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# Sirolimus-Induced Rash in a Kidney Transplant Patient

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## ABSTRACT

Sirolimus is an inhibitor of the mammalian target of rapamycin, which is used in kidney transplant immunosuppression. The clinical spectrum of cutaneous adverse events associated with sirolimus use varies, with maculopapular rash being an uncommon side effect very rarely reported in the literature. We present the case of a 78-year-old male renal transplant recipient who developed a diffuse maculopapular pruritic rash after starting sirolimus. This case report demonstrates that maculopapular rash is an uncommon sirolimus-related side effect that must be identified promptly so the medication can be discontinued and rash progression prevented.

## LEARNING POINTS

- Acneiform dermatitis, folliculitis, onychopathy, oral ulcers, rash and stomatitis are all common dermatological side effects of sirolimus.
- The occurrence of a diffuse pruritic maculopapular rash associated with sirolimus use is rare, but an important differential to keep in mind.
- Sirolimus cessation is required in case of diffuse pruritic maculopapular rash.

## KEYWORDS

Maculopapular rash, sirolimus, renal transplant

## INTRODUCTION

Sirolimus is a potent non-nephrotoxic immunosuppressive agent used to prevent rejection in renal allograft recipients [1]. Numerous side effects have been associated with sirolimus use, including anaemia, thrombocytopenia, leukopenia, hyperglycaemia, dyslipidaemia, delayed wound healing, lymphocele, peripheral lymphoedema and interstitial pneumonitis. Commonly experienced dermatological adverse effects of sirolimus include acneiform dermatitis, folliculitis, onychopathy, oral ulcers, rash and stomatitis [2, 3]. Herein, we describe the case of a 78-year-old man who developed diffuse maculopapular pruritic rash following the initiation of sirolimus therapy.

## CASE DESCRIPTION

A 78-year-old man with a history of hypertension, primary hyperparathyroidism, hyperlipidaemia, renal cell carcinoma with left nephrectomy, prostate cancer in remission, and end-stage renal disease treated with a transplant, presented with a 1-month diffuse maculopapular pruritic skin rash and hair loss. About 6 weeks previously his immunosuppressive therapy had been changed from azathioprine and prednisone to

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sirolimus and prednisone. His initial vital signs were normal. Laboratory results showed anaemia at 10.2 g/dl and a sirolimus level of 3.9 ng/ml. Upon examination, a generalized erythematous and scaly maculopapular rash covering the face, neck, upper extremities and back was observed (*Fig. 1*). To rule out transplant rejection and acute infection, an infectious work-up (HSV IgG, CMV DNA, EBV PCR and BK PCR) was ordered, which came back negative. The patient was passing enough urine, and his kidney function was stable. Following suggestions from transplant nephrology, sirolimus was held on presentation. A skin biopsy by a dermatologist revealed subacute pustular dermatitis with eosinophils and spongiosis that was consistent with a medication reaction (*Fig. 2*).

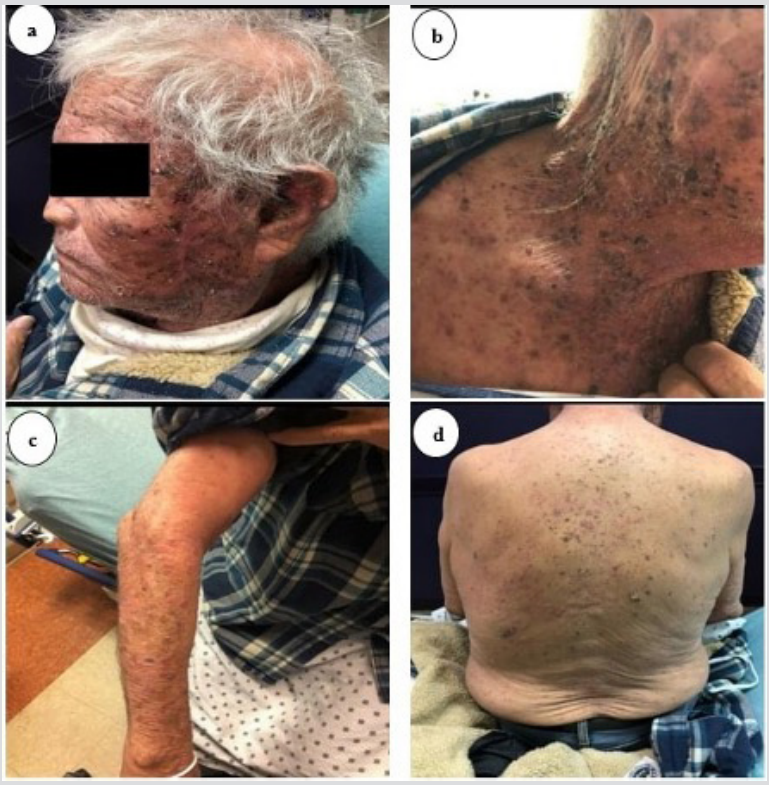


*Figure 1 (a–d). Erythematous maculopapular rash and plaques on the scalp, face, neck, arms, back and upper chest*

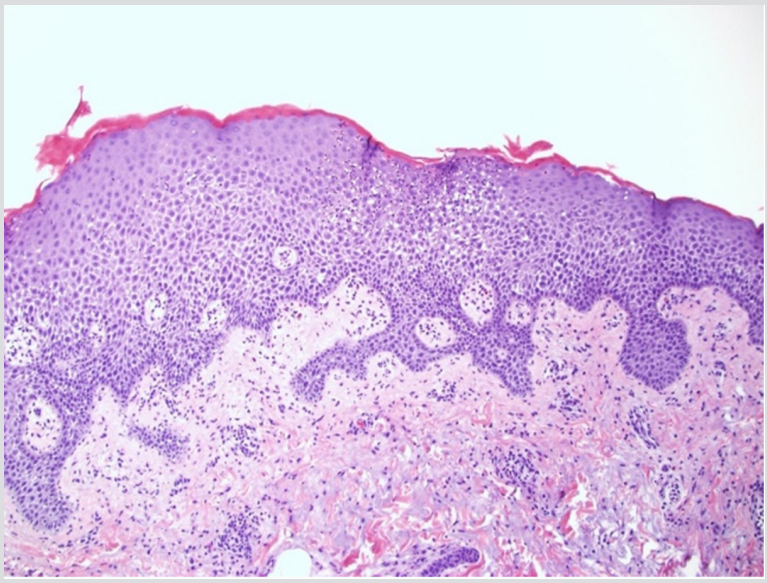

*Figure 2. Skin biopsy revealed spongiosis with scattered eosinophils and intraepidermal neutrophils suggestive of drug eruption dermatitis*

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It was determined that sirolimus was the causal agent based on the timing of the symptoms. The patient was started on topical steroid cream and high-dose oral prednisone with an 8-day taper to a daily home dose of 5 mg per day. The patient's rash continued to remarkably improve. Following the initiation of low-dose tacrolimus and close monitoring by dermatology and transplant nephrology, he was discharged from hospital in a stable condition. On follow-up, he showed complete resolution of the rash.

## DISCUSSION

Sirolimus is an immunosuppressant medication which is increasingly being used to prevent organ rejection in transplant patients. This potent immunosuppressant drug has been found to reduce calcineurin trough levels, resulting in fewer nephrotoxic effects [4]. However, a range of skin disorders have been reported to be linked to sirolimus use, with acne-like eruptions, oedema, xerosis, aphthous ulceration, epistaxis and nail involvement being the most common [5].

Diffuse pruritic maculopapular rash associated with sirolimus use is rare. Most such rashes are mild (resembling localized, mild seborrheic dermatitis) and occurred in 6–20% of patients in phase III trials [6]. To the best of our knowledge, severe diffuse maculopapular rash resulting from the use of mTOR inhibitors has been documented twice in the literature [7, 8]. One of these cases was a 56-year-old liver transplant recipient who developed maculopapular rash which completely resolved after he switched to mycophenolate mofetil. Furthermore, findings of a meta-analysis revealed an increased risk of developing skin rash in cancer patients receiving temsirolimus, which is an ester of sirolimus [9]. Our patient also had multiple underlying malignancies, which included renal cell carcinoma and prostate cancer in remission.

The precise mechanism causing maculopapular rash with sirolimus use is not clear. It has been hypothesized that there is a direct inhibitory effect on signalling pathways that regulate cell growth and tissue repair, with smaller keratinocytes found in those with reduced mTOR signalling activity [10, 11].

In conclusion, mild rash is one of the common complications of sirolimus use. However, our case highlights a diffuse maculopapular rash as one of its adverse effects. Drug-induced adverse events are often challenging to diagnose, and require keen clinical observation and discontinuation of the causative agent as the mainstay of treatment.

## CONCLUSION

It is critical to keep the rare adverse effect of a diffuse pruritic maculopapular rash in mind, especially in a patient on sirolimus, since stopping the medicine on time is critical for managing patient morbidity and mortality.

account for up to 16% of emergency department visits, data on reducing ADEs by medication reconciliation are rare [9]. Nevertheless, both hospital and community changes in medication should be monitored closely in solid organ transplant patients to prevent drug–drug interactions. Given the cumulative complications of drugs with a narrow therapeutic index such as tacrolimus, one should closely monitor its activity and any potential for drug–drug interactions such as acute tacrolimus toxicity as described in our patient.

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