

Radiotherapy for treatment resistant Darier's disease

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Abstract

Darier's disease is a rare autosomal dominant disorder of keratinisation. It is characterised by chronic, relapsing hyperkeratotic papules and plaques that can cause significant pain, recurrent infection, and impaired quality of life [1]. Patients with refractory disease may require systemic immunosuppressive or biologic therapies, which can carry risks including serious infection and increased risk of secondary malignancy [2,3]. Despite historical successful use, radiotherapy has more recently been avoided due to risk of secondary malignancy, challenges in treating larger body surface areas and availability of new medications. We present a case of treatment-resistant Darier's disease successfully managed with localized and subsequently total skin radiotherapy resulting in significant clinical improvement after failure of multiple conventional therapies. Evidence for radiotherapy in Darier's disease is currently limited to case reports. This case adds to the growing body of literature supporting its efficacy and highlights the role of radiotherapy in refractory disease.

Introduction

Darier's disease is a rare autosomal dominant disorder of keratinisation caused by pathogenic variants in the ATP2A2 gene, resulting in abnormal calcium signalling and impaired epidermal cell adhesion [4]. Symptoms are frequently exacerbated by heat, sweating, and ultraviolet exposure, leading to painful fissuring, malodour, and secondary infection, with a significant impact on quality of life [5]. Treatment options range from topical emollients to topical steroids and oral retinoids. Persistent disease has been shown to have variable response to calcineurin inhibitors and biologic agents [6]. As with other benign skin conditions; radiotherapy has been explored as a treatment option for severe, treatment-resistant disease.

The efficacy of radiotherapy in Darier's disease was first recognised through incidental clinical improvement observed in patients receiving radiotherapy for unrelated malignancies [7,8]. Since then, a small number of case reports have described radiotherapy as a successful primary treatment for refractory Darier's disease, suggesting it may represent a valuable therapeutic option in carefully selected patients [9,10].

This case report looks at the successful patch treatment of a case of treatment resistant Darier's disease and subsequent successful total skin electron therapy [11].

Case Description

A woman in her 50s with severe treatment-resistant Darier's disease was referred by dermatology for consideration of radiotherapy after failure of multiple medical therapies. Her disease was characterised by extensive, symptomatic skin involvement resulting in recurrent infections, repeated hospital admissions, and significant functional impairment that ultimately prevented her from working.



Figure 1: Skin prior to starting radiotherapy; Images from left to right; left abdomen, left anterior thigh, left anterior shin.

This patient's past medical and surgical history included Atrial Septal Defect (ASD) repair in 2022, depression, cholecystectomy, peptic ulcer disease, and vitamin B12 deficiency.

Prior treatments included: 11 months of ustekinumab, 6 months of guselkumab, 3 months of tofacitinib, 3 months of oral steroids, isotretinoin and valaciclovir in prophylactic and therapeutic doses. Multiple intensive topical agents were also trialled including Fucibet®, Betnesol®, Flamazine®, Betnovate®, Travocort®, Eumovate®, and Dermovate®. Applications for treatment with dupilumab inhibitors were also submitted but were declined.

Following discussion with the patient, a test area measuring 10 × 14 cm was planned, and a dose of 20 Gy in 10 fractions CXT was delivered to the left anterior thigh. The dose and fractionation schedule were selected following a review of the published literature describing successful outcomes in similar cases [12].



Figure 2: Images of set up pre-treatment, half way through radiotherapy, two weeks post radiotherapy.

Following a favourable response, with the treated area remaining in clinical remission for three months, a decision was made to proceed with Total Skin Electron Therapy (TSET). A total dose of 12 Gy was delivered over a two-week period using the Stanford technique.

Treatment was generally well tolerated. During the course of TSET, the patient experienced superficial skin discomfort, which was managed successfully with amitriptyline. Alopecia was also observed despite treatment planning measures aimed at minimising scalp dose. The skin discomfort resolved, and amitriptyline was discontinued two weeks following completion of treatment.

At three months following TSET, the patient remained in clinical remission with sustained symptomatic improvement and no requirement for further systemic therapy (Figure 3).



Figure 3: Images 3 months post TSET.
(Right thigh, left lower limb, posterior trunk)

Discussion and Conclusion

Initial localised radiotherapy successfully established disease remission and supported the subsequent use of total skin electron therapy, resulting in ongoing clinical remission with limited acute toxicity. Modern radiotherapy techniques enable precise treatment of superficial disease while minimising dose to deeper tissues. In this case, treatment-related toxicity was mild and self-limiting.

Although radiotherapy has traditionally been reserved because of concerns regarding late effects in benign disease, these risks should be balanced against the substantial morbidity associated with refractory Darier's disease and the cumulative risks of prolonged systemic immunosuppressive therapy. Careful patient selection and shared decision making within a multidisciplinary team are essential when considering radiotherapy as a treatment option.

We hope this case contributes to the growing body of evidence supporting radiotherapy as an effective treatment for selected patients with severe, treatment resistant Darier's disease. Further studies and long term follow up are required to better define its role, optimal treatment protocols, and long-term outcomes.

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