Content available at: https://www.ipinnovative.com/open-access-journals

IP Indian Journal of Clinical and Experimental Dermatology

Journal homepage: www.ijced.org/

Case Report

A dermatological odyssey: Levamisole's Triumph over warts, vitiligo, dermatophytosis, and pityriasis versicolor in a young patient

Abhinesh N[1], **Arisha Salam**[2]*

[1]*Dept. of Dermatology, Venereology and Leprosy, Tagore Medical College & Hospital, Chennai, Tamil Nadu, India*
[2]*Dept. of Dermatology, Andaman and Nicobar Islands Institute of Medical Sciences, Port Blair, Andaman and Nicobar, India*

ARTICLE INFO

Article history:
Received 07-01-2024
Accepted 16-02-2024
Available online 12-03-2024

Keywords:
Warts
Vitiligo
Dermatophytosis
Pityriasis Versicolor
levamisole

ABSTRACT

In our case, we observe the presence of various conditions within the same patient, including prevalent benign lesions caused by the human papillomavirus (HPV) known as warts. These warts, occurring in both mucosal and skin regions, can contribute to significant morbidity for affected individuals. Additionally, the patient exhibits vitiligo, a common acquired skin disorder characterized by well-demarcated white patches resulting from the loss of melanocytes in the epidermis. Although different theories exist regarding the pathogenesis of vitiligo, the exact etiology remains unknown. Alongside, the patient presents with two common fungal infections, namely pityriasis versicolor and dermatophytosis. The coexistence of all these dermatological conditions in a single patient highlights the complexity of the case.

1. Introduction

Warts, benign lesions caused by the human papillomavirus (HPV), can manifest in both mucosal and skin regions, with over 100 identified types of HPV. These lesions may occur at any site on the body. In contrast, vitiligo is an acquired pigmentary skin disorder characterized by the absence of pigmentary cells in the epidermis, resulting in white macules and patches. The condition is often associated with autoimmune disorders, with thyroid abnormalities being the most common. While the exact etiology of vitiligo remains unknown, various theories attempt to explain its pathogenesis. Vitiligo is further classified into three types based on distribution and pattern: generalized, segmental, and localized.

Additionally, pityriasis versicolor, also known as tinea versicolor, is a common, benign, superficial fungal infection affecting the skin. Clinical features include hyperpigmented or hypopigmented finely scaled macules, with the trunk, neck, and proximal extremities being the most frequently affected sites.

2. Case Report

A 25-year-old male patient, employed as a sailor in the Indian Navy, presented with complaints of multiple asymptomatic verrucous raised lesions on both upper and lower limbs for the past three months. Additionally, he reported asymptomatic flat white patches over the right shoulder and arm persisting for the past three years. The patient also experienced itching in the gluteal region and groin for the last month. Notably, there was no history of fever, atopy, or drug intake preceding the onset of these lesions. The patient mentioned a recent hospitalization for jaundice three months ago, after which the verrucous lesions appeared. During his hospital stay, he received treatment for jaundice and underwent a blood transfusion to address low hemoglobin levels.

* *Corresponding author*.
E-mail address: arisha.salam@gmail.com (A. Salam).

https://doi.org/10.18231/j.ijced.2024.016

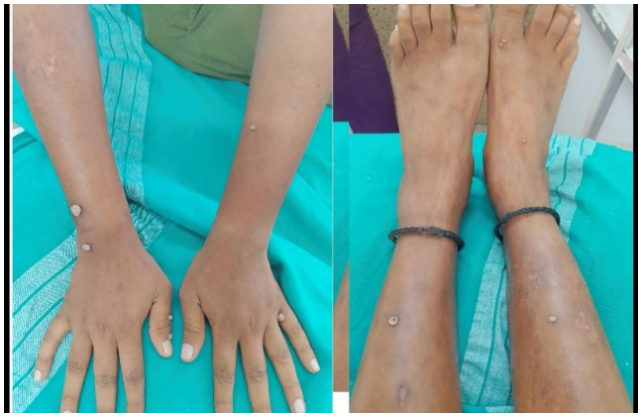

Figure 1: Clinical image of bilateral upper limbs and bilateral lower limbs showing verrucous papules and plaques.

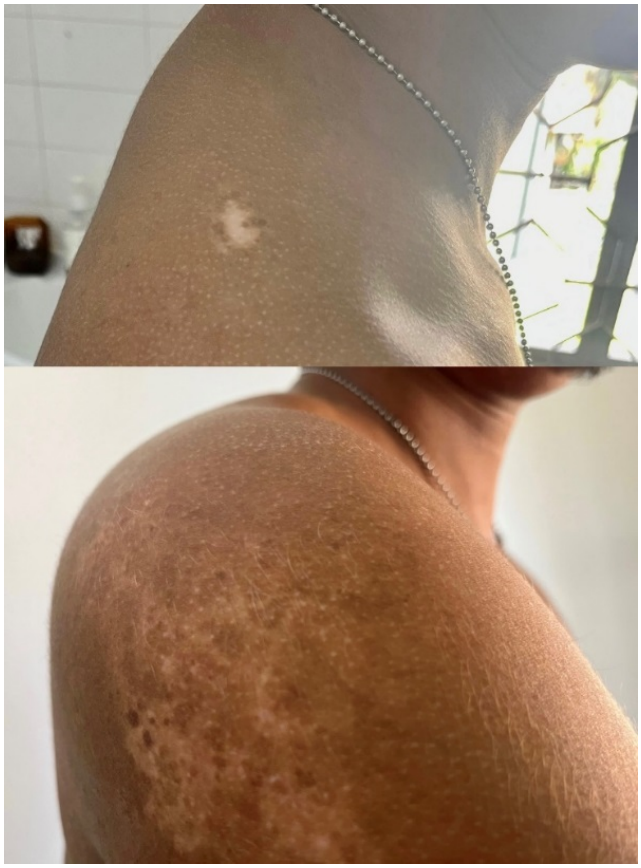

Figure 2: Clinical image of the depigmented irregular patch over the right shoulder with presence of leukotrichia.

Figure 3: Clinical image of the posterior aspect of the neck showing well defined hypopigmented patches with branny scales.

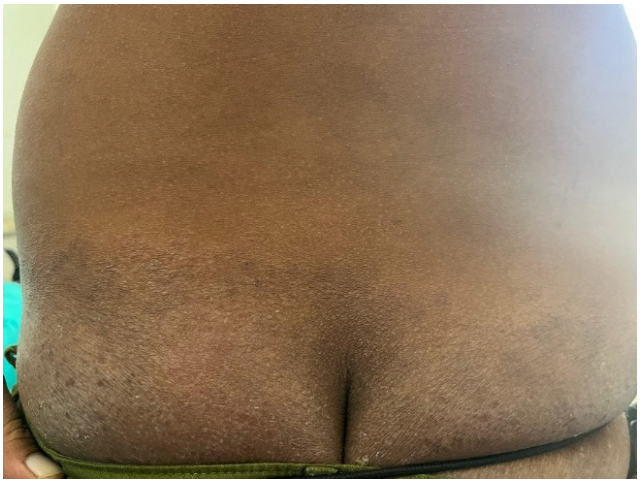

Figure 4: Clinical image showing annular plaques over the gluteal region.

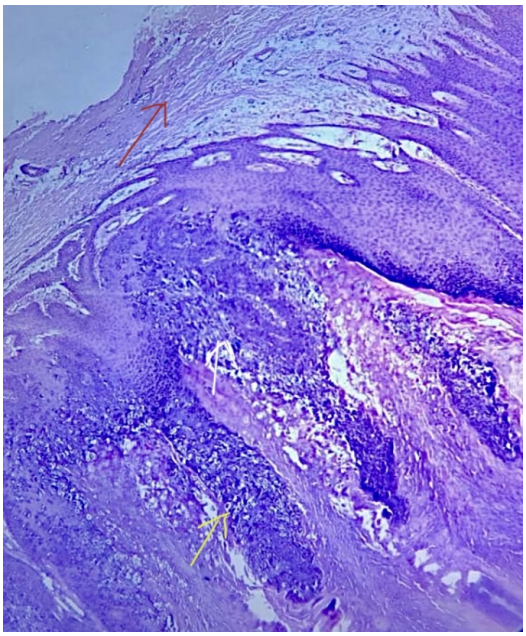

Figure 5: A 40x Hematoxyllin and Eosin stained histopathological image showing hyperkeratosis [red arrow], incurving of rete ridges [green arrow] and presence of koilocytes [white arrow].

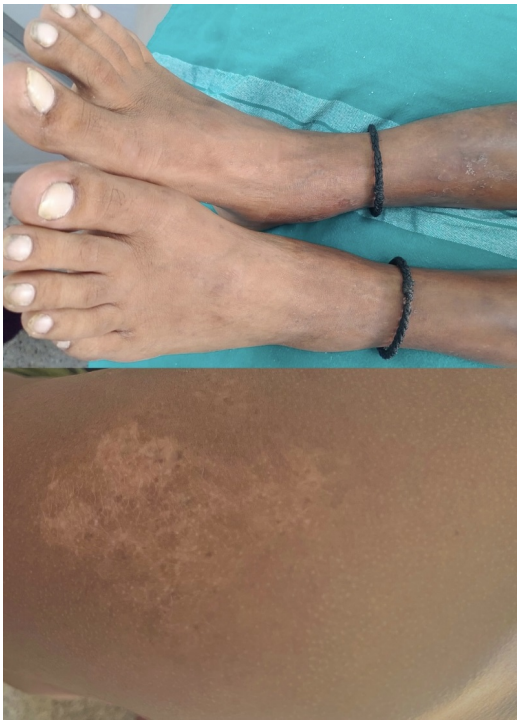

Figure 6: Clinical image showing no recurrence of warts and significant improvement in pigmentation of the vitiligenous patch.

On examination, there was presence of multiple verrucous papules and plaques over bilateral upper limbs and bilateral lower limbs [Figure 1]. There was 2-3 irregularly shaped depigmented patches with diffuse borders over the right shoulder and right upper arm. The hair over these patches showed presence of leukotrichia [Figure 2]. There was presence of hypo-pigmented patches with branny scales and pencil drawn like borders over the posterior and lateral aspect of the neck [Figure 3]. On examination of the gluteal region and groin, annular plaques with excoriations and central clearing was seen [Figure 4]. Skin scraping from the plaques over the buttocks showed presence of fungal elements. An excisional skin biopsy was taken from a verrucous papule over the forearm, which showed a histopathological picture of massive hyperkeratosis, acanthosis, papillomatosis and presence of koilocytes [Figure 5]. With this we confirmed the diagnosis of multiple verruca vulgaris with coexisting focal vitiligo, tinea versicolor and dermatophytosis.

The large lesions of verruca over the upper and lower limbs were excised by electrocautery and the smaller lesions were treated with cryotherapy and topical keratolytics. The patient was started on oral Levamisole 150mg for three consecutive days every fortnight for three months, along with daily oral zinc 20mg. Antifungal therapy, including topical miconazole and biweekly oral fluconazole 150mg, was administered for 6 weeks to address the dermatophytosis and tinea versicolor. Itching was managed with oral antihistamines. The depigmented patches over the right shoulder and arm were treated with topical tacrolimus 0.1% ointment in the morning and topical steroids at night.

After completion of three months of therapy, the patient exhibited significant improvement in pigmentation within the depigmented patches, and there was no recurrence of warts [Figure 6]. The superficial fungal infection resolved completely, with no evidence of new lesions.

3. Discussion

Warts, a prevalent dermatological concern attributed to the human papillomavirus, boast a plethora of available treatment options. Levamisole, often paired with cimetidine, has been utilized in managing stubborn warts.[1] In a double-blind comparative trial involving 48 patients with multiple recalcitrant warts, the efficacy of a combination of cimetidine and levamisole was scrutinized against cimetidine alone. Participants were divided into two groups, with one receiving oral cimetidine alone (30 mg/kg/day orally in three divided doses up to a maximum of 3 g/day) and the other receiving levamisole 150 mg tablets on 2 consecutive days a week, in addition to cimetidine. After a 12-week therapy period, the combination therapy group exhibited a marked to complete response in 75% of patients, compared to 41.6% in the cimetidine-only group. The average regression periods were 7 and 10

weeks, respectively.[2] Another study on 44 children with multiple stubborn warts revealed a complete response in 65% of patients on levamisole plus cimetidine, in contrast to 31.5% on cimetidine alone after 12 weeks of therapy. However, some randomized controlled trials failed to establish statistically significant improvement with levamisole in the treatment of multiple viral warts.[3]

In a double-blind, placebo-controlled, randomized trial involving 26 patients with chronic dermatophytosis due to Trichophyton rubrum, a more robust immunological response was noted with griseofulvin plus levamisole compared to griseofulvin plus placebo.[4] Despite similar clinical cure rates in both groups, indicating the potential immunomodulatory role of levamisole. Additionally, levamisole was found to expedite the remission of oral candidiasis when administered as an adjuvant with nystatin in patients with impaired cell-mediated immunity.[5]

Levamisole, either alone or as an adjuvant, has demonstrated utility in controlling the progression of vitiligo. A randomized, placebo-controlled, double-blind Indian study evaluated the efficacy of levamisole in limited vitiligo cases, revealing a higher proportion of patients without new lesions in the levamisole group after 6 months.[6] Another Indian study reported disease activity arrest within 2-4 months in 94% of patients treated with levamisole alone, with repigmentation observed in 64%. Considering these findings, levamisole emerges as a potentially safe and cost-effective adjuvant in vitiligo management.[7]

Levamisole, categorized as a U.S. Food and Drug Administration pregnancy category C drug, is considered safe during lactation. The adverse effects of levamisole are generally mild and transient, including abdominal symptoms, a flu-like syndrome, and arthralgias.[8] However, rare reports have highlighted severe complications such as agranulocytosis, multifocal leukoencephalopathy, ataxia, psychosis, myopathy, lichenoid eruptions, leg ulcers, fixed drug eruptions, necrotizing vasculitis, and retiform purpura. Notably, levamisole has been associated with cocaine adulteration, leading to cases of agranulocytosis in affected individuals.[9]

In a case study conducted by Takamich et al in Japan,[10] they presented an instance featuring multiple warts surrounded by depigmented halos and generalized vitiligo. Cryotherapy was employed to treat the warts, resulting in most of them undergoing involution. However, the depigmented halos and generalized vitiligo remained unchanged throughout the 6-month follow-up period. Some topical agents, such as imiquimod and diphenylcyclopropenone, have been documented to induce depigmented vitiligo.[11] These agents are believed to activate host immune reactions. While Berman affirmed that the gel did not induce depigmentation in some healthy individuals, the potential association between the gel and depigmentation remains a consideration.

In a study conducted by Kavya et al in Andhra Pradesh, investigating vitiligo with other coexisting conditions in the Dermatology, Venereology, and Leprosy (DVL) department of a teaching hospital, urticaria was observed in 4% of cases with vitiligo. This prevalence was higher than that reported in the study by Garg et al (1.5%).[12,13] Alopecia areata was identified in 2% of cases, aligning with findings from studies by Koranne et al (2.66%) and Vora et al (1.9%).[3,6] Psoriasis was noted in 2% of cases, consistent with Garg et al report of 2.5% in their study.[14] The incidence of psoriasis in this study was higher than that observed in Vora et al (0.4%) and lower than Mahajan et al's study (13.79%).[14,15] Atopic dermatitis was present in 2% of cases, similar to the findings in the study by Martis et al (2%).[16] Fungal infection, specifically tinea corporis, was observed in 2% of cases, comparable to Vora et al's findings (1.3%). Acne was identified in 2% of cases with vitiligo.[13,17] The most prevalent systemic comorbidity was iron deficiency anemia, affecting 20% of cases with vitiligo, followed by hypothyroidism (12%). Diabetes mellitus was present in 10% of cases, while 8% had dyslipidemia, and 2% had hypertension.

Rare instances of the coexistence of Morphea and Vitiligo vulgaris have been documented.[18,19] The association of morphea with homolateral vitiligo has also been reported. In a study by Salam A et al, a case report was presented on unilateral morphea following unilateral vitiligo in the same patient.[20]

In our case, the observation of verruca vulgaris coexisting with focal vitiligo at a distinct site raises the possibility of an immunocompromised state. Following the diagnosis of warts, the patient received guidance on preventive measures to minimize trauma and transmission risks. Specific instructions included avoiding nail-biting, using appropriate footwear around swimming pools, and wearing gloves when handling meat products. Emphasis was placed on the information that warts can sometimes resolve spontaneously, and the decision to pursue treatment should be carefully considered. The patient was educated about various topical treatments, their effectiveness, and potential adverse effects. Additionally, it was emphasized that no treatment produces immediate results, and multiple sessions would likely be necessary for optimal outcomes.

The patient's history of jaundice and blood transfusions suggests a potential hospital-acquired spread of the virus leading to the development of warts. The presence of long-standing focal vitiligo further hints at an autoimmune mechanism. However, intriguingly, oral levamisole emerged as a single therapeutic agent addressing all the conditions—vitiligo, dermatophytosis and verruca. Remarkably, significant improvement was noted in all aspects with the use of oral levamisole. This unique response underscores the complex interplay of immune

mechanisms in the manifestation and treatment of these dermatological conditions.

4. Conclusion

Levamisole, serving as an immunomodulator, exhibits potential applicability in numerous dermatological disorders. However, further substantiation through blinded randomized control trials and case-control studies across various dermatoses is imperative to ascertain its efficacy and compare it with established treatments. Despite this, owing to its cost-effectiveness, levamisole can be employed as an adjunct to established modalities. Achieving optimal outcomes in wart management necessitates an interprofessional team approach. The cornerstone of wart management lies in patient education, underscoring the importance of open communication between clinicians to mitigate the morbidity associated with warts. Simultaneous treatment of multiple diagnoses at distinct sites requires meticulous administration of safely interacting drugs for comprehensive and effective patient care.

5. Source of Funding

None.

6. Conflict of Interest

None.

References

1. Parsad D, Saini R, Negi KS. Comparison of combination of cimetidine and levamisole with cimetidine alone in the treatment of recalcitrant warts. *Australas J Dermatol*. 1999;40(2):93–5.
2. Parsad D, Pandhi R, Juneja A, Negi KS. Cimetidine and levamisole versus cimetidine alone for recalcitrant warts in children. *Pediatr Dermatol*. 2001;18(4):349–52.
3. Saúl A, Sanz R, Gomez M. Treatment of multiple viral warts with levamisole. *Int J Dermatol*. 1980;19(6):342–3.
4. Svejgaard E, Christiansen AH, Stahl D, Thomsen K. Clinical and immunological studies in chronic dermatophytosis caused by Trichophyton rubrum. *Acta Derm Venereol*. 1984;64(6):493–500.
5. Lai WH, Lu SY, Eng HL. Levamisole aids in treatment of refractory oral candidiasis in two patients with thymoma associated with myasthenia gravis: Report of two cases. *Chang Gung Med J*. 2002;25(9):606–11.
6. Khondker L, Khan SI. Efficacy of levamisole for the treatment of slow spreading vitiligo. *Mymensingh Med J*. 2013;22(4):761–6.
7. Roy R, Kalla G, Singhi MK. Levamisole in vitiligo of eyelids. *Indian J Dermatol Venereol Leprol*. 1996;62(3):199–200.
8. Quirt IC, Shelley WE, Pater JL, Bodurtha AJ, Mcculloch PB, Mcpherson TA, et al. Improved survival in patients with poor-prognosis malignant melanoma treated with adjuvant levamisole: A phase III study by the National Cancer Institute of Canada Clinical Trials Group. *J Clin Oncol*. 1991;9(5):729–35.
9. Sharda N, Shashikanth MC, Kant P, Jain M. Levamisole and low-dose prednisolone in the treatment of reccurent aphthous stomatitis. *J Oral Pathol Med*. 2014;43(4):309–16.
10. Ito T, Yoshida Y, Adachi K, Furue M, Yamamoto O. Wart with depigmented halo and generalized vitiligo. *Yonago Acta Med*. 2012;55(4):81–2.
11. Oh YJ, Shin MK, Lee MH. Narrow-band ultraviolet B treatment for dyphenylcyclopropenone-induced vitiliginous lesions. *Acta Derm Venereol*. 2012;92(1):102–3.
12. Vora RV, Patel BB, Chaudhary AH, Mehta MJ, Pilani AP. A Clinical Study of Vitiligo in a Rural Set up of Gujarat. *Indian J Community Med*. 2014;39(3):143–6.
13. Mahajan VK, Vashist S, Chauhan PS, Mehta K, Sharma V, Sharma A. Clinico-Epidemiological Profile of Patients with Vitiligo: A Retrospective Study from a Tertiary Care Center of North India. *Indian Dermatol Online J*. 2019;10(1):38–44.
14. Swati G, Vikram M, Karaninders M, Pushpinder C, Mrinal G, Yadav RS, et al. Vitiligo and associated disorders including autoimmune diseases: A prospective study of 200 Indian patients. *Pigment Int*. 2015;2(2):91–6.
15. Koranne RV, Sehpgal VN, Sachdeva KG. Clinical Profile of Vitiligo in North India. *Indian J Dermatol Venereol Leprol*. 1986;52(2):81–2.
16. Martis J, Bhat R, Nandakishore B, Shetty JN. A clinical study of vitiligo. *Indian J Dermatol Venereol Leprol*. 2002;68(2):92–3.
17. Finkelstein E, Amichai B, Metzker A. Coexistence of vitiligo and morphea: A case report and review of the literature. *J Dermatol*. 1995;22(5):351–3.
18. Brenner W, Diem E, Gschnait F. Coincidence of vitiligo, alopecia areata, onychodystrophy, localized scleroderma and lichen planus. *Dermatologica*. 1979;159(4):356–60.
19. Bonifati C, Impara G, Morrone A, Pietrangeli A, Carducci M. Simultaneous occurrence of linear scleroderma and homolateral segmental vitiligo. *J Eur Acad Dermatol Venereol*. 1920;20(1):63–5.
20. Salam A, Danny G, Kumar NA, Manohar A. Unilateral morphea following unilateral vitiligo: A rare occurrence. *Int J Res Dermatol*. 2021;7(3):463–5.

Author biography

Abhinesh N, Senior Resident https://orcid.org/0000-0001-9542-6298

Arisha Salam, Senior Resident https://orcid.org/0009-0009-8314-1207

Cite this article: Abhinesh N, Salam A. A dermatological odyssey: Levamisole's Triumph over warts, vitiligo, dermatophytosis, and pityriasis versicolor in a young patient. *IP Indian J Clin Exp Dermatol* 2024;10(1):85-89.