A Case of Systematized Epidermal Nevus (Nevus Unius Lateris) in a 20-year-old Filipino Female Treated with Ablative CO_2 Laser and Topical Tretinoin

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ABSTRACT

This is a case of a 20-year-old female with no known comorbidities presenting with verrucous plaques arranged in a unilateral blaschkoid distribution at birth. Biopsy was consistent with epidermal nevus hence patient was diagnosed as systematized epidermal nevus, Nevus Unius Lateris type. Gold standard treatment is full thickness surgical excision however, due to the extensive involvement, treatment of this condition remains a challenge. Hence, non-surgical combination of ablative CO_2 laser and topical tretinoin 0.1% were done. Thinner lesions (1-3 mm) showed lower recurrence (50%) as compared to thicker lesions (>3 mm) showing 100% recurrence after six months. Hence, another CO_2 laser session is needed. Quality of life was measured using the Dermatologic Life Quality Index (DLQI) with noted 35% improvement post-treatment.

Keywords: systematized epidermal nevus, nevus unius lateris, CO_2 laser, tretinoin, retinoid

INTRODUCTION

Nevus unius lateris is a rare systematized verrucous epidermal nevus characterized by confluent papillomatous, verrucous plaques distributed in a unilateral blaschkoid distribution. It is a rare benign congenital hamartoma derived from the ectoderm.[1] Systematized epidermal nevi in the absence of neurological manifestations, musculoskeletal, auditory and visual disturbances, as seen in epidermal nevus syndromes, are rare.[2,3] Lesions usually follow a benign course; and may enlarge, thicken and stabilize in size during puberty.[1] Maceration and superimposed bacterial infections may also occur on intertriginous areas.[1] There are rare cases of malignant transformation to basal cell, squamous cell, verrucous, and adnexal carcinomas.[4] Epidermal verrucous nevus has an estimated prevalence in the general population of 1/1000, and its variant nevus unius lateris represents only 0.01% of this total.[5]

CASE PRESENTATION

The patient is a 20-year-old female presenting with unilateral brown verrucous papules and plaques arranged in a blaschkoid pattern on the right arm, right trunk and chest, and right leg which were present at birth. She was born in a non-consanguineous marriage with no congenital anomalies. At birth, newborn screening and hearing screening were done with normal results. Although the lesions were extensive, they were no other associated symptoms and diseases such as neurologic, auditory, cardiac, endocrine diseases, amenorrhea,

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musculoskeletal disorders nor developmental delays. However, patient reported aesthetic concerns which affected her daily life as a college student. In the interim, verrucous plaques gradually increased in thickness and size on the same affected areas, not involving the left side of the body as patient grew older. There was also no appearance of systemic symptoms. Patient had not yet sought consult with any physician or institution and no other interventions were done. Patient then came in at the Philippine General Hospital Outpatient Department, Department of Dermatology, expressing her concern to decrease her skin lesions.

On physical examination, there are multiple well-defined irregularly shaped verrucous hyperkeratotic brown-gray papules and plaques on right arms and legs with blaschkoid and unilateral distribution which does not cross the midline as seen in Figure 1. Biopsy was done showing compact hyperorthokeratosis, papillomatosis, and epidermolysis of the granular layer. There is also a moderately dense perivascular infiltrate composed of lymphocytes and histiocytes in the superficial dermis as seen in Figure 2.

Quality of life of the patient was evaluated using DLQI prior to initiation of the treatment. Baseline DLQI score is 17. Patient also reported difficulty in daily life at school and constantly hid her skin lesions from other individuals. She expressed concern on non-surgical options which can address her condition. Hence, CO_2 ablative laser in combination with topical tretinoin 0.1% cream were initiated as treatment for this case.

Prior to treatment and documentation, informed consent from the patient was obtained. A CO_2 laser (Smaxel, IDS, Seoul, South Korea) was used in this study. CO_2 laser test spots on the foot were initially done two weeks prior to the scheduled laser session, and healing of the lesions were observed. After one week, there was good wound healing with no noted recurrence of the epidermal verrucous plaques on the anterior foot.

One CO_2 laser session was done per target area. The target areas were divided into the anterior leg, knee, and abdomen. Only one target area (around two palm sizes) was targeted per session to allow adequate healing. For the ablative settings, general CO_2 mode and normal pulse mode were used, with energy 215 mJ (0.215 Joules), 5 ms for the pulse duration and 25 ms for the rep time. Since ablation was done on the lesions, higher settings using a surgical handpiece was used. For the treatment proper, Lidocaine 1% was infiltrated on target areas. Cold air (Zimmer) was also done during ablation to decrease pain. Lesions were then ablated using a surgical pen in a paintbrush pattern to the level of unaffected dermis. Endpoints were pinpoint bleeding and charred appearance. Charred lesions were then curetted until epidermis was removed to ensure that the base was targeted. Pain numerical rating scale (NRS) score during the procedures was tolerable ranging from 1 to 3 out of 10.

Pruritus, pain, and erythema were noted immediately after the procedure, which all resolved after 24 hours. For the post-laser care, manipulation of scabs was avoided, topical fusidic acid was applied two times a day for seven days or until erosions healed. Mild cleanser, petroleum jelly, and sunscreen broad spectrum SPF50 ++ were applied daily.

In Figure 3, for areas with thinner lesions (1-3 mm) on the abdomen and leg, there was noted good healing and minimal post-inflammatory erythema with no recurrence (0%) and scarring four weeks after the CO_2 laser session as seen in Figures 3B and E. However, six months after, there was 50% recurrence of the target lesions ablated as seen in Figures 3C and F.

For the thicker lesions (>3 mm) on the anterior and lateral knee as seen in Figure 4, after four weeks, there was

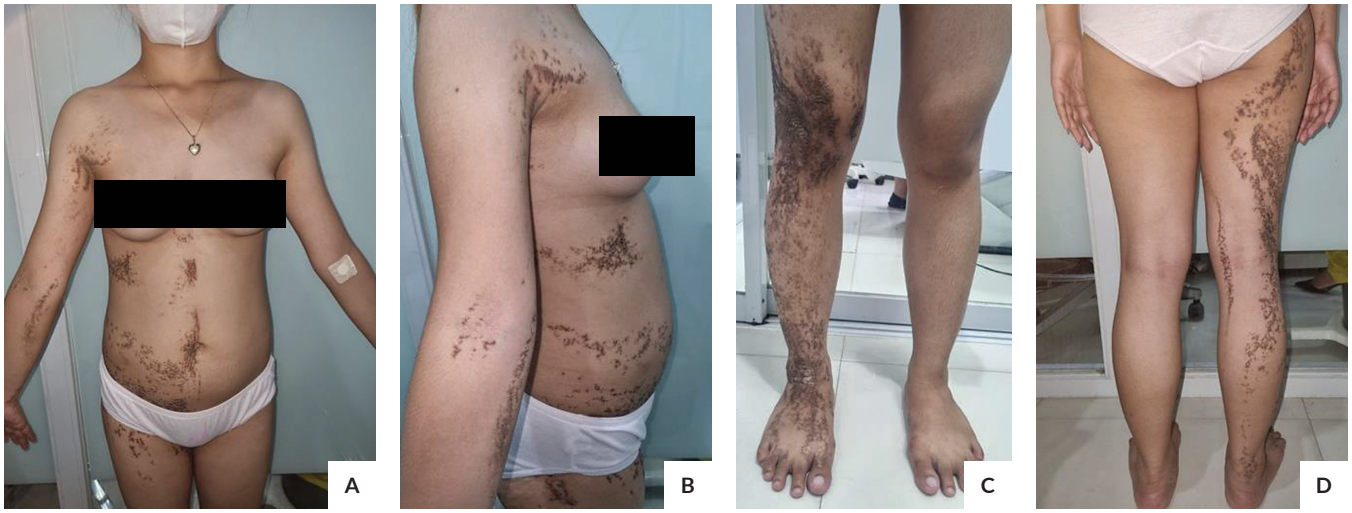

Figure 1. Baseline photos showing multiple well-demarcated, irregularly shaped, verrucous, hyperkeratotic brown-gray papules and plaques on the anterior trunk **(A)**, right upper extremity **(B)**, anterior right lower extremity **(C)**, and posterior right lower extremity **(D)**, arranged in a blaschkoid pattern and unilateral distribution that does not cross the midline.

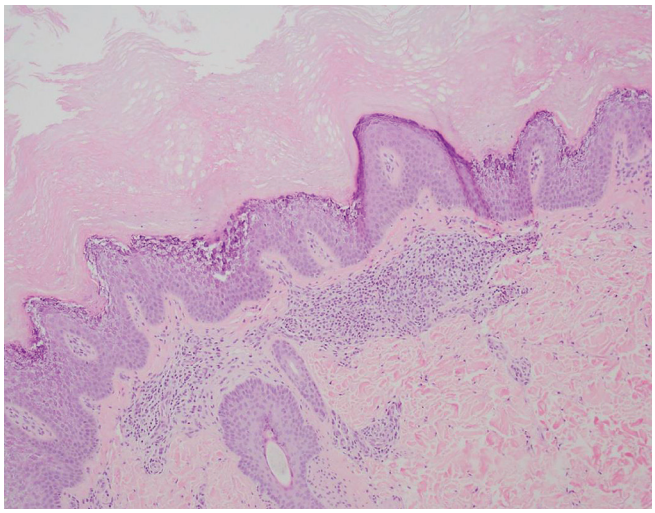

Figure 2. Histopathology of right leg showing hyperorthokeratosis, papillomatosis, epidermolysis of the granular layer, and moderately dense perivascular infiltrate composed of lymphocytes and histiocytes in the superficial dermis, consistent with an epidermal nevus. Magnification is 40x, H&E stain used.

more than 50% recurrence of the target areas (Figures 4B and E). And after six months, there was 100% recurrence of the thick lesions (>3 mm) on both the anterior and lateral target areas of the knees as seen in Figures 4C and F. The recurrence of the lesions may be attributed to the incomplete ablation of the thicker lesions. Hence, a second CO_2 laser session may be recommended to fully ablate the lesions.

Patient had monthly follow-ups after the CO_2 laser session for six months. Patient reported that there was no pain (NRS 0/10) on the target areas ablated on the 1st to 6th month post-laser. Patient was advised to apply topical tretinoin 0.1% cream daily, once at night, under occlusion using petroleum jelly two weeks after the laser procedure until six months. There was no pain on application of tretinoin. Adherence to treatment was assessed during monthly follow-ups until six months. However, patient was only able to apply topical tretinoin three to four times a week for six months. Inconsistent adherence to the topical tretinoin was due to frequency of application (daily) according to the patient.

In summary, it was observed that for thinner lesions (1-3 mm), percent recurrence was lower as compared to thicker lesions (>3 mm). Hence, this would warrant another CO_2 laser

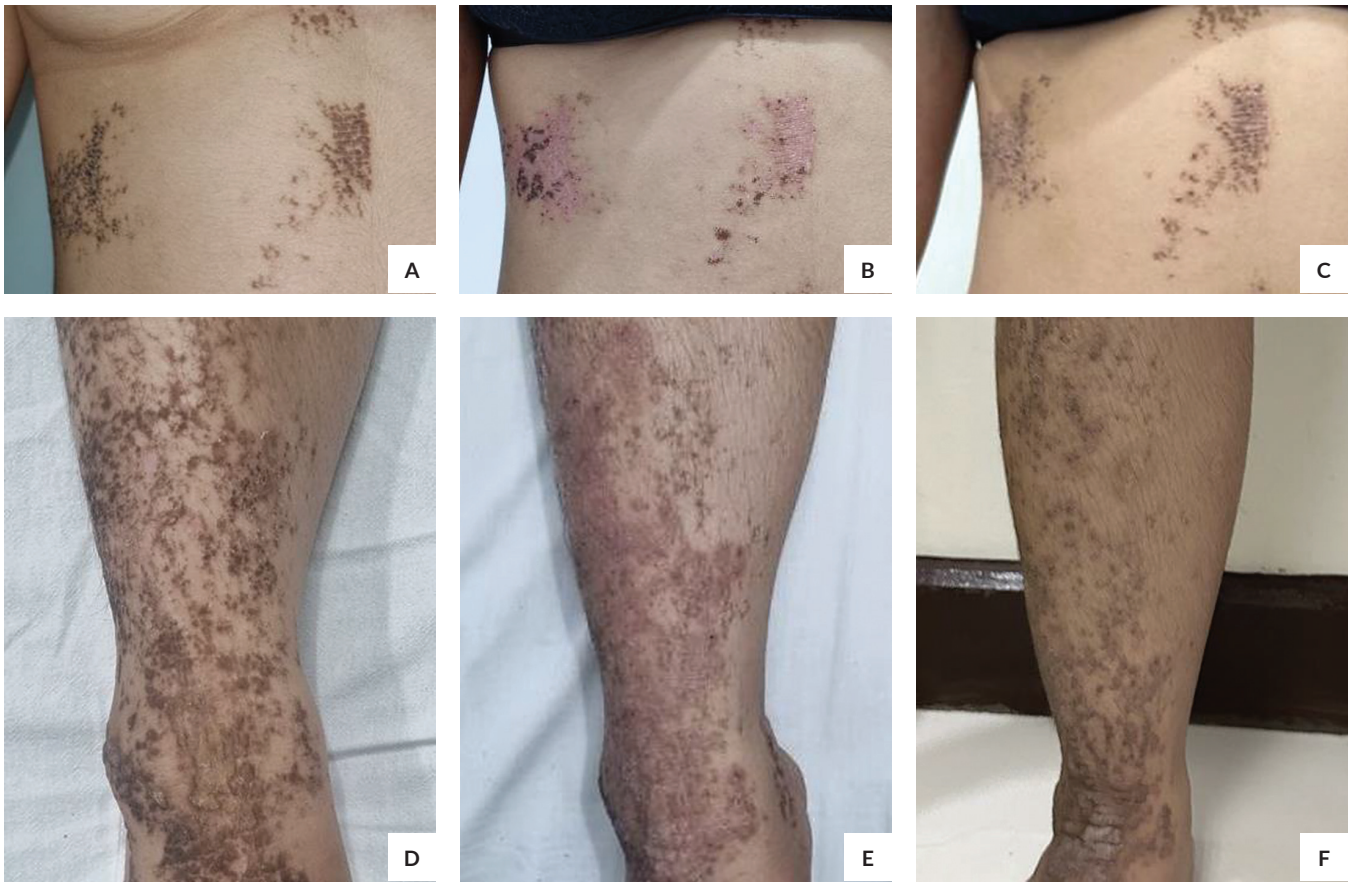

Figure 3. Thinner lesions (1-3 mm) on the abdomen and leg, respectively, at baseline **(A and D)**, four weeks after the CO_2 laser session showing no recurrence with post-inflammatory erythema **(B and E)**, and after six months **(C and F)** showing minimal recurrence (50%) and no scarring.

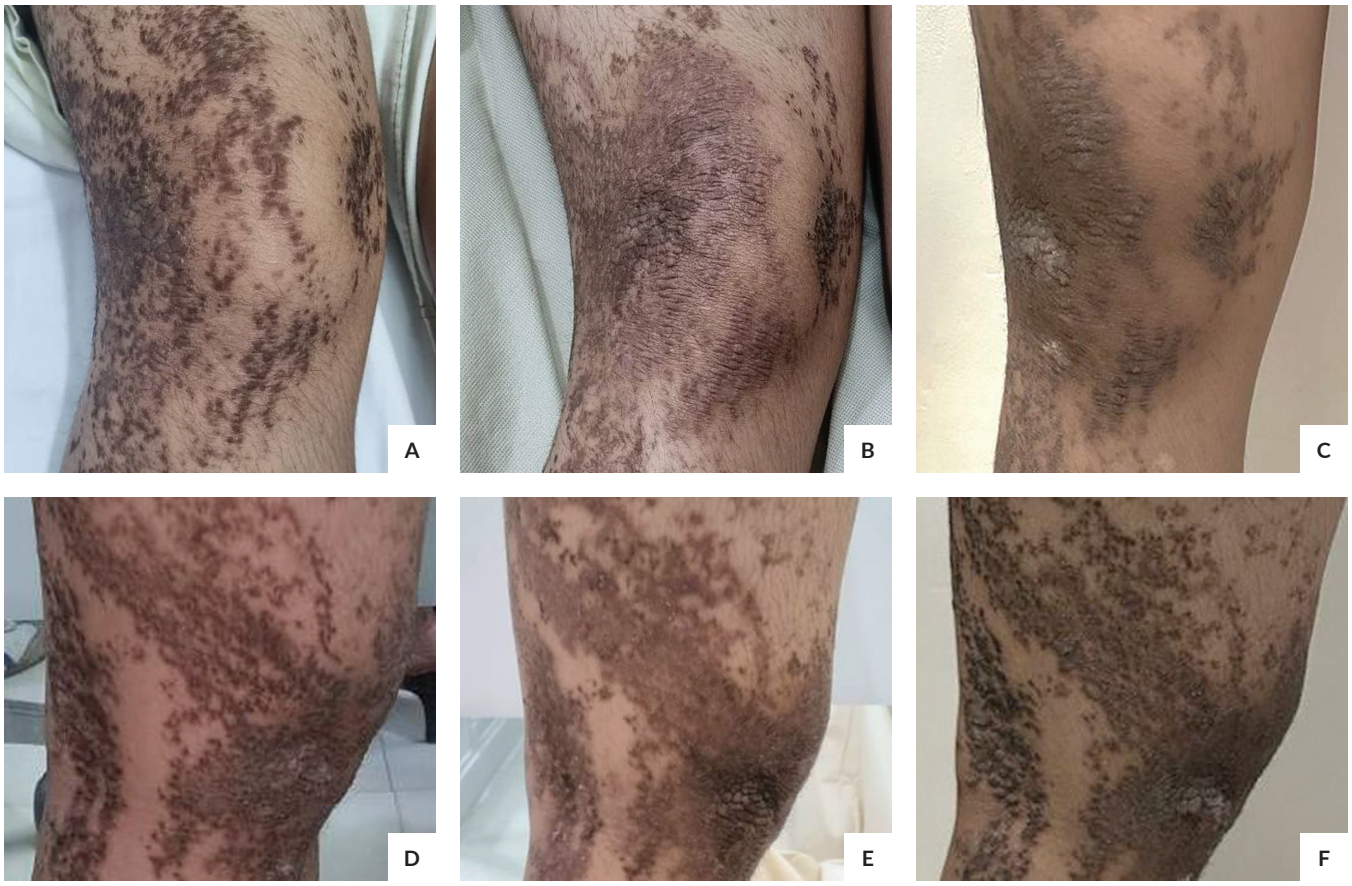

Figure 4. Thicker lesions (>3 mm) on anterior knee and lateral knee at baseline **(A and D)**, four weeks after the CO_2 laser session showing 50% recurrence **(B and E)**, and after six months showing 100% recurrence of the thick areas **(C and F)**.

session to fully ablate the lesions and to prevent recurrence. A second CO_2 laser session was offered however, patient noted satisfaction after one session and opted not to have another session on subsequent follow-ups. Quality of life using DLQI was recorded before and after the treatment. Baseline DLQI score prior to treatment was 17 and post-treatment was 11 with noted Improvement in DLQI by 35%. Patient also reported satisfaction with the decrease in thickness of the lesions having a significant impact in her daily life.

DISCUSSION

Pathophysiology

Nevus unius lateris is a type of systematized epidermal nevus affecting specifically one side of the body. Keratinocytic epidermal nevi, specifically, are derived from pluripotent cells in the basal layer of the embryonic epidermis. Although keratinocytes are the predominant affected cell type, there is accompanying overgrowth of the papillary dermis as well. These lesions result from cutaneous mosaicism, particularly postzygotic activating mutations.[6] 40% of keratinocytic epidermal nevi harbor RAS mutations (usually HRAS), and another 40% have an FGFR3 or PIK3CA mutation.[1] These mutations result in downstream activation and proliferation of keratinocytes.[1] Up to 10% have a mutation in KRT1 or KRT10 and characteristically exhibit epidermolytic hyperkeratosis on pathology.

Treatment Options

Gold standard of epidermal nevus lesions is still full thickness surgical excision however it requires extensive preparation and longer healing time.[1] Majority of patients are not amenable to this hence, we resort to non-surgical treatment options which are variable. For extensive lesions not amenable to surgery, nonsurgical treatments such as cryotherapy, electrofulguration, trichloroacetic acid, and topical tretinoin 5-FU can be used.[7] Cryotherapy has been successful in treating small lesions in a series of 11 patients; this treatment resulted in no scars, one recurrence, and one transient post-procedural hypopigmentation.[8,9]

Various lasers have also been used for epidermal nevus, however CO_2 laser and ER YAG specifically have shown good clearance of lesions with minimal recurrence rate in majority of the patients. In the studies of Alkhalifah et al. and Castro et al., majority of the patients noted clearance of the lesions with 50% recurrence and 20% recurrence, respectively

in both studies.[5,10] In the studies of Thual et al. and Park et al., there were noted fair and good results and clearance of the lesions however, there were 38% and 25% recurrence rate, respectively in a follow-up period of two years.[11,12] And in a recent randomized controlled trial of Osman and Kassab, they compared the efficacy of CO_2 vs ER YAG, noted no recurrence in a 6-month follow-up period for both lasers.[13]

CO_2 laser functions through an invisible infrared beam, emitting energy at a wavelength of 10,600 nm, which is absorbed by water.[1] This is used to coagulate, vaporize or ablate the tissues hence It can be used to treat extensive epidermal nevus lesions. In a case report of Sannino et al. last 2021, they used CO_2 laser to target the epidermal nevus lesions using one session. They divided the face into three separate areas and used dye laser to target post-inflammatory hyperpigmentation. The patient was followed up for the next two years with no noted recurrence of lesions.[14]

Tretinoin, is a type of retinoid. Its mechanism of action is through binding to retinoic acid receptors (RARs) alpha, beta, and gamma along with retinoid X receptors (RXRs) increasing collagen type I and III formation leading to decreased keratinization of epithelial cells.[1] Hence, it may also be used in keratinocytic epidermal lesions. Combination treatment with topical 0.1% tretinoin and 5% 5-FU under occlusion twice daily for three months followed by daily 5% 5-FU and twice daily 0.1% tretinoin for six months led to appreciable improvement in an extensive inflammatory linear verrucous epidermal nevus (ILVEN) in a 9-year-old boy. However, the lesion recurred after three to four weeks and the patient was maintained on treatment two to three times a month.[7]

Studies mentioned above have demonstrated various treatment options in epidermal nevus however recurrence is still common, hence treatment of epidermal nevi remain a therapeutic challenge. Cases above have demonstrated the use of lasers and topical retinoids however no studies have been yet reported regarding the use of combination of CO_2 laser and tretinoin as treatment in epidermal nevus and most especially in systematized epidermal nevus. In this case report, since surgical option may be difficult due to extensive involvement of the lesions, and patient was also not amenable to surgical interventions, another treatment used was combination of ablative CO_2 case and topical tretinoin with promising results most especially in thinner lesions but still with noted recurrence of the thicker lesions but were thinner compared to baseline.

CONCLUSION

Nevus unius lateris is a rare systematized epidermal nevus which may affect the daily lives, mental and psychosocial well-being of patients. Extensive lesions remain a therapeutic challenge due to frequent recurrence of the lesions hence treatment should still be individualized. This case report demonstrated a rare case of nevus unius lateris with no systemic involvement in the Philippines and the potential use of CO_2 laser and tretinoin on the extensive lesions. One of the limitations of this case report is the extensive involvement and varying thickness of the lesions which makes ablation more difficult resulting in recurrence in some of the areas. Other therapeutic challenges are monitoring of patient compliance to topical treatment and follow-up.

Tretinoin 0.1% cream and ablative CO_2 laser may be a promising therapeutic option for patients with extensive systematized epidermal nevi not amenable to surgical management. Thinner lesions (1-3 mm) have lower recurrence as compared to thicker lesions (>3 mm). However, some of the lesions, specifically thick lesions (>3 mm) noted recurrence hence one session is not enough to fully ablate lesions and subsequent CO_2 laser sessions are needed. Another consideration is to ensure adherence to topical tretinoin (daily application) to decrease recurrence of lesions. Although lesions recurred, there is improvement of DLQI by 35% six months post-treatment indicating that these treatment modalities would help in improving the quality of life of patients with extensive epidermal nevi.

Other recommendation for this case is addressing post-inflammatory hyperpigmentation and possible scarring. Monitoring of lesions for recurrence or malignant transformation, treatment compliance in the next years, and close follow-up should also be considered.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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