Head and neck cancer forum

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Dr Megan Carroll – Managing long-term effects of head and neck cancer treatment

MEGAN CARROLL: Good morning, my name is Dr Megan Carroll. I am one of the Radiation Oncology Registrars, and I too just work up the road at the Royal Brisbane. I am very honoured today to speak to you about the long-term side effects of head and neck cancer and its treatments. I used to be a radiation therapist, I really loved my job but I began to become more curious about the medicine and science around radiation oncology and wanted to be in a role that wasn't just focussed on treatment but one that looked after the long-term care of the patients. And that's where I diverted my track into medicine. Since I started radiation oncology, I have taken an interest into looking after head and neck cancer patients.

So I would like to congratulate everyone here today because you are not only survivors of cancer but have made it through one of the hardest forms of cancer treatment. Chemoradiation therapy is one of the most difficult. Not only while you have the treatment but in the long-term, trying to live and adjust with the side effects that affect your day-to-day living.

So during the presentation, I am going to be talking a little bit about, "Well, what is it a long-term side effect?", and try to cover a little bit of chemotherapy, surgery, but probably the great majority will be from radiation therapy. And talk a little bit about some of the treatments for those side effects that are available; and maybe discuss a little bit about how we are trying to reduce long-term side effects in the future as well.

I would like to focus my attention first on the lady that I have here on the slide; this is Julie McCrossin, an ABC journalist diagnosed with a head and neck cancer four years ago. She had a base of tongue and tonsil cancer and she went through chemoradiation. Today, she's one of the ambassadors for targeting cancer; and she's also the New South Wales Cancer Council Ambassador. Don't hold that against her.

I think she's an inspirational woman; and that's why I wanted to include her today because she's not only a survivor of cancer but she's been able to adapt and learn how to still live her life to the fullest, with the side effects that have accompanied her treatment. So she's still living out her passion, which is a journalist and MC; and I just think she's fantastic.

So what is a long-term side effect? If we take a radiation definition, it is a side effect caused by radiation therapy that will occur greater than 90 days after the treatment of radiation. And these can be anywhere from six months to five years sometimes side effects popping up ten years down the track. Using this broad definition, it can be used for surgery or chemotherapy. They are often irreversible and sometimes they can be progressive. That's why it's really important that we continue to strive to improve what we call the therapeutic ratio.

So that is the ratio of tumour response for a fixed level of tissue damage. We know that if we increase the dose of radiation, we can often get larger cell kill but we also get longer and more severe long-term side effects. So we are always trying to find ways in which we can get maximum tumour death but still maintain a person's quality of life.

There are a few ways in which we can do this. We are often looking at new radiotherapy techniques which tightly wraps that high dose of radiation around the tumour and minimises dose to normal, healthy tissue. And we can also look at different systemic agents which I will talk a little bit about later; that have potentially not as severe long-term side effects.

So I thought we would look at each different part of head and neck, from the eyes down to the neck. Each patient who goes through radiotherapy’s side effects are going to be what part of the party they have been treated. If you were a patient who has had a throat cancer, you are not necessarily going to be experiencing long-term side effects to the eye because this may not be near the surgical/radiation field.

So starting with the eye, one of the most common long-term side effects is having a dry eye; and there are a few different reasons this can happen. The actual duct, the lacrimal glands, because of radiation can have reduced numbers of cells that can make tears. There is a duct which transports those tears that are made in the glad to the actual eye and that can become narrowed because of radiation effects. So if you were to experience a dry eye, lubricating eye drops or artificial tears are one method to help but there's also a couple of surgical procedures that can be done.

So there can be a little stent popped in the little duct to open it up to allow those tears to flow back to the eye; as well as the punctual plug and that's in the second picture there. So there is a little hole, that tears that are naturally produced, escape down through. But if we are not making lots of tears, we want to try and accumulate them in the eye; so a little plug can be put in the eye, so that they pull and relieve the eye and make it feel a lot more comfortable.

Corneal damage can occur again because of radiation and it is due to an effect of depleted stem cells, and that can irritation and inflammation and ulcers. Topical steroids can help relieve that inflammatory process and there is a new topical eye drop on the market called "lifitegrast", and it's only been added recently to the Australian Therapeutic Goods Administration and it's something I would recommend that you would speak to an ophthalmologist about, if you wanted to use; but it's a lymphocyte function and associated antigen agonist which blocks the surface proteins from intracellular adhesion molecules which is essentially the two mechanisms which encourage inflammation, so if you stop that blockage from happening, you get less inflammation.

Cataracts are another side effect, which we see quite late and rare from radiation, and it can be caused from scatter radiation, low dose, not necessarily directly to the eye. With cataracts, you get an accumulation of abnormal fibre cells, and the lens has this wonderful ability to make new cells but can't expel these damaged cells. And these damaged cells are no longer transparent; they are cloudy. Because they can't be expelled, it builds up and you end up with a cataract. But luckily, thanks to wonderful Australian pioneers, micro-surgery is a quick and easy technique, where you can replace that cloudy lens with a new artificial lens; and sometimes even patients who have gone through this procedure, not even necessarily for side effect of radiation, end up not needing their glasses necessarily, with the new artificial lens.

So moving on to the ear. Sensorineural hearing loss, is hearing loss that can be caused by damage to the inner ear which has a component called the cochlear and, can be caused by damage to the auditory nerve. And both these mechanisms need to talk to each other; they need to work together.

One of the most common causes for this type of hearing loss is Cisplatin, a chemotherapy drug used for head and neck cancer to sensitise the tumour cells to make them more prone to death via radiation.

Unfortunately, it does have side effects on nerves not just within the ear but can also affect the nerves of the skin.

There are ways in which sensorineural hearing loss can be improved. A hearing aid is an option for people who still have some hearing. If people do have profound hearing loss, it can be the use of a cochlear. Hearing, though, is very complex; and whilst there are these two options, it might not be an exact replacement for normal hearing; but it's definitely a potential, if someone is experiencing hearing loss, to see their ENT surgeon, have some auditory tests done to see if maybe one of these two may be an option to help improve quality of life.

Interestingly, tinnitus, which can also be caused by chemotherapy, can sometimes be improved with a cochlear, if the person has had profound hearing loss.

Just touching on a little bit on peripheral neuropathy, Cisplatin can affect the sensation of the nerves on hand/feet. Luckily, it can reduce over time. So there isn’t a direct medication that helps improve the sensation but it is something that does tend to improve over time. Pain, however, we do have a few different medications that can help with neuropathic pain and one of the interesting ones is Duloxetine an anti-depressant, and for anti-epileptics, pregabalin or gabapentin...and have been useful for nerve induced pain.

I have included here wax build-up, when a person undergoes surgery near the inner ear, the anatomy of the ear changes; and it can cause a bit of swelling of the eustachian tube and it makes it very difficult to clean the ear and the natural process of which wax is normally removed by the body is very difficult and that, too, can have its impact on hearing; and that's normally a conductive hearing impairment. Going to the GP or ENT surgeon, though, to have the wax cleaned out by...can be a simple method, that can improve people’s hearing if it is related to a conductive hearing loss.

So as I mentioned before, tinnitus, which is ringing in the ears, can be quite obtrusive. Unfortunately, there's no pill which reduces that ringing, but there have been quite a few different studies looking at different kinds of cognitive behavioural therapies, different distraction techniques, and counselling, which has been found to be quite effective in in increasing people's quality of life. So whilst it doesn't reduce the tinnitus, it reduces its distress and the depression scales.

They have looked into many different things; looking at transcranial magnets, current stimulation and acoustic stimulation, but unfortunately none of these have really shown to reduce tinnitus or improve quality of life.

So dry nose. Unfortunately, radiation in particular can leave people with a dry nose that can bleed more frequently. So for dry nose, a simple lubricant or spray such as Nozoil can help. Bleeding can help, because of little veins, Telangiectasia, which are very delicate leaky blood vessels that are damaged due to radiation and may be more prone to bleeding. If a nose bleed was to occur, we would suggest padding, but if this was to be a problem, cauterisation in the long-term.

Dry mouth, this is probably one of the most common side effects of head and neck cancer, and it normally affects between 80 to 90 percent of patients. One of the mechanisms for this is with regards to radiation, it reduces the number of working serious acinar cells that make the saliva and, also, reduces the mucinous cells which produce the saliva, with submandibular saliva glands. It can cause people to change their diet, may have increased risk of dental caries and oral thrush.

What it tends to do is also change the chemistry of the saliva and that is one of the main reasons why going to see a dentist on a regular basis is important; because with that change in saliva chemistry, we do get that increased risk of dental caries.

So artificial saliva is one method for comfort; though I do notice within clinic, most people tend to prefer the regular water bottle, to keep their mouth moist during the day but to also aid with eating and drinking.

Hyperbaric oxygen has also shown to improve salivary function. Interestingly, this was found accidentally. There had been studies looking at hyperbaric oxygen for patients who had osteoradionecrosis, a weakened, damaged jaw bone from radiotherapy, and they found that they were producing more saliva when they were going through hyperbaric oxygen. Not the reason why they were there, but still a good outcome. Unfortunately, we still don't have large numbers of randomised trials to prove its effectiveness but it's something that you can talk to your doctor about, if dry mouth is something that continues to be a significant problem down the track after treatment.

So how does it work? Well, patients are placed in chambers that are pressurised to 2 to 3 atmospheres and they breathe 100 per cent of oxygens for a total of 20 to 40 dives and the elevated appreciate causes increased proportion of oxygen to dissolve the patients' plasma and that increased oxygen availability with tissue healing; and, also, helps to create new blood vessels in damaged tissue which improves the oxygenation and further healing in that damaged tissue.

I wanted to briefly also mention a medication called Amifostine, a drug which has been looked at in the process of having radiation therapy, which was looked at in dryness of mouth prevention. You may come across this in literature. It is an organic thiophosphate compound and the hypothesis was that it reduce the dry mouth. But there's been lots of conflicting evidence. In 2006, they did a big meta-analysis, grouped together lots of different trials, and it did seem to show a positive effect in reducing long-term dry mouth; but they included non-blinded studies so people knew if they were on the drug or not, and you could also have bias or placebo effect.

There was one phase three study which looked at this drug and found that there was an increase in oral mucositis, that's where you get ulcers in the mouth during radiation treatment. We are not sure why it caused this, but there's been conflicting evidence. So it's not a drug that we have enough evidence to recommend, and we also would like more experiments to be done, to make sure that it only has its effect on the salivary grands. We don't want it to have an effect on the tumour. We don't want the tumour to be less sensitive to the radiation.

So if you see it on the Internet, it is something that people have been thinking of trying to use, but there's not quite enough evidence there to put it into practice.

So as I mentioned earlier, osteoradionecrosis is a non-healing condition in which irradiated bone can become exposed through dehiscence or separation of the overlying mucosa and it can lead to jaw fracture.

Things that increase the risk of this occurring is when we have to treat at the very back of the mandible/jaw; if we have to use high doses which is often the case, 60 Gray or above, and if people have to undergo a tooth extraction in the future. So that's why at the head and neck meetings, when you get to do the speed dating with the doctors, you will also meet a dentist. The reason why the dentist is there is to see whether or not we can optimise a patient's dental care; can we use a filling, for instance, instead of having to give an extraction or are we better off extracting teeth now, rather than after radiation is given; all with an effort to try and reduce that patient's long-term risk of having osteoradionecrosis which is one of the rarer risks but still one that we need to be vigilant about; especially when good oral hygiene can help prevent it occurring.

So, again, with osteoradionecrosis, there is the option of hyperbaric oxygen therapy but there are also a number of surgical procedures that can be used; and this is more Dr Batstone's area. We often involve max fax in the care of our patients, who have developed osteoradionecrosis, for their expertise in helping to manage the problem; debridement or complete bone/soft tissue reconstruction are some of the things that the max fax surgeons can do to help people with fracture in the jaw bone.

There are a couple of medications. Again, we are still trying to get more data, but for some results that we have seen, these are looking quite promising. Pentoxifylline was originally used for vascular disorders. It improves blood flow because it is a vasodilator and it improves the flexibility of those red blood cells, when they transfer through the circulatory system and it's also been found to have an ability to dull down the inflammatory reaction, particularly fibrosis, which is the main reasons why lots of these long-term side effects, including ORN, occur in the first place. What is promising with this medication, it does reduce one of those inflammatory factors, which is called TGF beta, which has this ability to turn a fibro blast into a fibro site. Why I mention that: it is these little fibro sites that start making collagen and scar tissue. So the less number of fibro sites, the less scar tissue in the future and hopefully less of these sort of side effects.

Vitamin E is often used in combination with pentoxifylline and it itself is an anti-oxidant and can modulate that the inflammatory reaction. When you use both of those drugs together, you get less of the TGF beta, less fibrocytes, therefore let's scar tissue.

So looking this time at the joined within the jaw, so if you pop your finger just in front of your ear and move your jaw up/down, this is the area we are speaking about, the temporomandibular joint. This can be affected because of scarring, and causes trismus, so the inability to open the mouth completely. This can often affect people's ability to eat and speak. Some people, it can affect worse than others. So there's varying degrees of trismus.

Steroids can help but, also, physiotherapy and speech pathology. We will often make referrals to these two groups within allied health because they have wonderful exercises and different techniques that can help provide stretch to this joint.

A Therabite is placed in the mouth and then opened to allow gentle stretch of that joint area.

However, you don't need a Therabite to do that. Just using tongue depressors is equally as good. So you can start off with just a small stack and then gradually add one or two or more tongue depressors to give you that stretching effect. We often will give a pack to a patient that might be experiencing trismus within the clinic.

Hyperbaric oxygen, again, may have some effect on the fibrosis, as does Pentoxifylline and Vitamin E.

Moving further down now into the neck. Total laryngectomy can be very disabling for patients. Communication between loved ones, friends, your job, is vitally important to a patient's mental well-being; not just their physical. So we do try as much as we can to preserve the voice box. Unfortunately, it is not always possible, though, if a patient does present with an advanced stage of laryngeal cancer; sometimes the voice does have to be sacrificed, in order to increase our chance of overall survival.

But there are quite a few different techniques that we can try to help give a voice back. The three main topics/techniques are: electro larynx, tracheoesophageal voice restoration and oesophageal speech. The electrolarynx is the most used technique; it is an electronic device which transmits vibrations through the external tissue of the neck. The patient is still able to shape that sound, using their tongue, jaw and lips. That can be used straight after surgery; so that you can start talking to your loved ones straight away, because it can be quite frustrating for the patient, when they have to write literally everything down, especially with different medical teams popping up; and you have already given your story ten times to them having to write that down, it can be very frustrating. There are newer devices on the market as well, and they have got more ability to vary pitch. So this is aimed at hopefully being able to give people more expressive speech. So when you are sick of that, the second/third team, you can sell them to buzz off, "I have had enough," and they know you mean business.

So the second technique, tracheoesophageal voice restoration is a technique that actually - it is probably the most comparable to normal speech and it's hands-free. So if you are like me, and you are part Italian, you can still try and express yourself through your hands. It also allows clearer communication over the telephone as well.

So what it involves is a very small surgically controlled fistula, which is between the trachea and the oesophagus, so that there is a communication between the two and the opening is maintained by a one directional valve that protects the airway during swallowing but diverts air from the lungs across the pharyngeal oesophageal mucosa for voice, when the tracheostoma breathe valve is included. You don't need to use your hands to occlude it. When high pressured air gets moved from the lungs, it automatically closes, but remains open for soft breathing.

Oesophageal speech is the third technique, and this is probably the hardest technique to achieve; but some patients can do this. Again, it is a hand-free technique. What it involves is the patient rapidly intaking air into their oesophagus and then expelling the air from the oesophagus in a controlled manner, so it moves through the oral cavity and the vibrator resource is the...oesophageal segment. You don't need a device at all, but it does take a real amount of coaching from a speech pathologist, lots of practice, to be able to get that control.

Sometimes radiation can affect people's quality of voice. They still may be able to maintain what they would regard as a useful voice for communication but because of the fibrosis and the stiffness that radiation can cause on the vocal cords, it can mean that patients have to use a lot more effort to speak; and that can cause fatigue, essentially.

There are a couple of techniques, though, that can help people continue to use their voice in an effective way.

One is voice rehabilitation. So this has come from a Swedish paper; and patients underwent ten rehab sessions with the speech pathologist, 30 minutes a day, for over ten weeks; and this was direct exercises that were focussed on helping people remain relaxed, respiration, posture exercises. This has shown quite good results, to help people maintain their quality of voice.

The second thing that people can do is look at their voice hygiene. A lot of this is quite common or would make common sense, not to yell if you can help it; it must be difficult with naughty children or grandchildren, but these are the sort of things that they have recommended. If you are in a noisy situation, standing closer to the person that you wish to communicate to, so that you don't have to elevate your voice. Different techniques, too, such as yawning, regular swallowing of water, can all help preserve your voice.

So swallowing, or dysphagia, this is the difficulty of swallowing food. In the early stages of treatment, this is often due to pain that the treatment can cause, but in the long-term, we actually find that people can become deconditioned. So if you had a PEG, because of the dry mouth, loss of taste, pain, it can cause a bit of hesitancy to start using your mouth again to swallow. But like anything, if you don't use it, you can lose it. So those muscles need to be retrained and it's often with the help of a speech pathologist that we can help retrain people how to swallow.

What they will often do, of course, is a barium swallow, where you take in some dye and the speech pathologist can see whereabouts the deficit is of the swallow; because depending on where the problem is, means different exercises.

Swallowing in the long-term can also be caused by the constrictor muscles receiving a high dose of radiation; and similar process, scarring can occur there. So this is why I have put Pentoxifylline and Vitamin E there as we.

The constrictor muscles are called organ at risk, so we are forever trying to reduce dose to this area, if possible; and therefore reduce swallowing problems in the future. It can be difficult, though, if the tumour is nearby. We never wish to compromise the tumour outcome. We always have that as our first priority. But if the tumour is far away, and we can, we will reduce dose to those constrictor muscles.

Just as scarring can occur in other parts of the body, it can occur in the neck itself. Physiotherapy is an effective way to increase people's mobility within the neck. Sometimes the muscles themselves, there's a big one called the sternocleidomastoid; it can become quite stiffened from radiation. Sometimes it can be impaired by surgery as well; the nerves that supply the neck can be affected and affect those muscles. Physio with different stretching exercises and different massage techniques can help improve people's neck movement; and that can be really quite important even for simple things like driving. If you can just turn your head as opposed to having to turn your whole body, that can make life a lot easier.

Now, these side effects I mentioned here are quite rare but we do often recommend to people to have a thyroid function test once a year with your GP. If you have had radiotherapy, in the long-term, 10/15 years down the track, it can make that thyroid a little bit sluggish and underactive and thyroxine can be a simple replacement for that; and it is a very easy blood test to have.

I like this picture because you can see really clearly where the thyroid is. Those big blood vessels, the carotids, lymph nodes are right next-door. If we are aiming to treat lymph nodes with radiation or surgery, you can see how close these structures are; and why the radiation may affect the different parts of the body that we may not realise.

I have also included on there the carotid artery stenosis or narrowing of the artery. Big blood vessels often have arteries within their walls as well and the muscle can become fibrotic or hard and that can mean narrowing of the arteries. So it is really important not just from a heart perspective to keep up your exercise, diet, not smoking, reducing alcohol, because all these cardiovascular health strategies help us in the long-term with side effects of radiation. So we want to reduce the risk of complications of narrowed vessels. One of them can be stroke. It's very, very rare, but just day-to-day activities can also help reduce that.

Medical management may include statins, so that's a good thing to have a chat with your GP about. And for really serious long-term complications, there's always surgery, that may be an option, endarterectomy, if there's severe narrowing of those vessels.

As I was mentioning at the beginning of the talk, prevention is always better than cure; and that is something that we always endeavour. We are not just about trying to find ways to cure cancer, but we are also trying to find ways that we can improve quality of life at the same time.

So what we try to do within the radiotherapy sphere is find techniques that reduce dose to normal tissue, and we can do that increasingly well with tomotherapy, we can do that with a machine we have at the Royal, and VMAT, Volumetric modulated arc therapy, where we can wrap that high dose around the tumour and minimise dose to those normal tissues. And what I try to explain when we meet a new patient for the very first time is: your radiation oncologist is not just marking on the tumour where they want to treat; they are making on organs that they want to try and avoid. And that's our big aim; is both of those.

When we are able to put down our high dose, we need to make sure that we are treating where we need to treat. We can get dose escalation because we have more confidence in what we are treating; we don't want to have less margins and miss. So that is the other aspect of technology that has changed and allows us to have these tighter areas; because when we do a cone beam CT on our machines, we can say with great certainty that we are treating where we need to treat and not treating the normal tissue.

Within other areas of cancer treatment, we are also looking at ways to de-escalate treatment. So as mentioned earlier, P 16 positive cancers have a much better prognosis than similar cancer which have been initiated by alcohol and cigarettes. So much so, that we have even now got a whole new staging system for these cancer patients. They are not grouped together like they were because we know that these cancer patients do better. So they are now looking at trials at which we can maybe decrease the dose of radiation because we are looking at combining them with maybe immunotherapy. This is happening overseas. Hasn't hit here yet and we want to make sure that that decreased dose of radiation doesn't give a worse outcome. So for the time being, we are quite happy to see what the results are and if they are looking good, then that's something that we would take on board.

In a similar way, we are looking at using Cetuximab instead of Cisplatin with radiation therapy. Cetuximab fits into targeted therapy and it doesn't have the same side effect profile as Cisplatin because it is not a chemotherapy. It doesn't work to kill the cell. What it does, it stops the cell signalling to divide and grow. So it has its own side effects but they are not quite as severe as what we often see with Cisplatin so that is one way that we are trying to reduce the long-term side effects. So hopefully hearing, touch and kidneys, which are all affected by Cisplatin can be preserved in the future.

And there is also some trials looking at transoral surgery, in combination with radiation, which may eliminate the need for chemotherapy potentially; and in some patients, if they fit a certain tumour group, they may be able to have a robotic surgery alone; again, we are in early stages but we are constantly trying to improve ourselves, the treatment that we can often, so that we are not only getting high rates of cure but, also, increasing quality of life. Just at the very end there, I thought I would include a picture of what a tomotherapy machine looks like. And I have a few colleagues from a couple of years ago; some of them have now finished and gone on to work at other parts of Queensland. That is our pride and joy at the Royal, the tomotherapy machine. Thank you very much.