Use of Sirolimus for Refractory Cutaneous Dermatomyositis: A Retrospective Case Series

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Background

- Dermatomyositis is an idiopathic inflammatory myopathy that classically presents with symmetric muscle weakness and heliotrope rash, Gottron papules and photodistributed erythema
- Cutaneous lesions may be more refractory to treatment than muscular disease
- First-line systemic therapy for cutaneous dermatomyositis includes anti-malarials, methotrexate and mycophenolate mofetil, and second- and third-line treatments include intravenous immunoglobulin (IVIG), cyclosporine and Janus kinase inhibitors
- Sirolimus is a mammalian target of rapamycin (mTOR) inhibitor with immunomodulatory properties
- Sirolimus received FDA approval in 1999 for prophylaxis against organ rejection in kidney transplant patients
- Within dermatology, topical sirolimus was approved in 2022 to treat angiofibromas in tuberous sclerosis complex and is occasionally used for inflammatory dermatoses as well as orally for complex vascular anomalies
- Less is known regarding the outcomes of patients with recalcitrant cutaneous dermatomyositis treated with sirolimus
- We present a single center retrospective case series of four female patients (mean age: 71-years-old) who were treated with oral sirolimus for clinically amyopathic dermatomyositis, with a mean follow-up time of 9 years

Methods

- A total of six patients were identified who underwent treatment for dermatomyositis at our institution and who were also prescribed oral sirolimus
- Two patients were excluded from the study: one who received sirolimus following lung transplantation and one patient who did not initiate sirolimus
- All included patients started sirolimus after failing multiple other therapies, including azathioprine, hydroxychloroquine, and methotrexate (mean number of failed therapies = 5)
- Patients took a dosage of 1 to 2 mg sirolimus daily
- To assess response to sirolimus treatment, the primary endpoint was global improvement in cutaneous disease, based on clinical examination by a physician
- Treatment response was graded as complete, significant, moderate, or mild, and time to effect was recorded

Results

- Three of four patients achieved at least significant control of disease, including one patient with complete remission who was able to discontinue therapy without recurrence
- Three patients concurrently taking prednisone were able to decrease their dose while on sirolimus
- Adverse effects during sirolimus therapy included anemia, hypercholesterolemia, and peripheral edema
- One patient developed renal insufficiency during the course of treatment, which was likely secondary to a prior history of hypertension
- No clinically significant infections or new malignancies occurred during sirolimus therapy or follow-up
- One patient with lung cancer did not experience progression of malignancy despite 6 months of sirolimus therapy

Case	Age/gender	Diagnosis	MSA	Malignancy	Prior therapies	Outcomes	Concomitant treatments	Disease duration (months)	Sirolimus dose	Effect	Sirolimus treatment duration (months)	Adverse Effects
1	61/F	CADM	None	None	OCS, AZA, MTX, HCQ, MMF	All prior therapies were ineffective except OCS	IVIG, OCS (15mg/day decreased to 2.5mg/day)	98	1 mg daily, 2 mg daily	Moderate control of disease after 8 months on 1 mg daily, Complete clearance after 6 months on 2 mg daily	37, stopped with disease remission	None
2	65/F	CADM	None	None	OCS, AZA, MTX, HCQ, MMF	All prior therapies were ineffective except OCS	OCS (7.5mg/day decreased to 2.5mg/day)	178	1 mg daily, 2 mg daily	Moderate control of disease after 7 months on 1 mg daily, Significant control of disease after 11 months on 2 mg daily	142, remains on long-term therapy	HLD
3	78/F	CADM	Anti-PM/Scl-100	None	HCQ, MMF, MTX, AZA, IVIG, OCS	All prior therapies were ineffective except OCS	OCS (60mg/day decreased to 2.5mg/day)	193	1 mg daily, 2 mg daily	Mild control of disease after 6 months on 1 mg daily, Significant control of disease after 4 months on 2 mg daily	112, stopped due to side effects	Renal insufficiency
4	79/F	CADM	Anti-TIF1-γ (Anti-P155/140)	Lung cancer	HCQ, MTX, IVIG, RTX, MMF, AZA, apremilast	All prior therapies were ineffective	None	45	2 mg daily	Moderate control of disease after 2 months on 2 mg daily	6, stopped due to side effects	Peripheral edema, anemia

Table 1. Characteristics of patients included in the study.

Table legend:

F, female; CADM, clinically amyopathic dermatomyositis; MSA, myositis specific antibody; PM, polymyositis; Scl, scleroderma; TIF1-γ, transcriptional intermediary factor 1 gamma; OCS, oral corticosteroids; HCQ, hydroxychloroquine; MTX, Methotrexate; IVIG, Intravenous immunoglobulin; AZA, azathioprine; MMF, mycophenolate mofetil; RTX, rituximab; HLD, hyperlipidemia.

Discussion

- There is currently a dearth of published literature regarding the use of sirolimus in dermatomyositis
- Although sirolimus has been studied in randomized clinical trials to treat cutaneous sarcoidosis and inclusion body myositis, only a single published case report has described its use in treating dermatomyositis
- There is a known association between dermatomyositis and an increased risk of malignancy
- As sirolimus possesses antiangiogenic and antiproliferative properties, it may theoretically be used cautiously in concomitant malignancy
- Side effects of sirolimus include anemia, hyperlipidemia, increased creatinine and peripheral edema, which was consistent with the results of our study
- These adverse effects generally improve with sirolimus cessation, and the drug is otherwise well tolerated by patients
- This retrospective series is limited by the lack of a control group, small sample size, and subjective outcome measure
- Sirolimus trough level monitoring was inconsistent, and our cohort was exclusively women with clinically amyopathic dermatomyositis

Conclusions

- The safety and apparent efficacy of sirolimus in these patients suggests that the mTOR inhibitor may represent an underutilized treatment option for patients with refractory cutaneous dermatomyositis
- Further controlled studies in larger cohorts are needed to explore the safety and efficacy of sirolimus in this population, including in the setting of malignancy

References

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