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(CASE REPORT)

Cetuximab-based management of metastatic cutaneous squamous cell carcinoma in a heart transplant recipient: A case report and literature review

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Abstract

Background: Solid organ transplant recipients face a higher risk of cutaneous squamous cell carcinoma (cSCC) due to long-term immunosuppression. Managing metastatic cSCC in these patients is challenging because immune checkpoint inhibitors (ICIs) may cause graft rejection.

Case Presentation: A 67-year-old male heart transplant recipient developed multiple cSCCs with lung metastases during his illness. After surgery and radiotherapy, disease progression prompted systemic therapy with carboplatin and cetuximab. The patient achieved a complete metabolic response after seven cycles, with no graft rejection or severe side effects. Cetuximab maintenance therapy sustained the response.

Conclusion: Cetuximab offers a safe and effective treatment for advanced cSCC in heart transplant recipients, avoiding the risks of ICIs. This case shows that Cetuximab can be a good alternative treatment.

Keywords: Cutaneous squamous cell carcinoma; Heart transplantation; Immunosuppression; Cetuximab

1. Introduction

Heart transplantation improves survival in patients with end-stage heart disease, but long-term immunosuppression increases the risk of cancers, especially cutaneous squamous cell carcinoma (cSCC). cSCC accounts for approximately 10% of cases in heart transplant recipients and is often more aggressive, with a higher chance of metastasis compared to the general population [1]. These tumors commonly occur on the head and neck[2] . Immune checkpoint inhibitors (ICIs), are effective in non-transplant patients, are risky for transplant recipients due to potential graft rejection[3–5]. Cetuximab, an anti-EGFR monoclonal antibody, is a promising alternative, but its use in heart transplant patients is not well studied. This case report describes a heart transplant recipient with metastatic cSCC successfully treated with cetuximab, demonstrating a tailored treatment approach.

2. Case presentation

A 67-year-old male, with no history of smoking, alcohol use, or family cancer, underwent heart transplantation in 2021 for end-stage ischemic cardiomyopathy. He was maintained on tacrolimus (6 mg/day, mycophenolate mofetil (500 mg/day), and prednisone (5 mg/day). In May 2022, actinic keratoses on his forehead and vertex were treated with photodynamic therapy and cryotherapy, with regular dermatological follow-up.

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In October 2022, three exophytic, ulcerative lesions appeared on the left forehead, left vertex, and right wrist. (Figure 1)

Figure 1 Ulcerative, and exophytic skin lesion located on the dorsal aspect of the right wrist

Biopsies confirmed well-differentiated cSCC, staged per the 8th AJCC edition:

- Right wrist: pT2 R0, no vascular emboli or perineural invasion
- Left vertex: pT2 R1 (deep margin), perineural invasion present.
- Left forehead: pT1 R0, vascular emboli and perineural invasion presents.

In January 2023, surgical excision and local flap reconstruction were performed. Intraoperative fine needle aspiration of a left cervical lymph node showed metastatic cSCC. A PET-CT in March 2023 revealed hypermetabolic left cervical lymphadenopathy (level Va) and a postsurgical inflammatory frontal focus. Re-excision of the vertex lesion and lymph node dissection (15 nodes) confirmed metastatic spread with capsular rupture. Adjuvant cervical radiotherapy (69.96 Gy in 33 fractions) was given from May to June 2023.

In January 2024, PET-CT detected three bilateral pleuropulmonary nodules (12 mm right upper lobe, 10 mm left upper lobe, 19 mm right lower lobe) **(figure 2 and figure 3)**, treated with stereotactic radiotherapy in March 2024.

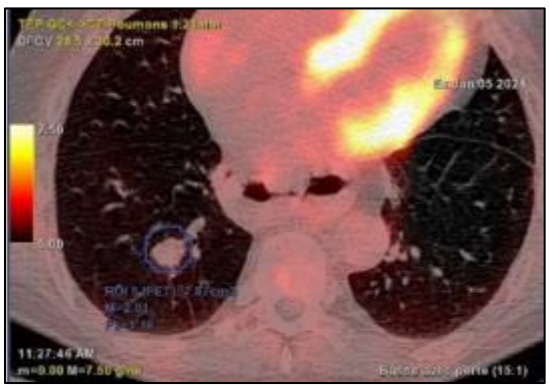

Figure 2 Hypermetabolic pulmonary nodule of 19 mm in right lower lobe

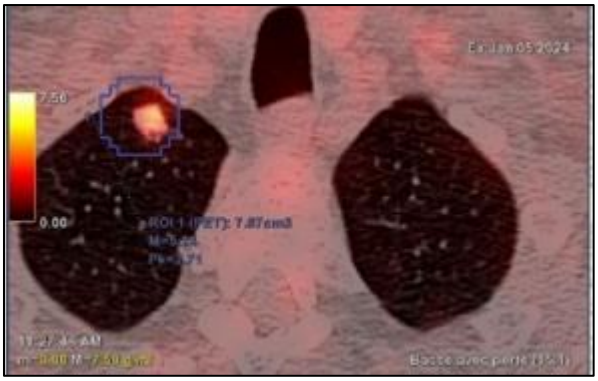

Figure 3 Hypermetabolic pulmonary nodule nodule of 12 mm in right upper lobe

In October 2024, a new 15 mm left lower lobe nodule and right basal condensation (SUVmax 2.9) appeared. (Figure 4)

Figure 4 hypermetabolic pulmonary nodule (left) and Pulmonary condensation in the apical segment of the right lower lobe (Right)

After multidisciplinary discussion, systemic therapy began with carboplatin (AUC5) and cetuximab (400 mg/m^2 loading dose, then 250 mg/m^2 weekly), alongside reduced immunosuppression (tacrolimus 4 mg/day). After seven cycles, a March 2025 PET-CT showed a complete morpho-metabolic response. Cetuximab maintenance (500 mg every two weeks) sustained the response, confirmed by a June 2025 PET-CT.

Side effects included grade II acneiform rash, xerosis with digital fissures, and grade I hypomagnesemia, managed with doxycycline, emollient and healing creams, and oral magnesium supplementation. No graft rejection or cardiovascular toxicity occurred, and the patient continues cetuximab maintenance.

3. Discussion

Managing metastatic cSCC in heart transplant recipients is complex, requiring both cancer control and graft protection. cSCC is a common cancer after a heart transplant (10% of cases), often head and neck-based (70%) and more metastatic than in no transplant patients[1,2].

Immunosuppression with tacrolimus, mycophenolate mofetil, and prednisone prevents graft rejection but promotes tumor growth by inhibiting T-cell activation[6]. In this case, immunosuppression likely drove cSCC development, as the patient had no significant UV chronic exposure.

Tacrolimus may increase skin cancer risk compared to sirolimus, which could offer protective effects[1], raising important considerations for long-term immunosuppressive strategies.

ICIs like cemiplimab are effective for advanced cSCC in the general population, with 47–50% response rates[7,8],but they carry a 41% graft rejection risk in transplant patients, including 20% in heart transplant cases[9].

PD-1 inhibitors (nivolumab, pembrolizumab) carry higher rejection risks than CTLA-4 inhibitors like ipilimumab, though the latter is less effective for cSCC [9]. Immunosuppressants may also attenuate ICI efficacy [3–5].

Other therapies such as bispecific antibodies or CAR-T cells, also risk rejection [10,11].

Cetuximab, targeting EGFR, overexpressed in 80–100% of cSCCs ,inhibits tumor growth and angiogenesis without compromising graft integrity [12].

In this case, carboplatin-cetuximab achieved a complete response, sustained with cetuximab maintenance. Literature supports these findings: a study of 10 cSCC patients ineligible for immunotherapy reported an 80% disease control rate with cetuximab, including 10% complete responses[13]. Two phase II trials showed 78% and 69% disease control rates with cetuximab, respectively, with better outcomes when combined with carboplatin [14,15].

Side effects were manageable, following guidelines [16]. The table below summarizes cetuximab tolerance in transplant recipients with various cancers and immunosuppressive regimens.

Table 1 Cetuximab Tolerance in Transplant Recipients

	cancer Type	**Transplant**	**Immunosuppression**	**Cancer treatment**	**Adverse Events**
Mydin et al. [18]	Piriform sinus SCC	Liver	Mycophenolate, tacrolimus	Cetuximab + radiotherapy	Acneiform rash and grade III dysphagia
JA, et al. [19]	Metastatic cSCC	Lung	Sirolimus	Cetuximab monotherapy	Grade 5 Toxicity
Holguin et al .[20]	Case I : Laryngeal SCC	Liver	Tacrolimus, mycophenolate, everolimus	Paclitaxel + Cetuximab	Grade III neutropenia
	Case II : Laryngeal SCC	Liver	Tacrolimus	Cetuximab + radiotherapy	GGT and PAL elevation , Acneiform rash and hypomagnesemia
Kalapurakal SJ et al. [21]	cSCC, Basal cell carcinoma	Kidney	Mycophenolate	Cetuximab monotherapy	No grade 3 and 4 toxicities
Julian A. Marin-Acevedo et al [13]	Advanced or metastatic cSCC	Kidney	Cyclosporine, prednisone Tacrolimus Tacrolimus, mycophenolate	Cetuximab monotherapy	Acneiform Rash (grade 1–2), Hypomagnesemia (grade 1–2)
		Liver	Tacrolimus, mycophenolate	Cetuximab + radiotherapy	Hypomagnesemia, Acneiform rash (grade 1–2)
		Heart	Tacrolimus, prednisone	Cetuximab + radiotherapy	Grade 5 toxicity

Immunosuppression was adjusted (tacrolimus reduced to 4 mg/day, mycophenolate discontinued), with close cardiology and oncology collaboration ensuring treatment success.

The sustained complete response indicates substantial efficacy of Cetuximab-based regimens in solid organ transplant recipients with advanced cSCC [17].

4. Conclusion

cSCC is a common and serious complication in heart transplant recipients, affecting up to 10% due to immunosuppression. Cetuximab is a safe and efficacious treatment option, avoiding the graft rejection risks of ICIs. This study and the supporting literature suggest that cetuximab could be a treatment of choice for advanced CSC in transplant patients, provided it is followed appropriately.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans subjects by any of the authors.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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