Diagnostic Delays for Non-melanoma Skin Cancers in Renal Transplant Recipients during the COVID-19 Pandemic: What is Hiding Behind the Mask?

Dear Editor,

The ongoing pandemic of coronavirus disease 2019 (COVID-19) was declared by the World Health Organization on March 11, 2020, and remains a global challenge. COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), transmitted primarily through respiratory droplets and aerosols. Even though the COVID-19 vaccine has become available since December 2020, the main preventive measures still include social distancing, hand washing, and the use of protective face masks.

By May 22, 2021, 3,437,545 deaths caused by SARS-CoV-2 have been registered by WHO, confirming the burden of this disease (1). Consequently, the pandemic has become a challenge for health care systems, as they had to be focused on the care of patients with COVID-19. During the first lockdown from March to May 2020, it was advised to postpone clinical visits whenever this could be done without risk. This recommendation was mainly aimed at older patients and those with chronic diseases, as it has been shown that they are at greater risk for complications from COVID-19.

Renal transplant recipients (RTRs) are at a greater risk for infections and different cancers due to their permanent immunosuppressive therapy. The most common malignancies in RTRs are skin cancers, particularly non-melanoma skin cancers. It has been estimated that RTRs have a 65-250 times higher risk for cutaneous squamous cell carcinoma (SCC), 10 times higher risk for basal cell carcinoma, and 2-5 times higher risk for melanoma when compared with the general population (2-4).

RTRs are at a higher risk for complications from COVID-19, not only because of their immunosup-

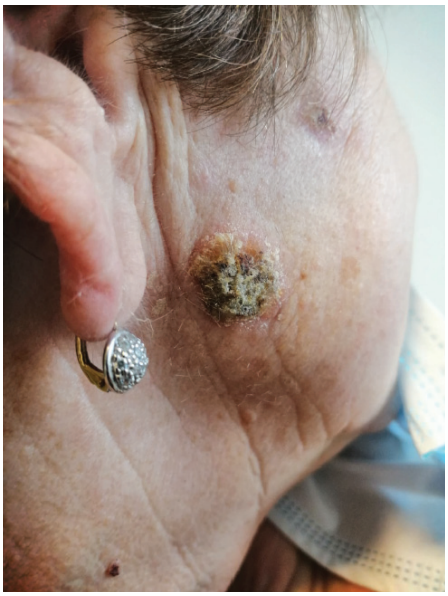

Figure 1. Cutaneous squamous cell carcinoma *in situ* (lower lesion) and actinic keratosis (upper lesion) on the patient's right cheek.

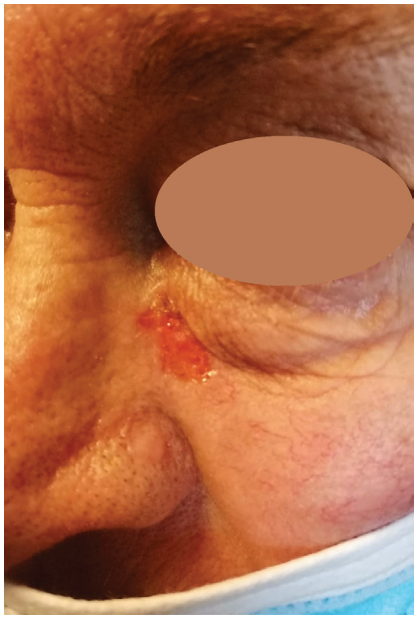

Figure 2. Basal cell carcinoma in the patient's left infraocular area.

pressive therapy but also because of different comorbidities, such as hypertension, cardiovascular disease, and diabetes mellitus (5). Therefore, RTRs tend to limit their medical visits and postpone clinical examinations for skin cancer screenings. Moreover, during clinical visits the patients are commonly asked to keep their protective masks on, increasing the risk of overlooking their facial skin changes.

Herein we present two RTRs who developed skin cancers during the COVID-19 pandemic, and the tumors were diagnosed with a significant delay.

Patient 1

A 67-year-old woman with unknown primary kidney disease received a renal allograft from a deceased donor in 2014. The immunosuppressive protocol included antithymocyte globulin induction with tacrolimus, mycophenolate mofetil, and steroid maintenance. In January 2020, she had noticed a reddish squamous lesion on her right cheek, which enlarged slowly. Since there were no other symptoms, she postponed the dermatologic examination. Additionally, she further postponed the visit to her physician during the pandemic as she wanted to avoid social contact as much as possible. One year later, at the nephrologist's examination, she was asked to take off her face mask for a skin check, and two skin tumors on her right cheek were noticed (Figure 1). One lesion was located at the angle of her mandible and presented as a hypertrophic, sharply marginated lesion with central crusting and a diameter of 2 cm. The other lesion was at the right zygomatic region and appeared as a scaly, erythematous lesion with a diameter of 7 mm. The patient was referred to a dermatologist, and a biopsy of both lesions was indicated. The pathohistological analysis revealed cutaneous SCC *in situ* for the mandibular lesion and actinic keratosis for the zygomatic lesion. SCC *in situ* has been excised, and actinic keratosis was treated by cryosurgery.

Patient 2

A 66-year-old woman received a renal allograft from a deceased donor in 2010 due to chronic glomerulonephritis without biopsy. The immunosuppressive protocol included basiliximab induction with tacrolimus, mycophenolate mofetil, and steroid maintenance. In June 2020, an erosion occurred at her left infraocular area and did not heal but instead gradually enlarged. The patient suspected that the "wound" developed due to the friction from the rim of her eyeglasses. Six months later, the nephrologist noticed the erosion which was 10×5 mm in size with a slightly elevated, pearl-colored margin (Figure 2). The patient was referred to a dermatologist who indicated tumor excision due to suspected basal cell carcinoma. The pathohistological analysis confirmed the clinical diagnosis.

DISCUSSION

Both presented patients did not inform their family physicians about their skin changes because they avoided all non-nephrological medical visits during the pandemic. The additional reason for the diagnostic delay was the fact that they kept the masks on their faces during most examinations, with the skin lesions behind the mask consequently remaining unnoticed.

The problem of diagnostic delay of skin cancers during the COVID-19 pandemic has been recognized by several studies. Canadian authors compared the number of biopsies for skin cancers during the first 15 weeks in 2020 and during the same period in 2019. They found a decrease in the number of biopsies for non-melanoma skin cancers (NMSC) and melanoma of 18% and 27%, respectively (6). A multicenter study performed in northern-central Italy showed that the number of skin cancer (NMSC and melanoma) diagnoses fell by 56.7% in weeks 11 to 20 of 2020 compared with the average number noted in the same periods of 2018 and 2019 (7). Furthermore, a single-center retrospective study in Italy demonstrated that the number of advanced skin cancers surgically treated between May 18 and November 18, 2020, was significantly higher than in the same period in 2019. These findings led the authors to conclude that the surgical excisions were postponed due to the delay in follow-ups, which resulted in increased incidence of advanced skin cancers (8).

RTRs are at particular risk of severe consequences from diagnostic delay with regard to skin cancers. Namely, skin cancers in RTRs are more aggressive and are associated with a higher incidence rate of metastases and recurrences than in the general population (9).

Therefore, RTRs should be advised to regularly check their skin for potential skin cancer, which includes self-examinations and dermatologic follow-ups.

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