Dupilumab as an adjuvant treatment for keloid-associated symptoms

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Key words: biologics; dupilumab; IL-13; IL-4 receptor; keloids; Th2 cytokines.

INTRODUCTION

Diaz et al[1] recently reported a case of a 53-year-old African American man with a serendipitous improvement in his keloids after 7 months of treatment with dupilumab for severe atopic dermatitis (AD). In the same study, using real-time polymerase chain reaction, the authors were able to demonstrate the overexpression of helper T cell type 2 (Th2) genes, notably interleukin 4 (IL-4) receptor and interleukin 13 (IL-13), in lesional keloidal tissue. Dupilumab is an IL-4 receptor blocker that effectively inhibits Th2 type cytokines and, therefore, may be a novel treatment option for difficult-to-treat keloids. Herein, we report a case of a patient who experienced a significant symptomatic improvement in her keloid without objective reduction in its size.

Abbreviations used:

AD:	atopic dermatitis
IL-13:	interleukin 13
IL-4:	interleukin 4
Th2:	helper T cell type 2

CASE REPORT

A 37-year-old South Asian woman presented with an exquisitely tender and inflamed keloid on the sternum from a previously ruptured cyst that started approximately 10 years ago (Fig 1). The patient had symptoms from the outset, which continued to worsen to the point where even the slightest touch from her clothing caused significant discomfort. Despite the use of topical anesthetics, cooling, and vibratory distractions, the patient was unable to tolerate intralesional steroids. Based on results from the aforementioned case report,[1] a trial of off-label use of dupilumab was agreed upon.

The patient was given a 600 mg subcutaneous injection of dupilumab, followed by 300 mg every 2 weeks thereafter. At her 4-week follow-up, the size of the keloid remained unchanged; however, the patient reported a noticeable reduction in pain (Fig 2). The patient underwent 3 months of dupilumab therapy in total that led to a near complete absence of her symptoms even without a reduction in the overall size of the keloid (Fig 3). The patient reported that she was now able to wear clothing comfortably without restrictions. At this point, the patient was satisfied with the outcome and declined any additional treatment, including the continuation of dupilumab. Approximately 4 weeks after her last dose of dupilumab, the patient reported that the itching and pain due to her keloid were slowly starting to return. As of today, the patient has still not returned for follow-up.

DISCUSSION

All wound healing starts with an inflammatory stage; however, a prolonged inflammatory phase may lead to excess fibroblast activity.[2] Maeda et al[3] were able to show that IL-4 and IL-13 stimulated human dermal fibroblasts to secrete transforming growth factor-β indirectly via periostin, which is thought to be central in abnormal scar formation. Therefore, pretreatment with dupilumab may be a therapeutic strategy for symptomatic keloids before any procedure is initiated. Alternatively, posttreatment with dupilumab may be considered for patients who are at high risk of keloid formation. This may be of particular relevance in patients who have sternotomy scars that can be very painful, difficult to treat, and profoundly negatively impact the quality of life.[4]

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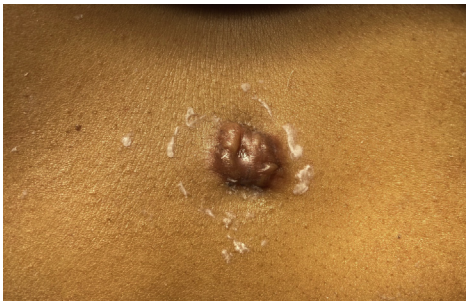

Fig 1. Photograph of the keloid at baseline.

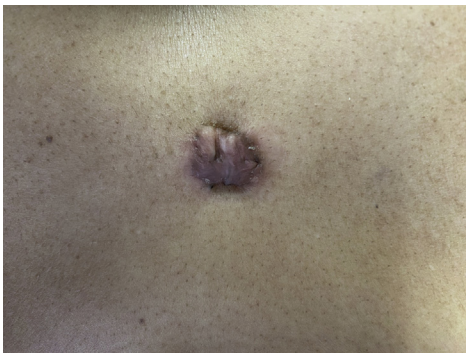

Fig 2. Four weeks into dupilumab treatment.

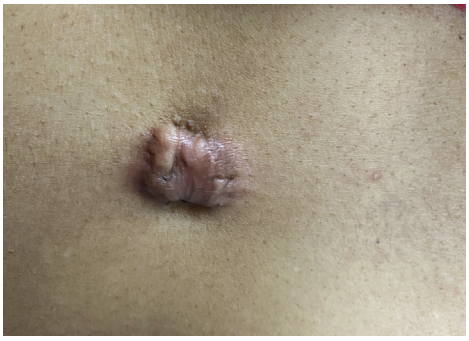

Fig 3. Twelve weeks into dupilumab treatment.

Compared with the previous case reported by Diaz et al,[1] our case had some important differences. Their patient had comorbid AD and was treated for 7 months with dupilumab, whereas our patient did not have an atopic history and was treated only for 3 months. Although patients with AD may have a higher risk of keloid formation,[5] IL-13 was also found to be overly expressed in lesional and nonlesional keloid skin in patients without a background of AD.[1] Therefore, a history of AD may not be predictive of responders.

Despite our results, questions remain. First, the optimal duration of treatment with dupilumab needs to be determined. Would a longer treatment course afford any additional benefit beyond what was seen in our patient? Or could our patient have achieved the same results with a shorter duration of treatment? Second, given the cost of biologics and their potential adverse events, how does one justify the use of dupilumab in this setting, especially if it is only for symptomatic treatment? Shared decision making to weigh the risks versus benefits of the treatment and the cost to the system will be critical.

In conclusion, we report our experience with using dupilumab as an adjuvant treatment for keloid-associated symptoms. Although our patient did not experience a reduction in the size of her keloid after 3 months of dupilumab treatment, she did have a remarkable improvement in her symptoms and was in a much better position to tolerate intralesional steroids. We hope that our case will encourage further research to better understand the role of Th2-mediated inflammation in abnormal scar formation so that it may serve as a target for future therapies.

Conflicts of interest

Dr Song has been a consultant, speaker, or investigator for the following companies: Sanofi & Regeneron, AbbVie, Janssen, Amgen, Novartis, Lilly, SUN, UCB, Incyte, and Castle Biosciences. Author Wong has no conflicts of interest to declare.

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