International Journal of Research in Dermatology
Saini B et al. Int J Res Dermatol. 2019 Nov;5(4):889-893
http://www.ijord.com

DOI: http://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20194689

Case Report

Topical corticosteroids induced hyper-pigmentation: a case report

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Received: 19 June 2019
Revised: 01 August 2019
Accepted: 03 August 2019

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ABSTRACT

Hyper-pigmentation is a common skin condition in which increased melanin production results in darker patches of skin. Although hyper-pigmentation is harmless but still mostly people wish to get rid of them because of increasing craze of beautification in India. Topical corticosteroids (TC) application showed quick amelioration of post-inflammatory hyper-pigmentation patches. Prolonged and unsupervised use of TC leads to skin atrophy and reappearance of hyper-pigmentation patches. We present two cases of hyper-pigmentation induced by TC misuse. In case-1, a 20 year old female came to OPD with a complaint of hyper-pigmentation and itch sensation along with drug history of Betnovate cream for the last 2 years for acne treatment. On examination, she showed signs of hyper-pigmentation on cheeks. She was counselled to stop the further use of Betnovate cream and prescribed demelanizing agents along with sunscreen and emollients. The patches improved significantly with above management within 15 days. In case-2, a 33 year old female came to OPD with complaints of redness over whole face, increased facial hair growth and burning sensation along with drug history of using Betnovate cream for 2 years. On examination she showed signs of hyper-pigmentation and redness on cheeks, bruise and tearing of skin and increased facial hair growth. She was counselled to stop the further use of Betnovate cream. She was prescribed retinoic acid cream, sunscreen agents, anti-allergic tablets and emollient cream. The patches improved significantly with above management within 15 days.

Keywords: Topical corticosteroids misuse, Hyper-pigmentation, Naranjo's ADR probability scale, Hartwig's severity

INTRODUCTION

Hyper-pigmentation is darkening of skin colour due to increased melanin production. Most common types of hyper-pigmentation include age spots, melasma and post-inflammatory hyper-pigmentation. Age spots, also called liver spots or solar lentigines are brown, tan or black spots that appear on skin after extended sun exposure on face and hands in older adults. Melasma, also called chloasma or "the mask of pregnancy" are large patches of darkened skin on forehead, face and stomach affecting women who are pregnant or taking control pills. Post-inflammatory hyper-pigmentation are patches of darkened skin that appear after an inflammatory skin condition such as acne or eczema on face or neck.[1] Other causes of hyper-pigmentation include reactions to drug use such as antimalarial drugs, topical corticosteroids and tricyclic antidepressants.[2-4] Chemicals added in topical treatments can also cause hyper-pigmentation.

There are a range of possible treatment methods and home remedies that people usually try without any dermatologist advice. Topical treatments usually include ingredients that lighten the skin, such as azelaic acid,

topical corticosteroids, hydroquinone, kojic acid, retinoids, such as tretinoin and vitamin C.[5] TC has been reported most commonly misused drug for hyper-pigmentation in studies conducted in the last 10 years.[6]

Basic purpose of starting the steroid cream is mostly to look fairer, beautiful and have a blemish free skin. TC has anti-inflammatory and pigment-lightening activity on the skin. TC produces rapid alleviation of unpleasant signs and symptoms of inflammatory changes on the skin. Unfortunately, this "improvement" is short-lived and can be followed by worsening of the original condition if TCs are used for a long duration or not used correctly. Steroids interfere with the synthesis of melanin by smaller melanocytes, leading to patchy areas of hypo-pigmentation which are reversible after discontinuation of steroids.[7]

Prolonged uses of TCs leads to epidermal atrophy, degeneration of dermal structure and collagen deterioration after several months. Continued or overuse of steroids can result in thinning of the skin as well as skin dependency on the steroid. Sun exposure to such a thin skin leads to darkening of superficial layer of skin, hence patients present with hyper-pigmented patches on sun exposed skin areas.[8]

CASE REPORT

Case 1

A 20-year-old female had been using Betnovate cream from 2 years for acne treatment without dermatologist prescription. Now she came to OPD with complaints of hyper-pigmentation from 1 year and itch sensation from 3 months. On examination, she showed signs of hyperpigmentation on face that was mainly on cheeks (Figure 1). Rest all the examinations were within normal limits. She was counselled to stop the further use of Betnovate cream. She was prescribed demelanizing agents for hyper-pigmented patches. She was advised sunscreen agents also. To relieve itching, emollients were given. The patches improved significantly with above management within 15 days.

Case 2

A 33-year-old female had been using Betnovate cream from 2 years for cosmetic purpose. She came to OPD with complaints of redness over whole face and increased facial hair growth for last 2 years. She also had burning sensation for 1 year. On examination she showed signs of hyper-pigmentation and redness on cheeks, bruise and tearing of skin and increased facial hair growth (Figure 2).

Rest all the examinations were within normal limits. She was counselled to stop the further use of Betnovate cream. She was prescribed retinoic acid cream, sunscreen agents, anti-allergic tablets and emollient cream. She was also advised for laser for increased facial hair growth. The patches improved significantly with above management within 15 days.

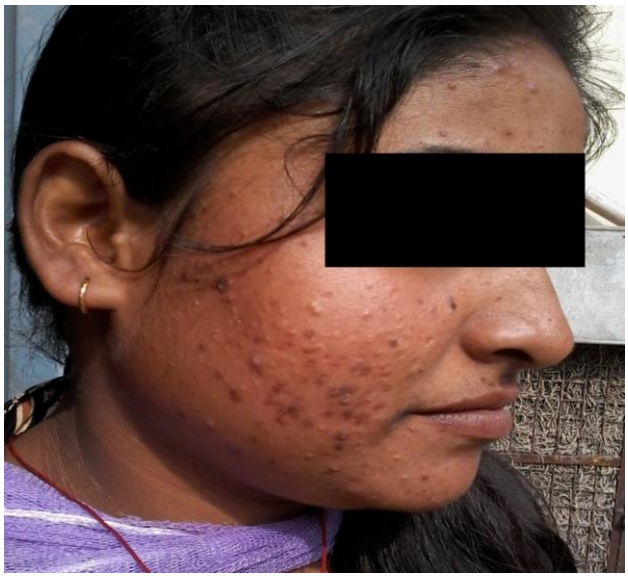

Figure 1: Hyperpigmentation with acne on cheek (case 1).

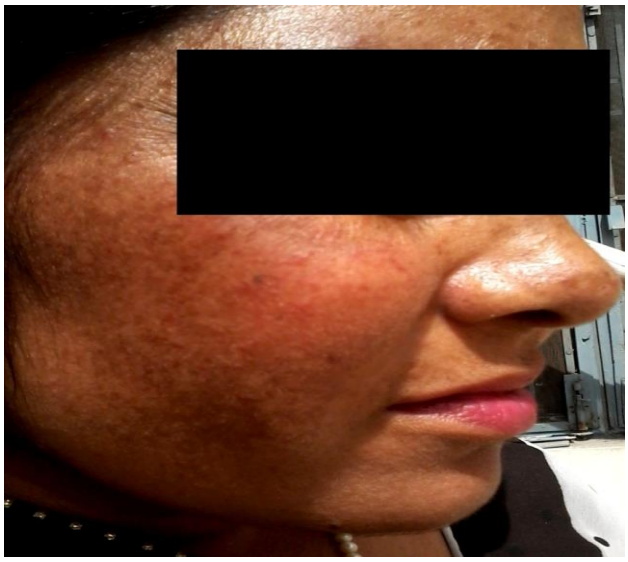

Figure 2: Hyperpigmentation and redness on cheek (Case 2).

For case-1 and case-2, ADR causality assessment was done. Naranjo's scale shown this ADR as probable (Table 1) and WHO scale shown it as probable or likely (Table 2). Severity was level 3-moderate according to Hartwig's severity assessment scale (Table 3). ADR preventability assessment with Shumock and Thornton Preventability Scale shows it was definitely preventable (Table 4). All the above assessments are summarized as analysis of ADR and depicted in Table 5.

Table 1: ADR Causality assessment (Naranjo scale).[9]

Question	Yes	No	Do not know	Score	
				Case 1	Case 2
Are there previous conclusive reports on this reaction?	+1	0	0	+1	+1
Did the adverse event appear after the suspected drug was administered?	+2	-1	0	+2	+2
Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	+1	+1
Did the adverse event reappear when the drug was re-administered?	+2	-1	0	0	0
Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	0	0
Did the reaction reappear when a placebo was given?	-1	+1	0	0	0
Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	+1	0	0	0	0
Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	0	0
Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0	0
Was the adverse event confirmed by any objective evidence?	+1	0	0	+1	+1
Total score				5	5

Score: ≥9=definite ADR; 5-8=probable ADR; 1-4=possible ADR; 0=doubtful AD.

Table 2: WHO-UMC causality categories.[9]

Causality term	Assessment criteria (all points should be reasonably compiled)	Case 1	Case 2
Certain	• Event or laboratory test abnormality, with plausible time relationship to drug intake. • Cannot be explained by disease or other drugs. • Response to withdrawal plausible (pharmacologically, pathologically). • Event definitive pharmacologically or phenomenologically (i.e., an objective and specific medical disorder or a recognised pharmacological phenomenon). • Rechallenge satisfactory, if necessary.		
Probable or likely	• Event or laboratory test abnormality, with reasonable time relationship to drug intake. • Unlikely to be attributed to disease or other drugs. • Response to withdrawal clinically reasonable. • Rechallenge not required.	✔	✔
Possible	• Event or laboratory test abnormality, with reasonable time relationship to drug intake. • Could also be explained by disease or other drugs. • Information on drug withdrawal may be lacking or unclear.		
Unlikely	• Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible). • Disease or other drugs provide plausible explanations.		
Conditional or unclassified	• Event or laboratory test abnormality. • More data for proper assessment needed. • Additional data under examination		
Unassessable or unclassifiable	• Report suggesting an adverse reaction. • Cannot be judged because information is insufficient or contradictory. • Data cannot be supplemented or verified.		

Table 3: Hartwig's severity assessment scale.[10]

Assessment criteria		Case 1	Case 2
Level 1	• An ADR occurred but required no change in treatment with the suspected drug		
Level 2	• The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. • No antidote or other treatment requirement was required. No increase in length of stay (LOS).		

Continued.

Assessment criteria		Case 1	Case 2
Level 3	• The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. • AND/OR an Antidote or other treatment was required. No increase in length of stay (LOS).	✔	✔
Level 4	• Any level 3 ADR which increases length of stay by at least 1 day (or) the ADR was the reason for admission.		
Level 5	• Any level 4 ADR which requires intensive medical care.		
Level 6	• The adverse reaction caused permanent harm to the patient.		
Level 7	• The adverse reaction either directly or indirectly led to the death of the patient.		

Mild=level 1 and 2; Moderate=level 3 and 4; Severe=5, 6 and 7.

Table 4: ADR preventability assessment (Shumock and Thornton Preventability Scale).[11]

Assessment criteria		Case 1	Case 2
1. Was there a history of allergy or previous reactions to the drug?	Definitely preventable	✔	✔
2. Was the drug involved inappropriate for the patient's clinical condition?			
3. Was the dose, route or frequency of administration inappropriate for the patient's age, weight or disease state?			
4. Was a toxic serum drug concentration (or laboratory monitoring test) documented?			
5. Was there a known treatment for the adverse drug reaction?			
6. Was required Therapeutic drug monitoring or other necessary laboratory tests not performed?	Probably preventable		
7. Was a drug interaction involved in the ADR?			
8. Was poor compliance involved in the ADR?			
9. Were preventative measures not prescribed or administered to the patient?			
10. If all above criteria not fulfilled	Not preventable		

Table 5: Analysis of the ADR.

Types	Case 1	Case 2
Causality- Naranjo	Probable	Probable
Causality- WHO-UMC	Probable or likely	Probable or likely
Severity- Hartwig	Moderate	Moderate
Preventability- Schumock and Thornton	Definitely preventable	Definitely preventable

DISCUSSION

Hyper-pigmentation is a harmless skin condition. Most patients want to get rid of them. Thus, they take treatment suggestions from their relatives and friends instead of proper dermatologist advice. They tend to continue the improper treatments for a very prolong period of time and present to dermatology OPD after worsening of their skin condition. In our cases, TC has been misused over 2 years for cosmetic purposes. Patient presented to the OPD with hyper-pigmented patches on face. Their facial skin had significant thinning as compared to other body parts, hence showing early signs of hyper-pigmentation than other body parts. Both the ADRs had causal association with drug used, moderate severity and were definitely preventable. Although hypo-pigmentation is a common ADR of TC misuse but hyper-pigmentation is also reported as ADR after TC misuse over 6 months. The incidence of hyper-pigmentation has been reported in few studies like Bhat et al, Jha et al, Manzoor et al.[6,12,13] Both our patients presented with hyper-pigmentation after chronic TC usage. The excessive, regular use of topical corticosteroids on the face results in an array of skin complications. Topical corticosteroids are very commonly abused drugs mainly in youngsters, especially females. Over the counter availability of these drugs in our part of world is a major cause of their abuse.

Depigmentation is commonly associated with steroid use. Hyper-pigmentation's are mostly seen in intraoral lesions.[14] The facial is skin is thin hence the penetration of the steroid's ointments is considerably higher in compared to other areas of body. Low potency steroids should be preferred for topical application in facial skin.

Various underlying mechanism are suggested as a cause of hyper-pigmentation. Use of the steroids leads to vasoconstrictive and anti-inflammatory effects leading to

the clearance of the primary dermatitis. On chronic unsupervised usage epidermal atrophy, degeneration of dermal structure and collagen deterioration is seen. After several months of usage, appearance of rosacea like features are noted. It makes the fragile skin susceptible to bacterial, viral, and fungal infections. Multiple pathways including rebound vasodilatation and pro-inflammatory cytokine release by chronic intermittent steroid exposure induce rosacea-like eruption which on resolution produces pigmentation.[15,16]

Facial hyper-pigmentation is a continued concern among new generation of Indian population. Successful treatment of facial hyper-pigmentation depends upon their underlying aetiologies. Patients should be encouraged to take advice of dermatologist for their hyper-pigmentation problem rather than applying topical corticosteroids without any proper advice.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Saini B, Kumar M, Bandyopadhyay A. Topical corticosteroids induced hyper-pigmentation: a case report. Int J Res Dermatol 2019;5:889-93.