

Skin Cancer in Kidney Transplant Recipients: A Nephrologist's Perspective

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Editorial

In course of preparing this article, one particular patient came to mind who encapsulates the issues in the current system as they relate to post-transplant patients and skin cancer. During a routine post-transplant follow-up – this patient had a successful kidney transplant for more than 10 years. I requested that she see a dermatologist for preventative skin cancer surveillance. In the past when I had made this request, she told me it was on her to-do list and promised to make the appointment soon. This time, however, she gave me a different reply. Between seeing her primary care provider three to four times a year, nephrologist twice a year, transplant nephrologist once a year, endocrinologist three to four times a year and cardiologist once a year, she was overwhelmed by the number of separate providers she had to visit. She further explained that while she may have new skin lesions and would think about making a dermatology appointment soon, she did not understand why one of the providers could not take care of it. Her frustration at the system was greater than her desire to possibly avoid skin cancer!

Skin cancer is the most common cancer in kidney transplant recipients. As immunosuppression increases the risk of skin cancer, transplant recipients are at an increased risk; and having once had a skin cancer, their cumulative risk of getting another skin cancer increases greatly. It is time to look at new approaches to handling skin cancer evaluations in post-transplant patients that takes into account their heightened risk factors as well the patients' already complex and time-consuming follow-up appointment schedules.

In our long term post-transplant kidney clinic, visits for patients with stable renal function who are on stable immunosuppressants usually focus on staying up to date on their health maintenance. Because of the prevalence of skin cancers, it is not uncommon to find patients who have experience with some form of skin cancer, either at present or in the past. In my clinical experience, when I talk about health maintenance to patients who have dealt with skin cancer, most of them are up to date with their usual age appropriate health maintenance including routine skin cancer screenings, colonoscopy, pap smear, mammogram and vaccination or bone density test. However, when I talk to patients who were never diagnosed with skin cancer about skin cancer risks and dermatology visits for skin cancer surveillance, the conversation often goes quite differently. Some say they were never told about skin cancer risk, others that they had heard about it in the past but have not paid much attention to it, and still some expresses that is on their "to do" list and will make appointment soon. But on subsequent visits the majority of those patients will have the same explanations about why they have not yet done anything about their skin cancer risks.

Non melanoma skin cancer; squamous cell cancer (SCC) and basal cell cancer (BCC) are the most common types of skin cancer in organ transplant recipients, accounting for more than 95% of all skin cancer [1]. Based on population based cohort study, standardized incidence ratio compared to general population is increased 65 fold for SCC, making it the most common cancer in organ transplant recipients, 10 fold for BCC, and 3.4 fold for melanoma. Although

standardized incidence of Kaposi sarcoma is increased 84 fold in transplant recipients, Kaposi sarcoma is still not one of the most common cancers in transplant recipients, as it is not a common cancer in general population [2]. Approximately 5 million people are treated for skin cancer in the US each year, with an average annual cost of \$8.1 billion [3]. The incidence of SCC is rising and has almost doubled in last three decades [4]. At around 8% the risk of metastasis of SCC in organ transplant recipients is significantly higher than general population [1]. Although SCC and BCC originating from epidermal and hair follicle keratinocytes are the most common cancer in organ transplant recipients, other less common but clinically significant skin cancers with significant morbidity and mortality are: melanoma from melanocytes and nevus cells; Kaposi sarcoma from endothelial cell; Merkel cell cancer from neuroendocrine cell; skin lymphoma from B and T lymphocytes and malignant fibrous histiocytoma from histiocytic or fibroblastic cells [5].

Cutaneous consequence of acute or chronic ultraviolet/ sun exposure can lead to different changes based on skin type and other different factors. In acute condition it can cause acute damage due to free mediators leading to erythema. In chronic or recurrent it can lead to benign changes of elastosis, wrinkles or cyst formation, or some consequence of cell death leading to atrophy and depigmentation and in severe cases somatic mutation leading to different form of skin cancer [6]. Risk factors for developing skin cancer include a history of skin cancer, age more than 50 year, significant sun exposure with sun burn as a child, fair skin complexion, resident of hot climate, and sun exposure more than one hour per day. Added to these, kidney transplant recipients have an increased risk based on any pre-transplant history of skin cancer, degree of immunosuppression and the fact that risk of skin cancer increases exponentially with the duration of immunosuppression [7,8]. Subsequent cumulative risk of skin cancer is also significantly higher after first skin cancer [9].

In a large cohort of more than 46,000 patients, graft or patient survival was not inferior with the diagnosis of non-melanoma skin cancer within five year of kidney transplantation [10]. But in another study in long term kidney transplant recipients with more than 30 year of transplant, five year survival (after 30th post-transplant anniversary) was 27% in patients with cancer (predominately skin cancer) vs 87 % in cancer free patient [11]. Similarly the patients with metastatic skin cancer had poorer prognosis, with high risk of relapse, poor graft and

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patient survival [12]. Moreover these patients endure the less studied burdens of skin cancer such as emotional stress stemming from the diagnosis of cancer and also risk of rejections due to modification of immunosuppression.

Although different institutes have their own guidelines and policies for skin cancer surveillance in kidney transplant recipients, it is highly recommended that kidney transplant recipients undergo routine skin cancer screenings. Kidney Disease/ Improving Global Outcomes (KDIGO) recommend informing high risk patients about the risks of skin cancer, minimizing sun exposure, use of UV blocking agents along with self-examination. It also recommends annual skin and lip examination by qualified health profession with experience in diagnosing skin cancer [13].

Going back to the patient, I did what time and my qualifications allowed: I recommended protective sun measures to her, and looked at her skin myself, ultimately finding a few lesions which appeared to be actinic keratosis. Even if I had had the necessary time, I ultimately wouldn't have helped her much, as I needed to send her to dermatology clinic any way for a possible biopsy. She has stuck with me not because her situation is unique, but the frustration she conveyed to me that day was so evident and genuine. Is it possible for us to be qualified to take care of this common condition in the solid organ transplant recipients? Can we establish a dedicated transplant dermatology clinic, so patients can have their annual skin check up on the same day and in the same setting as their other appointments?

Skin cancer in kidney transplant recipients is not a benign condition. Incidence and prevalence of invasive skin cancer is high and rising in these patients. Surely there must be a way to integrate their skin cancer surveillance into the post-transplant process that takes into account a plan for risk assessment, subsequent surveillance and follow up plans for the course of their transplant.

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