## Rapidly Progressive Radiation Dermatitis in a Liver Transplant Patient Using Tacrolimus-Based Immunosuppression

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Cite this article as: Akovalı ES, Şahin M, Öksüz DÇ. Rapidly progressive radiation dermatitis in a liver transplant patient using tacrolimus-based immunosuppression. Cerrahpaşa Med J. 2025, 49, 0021, doi:10.5152/cjm.2025.25021.

Solid organ transplant recipients require lifelong immunosuppression. Immunosuppressive patients have a higher risk of non-melanoma skin cancer.

Herein, we present a patient with squamous cell carcinoma (SCC) of the skin who had unexpected and rapidly progressive dermatitis during adjuvant radiotherapy (RT).

## Case

A 65-year-old male patient with a liver transplant 10 years ago presented with a nodule at the superolateral to his right eyebrow. The patient was treated by surgery. The pathology report stated that the tumor was grade 2 SCC. The tumor size was 1.2 cm, the depth of invasion was 5 mm, the surgical margin was 9 mm, and there was no lymphovascular invasion. Adjuvant RT was not considered. Ten months later, he noticed another nodular lesion near the primary location. Following wide local excision, the pathology revealed SCC, with invasion of the dermis, subcutaneous fatty tissue, and striated muscles, and a positive surgical margin. Adjuvant RT was recommended, and informed consent was obtained from the patient. Meanwhile, the gastroenterologist continued to administer tacrolimus at a dose of 0.5 mg twice daily.

The clinical target volume was defined as the tumor region with incisions plus 2 cm and the parotid lymph node area. Volumetric modulated arc therapy was planned at a dose of 60 Gy in 30 fractions. A tissue-equivalent bolus was used for adequate skin dose. Moisturizing cream was recommended at the beginning of RT. After 10 fractions, the skin reaction unexpectedly increased. RT continued without the bolus. Topical corticosteroid and lactokine-based R1-R2 system were added to treat the skin reactions. Serum tacrolimus concentration was 6.1  $\mu$ g/L. At the 17th fraction, RT was suspended due to grade 3 radiodermatitis (Figure 1). Due to this severe dermatitis, he was also weaned off tacrolimus and started on everolimus. After 1-week gap, RT restarted and completed without any other gap. Three weeks later, he had no more signs of acute radiation dermatitis. The patient was last seen at 5-year follow-up and had no signs of recurrence.

## Discussion

Radiotherapy represents a challenging treatment due to its immunomodulatory effects and the use of immunosuppressive drugs. RT is mainly applicable outside the transplanted organ. In the literature, there are limited data on RT for skin cancer in transplant recipients, as well as on the use of tacrolimus concomitantly with RT. Some publications stated grade 2 skin toxicity, while others did not report any severe toxicity.<sup>1</sup>

Campagne et al<sup>2</sup> investigated the adverse effects of tacrolimus in renal transplant patients and observed rare skin changes related to the maximum tacrolimus concentrations. However, none of the patients in the study were treated with RT.

Atypical side effects of oral tacrolimus such as hypersensitivity reactions and food allergies have been reported.<sup>3,4</sup> Radiation recall dermatitis has also been reported in cases of topical tacrolimus use.<sup>5</sup> In light of the data in the literature, we believe that tacrolimus, as a rare condition, may exacerbate radiation dermatitis.

Received: March 25, 2025 Revision Requested: June 29, 2025 Last Revision Received: August 25, 2025 Accepted: September 10, 2025 Publication Date: December 9, 2025

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DOI: 10.5152/cjm.2025.25021



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**Figure 1.** The patient had moist desquamation and bleeding induced by minor trauma on his eyelid.

In conclusion, adjuvant RT is an applicable treatment option for skin cancer in organ transplant patients. However, radiation

oncologists and transplant physicians should be aware of the potential skin toxicity of immunosuppressive drugs.

**Data Availability Statement:** The data that support the findings of this study are available on request from the corresponding author.

**Informed Consent:** Written informed consent was obtained from the patient who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

**Author Contributions:** Concept – E.S.A., D.C.O.; Design – E.S.A., D.Ç.O.; Supervision – D.Ç.O.; Materials – E.S.A.; Data Collection and/or Processing – E.S.A.; Analysis and/or Interpretation – E.S.A., M.Ş.; Literature Search – E.S.A.; Writing Manuscript – E.S.A.

**Declaration of Interests:** The authors have no conflict of interest to declare. Funding: The authors declared that this study has received no financial support.

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