

## Successful Treatment of Epidermal Nevus-associated Pruritus with Topical Ketamine–Amitriptyline–Lidocaine

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Inflammatory linear verrucous epidermal nevus (ILVEN) is a rare, linear, unilateral, pruritic eruption that usually presents during childhood. It is more commonly seen on an extremity, although cases on the head and neck area have been reported in the past (1). It is considered a variant of keratinocytic epidermal nevus; however, it has a significant histological similarity with psoriasis. Patients who have this condition usually complain of intense pruritus (2). Treatments that are regularly effective in psoriasis have shown low efficacy on the management of these lesions, as well as their related symptoms (3). We present here a case of successful treatment of pruritus associated with an epidermal nevus with the use of topical Ketamine 10% – Amitriptyline 5% – Lidocaine 5% in lipoderm base (TKAL). The preparation is widely used in the US for nociceptive pain and is prepared by a compounding pharmacy. All ingredients are FDA approved.

### CASE REPORT

A 24-year-old man presented to our Itch Clinic complaining of an extremely pruritic plaque involving his forehead and temple area, compatible with a diagnosis of ILVEN. The patient had this lesion since childhood, initially intermittently itching, however, over the past few years it became severely pruritic. He stated that itching was 9.5/10 in the itch Numeric Rating Scale (NRS; (4)), lasted several hours, presented 3–4 times a week, and was predominantly at bedtime, interfering with his sleeping pattern. Topical therapies including mid and high potency steroid ointments and multiple moisturizer creams had failed to relieve his symptoms. The past medical history and family history were insignificant otherwise. Cutaneous examination revealed a well-demarcated, linear, red, scaly plaque on his right forehead (Fig. 1), as well as multiple linear verrucous papules on his neck that were coalescing into a plaque. A biopsy of the forehead lesion was consistent with a psoriasiform epidermal hyperplasia with spongiosis and moderate inflammation, compatible with epidermal nevus with secondary inflammation. At that point, we decided to start him on TKAL applied on the lesions 1–3 times daily. After only one application, the patient noted significant improvement of his itch that lasted for more than 6 h. After 6 weeks of treatment, the patient returned to our clinic with complete relief of his pruritus and an itch rating of 0/10 on the itch NRS, and



Fig. 1. Well-demarcated, linear, red, scaly plaque on the right forehead consistent with ILVEN (post-treatment).

noted no side effects. In addition, there was significant reduction of the erythema and hyperkeratosis.

### DISCUSSION

To our knowledge, this is the first time that TKAL has been used to treat pruritus associated with epidermal nevi. We recently published a retrospective analysis that demonstrated the effectiveness of TKAL on chronic itch associated with different skin disorders (5). This analysis included 96 patients; noted side effects included mild burning sensation and redness in the application site. Only one patient reported dizziness but was able to continue with the therapy. Nonetheless, blinded controlled clinical studies are required to further evaluate TKAL's safety and utility (5). Since the lesions in our patient were limited to head and neck area where cutaneous penetration of drug is high, the effectiveness of this topical compound might have been favored. It is unclear if one compound is superior to the others or if the combination

of the 3 is more effective than each one individually, however we assume that targeting different ion channels in the peripheral nerve conduction will boost the effect. The suggested mechanism of action is related to blockade of N-methyl-D-aspartate receptors and Na<sup>+</sup> channels in peripheral nerve fibers that lead to analgesia (6). In addition, the cessation of trauma induced by scratching might reduce the koebnerization and inflammatory response in the lesion. ILVEN is characterized by an intense, hard to treat pruritus and management of this condition can be a therapeutic challenge. In spite of closely resembling psoriasis histologically, lesions are commonly resistant to antipsoriatic therapy. As seen in this case, pruritus is usually patients' chief complaint, and it significantly lowers their quality of life. Other treatments that have been anecdotally reported to provide some relief for this rare and bothersome disease were the use of high potency topical steroids (that in this case failed) and tacrolimus (7, 8). Full thickness excision of the lesion with or without a subsequent application of a skin graft seems to be the most effective treatment, however it generates a significant scar (9). So far laser therapy using Co<sub>2</sub> laser was not successful for ILVEN probably due to the deeper skin involvement of ILVEN versus epidermal nevi (10). It could be of interest to assess whether other topical anti-nociceptive drugs such as capsaicin in high concentration targeting TRPV1 channel have a similar antipruritic effect. Although prospective investigation is necessary to confirm its effectiveness in this condition, TKAL should be considered as a topical therapy to treat pruritus associated with epidermal nevi.

*The authors have no conflicts of interest to declare.*

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