Treatment of Childhood Vitiligo: A Case Report and Literature Review

YAHYA AM, FWACP[1], **SHEHU YM**, FWACP[2]

[1]Yusuf Maitama Sule University Kano, Nigeria.
[2]Bayero University Kano, Nigeria.
Corresponding Author: Yahya Aishatu Muhammad
Address: Yusuf Maitama Sule University Kano, Nigeria.
Email: aishayahya35@yahoo.com **Phone number:** +2348035054507

ABSTRACT

Vitiligo is an acquired disorder of skin pigmentation caused by selective loss of melanocyte function, with associated pigment dilution of the affected skin areas. It affects 0.1- 2.16 % of the world's population sparing no age group, sex, or race. More than 20% of cases of vitiligo are diagnosed before the age of 10 years. It is an autoimmune skin condition that is characterized by the presence of depigmented patches with a loss of natural colour. Vitiligo skin lesion appears amelanotic, without scales, and with a clear margin. Vitiligo has a great psychological impact on the lives of children affected. Treatment is often challenging in children as most of the modalities available cannot be used for them.

This case report is a typical example of how vitiligo can be treated in children using the available options for the age group. This report highlights the established guidelines for the treatment of vitiligo in children and identifies the gaps that exist in the treatment of vitiligo in children in this region.

Keywords: Childhood vitiligo, depigmentation, treatment, children

Traitement du Vitiligo Infantile: Étude de Cas et Revue de la Littérature

ABSTRAIT

Le vitiligo est un trouble acquis de la pigmentation de la peau causé par une perte sélective de la fonction mélanocytaire, avec une dilution pigmentaire associée des zones cutanées affectées. Elle affecte 0,1 à 2,16 % de la population mondiale sans épargner aucun groupe d'âge, sexe ou race. Plus de 20% des cas de vitiligo sont diagnostiqués avant l'âge de 10 ans. C'est une affection cutanée auto-immune qui se caractérise par la présence de plaques dépigmentées avec une perte de couleur naturelle. La lésion cutanée du vitiligo apparaît mélanotique, sans squames et avec une marge nette. Le vitiligo a un grand impact psychologique sur la vie des enfants touchés. Le traitement est souvent difficile chez les enfants car la plupart des modalités disponibles ne peuvent pas être utilisées pour eux.

Ce rapport de cas est un exemple typique de la façon dont le vitiligo peut être traité chez les enfants en utilisant les options disponibles pour le groupe d'âge. Ce rapport met en évidence les directives établies pour le traitement du vitiligo chez les enfants et identifie les lacunes qui existent dans le traitement du vitiligo chez les enfants de cette région.

Mots-clés: Vitiligo de l'enfant, dépigmentation, traitement, enfants

Introduction

Vitiligo is an acquired disorder of skin pigmentation due to the autoimmune destruction of melanocytes.[1] Environmental factors, genetic factors, and metabolic and cell detachment abnormalities play important roles in the aetiology.[2] It affects 0.1- 2.16% of the world's population sparing no age group, sex, or race[3] and about 50% of cases have onset during childhood. In Nigeria, the frequency of childhood vitiligo reported was 13.3%.[3] Childhood vitiligo affects more females than males.[4] Although vitiligo is not a rare skin disorder, the development of drugs for its treatment has been a neglected field of dermatological research.[4] Vitiligo presents as asymptomatic white macules or patches and can be segmental or non-segmental (localized, generalized, or universal).[5]

Childhood vitiligo can lead to depression, poor self-esteem, anxiety disorder, and overall poor quality of life among those affected and their families.[6]

Autoimmune disorders such as thyroiditis, atopic dermatitis, alopecia areata, pernicious anaemia, and diabetes mellitus are associated with vitiligo.[6] Most of the modalities of treatment of vitiligo cannot be used in children because of side effects, hence management of vitiligo in children is difficult. Treatment of vitiligo aims to stop the progression of the disease and to induce re-pigmentation of the affected skin areas to an acceptable cosmetic benefit. However, treatment is often disappointing. Various treatment modalities have been advocated for use in children. We herein report a case of a 6-year-old boy with vitiligo who was successfully treated with a combination of topical vitamin D3 analogue and topical corticosteroids.

Case report

A 6-year-old boy presented at our clinic with 2 months history of rapidly progressing whitish patches, initially involving the face and the hands, but later involving the upper trunk. There was no history of preceding trauma or rashes at the site. There was no history suggestive of autoimmune disorders, and a review of other systems was not remarkable. Full blood count, thyroid function test, and anti-nuclear antibody test were done, and the results were normal. There was no family history of vitiligo. Physical examination revealed depigmented and hypopigmented macules and patches on the face, the upper part of the chest (V-shaped), and fingers. [Figure 1] A clinical diagnosis of vitiligo was made. The patient was started on oral prednisolone 5mg daily, topical calcipotriol, and Mometasone furoate 0.1 %.

Oral prednisone was then tapered after 2 weeks to 2.5mg and stopped after another 2 weeks but the other medication was continued. After 3 months of treatment, there was significant repigmentation of the affected areas. [Figure 2]

Discussion

Vitiligo is the most common disorder that causes depigmentation of the skin. It presents as an asymptomatic lesion which can sometimes be associated with pruritus and a burning sensation of the affected skin.[7] It occurs due to melanocyte dysfunction and disappearance following synergistic effects of environmental factors, genetic predisposition, metabolic abnormalities, improper renewal, and alteration in inflammatory and immune responses.[6] Vitiligo has also been associated with auto-immunity.[8] Our patient however had no evidence of autoimmune disorders.

Vitiligo is classified into segmental and non-segmental. The non-segmental type is further divided into generalized, acrofacial, universal mucosal, and mixed types. Generalized vitiligo occurs randomly over the whole-body surface, often more on the pressure, friction, or trauma-predisposed areas. Acrofacial vitiligo is limited to the distal extremities and /or the face. It can involve other areas later and may become generalized or universal.[9] Mucosal vitiligo involves oral or genital mucosae. It may occur as part of generalized vitiligo or an isolated mucosal variety. Universal vitiligo is the type where 80-90% of the body is affected. Focal vitiligo presents with small, isolated depigmented macules and patches without a specific distribution pattern. Mixed vitiligo refers to the occurrence of both segmental and non-segmental types together .[10-11]

Segmental vitiligo (SV) is the type in which the depigmented macules have a segmental distribution. The lesions are usually limited to a single dermatome. The affected dermatome may be partially or completely affected.[12]

Segmental vitiligo is the most common type, followed by acrofacial vitiligo.[3] Other forms of vitiligo which cannot be classified as SV or NSV include punctate vitiligo (sharply demarcated 1-1.5mm macular depigmentation in a punctate form on any body part), hypochromic vitiligo (the lesions are present on seborrheic areas and limited to dark skin individuals). Follicular vitiligo presents with leukotrichia without depigmentation of the surrounding epidermis.[13] Our patient presented with acrofacial vitiligo which later became generalized.

Diagnosis of vitiligo is mainly clinical. However, the use of a Woods lamp can aid in diagnosis. Screening for autoimmune diseases such as thyroid and adrenal disorders is also important.[9]

Treatment of vitiligo in children is very important owing to its psychological impact on the child and the

family and to avoid the associated stigmatization. Various treatment modalities for childhood vitiligo exist. The first line option for the treatment of vitiligo according to the British Association of Dermatologists 2021 guidelines for the management of people with vitiligo is non-steroid option treatment.[14] The use of tacrolimus is considered the first line for the treatment of vitiligo in children because young children are at higher risk of skin atrophy from the use of topical steroids on their delicate skin. Non-steroid options should be used alongside potent topical steroids.

The high surface area to volume ratio in young children predisposes them to the side effects of steroids. The use of oral corticosteroids in young children can affect growth, hence should be used with caution.[14] Topical corticosteroids (TCS) are anti-inflammatory agents and in the paediatric population, the medium-potent ones such as betamethasone are better. They can be used daily or twice daily. They are best used for inflammatory vitiligo with a reported success rate of over 50% in childhood vitiligo.[15] Topical corticosteroids are relatively safe, but use should be limited to 2- 4 months to avoid local and systemic side effects from prolonged use.[16]

Calcipotriol is a synthetic vitamin D3 analogue, which seems to stimulate melanogenesis and stop the destruction of melanocytes by T-cells. Its exact mechanism of action is not known. It is applied once daily, but less effective than TCS.[16]

Topical calcineurin inhibitors (TCI) are good alternatives to topical corticosteroids for localized forms of vitiligo. They are immunomodulators used twice daily for facial and localized lesions among children older than 2 years; and they block calcineurin, preventing cytokine expression.[17] They cannot be used for children less than 2 years because of the risk of malignancies like skin cancers and lymphoma. They are expensive and when offered to our patient, the parents were unable to buy them because of their cost and unavailability in our environment. Hence, it was not used for our patient.

The second-line treatment option is the use of phototherapy (NB-UVB) and psoralen and UVA (PUVA). Phototherapy acts as an immunosuppressant and stimulates melanocyte activity.[18] Both UVB and UVA can be used and are even considered first-line therapy, especially for extensive lesions. Oral PUVA, topical cream PUVA, bath PUVA, and narrow-band PUVA can all be used. However, the risk of sunburn and low efficacy limit the use of broad-band UVB.

PUVA therapy involves oral intake of photosensitive psoralen which is followed by exposure to photo-activating UVA light (320-400nm) 2-3 times a week depending on the patient's response. It should not be used in children less than 12 years due to psoralens toxicity which can lead to ocular damage or gastric damage.[18] Topical PUVA is another valid option for the treatment of vitiligo in children. It involves topical application of 0.01-0.1% 8-methoxypsoralen in hydrophilic petrolatum or ethanol on the vitiligo skin then followed by exposure to UVA- irradiated with a dose of 0.12-0.25J/cm ^{2}. It is done 1 – 3 times a week, increasing the dose of the UVA until mild erythema develops.[19]

The third line of therapy is surgical therapy. Various surgical techniques are employed but suction blister epidermal grafting is preferred. They are not done commonly in children and should be limited to localized and stable lesions that are not responsive to conventional therapies. Another reason surgical treatment is not implemented in children is they are still growing; hence, lesions tend to extend and may not be stable postoperatively.[16,20]

Excimer laser is another treatment of choice in children with segmental vitiligo. Resistant lesions, acral lesions, and lesions in hidden places are favorable for the excimer laser. To obtain a good response with the excimer laser, a twice-weekly schedule should be used for 13 weeks. The treatment response rate depends on the anatomical site of the vitiligo.[20-21]

Another option for treatment with laser in children is the use of a UVA_1 target laser. Laser Alba allows limited, border lesions to be treated using a more appropriate dose of energy and shorter duration and less frequent treatment sessions. The treatment using laser Alba 355 has fewer side effects and therefore is well tolerated.[22]

Prostaglandin also plays a role in melanocyte proliferation and melanogenesis and topical application of prostaglandin E2 (PGE2) offers a new and potentially effective treatment of vitiligo.[23] Prostaglandin F2 is a reliable biomarker of oxidative stress and may be incriminated in the pathogenesis of vitiligo. Prostaglandin F2 alpha analog may be used in the treatment of vitiligo when applied topically.[23]

Drugs that inhibit the JAK/STAT pathways are also effective in the treatment of vitiligo. They stimulate Sonic Hedgehog and Wnt signaling implicated in epidermal pigmentation and melanocyte migration, proliferation, and differentiation. Ruxolitinib is the first JAK inhibitor approved to be used in the treatment of vitiligo, to be applied twice daily.[24] Topical tofacitinib a JAK1/3 inhibitor is also effective. Their efficacy is better on sun-exposed areas, with concomitant narrow band UVB (NBUVB) therapy, and on Fitzpatrick skin type IV to VI.

Depigmentation is another treatment option. This is done for widespread vitiligo using 20% monobenzyl ether of hydroquinone (MBEH). This should be used with caution in older children when they present with extensive vitiligo that is resistant to treatment, and in those that can understand the repercussion of the therapy.[25]

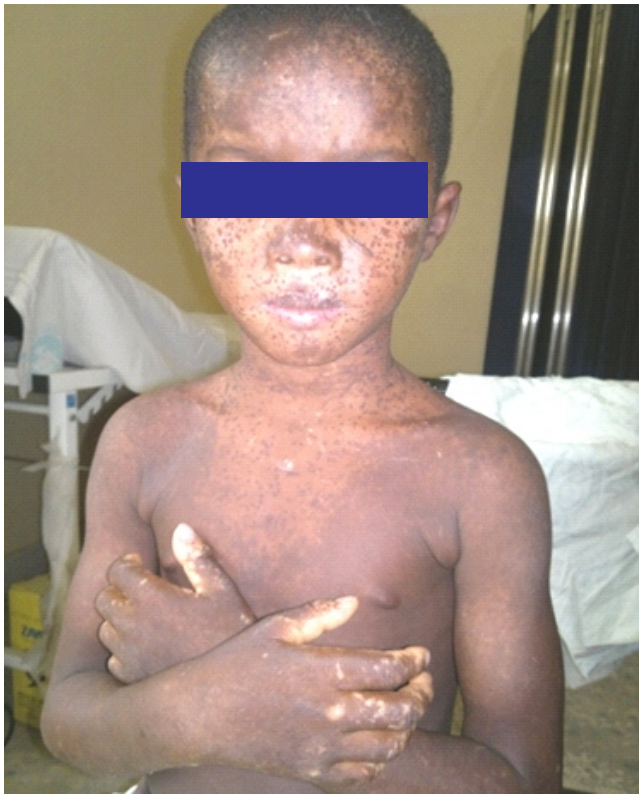

Figure 1: Patient at presentation

Systemic corticosteroids are used for patients with unstable vitiligo. It induces re-pigmentation and halts disease progression. They are administered for a short period or in a pulsed regimen due to their side effects.

Combination treatment: This has been proposed for the treatment of vitiligo in children in the last few years. Topical corticosteroids may be combined with calcipotriol.[26] This combination gives faster and better response and minimizes the side effects of each drug. Topical corticosteroids can also be combined with oral ones in progressive vitiligo.[27] Topical treatments can also be combined with phototherapies.

Adjuvant therapy: Cosmetic camouflage can also be used as a form of treatment for childhood vitiligo due to its psychological impact. The best cosmetic should be non-allergenic, have colour matching, not expensive, and be easy to use.[28] Cognitive therapy and psychological support are very important in children with vitiligo as well as their parents.[29]

The better outcome has been associated with vitiligo in sun-exposed areas and also when they occur in children.[7] We used mometasone (class III steroid) instead of tacrolimus because of the non-availability and non-affordability of tacrolimus. A combination of topical calcipotriol (Dovonex) and topical steroids

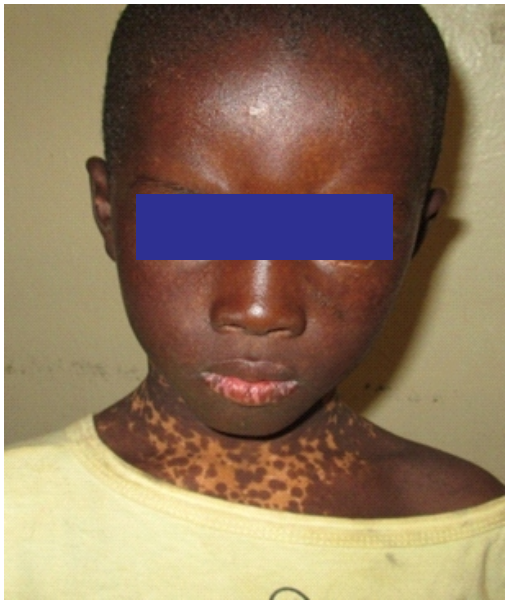

Figure 2: After 3 months of treatment, there is total repigmentation of the facial lesions and improvement of the lesions on the neck

is more effective than each medication given alone.

In conclusion: The use of the combination of topical calcipotriol (Dovonex) and a topical steroid may therefore be promising in the treatment of childhood vitiligo. However, further studies need to be done in this area. The best choice of treatment for childhood vitiligo depends on the age, psychological factors, extent and distribution of the lesion, whether the vitiligo is stable or non-stable, the socioeconomic status of the patient, and also the availability of treatment options.

Conflict of interest: Non

Funding: Nil

References

1. Halder RM. Vitiligo update. *Semin Cutan Med Surg*. 2009; 28: 86-92
2. Bergovist C, Ezzedine K. Vitiligo: A Review. *Dermatology*. 2020; 10: 1-22
3. Ehiaghe L. Anaba Adebola O. O. Clinical characteristics of childhood vitiligo in Nigeria. *Int J Contemp Paediatr* 2019; 6: 578 – 582
4. De Barros J, Filho C, Abreu L, De Barros J, Paschoal F, Nomura M, Marques E, Martins L. A study of Clinical profiles of Vitiligo in different ages; An analysis of 669 outpatients. *Int. J Dermatol.* 2014; 53:842-848.
5. Kruger C, Schallreuter K. A review of the worldwide prevalence of vitiligo in children/adolescents and adults. *Int J Dermatol*. 2012; 51: 1206 -1212.
6. Ezzedine K, Sheth V, Rodrigues M, litefat H, Hamzavi M, Amit G, et al. Vitiligo working group. Vitiligo is not a cosmetic disease. *J Am Acad Dermatol*. 2015;73:883-85.
7. Mu E, Cohen B, Orlow S. Early-onset childhood vitiligo is associated with a more extensive and progressive course. *J Am Acad Dermatol*. 2015;73: 467-470.
8. Nicolaidou E, Mastraftsi S, Tzanetakou V, Rigopoulos D. Childhood vitiligo. *Am J Clin Dermatol*. 2019; 20(4): 515-526.
9. Fricain M. Weidmann P, Roche Y, Fricain J. Labial vitiligo associated with fastice disorder: a case report. *Journal of Oral Medicine and Oral Surgery.* 2018; 24 (4): 167-169
10. Ezzedine K, Lim HW, Suzuki T, Katayams I, Hamzavi I, Lan CC et al. Vitiligo global issue consensus conference panelist. Revised classification/nomenclature of vitiligo and related issues: the Vitiligo global issues consensus conference. *Pigment Cell Melanoma Res*. 2012; 25 (3): E1-13.
11. Ezzendine K, Gauthier Y, L eaute-Labreze C, Marquez S, Bouchtnei S, Jouary T et al. Segmental vitiligo associated with generalized vitiligo (mixed vitiligo): a retrospective case series of 19 patients. *J Am Acad Dermatol*. 2011; 65: 965-971.
12. Ezzendine K, Diallo A, Leaute-Labreze C, Seneschal J, Ballanger F, et al. Halo naevi and leukotrichia are strong predictors of the passage to mixed vitiligo in a subgroup of segmental vitiligo. *Br J Dermatol*. 2021; 166: 539-44.
13. Hann S, Lee H. Segmental vitiligo: clinical findings in 208 patients. *J Am Acad Dermatol*. 1996; 35: 671-674.
14. Elefheriadou V, Atkar R, Batchelor J, McDonald B, Novakovic L, Patel JV et al. British Association of Dermatologists guidelines for the management of people with vitiligo. *Br J Dermatol*. 2021; 186; 18-29.
15. Cho S, Kang H, Hahm J. Characteristics of vitiligo in Korean children. *Pediartric Dermatol*. 2000; 17: 189-193
16. Amrinder J, Kanwar M, Sendhil Kumaran. Childhood Vitiligo: treatment Paradigms. *Indian J Dermatol*. 2012; 57: 466-474.
17. Manzoni A, Weber Mb, Nagatomi A, Pereira R, Towsend R, Cestan T. Assessing depression and anxiety in the caregivers of paediatric patients with chronic skin disorders. *An Bras Dermatol* 2013; 88): 894-899.
18. Gianfaldoni S, Zarrab Z,Lotti T. Phototherapy and vitiligo RE-pigmentation. From PUVA to micro-focused phototherapy. *Journal of Pigmentary Disorders*. 2014; 1: 102.
19. Tamesis ME, Morelli JG. Vitiligo treatment in childhood. A state-of-the-art review. *Paediatr*

Dermatol. 2010; 27: 437-445.

20. Cho S, Kang HC, Haahm JH. Characteristics of vitiligo in Korean children. Pediatr Dermatol. 2000; 17: 189-193.
21. Giafaldoni S, Tchernev G, Wollina U, Lotti J, Rovesti M, Satolli F et al. Vitiligo in children: What is new in treatment? *Macedonian Journal of Med Sci*. 2018; 6: 221-225.
22. Tchernev G, Wollina U, Franca K, Lotti J, Satolli Fet al. Useful treatment with UVA 1 laser of non-responder patients. *Macedonian Journal of Med Sci*. 2018; 6: 43-45.
23. Parsadi D, Pandhi R, Dogra S, Kumar B . Topical prostaglandins analog (PGE2) in vitiligo- a preliminary study. *Int J Dermatol*. 2002; 41: 942-945.
24. Rosmanin D, Pandya A, Lebwohl M, Grimes P, Hamzavi I, Gottlieb A et al. Ruxolitinib cream for treatment of vitiligo: A randomized, controlled phase 2 trial. *Lancet* 2020; 396:110-120.
25. Grimes P, Kelly A, Cline D, Nordlund JJ, Jareatt MT, Rogers M, et al. Management of vitiligo in children. *Pediatr Dermatol* 1986; 3: 498 – 510
26. Scherschun L, Kim J, Lim H. Narrow-band ultraviolet B is a useful and well-tolerated treatment for vitiligo. *J Am Acad Dermatol* 2001;44: 999 – 1003
27. Travis L, Silverberg N,. Calcipotrien and corticosteroid combination therapy for vitiligo. *Pediatr Dermatol.* 2004; 21: 495-498.
28. Tedeschi A, Dali Oglio F, Micali G, Robert A, Schwartz M, Camila K et al. Corrective camouflage in pediatric dermatology. Cutis, 2007; 79:110-2.
29. Schwartz R, Sepulveda J, Quintana T. Possible role of psychological and environmental factors in the genesis of childhood vitiligo. *Rev Med Chil*. 2009; 137: 53-62.