopy but that’s also similar to what happens on a dislocation and you’re right, I have a patient that’s recent to the clinic that’s going to have a laryngeal EMG because that can be easily diagnosed and that would indicate a different procedure.

I agree that I like to use injection medialization in children that have a problem that hasn’t recovered or if they’re having some sort of dysphagia. Usually kids recover completely or recover some function like swallowing and don’t necessarily present with the same symptoms as an adult with regard to dysphagia or difficulty feeding, sometimes not much of an issue. Generally they maintain hoarseness and might need a better functional outcome which is the reason to go ahead and do injection medialization.

Many times with respect to the re-innervation procedure, it’s a great procedure for when you know you’re going to cut the nerve and you have a paraganglioma. Many times when you’re doing thyroid surgery which is a much more common surgery, and you close area, when you go back to do the re-innervation, you almost can never find the stump of that nerve. It’s impossible. So that the most common procedure I’ve been associated with or that I’ve done is taking a small cup of muscle from where the ansa has innervated one of the strap muscles and actually implanting that through a thyroplasty and it usually takes as long as you can implant it into the bed of the thyroarytenoid muscle. That provides just the tone and it’s amazing that after about three months the patient has to be willing to undergo three months of breathiness with no recovery until re-innervation occurs.

Yours was a very good talk, overall very thorough. Thank you.
BIBLIOGRAPHY


