TRANSCRIPT

S2.E1 – Basal Cell Carcinoma (BCC)

Dr. Blake Mumford: *A disease more repulsive and distressing can hardly be conceived than a rodent cancer of the face. It removes whole organs but restores nothing. In its front, all is healthy, behind it is vacancy and frightful disfigurement.*

Welcome to season two of *Spot Diagnosis*, a podcast about all things dermatological, brought to you by the Skin Health Institute in Melbourne, Australia. I am Dr. Blake Mumford, Education and Research fellow at the Institute.

Alvin Chong: I'm Associate Professor, Alvin Chong, Director of Education and Specialist Dermatologist. Blake and I are your co-hosts.

For season two, Blake will be taking over from Dr. Tom Kovi, who has been accepted into the dermatology training program. We would like to thank Tom for his help in establishing this podcast and also congratulate him on his new role.

As some of you may have guessed, today's topic is basal cell carcinoma, or BCC. The illustrative opening quote comes from Doctor Charles Moore's seminal work, *The Rodent Ulcer,* published in 1867.

Blake: Our guest today is Dr. Michelle Goh, a consultant dermatologist at the Institute, where she works in the Skin Cancer Assessment and Transplant Dermatology Clinics. Michelle is without a doubt one of the busiest and most experienced dermatologists in Melbourne. She is the current Victorian examiner for the Australasian College of Dermatologists and has consulting positions at several hospitals, including: The Peter MacCallum Cancer Center, St Vincent's Hospital, Melbourne, The Austin, The Alfred, and finally, The Royal Melbourne Hospital. Michelle has a particular interest in skin cancer. Michelle, welcome to *Spot Diagnosis*.

Dr. Michelle Goh: Thank you very much, Blake and Alvin, for inviting me to this podcast.

Blake: Michelle and I would like to dedicate this podcast to the memory of Professor Oscar Colegio, a brilliant shining light in the field of transplant dermatology. He was also our friend.

Now, Michelle, we're starting a new tradition this season where we ask our guest speakers to tell our listeners an obscure, interesting dermatological titbit that the listeners might not know.

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Michelle: Since this podcast is about basal cell carcinomas, BCCs, the most common skin cancer, do you know any famous people who have been affected by BCCs? Well, Hugh Jackman, our own well-known Australian actor, best known for his role in the *X-men* franchise, has had multiple BCCs. He constantly urges his fans to get themselves checked for skin cancer. Thankfully, his superhuman wolverine regenerative powers saw him recover quickly after his surgical procedures.

Blake: Thanks, Michelle, that was interesting. Now, before we start picking your brain, we're going to give our listeners a brief overview of what basal cell carcinoma is, and why they need to know about it.

Basal cell carcinoma has been called many things over the centuries. The other term most of us would know is the *rodent ulcer*, coined by Hermann Lebert in 1851. But it was way back in 1755 that BCC was first recognised as a distinct clinical entity by Jacques Daviel. Daviel's discovery that these ulcers could be treated with surgery was unfortunately ignored for the remainder of the 18th century.

So, what is basal cell carcinoma and why is it important? BCCs are one of the keratinocyte carcinomas, the other being SCC. These are cancers which arise from keratinocytes, the cells which make up a vast majority of the epidermis. BCCs are the most common type of skin cancer. In fact, BCCs are the most common type of cancer, period. To give you some perspective, in Australia, the incidence of keratinocyte carcinomas, BCCs and SCCs, is five times all other cancers combined. It is estimated that 70% of Australians will have at least one skin cancer by the time they reach age 70.

In a paper published in the *Medical Journal of Australia* in 2017, Pandeya and co-authors[i] found that 7% of Australians will have had a keratinocyte carcinoma removed over a three-year period. Approximately 900,000 keratinocyte cancers are removed per year in Australia and BCCs make up about two-thirds of these, so roughly about 600,000 lesions.

The cost of treating keratinocyte carcinomas is enormous. Francine[ii] estimated the total cost of keratinocyte carcinomas to the Australian health system in a single year would be $703 million.

Ultraviolet radiation exposure is the predominant cause of BCCs, with the majority occurring after the sixth decade of life. Men are more likely to get BCCs and lighter skin types, as one would expect, are at higher risk. BCCs also have a higher incidence in the warmer more northern latitudes.

Alvin, I'm starting to feel a bit nervous. I am a Caucasian male who grew up in Queensland.

There are many different histological subtypes of BCC that have been described in the literature, but there are only three main clinical types that you need to worry about:

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nodular, superficial and morphoeic. Whilst these are histological subtypes, clinically, they have unique characteristics as well, which we'll talk about in more detail later.

Now that you've been given a brief overview, I think it's time to get our experts to answer some of our gnawing questions about the rodent ulcer. Get it? Gnawing questions? Rodent ulcer?

Okay, moving on. I've got two experts in the hot seat today, because both Michelle and Alvin are experts at skin cancers. Let's start with Michelle. What causes BCCs, Michelle?

Michelle: As you mentioned earlier in the introduction to this podcast, Blake, ultraviolet light is the principal environmental cause for BCCs. The fair skin type is the host factor for increased risk. UV radiation induces mutations. Studies have shown that tumor DNA of BCCs carry the highest mutational burden of all cancers and the majority of these have the UV signature mutation.

Alvin: Michelle, what are the risk factors for having BCCs?

Michelle: People with a very fair skin phenotype that sunburns easily and does not tan, a tendency to freckling, red hair and blue eyes. With UV sunlight exposure, intermittent high intensity sun exposure, such as recreational or occupational exposure, and childhood sunburns are the predominant risk factor for BCC, as compared to chronic cumulative sun exposure, which plays a critical role for the development of SCC.

Apart from skin type and ultraviolet light, less common risk factors for BCC are arsenic exposure, such as from contaminated food and water and historical medicinal products, ionizing radiation, especially people who have had radiation therapy at a young age. This may sound crazy but historically, young were treated with radiation therapy for acne and, in adulthood now, we see patients who present with multiple head and neck BCCs.

Immune suppression is another factor which increases the BCC incidence five to ten-fold. There are also several rare genetic syndromes that have increased rates of BCCs. The most notable is Gorlin Syndrome, also known as nevoid basal cell carcinoma syndrome.

Blake: Michelle, in our opening quote, Dr. Charles Moore mentioned things like frightful disfigurement and devouring whole organs. Are BCCs really that dangerous?

Michelle: BCCs are typical indolent, slow-growing and usually only cause gradual local invasion of tissues, so they are usually not dangerous if the tumors are detected and treated early. However, BCCs can become dangerous if lesions are neglected and left untreated and so left to grow very large and deep, especially if they were to invade into vital structures. The term “rodent ulcer” that was mentioned before also refers to some of

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the historical presentations of extremely large ulcerated BCCs that have invaded through bone and soft tissue, such that even internal organs are on view.

BCCs can also be dangerous at what we call high-risk sites, which are mainly the regions around the eyes, nose and ears. The high-risk BCC histological subtypes for deep and wide sub-clinical invasion are the morphoeic or infiltrative BCCs, basisquamous BCCs and BCCs with perineural invasion. Rarely, they can metastasise.

Alvin: So they can be dangerous if left alone. What do BCCs actually look like?

Michelle: They look different depending on their histological subtype. Nodular BCCs occur mainly on the head and neck. Classically, they are slow-growing asymptomatic nodules and usually, it is many months before they present themselves. They can ulcerate, they can bleed and scab intermittently. On examination, it is a red firm papule or nodule, with telangiectasia.

Blake: **Skin tip time**. An intermittently bleeding, non-healing lesion in the head and neck area is suspicious for BCC.

Michelle: The second type of BCC, superficial BCCs, look quite different from their nodular counterpart. They are flat, red, sometimes scaly, more frequently found on the trunk or limbs. They are usually asymptomatic but can be itchy. They can be misdiagnosed as inflammatory problems like eczema or psoriasis, but they do not respond to topical steroids.

Blake: Wow, I think it's time for our second **skin tip** already. A red patch or plaque on the trunk that does not respond to topical steroids is a superficial BCC until proven otherwise.

Michelle: The BCC can have both superficial and nodular components. For example, a superficial BCC that has been left to grow for a long period of time can end up with invasive nodular components as well.

Morphoeic or infiltrative BCCs are another subtype of BCC. These can be difficult to diagnose. They are like the black sheep of the family. They present as a firm scar-like or indurated plaque, often on the head and neck. Fortunately, these types are less common. All BCCs can be pigmented so they can mimic melanomas.

Blake: Gosh, Michelle, that morphoeic BCC sounds like that cousin that no one really wants to talk to at Christmas dinner. Are there features on dermoscopy that can help diagnose BCC?

Alvin: I'm glad you asked that question. Dermoscopy is actually very useful in the diagnosis of BCCs, and for us dermatologists, is an important part of our physical

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examination. When we look under the dermatoscope we can see micro aborising vessels, a milky pink color, and ulceration. These are findings which are quite specific and sensitive for BCCs. In addition, you can see pigment in globules and clumps.

Blake: Okay, it's time for our third **skin tip** already. This one is brought to you by Professor Alvin Chong who's too modest to mention it but actually wrote a paper[iii] on the dermoscopic appearance of BCC. Our skin tip is, dermoscopy is very helpful in the diagnosis of BCC.

Alvin: All right. Now apart from clinical examination and looking under the dermatoscope, how else can BCCs be diagnosed?

Michelle: Alvin, a preliminary biopsy is often useful, particularly for less experienced doctors. These can be punch biopsies or shave biopsies. Generally, a nodule should be diagnosed with a punch biopsy, whereas flat lesions can be diagnosed with shaved biopsies. It is also useful to do a biopsy first before performing large or potentially cosmetically disfiguring surgical procedures.

Blake: Okay, Michelle, the histopathology report has come back confirming the diagnosis of BCC and my patient is super impressed with my clinical acumen. We've appropriately celebrated with a COVID-19 social distanced elbow bump, what are the treatment options now for this BCC?

Michelle: Blake, it depends on the subtype and the patient factors. Perhaps starting with the commonest type, the nodular BCC. These are often on the head and neck area. Surgical excision with clear margins is the usual way these are treated. This has the lowest recurrence rate (around 5%) and is curative. Sometimes radiotherapy is used if the patient cannot tolerate surgery.

There are more options for the treatment of superficial BCCs. They can be surgically excised, like nodular BCCs, they can also be treated with other modalities such as topical imiquimod cream. Specialists can also use methods such as serial curettage, photodynamic therapy, and, rarely, cryotherapy or radiotherapy.

Alvin: How would you use topical imiquimod in the treatment of superficial BCCs?

Michelle: Imiquimod is approved by the Australian Pharmaceutical Benefits Scheme for immune-competent patients who have biopsy-proven superficial BCC that is not suitable for other forms of treatment. Imiquimod is a topical cream that is self-applied by the patient. It works by immune stimulation against the tumor. For BCC the recommended regimen is five consecutive days per week for six weeks. The expected local reactions are redness, itching, burning, and then erosion, weeping, scabbing or crusting. Secondary

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infections can occur, but the severe skin reaction is usually a result of the significant inflammatory reaction against the tumor.

Uncommonly, systemic side effects can occur if the immune activation is very exaggerated. Symptoms include flu-like symptoms, fatigue, headache, nausea, muscle aches and pains, and fever. Patients are asked to stop the treatment if the local reaction becomes severe or if they develop systemic symptoms.

It has a success rate of around 80%, so about eight out of 10 lesions respond to the topical treatment. For low-risk superficial BCC, it is a good first option.

Blake: Wow, I can't believe how far we've come in such a short period of time. In the 18th century, we couldn't do much and nobody thought we could cure these and now we can cure them by rubbing a cream on them. What about that black sheep of the family? That cousin that no one wants to talk to, the morphoeic BCC? How do we treat that?

Michelle: Surgical excision is the treatment of choice for infiltrative or morphoeic BCCs. These are tumors that have a tendency to infiltrate deeper than what we can see clinically. A wider clinical surgical margin is recommended to reduce the risk of incomplete excision. Larger infiltrative or morphoeic BCCs close to critical structures on the face should be considered for Mohs micrographic surgery or delayed reconstruction of the surgical defect after histopathological examination confirms that the surgery has achieved clear microscopic margins.

Blake: Okay, Michelle, I've just excised a lesion and at the time thought, "Yes, I've nailed it. I definitely cut it all out," only to get the pathology report back later with a positive margin. How should I approach this?

Michelle: Blake, in this scenario, surgical re-excision is the treatment of choice. If the histological subtype is not aggressive, so meaning the nodular or superficial subtypes, then standard surgical re-excision with an appropriate additional margin can be done. Referral to a specialist should be considered for incompletely excised BCC with aggressive histological subtypes, or BCCs in cosmetically sensitive sites, or near vital structures.

Alvin: Is there a place for just observing these, Michelle?

Michelle: Yes, Alvin, sometimes an incompletely excised BCC can be observed. This is if the histology of the lesion is low risk, and there is only one margin involved, and in a low-risk site, such as the back, then close observation may suffice.

Blake: Okay, are there any red flags that you should worry about in BCCs, apart from the ones that we've already mentioned?

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Michelle: The high-risk sites are those lesions that are near the eyes, ears and nose, and the aggressive BCC subtypes are the basisquamous and BCCs with perineural invasion. Morphoeic or infiltrative BCCs have deeper invasion and greater subclinical extension.

Blake: When should I refer a patient with a BCC off to a specialist?

Michelle: Referral to a specialist should be considered for high-risk tumor factors such as a BCC that has not been cleared despite multiple attempts at excisions, or recurrent tumors, and especially BCCs with aggressive histology or perineural invasion.

Tumor sites may also be a factor for specialist referral. Tumors in cosmetically sensitive sites of the face, and high-risk sites near the eyes, nose, lips or ears, tumors on the distal limbs or large BCCs that require complex reconstruction. Patient factors are also another consideration. Some patients may have associated comorbidities. They may require sedation or general anaesthetic for the procedure because of the intolerance of local anaesthetic surgery in the clinic.

Blake: Michelle, what sort of things can go wrong like if you did try to excise a lesion around the eyes or the ears?

Michelle: Well, you may find that the tumor extends deeper and wider than what you suspected clinically before you started the procedure, so you're unable to completely excise the tumor or you may find that you have a defect that is a lot bigger than you anticipated and may not be able to close the defect on the day and may need additional help.

Blake: Why is it important to examine the rest of the skin when you've found a BCC?

Michelle: Having had one BCC means that this person has the genetics, skin phenotype plus the history of risk factors, especially sun exposure, to have the risk of skin cancer on all their skin, and especially at all their sun damaged sites. Not only are they at risk of BCCs elsewhere, they are at risk of other types of skin cancers which are potentially more dangerous, such as squamous cell carcinoma and melanoma.

Blake: Okay, guys, it's my favorite time of the podcast again, it's time for another **skin tip**. Skin that has grown cancer can definitely do it again. Any diagnosis of a skin cancer should prompt a full skin examination for other lesions.

Moving on, how do you follow up someone whom you've just diagnosed as having a BCC?

Michelle: The follow-up after surgery is to ensure that the tumor is completely removed on histology and that the surgical wounds have healed satisfactorily, or if the BCC was

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treated with non-surgical methods, the follow-up is to check that the BCC is cleared clinically.

Further review down the track is to check for tumor recurrence and for new emergent skin cancers. The interval between follow-up reviews depends on the skin cancer risk profile of the person and tumor factors.

In-between the medical appointments, all patients are advised to be always aware of their own skin and to perform regular self-surveillance and to also seek earlier review if there are any new or changing skin lesions of concern.

Blake: Going through medical school, during my very brief dermatology teaching, I was told that BCC essentially never metastasised but that's not entirely true, is it? Michelle, I understand you're of something of an expert in these rare corner cases. Can you tell us a bit more about it?

Michelle: Metastatic BCC is indeed really rare, Blake, and usually occur from very locally advanced tumors. Metastases usually come from very large tumors that have been neglected for years, with delayed, inadequate surgical management. Furthermore, large tumors often have multiple mixed histological patterns, including the morphoeic or infiltrative patterns, which have subclinical deep extension. Metastatic BCC is extremely rare, estimated to be one in 20,000 to 40,000 cases. Approximately 1% of BCCs present as locally advanced and surgically unresectable because of their anatomical site.

Alvin: How would you treat locally advanced or metastatic BCC?

Michelle: We would discuss locally advanced or metastatic BCCs in MDT, multidisciplinary meetings. If the advanced tumor is not treatable by surgery or radiation therapy for a variety of reasons then hedgehog inhibitor therapy, and the names are: vismodegib or sonidegib, can be obtained through special authority on the Australian Pharmaceutical Benefits Scheme. These drugs inhibit the hedgehog signaling growth pathway of BCCs. It is an oral medication taken daily. The side effects of this drug, which build-up in severity over months, are the limiting factor for patient tolerance for ongoing treatment. The side effects are universal to all patients because they relate to the mode of action of the drug on cellular growth pathways but the severity of the side effects for each individual is variable. The main side effects of note are: hair loss, loss of taste, lack of appetite, weight loss, muscle cramps, and general fatigue.

Hedgehog inhibitors merely suppress and regress the BCCs but do not completely eliminate the tumor. Once the drug is stopped, the tumors often regrow slowly again. Some patients who are intolerant of continuous therapy because of the severe side effects take intermittent therapy to keep the advanced BCCs in control as they are usually slow-growing tumors.

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Blake: I'm really surprised that we actually have some kind of treatment for what is, in all aspects, a fairly rare disease. That's great news that we at least have something. How do you approach a very old frail nursing home patient who is either not fit for surgery or just doesn't want surgery? Is there anything that can be done to help this patient?

Michelle: In this case, firstly, a thorough assessment of the patient including their medical comorbidities, and the reasons why surgery is contraindicated, logistics of treatment, the patient wishes and their reasons for them, and the patient's cognitive ability. If appropriate, the decision should be made in conjunction with the medical treatment decision-maker, the GP, and the nurses and carers at the age care facility to get a comprehensive view of the whole scenario.

The characteristics of the skin cancer also need to be taken into account. The histological subtype, its growth pattern, size and clinical morphology, the anatomical site, and in what way it is causing symptoms such as pain, bleeding, ulceration, and functional impact.

Ideally, decisions in such a complex psychosocial setting are made with MDT input, and after discussion with all relevant parties. An indolent lesion that is asymptomatic and clinically non-aggressive can be actively monitored. Superficial lesions can be managed palliatively in the short-term with topical therapies. However, often an exophytic or deeply invasive tumor that is obviously enlarging requires treatment for symptom control even if the patient is frail with multiple comorbidities. Radiotherapy and surgery are often required to prevent progression of large tumors to further complications such as bleeding, ulceration, and infection. A formal anesthetic review is also essential to reassess the patient's said fitness or lack of fitness for surgery. Other methods of anesthesia such as regional blocks for example could be alternative options for a patient who is medically high risk for sedation or general anesthesia.

Alvin: It's actually a very complicated scenario. I think what we're often faced with is, a patient's family not wanting anything aggressive and yet these tumors are extremely troublesome and causing significant morbidity. I think the role for surgery is still present even in these kind of cases.

Blake: That's very good insight from both of you. Thank you. Okay, before we wrap up this episode, I need to get at least one more quote in and this one comes from the British plastic surgeon, Mr. John Bennett[iv]:

> *"One should not consider the chances of success when treating this disease but the price of failure. Often for the patient it is at the cost of a slow, insidious and disfiguring death."*

On that morbid note, that concludes our episode on BCC. Stay tuned because the next episode, we'll be talking about the other keratinocyte carcinoma, SCC.

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Alvin: Thank you, Michelle, for sharing your time with us.

Michelle: Thank you, Alvin and Blake.

Blake: We would also like to thank Joanne Coughlin and Peter Monaghan at the Skin Health Institute.

Alvin: We hope you've enjoyed this episode of *Spot Diagnosis*. 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.

Blake: For listeners who want more information on this subject, a transcript of this episode and links to other resources can be found on our website, spotdiagnosis.org.au

Also, the Skin Health Institute, based in Carlton, Melbourne, hosts a series of GP education events. Our workshops cover a variety of important dermatological skills and topics including dermoscopy, as well as hands-on workshops for GPs and GP trainees using pigskin where we demonstrate biopsy and surgical excision techniques. These are run by Professor Chong and a team of specialist dermatologist educators.

Alvin: I just want to highlight a great resource for clinicians put together by the Cancer Council's Clinical Guidelines Network. It is on keratinocyte cancers. This has been approved by the National Health and Medical Research Council and both Michelle and I were involved in the working party to write it. It is available online in an easy to use format at https://cancer.org.au/health-professionals/clinical-guidelines/

That is a mouthful, but you can find this link in the podcast description and on our website at spotdiagnosis.org.au.

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 and join us next month for our podcast on squamous cell carcinomas and actinic keratoses.

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