Dr. Linda Yin:

Hi everyone, welcome back to another episode of ENT in a Nutshell. I am joined again today by Dr. Semirra Bayan. Dr. Bayan thanks for coming back.

Dr. Semirra Bayan:

Great to have the gang back together talking about glottic cancer, Linda.

Dr. Linda Yin:

Yes, perfect. We're talking about early glottic cancer today, so that means T1 or T2 cancers that come from the true vocal cords. Now larynx cancers are of course a huge subject in both laryngology and head and neck cancer which are two of our primary subspecialties, but today we're talking specifically again about early cancers only. For details on advanced cancers and the cancers of other sub sites of course, other podcasts are forthcoming. Let's go on to presentations. So how does a patient with an early glottic cancer typically present to your clinic?

Dr. Semirra Bayan:

Well, most often a patient will come to clinic with a symptom of hoarseness. So that's the most common symptom that this presents as. Glottic cancer is pretty unique because it can be caught relatively early secondary to the fact that they'll have changes to their voice even with smaller lesions. However, hoarseness we learned in prior talks can be a lot of different things. So what type of hoarseness do they present with? Well, generally it's raspy and strained though with larger lesions you can have a more breathy and strained quality to the voice. So the type of hoarseness can vary, but most often it's hoarseness.

Dr. Semirra Bayan:

I've had patients in the past also present with global sensation or chronic cough as well. Very rarely will people have trouble with swallowing or pain with swallowing as an original presentation, even referred otalgia just because of the early nature of these cancers it's relatively rare to have. Hemoptysis is ones that maybe they discuss in the books but again, because of the small nature of these lesions it's unusual to present with hemoptysis and things like airway obstruction, again unless you have a large mass but that's often not seen in its early stages.

Dr. Linda Yin:

So how about the epidemiology of this disease, how common are early glottic cancers in the United States?

Dr. Semirra Bayan:

Laryngeal cancer is the second most common head and neck cancer in the US, most commonly you see it in men though... but women obviously get glottic cancers as well. Between 10 to 15,000 cases are seen every year in the United States. Glottic cancer itself is the most common site of laryngeal cancer. Again, early cancers are common in the glottis and the most common ones in the larynx are glottic cancer. The incidence of them has decreased with time and that's likely secondary to declining rates of smoking and alcohol abuse, but while the incidence is decreasing there have been reports showing actually an increase in numbers of patients under the age of 30 years or patients who are non smokers where that actually has changed and is on the rise.

Dr. Linda Yin:

We alluded to this already, but what are some of the biggest risk factors for developing this disease?

Dr. Semirra Bayan:

As we mentioned before smoking and alcohol use are the probably biggest factor that we traditionally see, patients of prior radiation are another group that you can have glottic cancers in. HPV is one that's still up for discussion. Patients who have recurrent respiratory papilloma for instance, there're reports of conversion. Again, that's not quite confirmed yet, we don't know how often that does happen. You can't have HPV related cancers too, though again the prevalence of that I think is still not quite defined. Others talk about exposure to carcinogens like metals, plastics or wood dust. And then as we had mentioned in the prior question you can see this in non-smokers or people have no other exposure history, and I think it really brings into the question what other factors playing a role here. That brings up again the possibility of HPV related cancers, potential genetic contributors or some other type of viral contributor that could potentially be playing a role, we still don't understand that though.

Dr. Linda Yin:

Moving on to physical exam now. When you're examining a patient in clinic, what are you looking for on endoscopy?

Dr. Semirra Bayan:

So as we talked about in our Benign Lesions podcast, a good exam is so important and that's especially important when you're examining someone with cancer. So you not only want to look at the lesion itself, but you want to know where is it. So the first thing to look at is, is it on the medial aspect of the chord, the superior aspect of the chord, what portions of the chord does it involve? You want to look to see if there's extension into the ventricle or across the anterior commissure, as well as extension into the sub glottis. The evaluation of the movement of the vocal cords is very important because that changes the stage if you have a vocal cord that is not moving, and then looking at the composition of the lesion itself.

Dr. Semirra Bayan:

When I say that I mean going beyond seeing if something is [inaudible 00:04:38], or leukoplakic, or exophytic, you're looking at the vasculature. So the glottis is such a different type of organ than other areas of the head and neck, because I think cancers look a little different there. It's unusual in that you have those three layers of the vocal cord, you have your epithelium, your superficial lamina propria and then you thyroarytenoid muscle. The superficial lamina propria is pretty important, that's the meat and potatoes of how we're voicing, and it has within it the blood vessels of the vocal cord, and it's those blood vessels that I pay the most attention to. So in 1966 Jako and Cline, Souza first commented on changes in the vasculature that you can see with dysplasia in carcinoma. So if you think about how a cancer grows and survives, the one big thing that has to happen is angiogenesis or the formation of new blood vessels. So cancer needs blood vessels to grow and survive. What you see in dysplasia settings is often an obscuration of the underlying blood vessels where you can't see those.

Dr. Semirra Bayan:

So thickening of epithelium, region vascular stippling within the dysplasia. Once you get to more severe things like CIS or cancer itself, which you'll see is more aberrant and complex looping microvasculature, and really there's no other area at least in the head and neck that you can see that as well than you can

on the glottis. So I get a very close look and I look at those blood vessels, and that's a very important part not only in diagnosing and understanding, "Okay, is this something I should be worried about or not?" But then once you've treated a patient for cancer, it's also a great way to monitor too by studying those blood vessels. So it's all about the blood vessels.

Dr. Linda Yin:

All right, and what about the lesion itself... the cancerous lesion, what does that typically look like?

Dr. Semirra Bayan:

It can vary, you can see it presenting exophytically, it can be an ulcerated lesion, sometimes you'll have an area of leukoplakia overlying it with some underlying erythema. At times lesion can be friable or erythematous. You can have erythroplakia as well. So there's a variety of ways that it can often present.

Dr. Linda Yin:

Okay. Outside of the scope exam itself focusing specifically on the true chords, anything else or any aspects of the physical exam to pay attention to?

Dr. Semirra Bayan:

Well, was part of a good flexible exam, you want to make sure there's no other cancers in the upper aerodigestive tract, so that no other mucosal changes that you see in anywhere along the nasal pharynx to the larynx. I usually do a good neck exam as well, palpate make sure there's no [inaudible 00:07:11]. The only other aspect that at least in a voice clinic we often will do is evaluate the quality of the voice. So we pay attention to the kind of pretreatment vocal quality by getting a sampling of the voice, as well as in most instances obtaining acoustic and aerodynamic measures. That can be helpful in the post operative setting. It creates a more objective marker to kind of see the way the patient's voice improved, and then also our kind of numbers for the patient to look at to see how they've improved as well.

Dr. Linda Yin:

What are some other conditions that are on your differential diagnosis for early glottic cancer?

Dr. Semirra Bayan:

Well, if you have a patient that's an active smoker you can sometimes see laryngitis sicca. Which can be pretty extensive and can sometimes look like cancer but always kind of have that in the back of your mind. Usually, the epithelium will look inflamed, you'll have thick crusting that'll sit over the vocal cords. Hyperkeratosis is another one that can sometimes seem like cancer though it's not, and that'll present often as large areas of leukoplakia. You can have precancerous lesions which we discussed a little bit before that can be mild, moderate or severe dysplasia or carcinoma in situ. Papilloma can sometimes look like cancer and cancer can sometimes look like papilloma. So you have to be very careful especially in the adult in diagnosing papillomas. You can have other benign vocal fold lesions as well. Polyps and granulomas are probably the ones most often that are either mistaken for cancer or cancer is mistaken for it. And the last few ones would include infections like laryngitis. So a fungal laryngitis is a type of leukoplakia that you can find and it could sometimes be mistaken for cancer or vice versa.

Dr. Semirra Bayan:

The more uncommon types of fungal laryngitis like blastomycosis can actually look like cancer, and be treated as cancer but obviously not be that. Then lastly is autoimmune disorders like GPA, sarcoid lupus and relapsing polychondritis.

Dr. Linda Yin:

It can always be sarcoidosis.

Dr. Semirra Bayan:

Always be sarcoidosis.

Dr. Linda Yin:

All right. Now, moving on to pathophysiology. So I think it's important before we go any further in talking about the disease process to better define the anatomy of the glottis for the listener. Can you give us a brief overview, we already talked about the different layers but also, talk about different components anatomically to the glottis.

Dr. Semirra Bayan:

Yeah, so the glottis itself refers to the vocal cords. So it's the vocal cords and a portion of the... arytenoids is considered the glottis. The layers of the vocal cords go from superficial to deep. So you have your epithelial layer which is a stratified non keratinizing squamous epithelium. This is the origin of your glottic squamous cell carcinomas. You have your superficial lamina propria, which is varying degrees of collagen and elastin. As you go deeper there're different layers to this superficial lamina propria. As we mentioned before that's our meat and potatoes. That's what we use to voice, that's what helps our vocal cords vibrate. You have your thyroarytenoid muscle underneath that, which includes both thyroarytenoid and your vocalis muscles, and then above the glottis is the supraglottis. So that involves the ventricle, which is the space in between the true and false chord that's the superior boundary of your glottis, and then below your glottis is your subglottis. Usually that's defined as starting a centimeter below the upper surface of the true vocal cords.

Dr. Linda Yin:

Which of these components do you need to achieve a good voice after surgery?

Dr. Semirra Bayan:

So, that's a great question. There are two big things that you need to attain a good voice and that's surgery or no surgery. One of those is glottic competency, so how well your glottis can close and the other is mucosal pliability. So the mucosal pliability is secondary to our superficial lamina propria. So again that's an important aspect of how we voice. So when you're treating early disease like the ones we're discussing, you have to have a really healthy respect for the mucosal pliability portion of how we voice, and that'll kind of segue into some of the other things hopefully we'll talk about a bit later.

Dr. Linda Yin:

Can you discuss the barriers to early spread of glottic cancers, compared to cancers that involve the supraglottis and the subglottis?

Dr. Semirra Bayan:

Yeah, that's a great question and I think that comes into play quite a bit when we are talking about early cancer. The big player in our barrier in early cancer is our conus, so our conus elasticus that's our inferior lateral barrier. That extends from the cricoid cartilage to our vocal ligaments. When you move past the conus most lateral to that is our paraglottic space. So once a cancer has invaded or gone past the conus and gone into the paraglottic space that upstages your cancer. So conus is a big and very important barrier. Everything inside the conus does not have a lot of lymphatics and because of that, that's why early cancers don't tend to have lymphatic spread and we'll talk about later, you don't need to do neck dissections for early cancers and it's all thankfully because of the kind of conus elasticus.

Dr. Semirra Bayan:

Probably the other barrier that we talk about and probably not enough is this Broyles tendon, right? So that's the insertion of the vocal ligament into the thyroid cartilage, and I think that can be actually a barrier to spread at the commissure, and so he will talk about it also being a weak point. So let's clarify that because that's I think a bit of a debate. Everyone fears the anterior commissure because they talk about once you get past the Broyles tendon you're in trouble. That's true for a certain point, so you have to think about what it's made up of. So the Broyles ligament is made up of the vocal ligament, your thyroepiglottic ligament and the inner perichondrium of your thyroid cartilage.

Dr. Semirra Bayan:

So the commissure itself is part of the vocal cord, it's actually pretty thick. If you have disease that's just confined to that area that's not a dangerous place necessarily to get disease. It can be a hard place to expose but that doesn't mean it's a dangerous area. Now once you go above or beyond that you don't have that same barrier, and that's where you can get yourself into developing more advanced disease. Now you're past the area of where the conus elasticus is, your past that Broyles tendon. You don't have those barriers to spread and that's where you can get more advanced disease once you get above or below that point, but the Broyles tendons actually pretty important because you never want to fear the anterior commissure can be in the right circumstance a pretty safe area to have disease.

Dr. Linda Yin:

Moving on now to carcinogenesis, what is the mechanism behind glottic cancers that develop with cigarette smoking?

Dr. Semirra Bayan:

So historically, about 95% of patients with glottic cancer are smokers. What happens in those situations is the carcinogens causes mutations and most often that's in the p53 gene, and then those changes are what's leading to changes in the laryngeal squamous epithelium. But this cancer can occur in non-smokers and non-drinkers as well, so there's obviously other processes at play in those situations.

Dr. Linda Yin:

Okay, let's talk a little bit about leukoplakia. So we've already kind of thrown this term around a little bit. Does leukoplakia always mean severe dysplasia? Or... I've heard it in that context, but can you define it better for us?

Dr. Semirra Bayan:

Yeah, I think leukoplakia is thrown around quite a bit. It can mean something very different than just dysplasia. So, the word leukoplakia just means white patch. So leukoplakia can be fungal, leukoplakia

compete dysplasia, you can see leukoplakia as cancer but leukoplakia is just describing the lesion itself. It's making absolutely no diagnosis.

Dr. Linda Yin:

So in other words, a clinical term leukoplakia should really be distinguished from the pathology that we see. Pathologically now when we talk about precancerous lesions in the glottis, what does that look like and what does the spectrum look like?

Dr. Semirra Bayan:

So you can have a spectrum that starts with hyperplasia, which is just an increased number of cells. I consider it almost like a callus, say the thicker epithelium that you can see for instance in smokers, that's not necessarily a risk factor for malignancy. Then you get into your dysplasias, which we could probably have pathologists sit here and look at slides and argue over what's mild, moderate or severe, because I think there's somewhat of a subjectivity to it based upon the pathologist that's looking at it. When it comes down to in defining mild, moderate or severe, is the level of amount of nuclear abnormalities that are seen within the cells and then the depth of those abnormalities. So mild involves a little less of the epithelium than moderate, and then moderate a little less than severe. Again, it's all relatively subjective. So while they do have some grading obviously that goes on in making those decisions, you can also have different pathologists make different diagnoses on the same slides.

Dr. Linda Yin:

And I think because of that subjectivity I've heard a lot of different rates thrown around for the rate of malignant transformation, for severe dysplasia into cancer. This is heavily pimped sometimes of residents, but can you talk a little bit about the risk of malignant transformation and what that really is for severe dysplasia?

Dr. Semirra Bayan:

I can give you a percentage today. I think you can read different types of literature that will give you slightly different percentages. As a rule, I typically quote around 30% chance of it ever transitioning into a malignancy once you get to the more severe stage. When you're talking about dysplasia, I think the more severe it's graded the higher risk that you have at transitioning to malignancy. That's what you should really take away from that, and that delves a little bit into severe dysplasia and the concept of severe dysplasia and carcinoma in situ, which again pathologists could debate, is it the same thing or two different things? But either way severe dysplasia and carcinoma in situ I treat like cancer. Now to distinguish severe dysplasia and carcinoma in situ from cancer, the only difference between the two is invasion of the basement membrane of the epithelium. So that transitions a little bit into the importance of obtaining a good biopsy and the need when you have dysplasia especially severe dysplasia to treat completely.

Dr. Semirra Bayan:

So you have to think of cancer is not a linear disease, meaning because that difference between dysplasia and carcinoma involves that very thin basement membrane of the epithelium, you just can't guarantee that the particular area that you biopsied represents the entire area of your disease. So sometimes you'll have a pathologist that will tell you that it's carcinoma in situ with small areas of microinvasion. You can't assume that that's the only area that has microinvasion. There's bound to be other areas that have micro invasion and that's not CIS, that's cancer. Because there can always be

pockets of carcinoma especially when you start to deal with things like carcinoma in situ. It's best to treat it entirely and it's best to treat it essentially like it's a cancer.

Dr. Linda Yin:

All right, I think that's a good segue too into our workup since we're talking about biopsies. So tell me a little bit about how you choose to biopsy these patients, are you doing it in the office or in the operating room?

Dr. Semirra Bayan:

I tend to not be a fan of doing things in the office, unless the patient for some type of medical reason cannot tolerate a general anesthetic. The reason being is you have more control in the operating room. In the office, you always run the risk of not necessarily taking enough tissue. So that means you just wouldn't get a representative sample of tissue for diagnosis. There you are looking at something that looks like cancer, and they can't tell you it's cancer and now you're having to go to the operating room anyway to get a biopsy. I mean you've seen the [smoke 00:18:52] biopsy forceps that you can get pass through the scope. They're not very large, you're not getting a large sampling of tissue. So my preference is to get not only a biopsy, but a micro flat biopsy. What that involves is taking the lesion, trying to separate it from the underlying healthy portion of the vocal cord to its depth. So it's allowing you to accurately assess the depth of the lesion, and obtain an appropriately sized piece of tissue and a representative area of glottis that gives you an accurate diagnosis.

Dr. Linda Yin:

Let's move on now to talk about the staging part of the workup. So we already said that we're talking exclusively about T1 and T2 glottic cancers. How are T1 and T2 identified and what is the distinction between them?

Dr. Semirra Bayan:

When we're discussing T1 cancers that involves... T1 are just limited to the vocal folds only. So, it can involve not necessarily the entire vocal cord. For instance, you can have it just at the anterior posterior aspects of the vocal cord, but it's the vocal cords themselves. Within T1s you can have a T1a cancer which is just involving one vocal fold or a T1b or... I remember it is bilateral, so involves both vocal folds. T2 is extension into either the subglottis with the vocal cords included, so vocal cords and subglottis or supraglottis and or any type of reduced mobility but not cord fixation. So you don't necessarily have to have that reduced mobility, but you do have to have at least extension to subglottis or supraglottis.

Dr. Linda Yin:

Let's talk a little bit about vocal cord fixation. So that's kind of the distinguishing characteristic from an early versus a later T3 glottic cancer. So T3s we now have full vocal cord fixation, what is happening when the vocal cord is fixated in terms of actual invasion into surrounding structures?

Dr. Semirra Bayan:

Well, when you see fixation you do have to worry about involvement of the muscles surrounding the arytenoid vocal process. So that could indicate involvement of the thyroarytenoid muscle, the lateral cricoarytenoid muscle, the posterior cricoarytenoid muscle, the interarytenoid muscles. And you can see that in a more advanced stages such as T3 where they're invading the cricoarytenoid joint, or even more advanced disease where you have extra laryngeal spread and you get perineural invasion.

Dr. Linda Yin:

Got it. So, in general vocal cord fixation is a bad sign and takes somebody out of the category of an early glottic cancer?

Dr. Semirra Bayan:

Correct.

Dr. Linda Yin:

How about the risk of nodal disease including occult nodal disease? How do we work that out for an early glottic cancer? Or is workup even necessary for nodal disease?

Dr. Semirra Bayan:

So if you're looking at just T1 cancers, that goes back to some of the stuff we talked about with anatomy. If you're confined within the conus elasticus, embryologically the way the larynx forms is because of that there's very sparse lymphatic drainage within that area confined within the conus. That's why T1 cancers you really don't have lymphatic spread in those types of cancers. So you don't necessarily need to get imaging or workup for nodal disease though I would say you could always get imaging to evaluate for paraglottic spread, which would obviously upstage you. Supraglottis is a little different. That's a sharp contrast because now you're looking beyond the conus, and those have a much higher propensity to spread. So I think if you have the higher stage of disease or the ones where you want to evaluate for lymphatic spread, but very early stages including... I mean most importantly T1, you do not need to get further workup for that.

Dr. Linda Yin:

Good. You talked a little bit about imaging in terms of a CT, is that typically the only image that you need? And are there any other modalities that we should consider for workup?

Dr. Semirra Bayan:

I will sometimes get a CT with contrast. In fact, I usually do it especially if it's a more extensive T1 and that helps characterize exactly where the disease is and identify if there's paraglottic spread, and make sure if there is that there's no invasion to the thyroid cartilage because obviously both of those things upstage you. Sometimes it's a little bit difficult for the radiologist to tell you definitively though if there is paraglottic spread. I've had certain situations where I have obtained an MRI and once that I am worried about it and they can't tell me definitively if it's spread there or not. MRI is not used classically though, more in Europe I think it is than the United States. There have been some studies that show it can be helpful in identifying paraglottic spread but more traditionally use CT, and then PET-CT and a CT chest are generally not used in an early stage. Though obviously if someone has a smoking history, you can obtain a CT chest if there's any concerns for other secondary cancers.

Dr. Linda Yin:

Okay, moving on to treatment. So before we even talk about the treatment for early glottic cancer, let's talk about the management of the pre-cancer so the dysplastic lesions. We talked a little bit about this in the biopsy session too, but what are your options for management of the dysplastic colitis?

Dr. Semirra Bayan:

Why I'm relatively aggressive with dysplasia, so I will treat it completely at the time of surgery either all in one surgery or in a staged fashion if it's crossing the anterior commissure. So its surgical excision is my primary way to treat dysplasia, very rarely do you resort to radiation therapy. In fact, I can't really think of a recent situation where I would have done that. I'll encourage smoking cessation, reduction in alcohol intake if the patient is a smoker, and then follow up is dependent on the diagnosis itself. So for instance if I have a patient with a mild or moderate dysplasia, I'll generally see them every two to three months for the first year. And then depending on how they're doing if they haven't had a recurrence in a while, then we can increase that time to every three to six months if needed and so on. Now, if it's carcinoma in situ for severe dysplasia, I basically treat that like cancers.

Dr. Semirra Bayan:

So I prefer to see them within a relatively short period of time. So for me every four to six weeks for the first year, and then you can move up to two to three months for... after that, and then every six months after that and then a yearly for five years or so.

Dr. Linda Yin:

Earlier you mentioned that for a suspected diagnosis of cancer, for the first time that you're biopsying one of these lesions, you prefer to do it in the operating room setting. How about a patient with a dysplastic lesion that you've been following that you've may be treated in the past and is once again showing dysplastic lesions? Would that patient ever be a candidate for any in office interventions?

Dr. Semirra Bayan:

That's a great question. So dysplasia I think especially in the mild and moderate form can sometimes behave a little differently than cancer itself. So you can treat or remove it completely, and I think there's a certain group of patients that just tend to regrow their epithelium in a dysplastic manner, so it ends up becoming a recurrent disease. These patients become your patients forever because of that. So my general mantra is if I have biopsied a patient twice and proven that that dysplasia is just dysplasia, that we don't have areas of cancer, they are then good candidates for in office laser procedures at that point. That being said, if there's any concern for potential cancer, I take that to the operating room. I don't treat cancer in the clinic as a rule, unless there's some extenuating circumstance to do that.

Dr. Linda Yin:

Moving on now to the invasive cancers, when we treat an invasive glottic cancer what are the primary goals of treatment?

Dr. Semirra Bayan:

Well, the first goal of treatment as there is for any cancer that you have is cure or complete oncologic resection, so that's the primary goal of treatment. Secondary goal is preservation of laryngeal function, and that comes down to voice outcomes. We're talking about the larynx and that's especially important as a laryngologist to try and preserve. So, when you have disease like early cancer which is generally slow growing as a rule, not metastatic. If you have a surgical option that can be oncologically sound which we do. Wow, you should be really worried about preserving the voice too. That should be high up there and I think voice outcomes for me is almost as important as getting a good oncologic resection. Secondarily our swallow outcomes I think especially for things like T1 and T2 cancers, that's a little bit less of a worry just because they still have good and full glottic function.

Dr. Linda Yin:

All right, and when we talk about treatment options now, what are the primary options that are available to us?

Dr. Semirra Bayan:

So there's two primary options. The mainstay of treatment is single modality therapy, so you have either surgery or primary radiation. Both are essentially equivalent in regards to local control and laryngeal preservation rates. The cure rates generally has a real range between 85 to 95% whether you're looking at TLM laser surgery or radiation. Most of this data does come from retrospective trials. There's really no randomized control trials examining this. So you really have to look at the treatment and what's going to be best for that particular patient. So that not only depends on patient preference, it depends on the ability to withstand a surgery. So, their medical history plays a role in your decision making, and also their ability to be exposed endoscopically if you're planning on doing a laser resection, so you can't treat what you can't see. So if a patient cannot be exposed appropriately, that's probably someone you consider radiation on.

Dr. Linda Yin:

Can you tell us a little bit about the specifics of radiation therapy and what the patient actually goes through when they choose radiation?

Dr. Semirra Bayan:

When radiation is given for laryngeal cancer the field is generally very limited it's given over a period of five to seven weeks. Usually about 50 to 70 [gray 00:28:45] is given depending on the radiation oncologist that is treating them. There are a lot of complications with radiation now. Patients have issues with mucositis that can necessitate hospitalization and require treatment breaks, they can have oedema from their radiation. Sometimes the oedema can create the need for airway obstruction in a tracheostomy, and there's always secondary issues with posterior glottic stenosis or full glottic stenosis, esophageal stenosis years down the road. That means the patient may need to salvage laryngectomy, especially if they have any type of treatment failure or they have a non functional airing. So radiation does not come without its risk. Let's take another minute to talk about what radiation does to the voice too, and I'm not trying to sit here and hate on radiation but it destroys the mucous glands within the [saccular 00:29:34]. Those glands are important for the surface hydration that's necessary for glottic vibration and for sound production.

Dr. Semirra Bayan:

Your vocal cords themselves don't have mucus glands they're producing lubrication, that comes from the saccular. Radiation destroys that. Radiation also impacts your vasculature. It radiates both disease tissue and non-disease areas. So areas that may be in a laser surgery you wouldn't touch, those get touched by radiation. It changes the microvasculature of the larynx, it changes the composition of the superficial lamina propria. As a rule, the vocal cords become more stiff. Their voices do change, and it goes back to preserving that maximum pliability, the superficial lamina propria our meat and potatoes, that gets affected when we talk about radiating early cancers. Radiation is also a one time treatment so you can only do it once, you can't repeat it again as a rule. So there's really no backup plan at that point besides a salvage laryngectomy if treatment fails.

Dr. Linda Yin:

So, what options surgically can we offer the patient that has an early glottic cancer?

Dr. Semirra Bayan:

So, surgery can involve either endoscopic surgery or open surgery. I think more traditionally nowadays we offer transoral laser surgery that involves laser excision of the tumor and using either a CO2 laser or KTP laser. Other options though include an open partial laryngectomy, that has been in the past what was traditionally the treatment of choice for these types of cancers. So it's becoming less and less common nowadays.

Dr. Linda Yin:

So endoscopically with TLM or transoral laser microsurgery, what are some techniques that are important to understand for the early learner?

Dr. Semirra Bayan:

So, in order to discuss techniques we have to discuss the difference between the CO2 laser and the KTP, because they actually have two different ways that they work and the techniques are different. So, a CO2 laser absorbs the water, so it vaporizes the tumor. I consider it a cutting laser, so it's a cutting laser. It cuts through tissue. The CO2 laser was initially pioneered... the first attempts of using it or in the late '60s or early '70s by Jako, Vaughan and Strong at BU. So, that was kind of the first group to use the CO2 laser. The laser utilizes the Steiner's concept of resection. So you're coming across the tumor, you're taking a rim of healthy tissue to resect the entire cancer, so that's CO2. KTP has a very different concept and it utilizes the theory of ultra-narrow margins.

Dr. Semirra Bayan:

So we'll get a little bit into that, but the KTP laser is a photoangiolytic laser, it's absorbed by oxyhemoglobin. The original concept for its use was developed Zeitels. So he had studied the work of Rox Anderson who was a dermatologist... who is a dermatologist at Mass General. Developed the KTP laser to use for dermatologic conditions, and then Zeitels himself started using it for dysplasia and early cancers. The KTP laser like I said is photoangiolytic, it induces selective heating of the lesion subepithelial and intralesional microcirculation, and it minimizes thermal trauma because of that. So you're not really cutting through tissue your photoablating the surrounding vasculature. It minimizes fibrosis of the extra lesional healthy, underlying normal glottic soft tissue which optimizes your pliability which obviously you need for vibration and voicing as we've talked before. This all goes back to that concept of angiogenesis which I think we've discussed a little bit. In order for tumors to grow and survive they have to grow new blood vessels, and those blood vessels are what feed the lesion to grow.

Dr. Semirra Bayan:

The big difference between CO2 and KTP is the concept of ultra-narrow margins, and it comes a little bit back to that angiogenesis theory. So, Jim [inaudible 00:33:31] and Zeitels, their group did a very intricate study looking at a hamster cheek pouch model. That particular model grew different sizes of squamous cell carcinoma, and then they just photoablated those lesions, they were of different sizes. What they found was that when you get to a very small lesion, so less than two millimeters just photoablation involuted and removed the disease. So, they just photoablated the lesion and the disease was gone. What that tells us is when you're at that very fine layer between normal and abnormal tissue, the photoablative laser can involute and remove disease without kind of impacting the underlying healthy tissue in a manner that you just can't get with a CO2 laser, and that's the concept of ultra-narrow

margins. It allows you to preserve as much superficial lamina propria as you can, and as much normal functioning tissue as possible which in the end optimizes voice outcomes.

Dr. Linda Yin:

Yeah, so let's talk a little bit about margins. This for me at least in my mind is somewhat of a controversial topic. I've certainly heard different arguments for this in terms of the necessity and the width of a margin that we need to take early glottic cancers. Can you tell us a little bit about this debate?

Dr. Semirra Bayan:

Yeah, there's quite a debate with this and I think there're differing thoughts based upon what technique you choose to use in regards to KTP versus CO2. So there're studies that show close positive margins can be independent risk factors for recurrence and poor survival, but there're others that do not show there's really significant variation especially when you're looking at early cancers. I would argue that when you're working in a small area such as the glottis, and you take a very small biopsy which we all do once we've made a resection, sometimes it's really hard for your pathologist to interpret that. And then it's hard for you to interpret how to interpret what the pathologist is saying. So in the end there're times where your margins may not even be helpful.

Dr. Semirra Bayan:

I found that really close observation after surgery, especially when you're focusing on that microvasculature concept, you're studying the blood vessels of the vocal cord. You can follow someone closely and detect disease relatively easily if there's any recurrence, and then you treat it. You can treat it with a laser, it's relatively easy to do rather than removing a large piece of the vocal cord that maybe you didn't even need to resect just to get your margin. Again, it goes back to do you kind of follow the concept of Steiner's method of removing the CO2 laser and taking out larger margin of healthy tissue with you when you're resecting? Or are you doing ultra-narrow margins and following closely knowing that you're involuting disease, and following them closely and watching that microvasculature to make sure you don't have recurrence?

Dr. Linda Yin:

Now I've heard some people refer to certain early glottic cancers as unfavorable especially from a surgical perspective. Can you tell us what they mean by that?

Dr. Semirra Bayan:

So when you talk about unfavorable when it comes to early cancers, those are ones that either can be exposed appropriately or the ones that seem to be a little bit more advanced and those I would argue perhaps need to be upstaged to T3 at that point. Those are ones who have reduced vocal cord mobility, so those who really have to be careful about because is it reduced mobility or is it no mobility? And if it's no mobility, then you're looking at a T3 lesion. If you have significant extension into the subglottis or supraglottis that goes into our talk about lymphatic spread, you definitely increase the risk of having metastatic disease at that point. I would say especially in the subglottis you have a lot less control over how much you can accurately resect endoscopically to get a good sound oncologic margin as well, and a much higher rate of metastatic disease at that point.

Dr. Semirra Bayan:

Some people would also comment on the anterior commissure potentially being unfavorable, that's a point of contention. Because some of that comes down to if you can expose it appropriately or not. It goes back to our discussion of the anterior commissure ligament itself, what it's composed of and the fact that if you're confined just to the commissure within the anterior commissure ligament, you have a nice barrier but above and below that you don't and you have to define those two differences before you say something's unfavorable.

Dr. Linda Yin:

So you said don't fear the anterior commissure, and as we've learned involvement of anterior commissure is not necessarily on its own a negative prognostic factor. But what are some special considerations that we have to keep in mind when we're operating in this area? Are there any technical challenges?

Dr. Semirra Bayan:

There can be quite a bit of technical challenges. So while I say you shouldn't fear the commissure, I think you should respect the commissure and I think the biggest technical challenge is exposure. So most of the time we struggle is just because we can't see, so that's a pretty big aspect that you have to take into consideration. I put a big plug in for utilization of Glottiscopes and I like to use the Suspension Gallows. I think it gives you a level of visualization of the anterior commissure which is difficult to achieve with other types of fulcrum laryngoscopy. That being said you don't necessarily need it to get good exposure. If you have a fulcrum laryngoscopy you can certainly use it, anterior taping of the neck can often be a very helpful and pushing the larynx up towards you to be able to see the commissure. If, for instance you have larger false cords may be obscuring a portion of [UV 00:39:09] can do a partial complete vestibulectomy too to help with your resection, to be able to kind of expose the commissure itself if you need to.

Dr. Linda Yin:

What about management of the neck? We already talked about how uncommon occult neck disease is, and to the point that we don't usually even need to work this up. But just to cement this concept in, is there any role in elective neck dissection in early glottic cancers?

Dr. Semirra Bayan:

No role for elective neck dissection for early cancers, unless you feel like you are working with a cancer that's not early, in which point you upstage the patient and then you're talking about a completely different discussion. In regards to swallowing, I can't think offhand of any particular studies evaluating this though I would say swallowing in the long term especially with radiation you can have issues. You don't have as much problems as a role with transoral laser surgery. Voice outcomes is a tough one, mainly because most of the studies if not all the studies are retrospective. They don't utilize consistent acoustic and aerodynamic measures. They're often very small subsets of patients and many times they're relying on subjective voice evaluation measures rather than objective voice evaluation measures. The follow up for most of the studies are often quite poor. So I don't think you can really make any lasting conclusions at least based on the literature.

Dr. Semirra Bayan:

I could give you my subjective take, but I don't think that would be very appropriate in this setting. But as a rule if you look at these studies, which again I don't think are always very strong, I think there's relative equivalency if not maybe leaning towards some superiority towards trans or a laser surgery.

Dr. Linda Yin:

For patients that do require a more extensive resection, are there any reconstructive or rehabilitative options for them to achieve a better voice?

Dr. Semirra Bayan:

For those who have an early cancer that requires four oncologic purposes, more tissue to be taken. I mean obviously the primary goal of transoral laser surgery is a complete and optimal oncologic resection. For those that do require more tissue to be removed, you end up having a larger glottic defect and that goes back to our original concepts that we talked about in the beginning of needing to voice you need good mucosal pliability and a good glottic competency. When you lose that glottic competency your voice declines. So for those where that is the situation reconstruction options would include fat injections to provide more paraglottic support. You can also sometimes do a thyroplasty as well for those same types of concepts. For patients that lose a large portion of the muscular membranous portion of one vocal fold, as long as you preserved pliability in other areas. If you can restore that glottic competency, you can actually have a very, very serviceable voice as long as you've preserved superficial lamina propria and other areas.

Dr. Linda Yin:

Excellent. I think you've answered all of the burning questions that I had, and I think that's Early Glottic Cancers in a Nutshell. Are there any other things that we haven't covered that you think should really be addressed?

Dr. Semirra Bayan:

No, not that I can think of.

Dr. Linda Yin:

Great. Well, thank you so much for coming back on the show and chatting with me.

Dr. Semirra Bayan:

Thanks for having me Linda, It's great to be here today.

Dr. Linda Yin:

Okay, let's move on to some key summary points now from the talk. Early glottic cancers are made up of T1 and T2 lesions of the true vocal cord. T1 lesions are confined to the vocal cord only, but can include the anterior and posterior commissure. T2 lesions extend into the supraglottis or the subglottis. Unlike some other cancers in the head and neck, glottic cancers can have onset of hoarseness early on and therefore patients can present with an early stage disease. The glottis is the most common sight of laryngeal cancer. The biggest risk factors for glottic cancer include smoking and alcohol use traditionally, but there is a new group of younger non smokers who are getting this disease and incidence in this group may be rising. A good physical exam for an early glottic cancer includes a careful laryngoscopy and this should not only examine the tumor itself, but also any surrounding vasculature that may serve to

feed the tumor. As opposed to supraglottic or subglottic cancers there are several natural barriers that can keep a lot of cancers relatively protected from spreading outside the larynx. The most important of these barriers include the conus elasticus as well as Boyle's tendon.

Dr. Linda Yin:

There are a number of premalignant lesions in the glottis and this can range from mild dysplasia to severe dysplasia. The exact risk of cancer and each of these categories is not exactly known, but in general severe dysplasia is the same as carcinoma in situ and should be treated with caution. Carcinoma in situ is distinguished from an invasive carcinoma only by invasion through the basement membrane. In terms of a workup, imaging is not typically needed as the risk of nodal spread is low. But a CT scan within cuts through the larynx can be helpful in characterizing the local disease. It's important to remember that vocal cord fixation upstages a tumor, and we'll make it a T3 rather than an early glottic cancer. Treatment options for early glottic cancers can include primary radiation therapy alone, or surgery as the only modality treatment. Both are essentially equally effective at local control and laryngeal preservation, although some studies do show some variability. Historically, surgery was done through open approaches but it's now most commonly done through transoral laser microsurgery. Either the CO2 laser or the KTP laser can be used with different techniques.

Dr. Linda Yin:

The voice outcomes after both radiotherapy and surgery can be quite variable, but in general voice outcomes after transoral laser microsurgery, tend to depend on the extent of resection. As such, the goals of surgery should always be to optimize oncologic resection but at the same time at maximizing laryngeal preservation and function.

Dr. Linda Yin:

Okay, let's move on to our question session now. So, for this I'll be providing some high yield questions that highlight some key points from this talk, and then I'll be taking a brief five second pause so that the listener can think about the answer, and then I'll provide the answer. The first question is what is the most common subsite that is involved in laryngeal cancer? The most common subsite of the larynx involved in squamous cell carcinoma is the glottis. Next question, what are the superior and inferior boundaries of the glottis? The superior boundary of the glottis is the ventricle that is the space between the false and the true cords. The inferior boundary of the glottis is the subglottis, and the subglottis is defined as starting about one centimeter below the upper surface of the true vocal fold.

Dr. Linda Yin:

What is Boyle's tendon? Boyle's tendon is the insertion of the vocal ligament onto the thyroid cartilage. The tendon itself is made up of the vocal ligament, the thyroid epiglottic ligament and the inner perichondrium of the thyroid cartilage. The ligament itself can serve as a barrier in the anterior glottis towards spread of beyond the glottis. Otherwise, in the anterior portion of the thyroid cartilage is above and below boyle's ligament. This can be weak points for glottic cancers to spread. A patient presents to the clinic with lesion that appears like an early glottic cancer in the mid portion of one vocal cord, and this lesion is crossing over the anterior commissure onto the contralateral side. There's nodal disease or [inaudible 00:47:01] disease, how would this tumor be staged? So this tumor is involving the bilateral vocal folds but not going to the supraglottis or subglottis. This is a T1b N0, M0 glottic squamous cell carcinoma.

Dr. Linda Yin:

Which type of treatment gives better cure rates for glottic cancer, radiation or surgery? This is a trick question. Patients should be counseled that radiation therapy and surgical therapy are essentially equally effective from the oncologic control perspective. Again with cure rates usually higher than 85%. Alright, well that concludes our episode on early glottic cancers. Thanks again for tuning in.