



Nevus Unius Lateris (NUL) in a Three-Year-Old Child Treated by Tretinoin 0.025%, Desoxymethasone 0.25%, and Urea 20% Cream

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ABSTRACT

Background: Linear verrucous epidermal nevus is the most frequent variant of the epidermal nevus classification. Linear verrucous epidermal nevus is characterized by the proliferation of epithelium arranged in a configuration that follows Blaschko's line. Nevus unius lateris (NUL) is a variant of the verrucous epidermal nevus, which has a unilateral distribution of lesions. Lesions are usually found at birth or in the first year of life as brown to grey verrucous papules or papillomatous plaques. The management of NUL is challenging as the results are varied and there is a high risk of recurrence. **Purpose:** to report a case of NUL and its management, especially in children. **Case:** A 3-year-old girl presented with brownish spots and multiple small lumps on the left buttock that have extended to the left leg since she was 9-days-old. On dermatologic examination, there were numerous hyperpigmented verrucous papules and plaques along the Blaschko line over the affected area. In this case, the diagnosis of NUL, is based on clinical symptoms and dermoscopy examination showed multiple large brown oval or round structures with hyperpigmented brown border. The patient was treated with combination topical therapy of tretinoin 0.025%, corticosteroid desoxymethasone 0.25%, and urea 20% cream, and the lesion improved within four weeks. **Discussion:** Epidermal nevus is often cosmetically disturbing. The treatment is still challenging and various, including surgical and non-surgical, but none is ideal and could potentially recur over months or years. A topical corticosteroid as an anti-inflammatory agent combined with tretinoin as an anti-proliferative agent may be effective. In addition, urea 20%, which is mildly keratolytic, may be beneficial. **Conclusion:** Topical combination therapy of tretinoin, desoxymethasone, and urea is non-invasive, tolerable, and effective for children.

Keywords: Blaschko line, Corticosteroid, Epidermal Nevus, Tretinoin, Urea.

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| Article info |

Submitted: 28-03-2022, Accepted: 11-07-2023, Published: 31-07-2024

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BACKGROUND

Linear verrucous epidermal nevus is the most frequent epidermal nevus, a group of congenital malformations originating from ectoderm cells during embryogenesis. Linear verrucous epidermal nevus is characterized by the proliferation of epithelium arranged in a configuration that follows Blaschko's line.¹ When only affecting one region asymmetrically, it is called nevus unius lateris. Lesions are usually found at birth or in the first year of life as brown to grey verrucous papules or papillomatous plaques. Epidermal nevi can be accompanied by neurological,

musculoskeletal, and visual disturbances known as epidermal nevus syndrome.^{1,2}

The incidence of epidermal nevus occurs in 1 in 1000 live births. Among 10,000 patients with skin tumors in the United States, 4 cases of NUL, or 0.01% ,were reported.³ In Sanglah General Hospital since 2018, there have been 2 cases of NUL in children. About 80% of cases appear in the first year of life; the rest appear in adolescence.⁴ Most cases are reported to be sporadic, and familial connections are rare.^{4,5} The management of NUL is challenging due to varied results and a high recurrence rate.⁶

CASE

A 3-year-old girl presented with brown spots on the buttocks up to the left foot; they first appeared when the patient was 9-days-old as a brown spot on the left side of the buttocks. The brown area had increased in size and amount with a rough surface and spread along her left limb since she was 1-year-old. The patient denied complaints of redness, itching, and pain. There was no delay in her development process. A history of seizures, learning difficulties, hearing loss, and visual disturbances was denied, as was a family history of the same complaints.

On physical examination, the general condition was good and *compos mentis*. Vital signs were within normal limits. The body mass index and other general examinations were normal. Dermatologic examination on the gluteal, femoral posterior, and pedis sinistra regions showed multiple hyperpigmented papules with verrucous surfaces that partially coalesced into plaques and were arranged linearly following the Blaschko's line (Figures 1a-b).



Figures 1a-b. Multiple hyperpigmented papules with verrucous surfaces that partially that coalesced into plaques and are arranged linearly following the Blaschko's line.

Dermoscopic examination revealed an irregular globular pattern. There were multiple large brown oval or round structures with a hyperpigmented brown border surrounded by hypopigmented area (Figure 2). Histopathological examination was not done because the patient was too young and not cooperative, according to the parents.

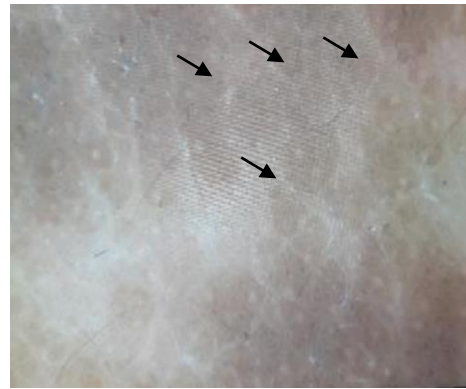


Figure 2. On dermoscopic examination, large brown oval or round structures with hyperpigmented brown border surrounded by hypopigmented area (black arrows).

This patient was diagnosed with nevus unius lateris (NUL) based on the clinical and dermoscopic examinations. The patient was treated with tretinoin 0.025% cream topically every 24 hours (applied at night), desoxymethasone 0.25% cream topically every 12 hours, and urea 20% cream topically every 12 hours on the lesions. We informed the parents to notice if there were any neurological disorders, developmental disorders, visual disturbances, or side effects of the topical drugs such as redness, peeling skin, or burning sensations, including the risk of recurrence. After four weeks of therapy, the lesions improved, leaving erythema and hypopigmentation (Figure 3a-b). Afterwards, we modified the treatment into tretinoin 0.025% cream topically every 48 hours (applied at night), desoxymethasone 0.025% cream topically three times a week, and urea 20% cream topically every 12 hours on the lesions to prevent a recurrence.

DISCUSSION

Epidermal nevus is a cutaneous mosaicism due to post-zygotic genetic mutations in epithelial proliferation. Nevus unius lateris (NUL) is characterized by a unilateral distribution of the lesion following the Blaschko line.^{3,4} The genetic mechanism of nevus unius lateris results from cutaneous mosaicism; post-zygotic mutations during embryogenesis consist of 40% RAS mutations, 40% FGFR3, or PIK3CA 20% KRT11 or KRT1 mutations.^{4,7} The lesions are usually found at birth or in the first year of life, develop during childhood, and stabilize at puberty.⁴ Sometimes, it may be accompanied by other epidermal nevus syndrome disorders, consisting of skin, nerve, eye, and musculoskeletal disorders.³ In this case, the skin manifestation is consistent with other

literatures without any manifestation of epidermal nevus syndrome.

The principal diagnosis of NUL is based on clinical symptoms and dermoscopic examination, but histopathological examination can also be considered to confirm the diagnosis.⁵ Dermoscopic examination shows irregular pigment and globular patterns.⁸ In this case, the patient was diagnosed as nevus unius lateris (NUL) based on the clinical symptoms and dermoscopic examination. Histopathological examination was not performed due to the parents' refusal, and the patient was not cooperative.

Patients often complained about epidermal nevi for cosmetic reasons. There are various therapy options, but none are ideal or satisfying and can recur several months or years later.^{2,3} Management of NUL consists of surgical and non-surgical therapy. Surgical excision is a definitive therapy with a low recurrence rate but often leave scars, so surgery is recommended only for small lesions. Electrofulguration, cryotherapy, dermabrasion, and electrosurgery may be performed, but there is a risk of recurrence and scar formation.^{2,9} Light-based therapies such as CO2 laser, Nd: YAG, and 585 nm pulsed dye laser may provide effective results. However, recurrences may occur months or years after the nevus removal by any method.^{2,10} Topical therapies that can be used are keratolytic agents, combinations of retinoid and 5-fluorouracil (FU), salicylic acid, calcipotriol, dithranol, chemical peels, occlusive topical corticosteroids, and podophyllin.¹¹⁻¹³ Urea 20% as a keratolytic agent increases the penetration of other topical substances (for example, corticosteroids) and it is a penetration enhancer to optimize the effects of other topical agents. The potential mechanism of urea is to dissolve keratin by promoting the breakdown of hydrogen bonds.^{4,14} Topical corticosteroids under occlusion combined with tretinoin show good improvement. Corticosteroid has antiinflammatory and immunomodulatory effects, and tretinoin has antiproliferative effects on keratinocytes, normalizing abnormal differentiation and down-regulating epidermal growth factor and hyperproliferative keratins. These modalities may improve the irregular nevus surfaces while having a high recurrence rate.^{2,15}

Another study found that the combination of tretinoin 0.1% and 5-FU with occlusion within 2 months showed effective improvement. However, recurrences occurred when it was stopped.¹¹ A combination of topical tretinoin 0.1% cream every 12 hours and 5-FU every 24 hours for 6 months showed good results and recurred within 3-4 weeks after

stopping therapy.¹² Another study in a 11-year-old child treated with tacrolimus 0.1% and fluocinonide topically every 12 hours with occlusion for 2 weeks, then continued without occlusion for 10 weeks, showed promising results and no recurrence within 24 months after therapy. A study done by MJ et al. using a combination of calcipotriol and betamethasone dipropionate in a 5-year-old child for two months showed thinning of the lesions.⁹

In this case, the patient was treated with tretinoin 0.025% cream, urea 20% cream, and desoxymethasone 0.25% cream for 4 weeks. The lesions were peeled off and became thinner. The topical treatment modality was chosen because the patient is a child and the treatment is simple, affordable, non-invasive and effective. The most common side effect of topical tretinoin is local skin irritation.^{4,12} Patient in this case experienced redness and pain on the peeling lesion where the tretinoin was applied with occlusion. Due to the improvement of the lesions, tretinoin over the gluteal and femoral regions was discontinued; although treatment on the pedis region was still continued.

Epidermal nevus has a risk of recurrence that may occur within several months to several years after discontinuing the treatment.^{4,11,12} Study by Alonso-Castro et al. stated that the epidermal nevus recurrence rate was 30%.³ Nevus unius lateris (NUL) is a rare form of epidermal nevus. Topical therapy combination of tretinoin 0.025% cream, desoxymethasone 0.25% cream, and urea 20% cream provides a significant result with mild local irritation due to tretinoin. The safety profile and adverse effects of the use of tretinoin and desoxymethasone in children need constant monitoring. NUL is a highly recurrent condition. There are various treatment options, but none are ideal or satisfying and may recur several months or years later.

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