TRANSCRIPT

S1.E5: Melanoma (Part 2)

Dr Tom Kovi: Hello and welcome back to *Spot Diagnosis*.

This is the second part of our melanoma episode. We are joined by Associate Professor Victoria Mar. In this part, we'll be talking about how melanoma is treated and prevented. There's lots to talk about so we'll get cracking.

Associate Professor Alvin Chong: Okay, Tori, we diagnose a melanoma and it is excised narrowly on an excisional biopsy. What do we do next?

Victoria: Next, we want to have a good look at the pathology report. Obviously, if there is any concerns with the pathology, or it doesn't correlate with what we saw clinically, we'd want to give our friendly pathologists a call to have a discussion about what it all means. That's important. The next thing is obviously explaining the pathology report to the patient. If the melanoma is invasive and if it's more than a millimeter in thickness we'd recommend consideration of a sentinel node biopsy for further staging.

A sentinel biopsy is a staging procedure. It has to be done at the same time as the wide local excision. The first draining lymph node is what we call the sentinel node, so excising that and testing it to see if there has been any early spread of melanoma is important in the staging process.

Alvin: If it is positive what does that mean?

Victoria: If the sentinel node is positive it means that you're at higher risk of developing metastatic disease in the future, so it makes a difference in terms of prognosis. It used to be that if you had a positive sentinel node the surgeons would do a completion lymph node dissection which is removing all the lymph nodes in that area to reduce the risk of recurrence. But there was a big trial thatzreported at the end of last year that showed there is actually no survival benefit in doing that.

Currently, if you have a positive sentinel node you won't have any further surgery in most cases to remove the lymph nodes which is good news for patients really because that was quite a morbid procedure. If you do have a positive sentinel node though you will be considered for what we call adjuvant therapy: additional medical therapy to reduce the risk of the melanoma coming back.

Alvin: These are for melanomas where the Breslow thickness is more than a millimeter.

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Victoria: Correct, so it also might be for patients who have slightly thinner melanomas between 0.8 and 1 mm if there is other prognosis features, such as ulceration, mitoses.

Alvin: What about thin melanomas, let's say a 0.5 mm thick melanoma, you would still recommend wide local excision?

Victoria: Correct. They should have a wide local excision. With any invasive tumor, we recommend a 10 mm margin and, if it's in situ, only a 5 mm margin. That is really to reduce the risk of recurrence locally in the skin. The chance of having any further spread from a very thin tumor is so low. So we set a cutoff for a sentinel node biopsy of about 5% risk of having spread to the lymph nodes already.

Alvin: You've cut out a melanoma in a community, so 1.5 mm melanoma narrowly excised, who would you refer to for the next steps?

Victoria: I think particularly for people who are in good health and would be considered for adjuvant medical therapies, it's a good idea to refer to a multidisciplinary center. The sentinel node result will often determine whether they can access medical therapies as adjuvant treatments to reduce the risk of their melanoma coming back. The field is changing so rapidly at the moment, trials are available for people at different stages.

Tom: So, that's our tip number one. Any melanoma greater than 1 mm should be referred to a multidisciplinary melanoma unit for consideration of sentinel node biopsy, adjuvant therapy, and clinical trials

Tom: Once a patient gets diagnosed with melanoma and then treated, how do we follow up someone who has had melanoma?

Victoria: Follow-up is really important because we know that the risk of the melanoma coming back whilst it diminishes with time, patients already prove that they can grow one essentially. They hold all the right ingredients, so the risk of getting a second primary unrelated melanoma actually increases with time. The follow-up schedule really is determined by their risk of developing further disease.

Thick tumors with poor prognostic features will be followed up more closely initially and thinner tumors which are lower risk could be followed up annually. Essentially, the highest risk time for recurrence is in the first two to three years. If patients are going to have a recurrence they usually recur within the first two to three years. That's about 80%. And less than 5% of patients will recur after five years.

It's important really to have lifelong follow-up at least to check skin for other primary melanomas, to check their lymph node basins and ask them about any symptoms that can't be explained for other reasons.

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Alvin: Tori, what if someone does develop a recurrence of melanoma? For example, the lymph node starts to enlarge, what do we actually do then?

Victoria: It's a good question. If somebody presented with a lump under their arm, a lymph node that they're suspicious of, it's important to get a diagnosis. The first thing is to do an ultrasound and a biopsy, often a core or an FNA. It can be done under ultrasound guidance to get a tissue diagnosis and confirm melanoma. If melanoma is confirmed, they can be referred directly at that stage to a multidisciplinary team. A further staging would be requested, usually, a PET scan and an MRI of the brain at that point to make sure that there's not more distant disease as well.

Alvin: The reason why the skin is checked at follow up visits, is it because of the increased risk of getting another melanoma?

Victoria: About 10% of patients with a first melanoma will develop a second, third or fourth primary melanoma over their lifetime. It's important to check the rest of the skin and make sure that there's no other lesions of concern as well as managing the initial melanoma.

Tom: That's our tip number two. When following up a patient with melanoma we should perform a full skin examination to look for further primary and other skin cancers as well as checking the nodal basins and the scar site.

Tom: There have been some important breakthroughs in the management of melanoma, can you tell us about these?

Victoria: It's been a really exciting time to be part of melanoma research and management. Our patients have benefited hugely from some of the breakthroughs. We've now got a number of options in terms of treatment of metastatic disease. Those drugs are being used earlier and earlier in the management of melanoma to prevent more distant metastatic disease as well.

The two main classes of drugs that we have available to us now are immunotherapies - which essentially harness the body's immune system to fight the melanoma - and also targeted therapies. About 40% of melanomas harbor what's called a BRAF mutation, and the targeted therapies essentially switch off melanoma cells that have that mutation and cause the tumor to shrink quite quickly.

Tom: Which one is more effective?

Victoria: That's a really good question, Tom. There are pros and cons of both approaches really. The BRAF targeted therapies are extremely effective for most people that have the BRAF mutation but the effect is short-lived. We usually see a response to therapy quickly over weeks but then resistance can develop usually over about seven to nine months.

The immunotherapies are not as effective in as many people but, when they are effective, their longevity is much better so the duration of response is improved and can be over many, many

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years. About 50% to 60% of patients will respond to immunotherapies, and they'll have a more durable response, but the BRAF inhibited therapies have a quick response in most patients, but resistance occurs.

Tom: I understand that the immunotherapies are quite different from the conventional chemotherapy. Can you tell us about some of the side effects of immunotherapy?

Victoria: Immunotherapies really work by revving up your immune system to fight the cancer. In doing so the immune system can start attacking normal tissues as well.

There are a lot of autoimmune type syndromes that you can get with the immunotherapies: colitis, hepatitis, thyroiditis and so on. Some of these can persist despite stopping therapy. So, they can be lifelong as a consequence of treatment.

Alvin: Okay, now Tori we're going to move right along to prevention of these skin cancers. In Australia we have had the good fortune of having a very long and extensive public health campaign called *SunSmart*. Can you tell us something about whether these campaigns have been effective?

Victoria: Really these campaigns have been pretty much the most effective thing to reduce the incidence of melanoma in the country. They've been extremely cost-effective in terms of reducing incidence and health costs associated with melanoma but also we do now see a drop in the incidence of melanoma amongst young people. That's probably due to the campaign efforts which started in around the '80s, *Slip Slop Slap*, to try to increase awareness about the importance of sun protection.

Alvin: Just remind us, what is *Slip Slop Slap* again?

Victoria: We want to slip on protective clothing. We want to slop on the sunscreen and slap on a hat and we also want to put sunglasses on and seek shade where we can as well.

Alvin: Tori, tell us a bit about your advice on the use of sunscreen.

Victoria: Sunscreen is one really important measure for sun protection. Also, adequate protective clothing is really important and I would argue easier to put on than sunscreen every day. But we do recommend putting sunscreen on to all the areas that are exposed, that you can't cover up and obviously some days it's just going to be too hot to wear full long sleeves and trousers. On areas that are still exposed, 30 to 50-plus sunscreen is recommended when the UV level is over three.

Alvin: Combining sunscreen, clothing and seeking shade is much, much better than just putting a little bit of sunscreen and spending all day in the sun, right?

Victoria: Absolutely. If you put on a little bit of sunscreen and still go out and bake, you're still going to get sunburnt.

Alvin: Yes. I see it a lot. People with a little bit of sunscreen on getting sunburned slowly.

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Victoria: You always miss areas, don't you? It's important to reapply it and make sure that you've put it on properly. The trap is when you're at the beach and you're building sandcastles and you've got sand covering places. It's important to put it on before you go out in the sun and make sure that you can get all the areas that are exposed.

Alvin: The other thing I often see is kind of double standard if you go to any Australian beach in the summer, you see that the children are very well protected with rashies and hats and sunscreen and all the adults actually getting burned because all they have on is a budgy smuggler and a little bit of sunscreen. I think for listeners out there, just remember people will see what you do so it's better to model good behavior.

Victoria: There are some really good rashies out there for adults as well. Kids have a good range of rashies with long sleeves and so on but there are some really good long-sleeved rashies and products for adults. It's worth the investment.

Alvin: Are you worried about vitamin D deficiency with sun protection?

Victoria: Not from the amount of sunscreen and so on that we use. I think firstly it's important to prevent skin cancer and then vitamin D levels shouldn't really be affected by sunscreen application. It is a theoretical risk, but in reality, there's no difference in vitamin D levels in people who have been applying sunscreen every day compared to those who have just put it on intermittently. Really I'm not concerned about sunscreen affecting vitamin D levels and, of course, vitamin D levels are going to fluctuate through the year as well.

Tom: I heard that there was a recent change in the recommendation regarding sunscreen use in the Australian guideline. Do you mind to comment on that?

Victoria: Yes. It used to be that we recommended applying sunscreen before any planned exposure or prolonged exposure and people often do think to do it before they go to the beach for instance but it's really the incidental exposure where we end up getting burnt, where we are not expecting it. Particularly on those days which are overcast and we don't realise that the UV level is quite high. Now, the recommendation is really that we should be applying sunscreen daily in the morning before we go out, when the UV level is predicted to be over three.

Tom: Do you have any tips in terms of how much should people apply sunscreen?

Victoria: You've actually got to apply quite a bit for it to be the recommended dose and to give you adequate coverage. It's about one teaspoon per body part as a general guide. It's about five ml. It ends up being quite a lot if you're covering the whole body but hopefully, you've got good protective clothing for most parts.

Tom: How often do people need to reapply sunscreen?

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Victoria: We'd recommend every two hours, but it might be more frequent if you're sweating a lot or if you're doing a lot of swimming.

Tom: That's our tip number three, when the UV level hits three, people should be advised to apply sunscreen as part of their morning routine.

Alvin: Tori, there have been increasing amounts of articles being published where AI is seen as being equivalent, if not even better, than some human dermatologists in diagnosing skin cancer and melanoma.

Victoria: Not you or me obviously! [laughter]

Alvin: No. We're just so good!

Victoria: [laughs]

Alvin: Actually, you're better than me. We went to the World Congress and we actually challenged some machines and AI and I lost to the machine but Tori beat it.

Victoria: I think it took us a few goes. [laughter]

Alvin: Okay. What do you think of this AI situation?

Victoria: I think it's really exciting actually. Essentially there have been a few publications that have shown that the computer can diagnose melanomas at least on par with dermatologists. It's a little bit of an artificial setting in that dermatologists are shown photographs and asked to give a diagnosis. Whereas in clinic it's pretty different. We see a patient, we actually take a history of the lesion and that influences our diagnosis I think quite a bit.

It's an artificial scenario and I think given more information, the dermatologist would probably still come out on top. But the computers are getting pretty good and I think in time they will be a really useful thing for us to have in clinic as a bit of a second opinion, which I think is a great thing to have. It's nice when you're working in a team and you have somebody next door that you can say, "Hey, have a look at this. What do you think?" I think the computer will be able to take that role for us.

Alvin: I think what could be interesting is the development of apps to diagnose skin cancer. I think that's a different beast altogether. Do you have any comments on that?

Victoria: I think it's difficult when the technology is in the hands of people who might not know what to do with the information. I suppose I worry that if a patient were to use it or someone in the community was to use it on a lesion and it gave a high probability of melanoma, what they might do with that information and these apps haven't been validated accurately. We don't know really how good they are in essentially getting better outcomes for melanoma in the community. So, I

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think we've got to be cautious with apps. There is some great potential out there, but at the moment they're a little bit untested.

Tom: Just before we finish our episode, where can our listeners find out more about melanoma?

Victoria: There are some really good websites to look at and the Melanoma Guidelines give a really good wealth of information and also guidance on practice. The Wiki guidelines on the Cancer Council Australia website is an excellent resource.

Tom: That concludes our episode on melanoma. Thank you very much, Professor Mar, for joining us today. We would like to thank Cancer Council Australia for their Supporting People with Cancer Grant. We would like to also acknowledge our production team, Maddie Chwasta for podcast editing, Peter Monaghan and Joanne Coughlin for podcast production support.

Thank you for listening to another episode of *Spot Diagnosis*. We hope it's been educational for you. Stay tuned for our next episode.

Alvin: We hope you have enjoyed this podcast. Remember, these podcasts are not meant to replace medical advice. If you have a skin condition that requires attention, we strongly encourage you to see your medical practitioner.

Tom: For those who would like to access some further information of this subject, we have placed a transcript, together with some further education and information resources for you on our website. I also want to do a shout out for the GP education events that we run at the Skin Health Institute. Just go to spotdiagnosis.org.au.

Alvin: Please share Spot Diagnosis with your friends and colleagues. Rate and review us. Let us know what you think. We would really appreciate your feedback and any suggestions. Thank you for listening.

More information, and other dermatology education resources, can be found on our website at www.skinhealthinstitute.org.au/podcasts

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