Professional Development Dermatology

UCD CHARLES INSTITUTE SEMINAR SERIES

UCD School of Medicine
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Charles Institute of Dermatology

Insights on a vulnerable patient population

Attendees at UCD's Charles Institute Seminar Series heard a presentation from Consultant Dermatologist ***Dr Aoife Lally*** *on the risks and prevalence of skin cancer in immunosuppressed patients*

The Charles Institute, Ireland's national dermatology research and education centre, played host to a range of guest speakers who covered a variety of topics ranging from skin cancer to psoriasis, among others. The series, which was sponsored by RELIFE (part of the A.Menarini group), was designed to provide expert advice from a range of distinguished national and international experts in their respective fields and was chaired by Prof Desmond Tobin, Professor of Dermatological Science at UCD School of Medicine and Director of the Charles Institute of Dermatology. The seminars were broadcast to attendees with a special interest in dermatology in other locations, who accessed the talks remotely via an audio-visual link.

Attendees at the series heard a presentation from UCD Associate Clinical Professor Aoife Lally, Consultant Dermatologist at St Vincent's University Hospital in Dublin, on the topic 'Skin Cancer in Immunosuppressed Patients: The Evolving Picture'. Dr Lally provided an overview of skin cancer in immunosuppressed patient populations, including solid organ transplant recipients, patients with chronic lymphocytic leukaemia and patients with inflammatory bowel disease (IBD). Dr Lally also presented case studies and a range of clinical research, as well as an outline of planned collaborative skin cancer studies.

Dr Lally explained that the data she presented came predominantly from renal transplant recipients, but all solid-organ recipients have an increased risk of skin cancer. "The old data suggest that the risk increase is between 40-to-250 fold for squamous cell cancer (SCC) — that's the highest risk estimation, but most studies state that the risk is between 40-to-120 for SCC," she told the seminar. "The important thing to note is that in the immunocompetent general population, basal cell cancers (BCCs) are far more common than SCCs, at a ratio of between 2.5-3-to-one. However, post-transplant, this ratio is reversed and SCCs are the more common skin cancer post-transplant in this immunosuppressed group." Recent studies have shown that the risk of keratinocyte cancer post transplant is declining, likely due to changes in immunosuppression regimens as well as improved sun protection awareness of patients, Dr Lally added.

Keratosis

Melanoma is also more common in these patients, Dr Lally explained, as well as more rare cancers that have a viral aetiology, although these are generally smaller in number. She also highlighted the original Australian study, which showed that these patients often have multiple tumours that are highly aggressive and have high rates of recurrence and metastases compared to the immunocompetent population. "Unsurprisingly, sun-exposed sites are affected and there is a high prevalence of actinic keratosis," she continued. "Actinic keratoses are areas of keratinocyte dysplasia — not full thickness, but there is a risk of progression to SCC. The literature shows the risk to vary from between 1-in-1,000 to about 1 per cent, but the risk is much greater when large areas are affected — so-called 'field-change'." Studies have shown that there is an association between amount of field-change and keratinocyte cancer risk in this group of patients, she told the attendees.

Males more commonly develop skin cancer than females and the patient's age at transplantation and their time post-transplant are also important considerations to bear in mind, said Dr Lally. "The time since transplant is a surrogate marker for exposure to immunosuppression — the longer the time post-transplant, the greater the risk that these patients will develop a skin cancer. Interestingly, if a patient is transplanted at a younger age, the lag-time between transplant and development of a skin cancer is longer compared to when a patient is transplanted at an older age, and this has implications in terms of screening patients, giving them advice post-transplant, and trying to get them engaged in services for cutaneous surveillance."

Dr Lally also presented her research on the prevalence of skin cancer in patients with inflammatory bowel disease (IBD) and summarised: "Overall in our research, the risk we found for developing non-melanoma skin cancer in patients with IBD was a more than five-fold increased risk in those who had thiopurine exposure only, and in those who had exposure to thiopurine and/or anti-TNF agents, there was a more than 6.5-fold increased risk, even when we allowed for confounding factors in this analysis."

Skin cancer

Skin cancer is a significant burden of disease for many immunosuppressed people, for various reasons, and there are growing numbers of immunosuppressed patients presenting to Dr Lally's clinic, she explained. "Traditionally, it was predominantly the solid-organ transplant patients we would see day-to-day, but it is now patients with IBD, patients with haematological malignancy, patients with rheumatoid arthritis and patients who are HIV-positive — those who are HIV-positive even have an increased risk of skin cancer when they are taking antiretroviral therapy. So it's important to be aware of all the groups of patients who are at risk because of the significant disease burden. Multidisciplinary team input is often required, because if you are going to modulate or modify immunosuppression regimens, that requires input from the physicians looking after these patients at their primary diagnosis."

The treatment and diagnosis landscape for immunosuppressed patients with skin cancer is changing, explained Dr Lally, partly because this patient population is growing larger. She also touched on the value of collaborations with the Charles Institute to foster translational research. "Melanoma is the fourth-most common malignancy in Ireland and has been somewhat neglected by various public funding and cancer awareness bodies compared to cancers such as breast, lung, colon and prostate," Dr Lally told the seminar. "These all have cancer programmes that are funded for screening, or have specific National Cancer Care Programme funding for specific positions in hospitals."

Nevertheless, overall five-year survival for melanoma is 91 per cent, but there are significant numbers of patients who develop advanced melanoma, however survival rates are improving, she added. "Five-year survival at stage 4 melanoma was around 10-to-15 per cent but with the advent of targeted therapies and immunotherapy, the picture is changing… patients who are on combination immunotherapy have about a 52 per cent five-year survival rate now for advanced melanoma."

Medication therapies

During a lively Q&A session, Prof Tobin commented: "I am taken by the fact that our successes in other areas of public health, for example people living longer and enabling them to have more transplants, are bringing with them the downside of providing more time for skin cancer to appear in an elderly population or increasing numbers of transplanted individuals." Referring to some challenges facing researchers, including those at the recently launched Precision Oncology Ireland initiative, Prof Tobin asked about "the potential for mis-sequencing the administration of potent anti-cancer drugs that could inadvertently alter cancer cell subpopulations in a tumour so as to potentially facilitate the emergence of more aggressive clones in a tumour. Different types of drugs may damage tissue and can possibly "set the scene for further problems with tumour development", he posited. Prof Tobin also pointed out the complex relationship between an individual's biology and their response to both the level (dose) and type of drug they are exposed to.

Dr Lally replied: "The patient's biology is certainly important because the majority of skin cancers, whether they be SCC, BCC or melanoma, will occur in fair-skinned individuals who have had a pattern of UV exposure, whether that be childhood sunburn or intermittent, high-density sun exposure, or chronic UV exposure leading to increased SCC risk," she said. "The drug is certainly also important, because we know the duration of exposure is also a significant factor. For example, I would be very reluctant to prescribe azathioprine for some of the cutaneous non-skin-cancer conditions that I manage.

"The metabolites are embedded and therefore with any UV exposure, a person could be predisposed to cutaneous malignancies," she continued. "The patient factors are certainly key. When I worked in Oxford [where she conducted research], the majority of patients were fair-skinned. When I moved to London [where she was Clinical Lead for Skin Cancer in Immunosuppressed Patients at the Royal Free Hospital], there was a much more mixed population, so the skin cancer rates overall were lower. I think [biological] patient factors and behaviour are key, but the iatrogenic aspect of the medication also has to be considered, and that's something that we can definitely modify — if we can use a more skin-friendly immunosuppression regimen, that's very important."

Dr Aoife Lally

In patients with IBD, it is still unclear as to why these patients get more BCCs than SCCs and neither large epidemiological or cohort studies have addressed this yet, she added.

Speaking to the ***Medical Independent (MI)***, Dr Lally commented on the amount of dermatology training that is given to trainee GPs, relative to the amount of dermatology-related presentations they will see each day. "It is my opinion that trainee GPs do not have enough dermatology training — but naturally, I am biased. A GP trainee may go through their entire training without formal dermatology training/attachment to dermatology clinic, and yet up to a third of primary care consultations may be skin-related. There are some initiatives where GP trainees are linked-in with dermatology departments in Ireland for placements during their training, but it is not universal across the country or mandatory, unfortunately."

It was also put to Dr Lally that certain diseases have a stigma for patients, as they are seen as 'self-inflicted', such as lung cancer. But is there a similar stigma associated with skin cancer? "In my experience, there is not a tremendous stigma with regard to skin cancer, but some patients who have used sunbeds, for example, may feel guilty about their behaviour," she said. "In general, the issue is to educate patients that they can get sun damage even in Ireland and that sunbathing is not the only form of sun exposure — outdoor hobbies/work, etc, are important risk factors for patients to modify their sun protection habits around."

Dr Lally was also asked to expand on the types of patient education that are needed to reduce the incidence of skin cancer. "Patient education should include advice on year-round sun protection behaviour," she told ***MI***. "This should include care when outdoors for work or hobbies — chronic, ongoing sun exposure is a risk factor for SCC, in particular."

RELIFE has had no input into the content of this article or series of seminars