SEVERE STRIAE AND STEROID ACNE AS SIDE EFFECTS CAUSED BY LONG-TERM SYSTEMIC CORTICOSTEROID TREATMENT: A CASE REPORT AND REVIEW OF THE LITERATURE

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ABSTRACT Background: Systemic corticosteroids are often used in dermatology. The anti-inflammatory and immunosuppressive properties of corticosteroids make this agent as the first-line option in many disorders such as autoimmune and bullous diseases. However, there are also potential side effects and dermatologists who prescribe corticosteroids have to be aware of them. **Case Summary:** We report a 16-year-old girl with a history of taking oral methylprednisolone in the past eight months who came with an acne-like eruption on the face, chest, and extremities as well as lines on the skin. Physical examination revealed monomorphic papules on the facial, thorax, and superior and inferior extremities region. Comedones were absent. Striae were found in the bilateral femur, abdomen, and mammary region. The patient was diagnosed with acneiform eruption and striae distensae rubra. Treatment using a combination of topical clindamycin and tretinoin showed clinical improvement of the acneiform eruption after three months of therapy. However, striae did not show improvement despite topical application of tretinoin and Centella asiatica extract. **Conclusion:** This case demonstrates the importance of understanding the cutaneous side effects that may result from chronic systemic corticosteroids administration as well as the evidence-based management.

KEYWORDS cutaneous side effects, systemic corticosteroid, striae, acneiform eruption

Introduction

Since its first discovery in 1935 by Kendall et al., the use of corticosteroids has been extensively developed and used in various medical fields, including dermatology.[1] Systemic corticosteroids are potent immunosuppressive and anti-inflammatory agents that play an essential role as the first-line treatment in various dermatological disorders such as connective tissue disease, bullous diseases, and autoimmune diseases.[2-4] Corticosteroid is a class of chemical comprising both natural and synthetic hormone with various physiological effects. There are two types of corticosteroids, glucocorticoids and mineralocorticoid. Glucocorticoids regulate metabolism and inflammation, whereas mineralocorticoids regulate levels of sodium and water. Corticosteroids have a wide spectrum, ranging from exclusive glucocorticoid effects, combination to mineralocorticoid exclusive, which is an essential factor to be considered.[5]

However, the side effect of musculoskeletal, metabolic endocrine and dermatological may occur; where the incidence and severity increased with increasing dose and duration of use.[1-3] In the dermatology, side effects may vary, such as skin atrophy, habitus cushingoid, eruption acneiform, easy bruising, alopecia and hirsutism, perioral dermatitis, and stretch marks.[6]

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Clinical photos at the first visit -
Figure (A) Acneiform eruption
and moon face appearance.
Figure (B) and (C) acneiform eruption
on the upper extremities.
Figure (D) and (E) The striae on anterior and posterior
trunk accompanied
with an acneform eruption on the thorax.
Pictures (F) and (G) striae and acneform eruptions
on the superior and inferior extremities.
Pictures (H) picture buffalo hump on the posterior trunk.

Case Report

A 16-year-old girl was consulted from the paediatrics department with a chief complaint of pimples on the face and the entire body since seven months before admission to our outpatient clinic. The patient did not complain about pain or itchy. Pimples started to appear in the back and thighs for six months before admission which then extended to the chest, arms, and stomach. Her body weight increased from 44 kg to 57 kg. Her menstrual cycle became irregular and was diminished in volume. The patient had never taken any treatment for her skin complaint. History of drug allergy and food were denied.

The patient was diagnosed with lupus nephritis by the pediatric department eight months earlier and was given daily oral methylprednisolone 64 mg (32 mg in the morning and evening), captopril 12.5 mg bid, 400 mg calcium and vitamin D 200 IU. Physical examination showed that the patient was in a good general condition with a blood pressure of 124/89 mmHg, heart rate of a 90x / minute, the temperature of 36.70C, and respiratory rate of an 18x / minute. Patient weight was 57 kg with a height of 153 cm. Moon face appearance was observed (Figure A). Dermatological examination showed multiple papules and pustules with uniform size distributed discretely on the facial region, thorax, both superior and inferior extremities, with no comedones found (Fig A-G). In addition, violaceus erythematous striae was observed on the mammary, anterior thorax, superior and posterior trunk, abdomen, left and right thighs (Fig D-G). Buffalo hump was found on the superior posterior trunk.

Blood investigation showed leukocytosis 13,800 / ul. Kidney function, liver function, albumin, and electrolytes were within normal limits. Urinalysis showed proteinuria +2, erythrocytes +2 and leukocytes +1. Antinuclear Antibody (ANA) test was positive.

According to the history, physical examination, and supporting examination, a diagnosis of acneiform eruption and striae rubra et causa systemic steroid was established. The patient was given a combination of clindamycin and 0.025% tretinoin applied topically in the morning and evening. At sites with the acneform eruption, lesions were given tretinoin 0.1%, and Centella Asiatica plant extracts were applied to the striae. The patient was given information about the cause of the condition and moral support as she was frustrated with her condition. The importance of continuing methylprednisolone to control the underlying diseases was emphasized.

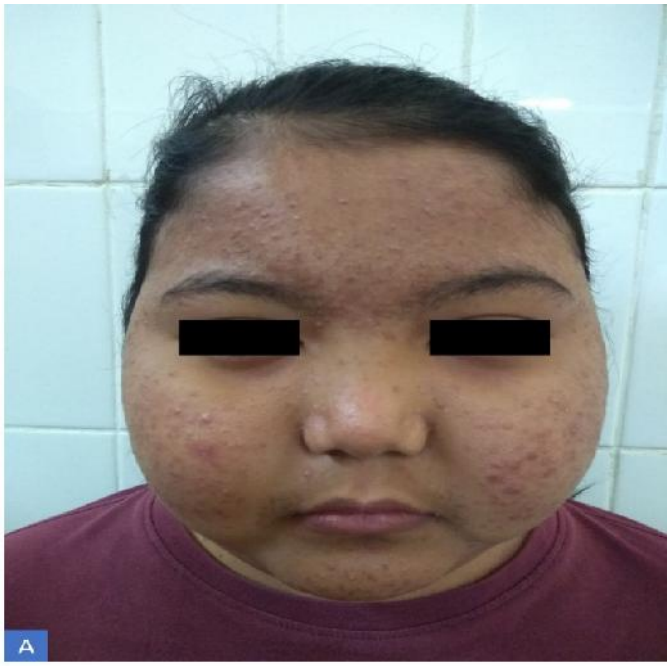

Fig.1.A.

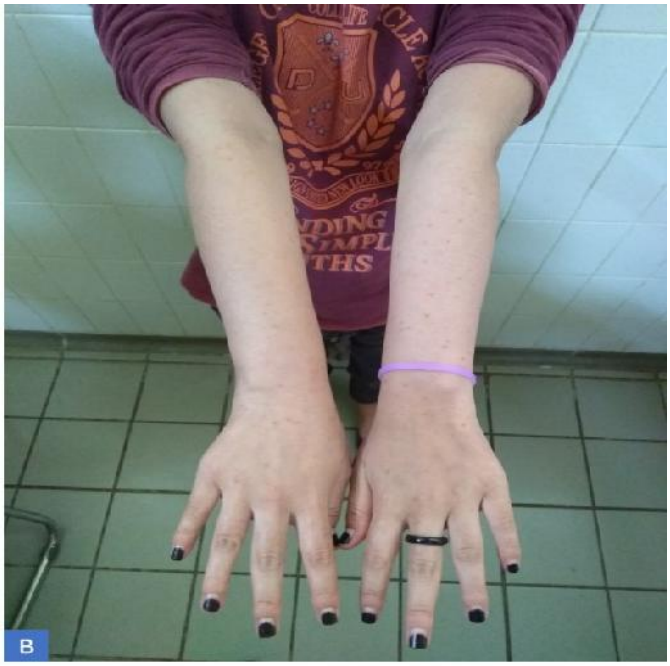

Fig.1.B.

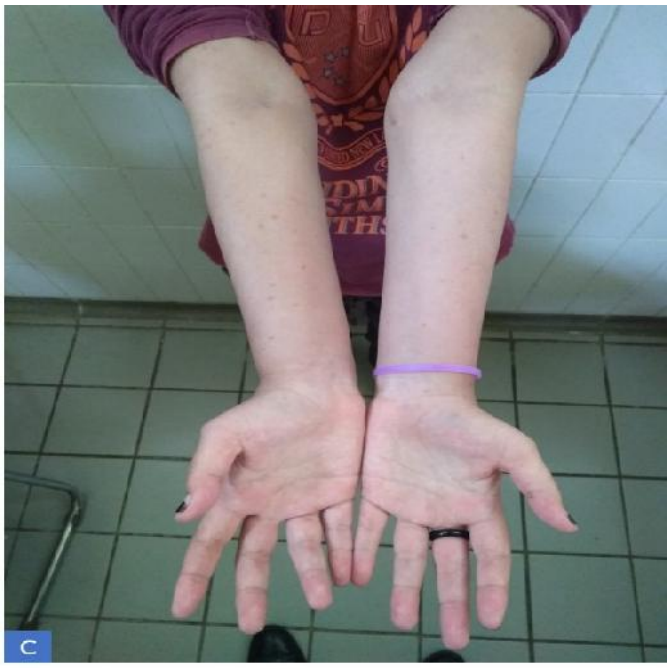

Fig.1.C.

The first follow-up month -
Pictures (HM) no changes in the number and distribution of papules on the facial region, trunk, and superior and inferior extremities.
Pictures (IM) showed striae was expanded.

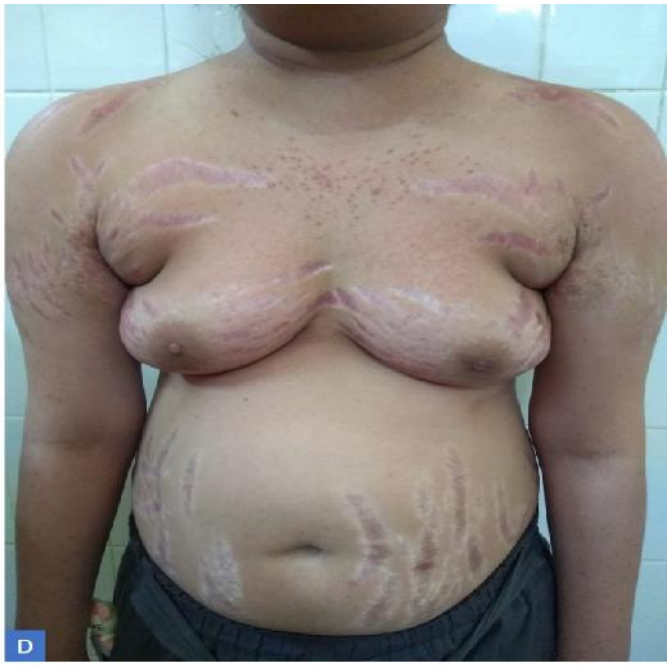

Fig.1.D.

One month later, there was no change in the number and distribution of papules and pustules on the facial region, thoracic, and superior and inferior region (Figure H-M). The striae appeared to be more spacious, and new lesions appeared (Figure K-M). Laboratory tests showed leukocytosis 14,200/ul, Hb 13.4 g/dl, random blood sugar 216 mg/dl, normal renal function, liver function, and electrolytes. Urinalysis showed proteinuria +2, glucosuria +1, +3 erythrocytes and leukocytes +1.

At the second month of follow up, the number of papules was reduced, but the striae kept on expanding. Previous treatments were continued.

The clinical picture at the second-month follow-up - Pictures (NS) looked papules on the facial region, trunks, and extremities began to decrease. Pictures (PS) showed striae expanded.

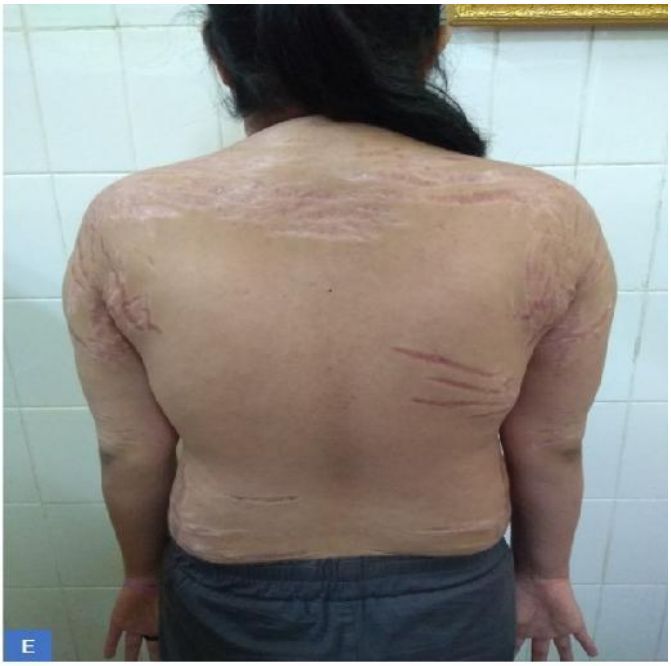

Fig.1.E.

Discussion

This case discussed the cutaneous side effects of long-term use of systemic corticosteroids in a 15-year old girl with nephrotic lupus and Cushing's syndrome. On physical examination, there

Fig.1.F.

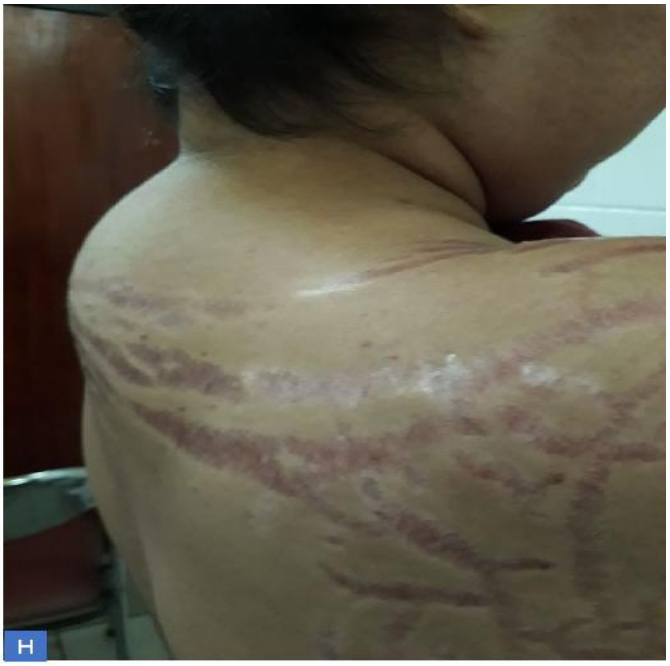

Fig.1.H.

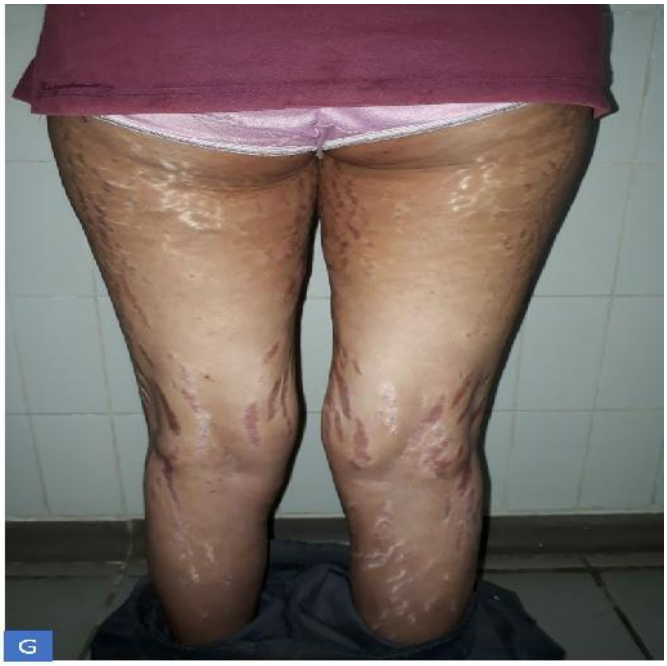

Fig.1.G.

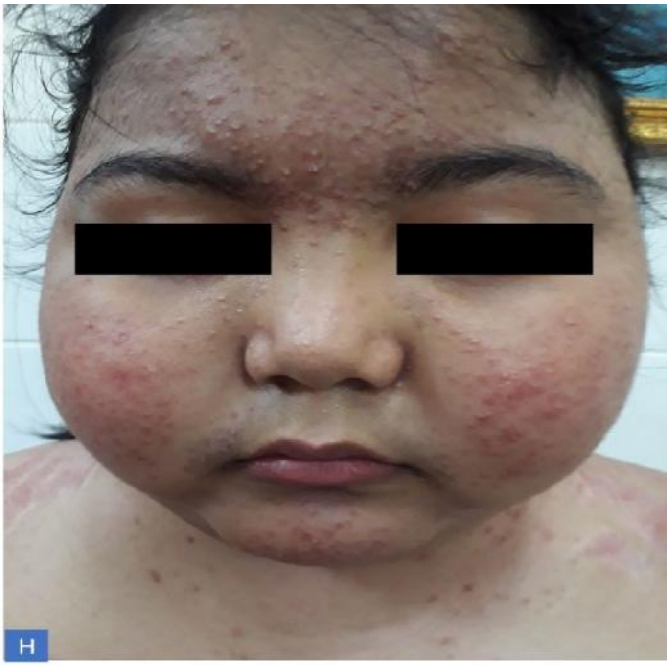

Fig.2.H.

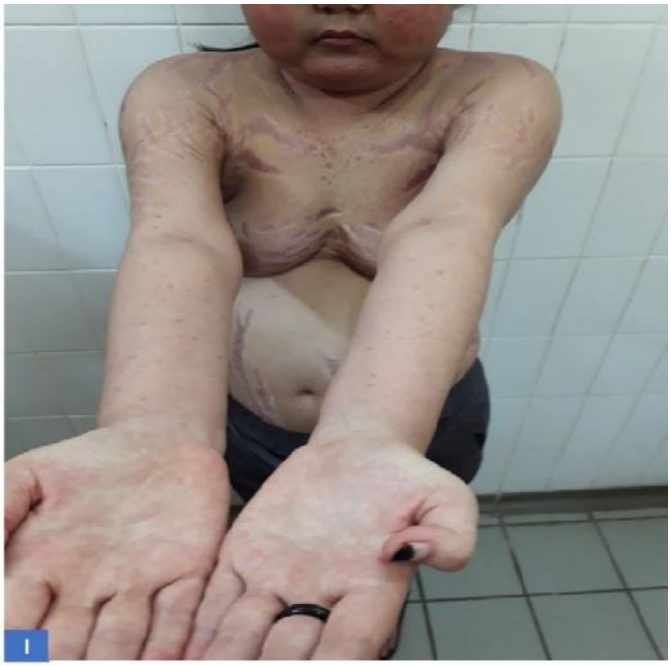

Fig.2.I.

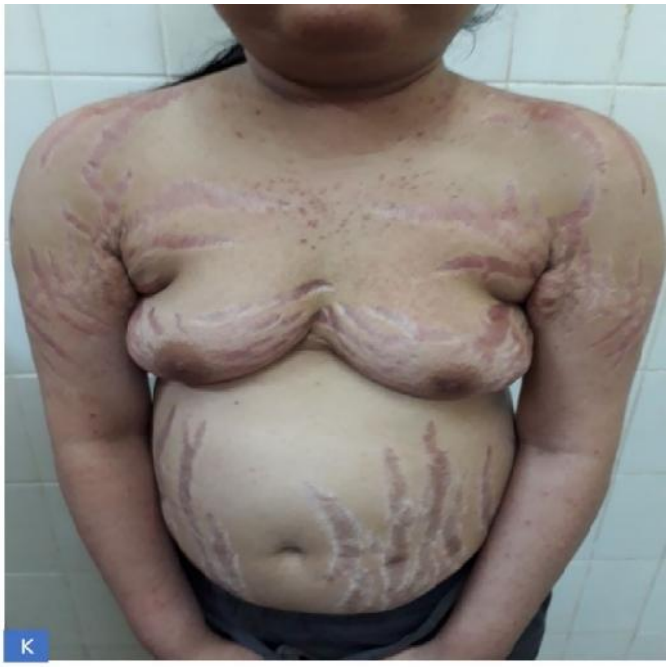

Fig.2.K.

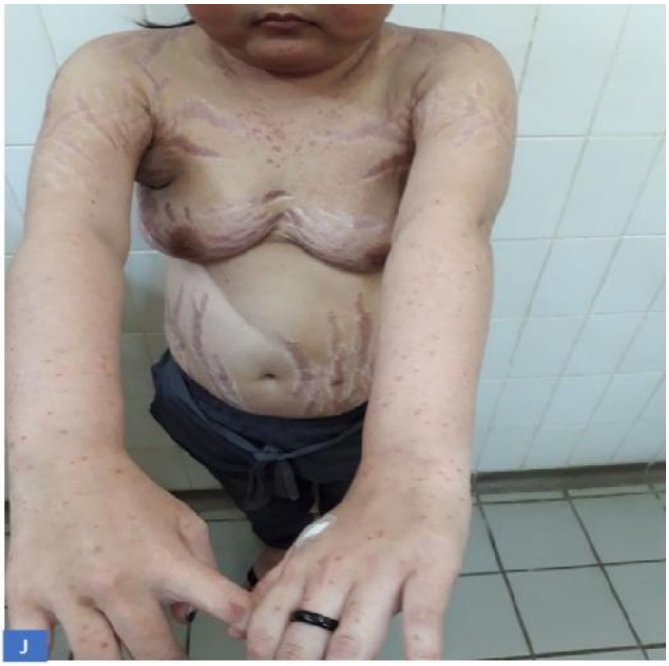

Fig.2.J.

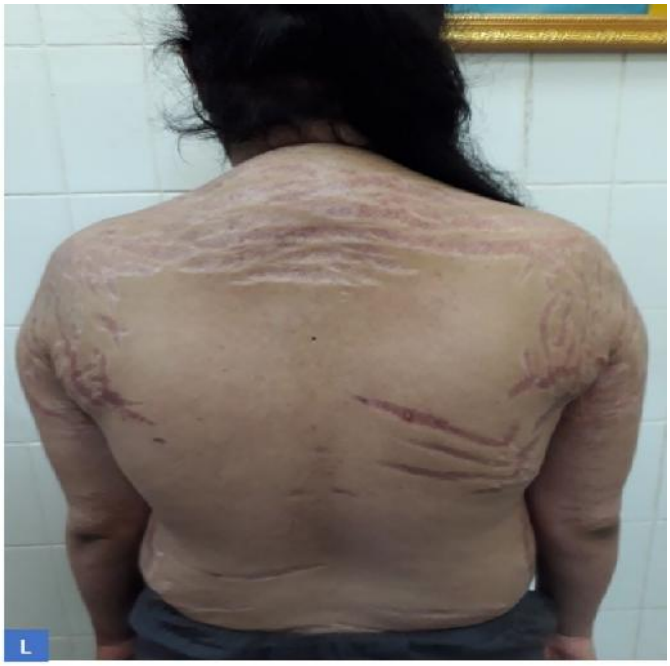

Fig.2.L.

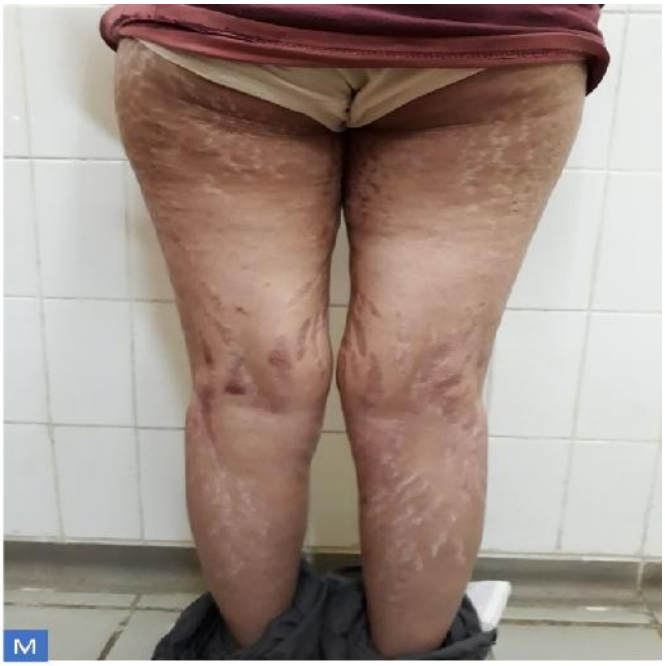

Fig.2.M.

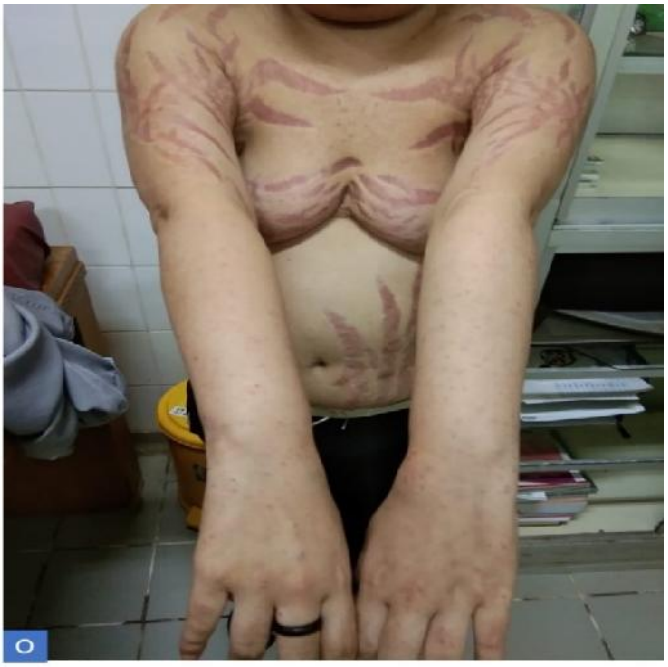

Fig.3.O.

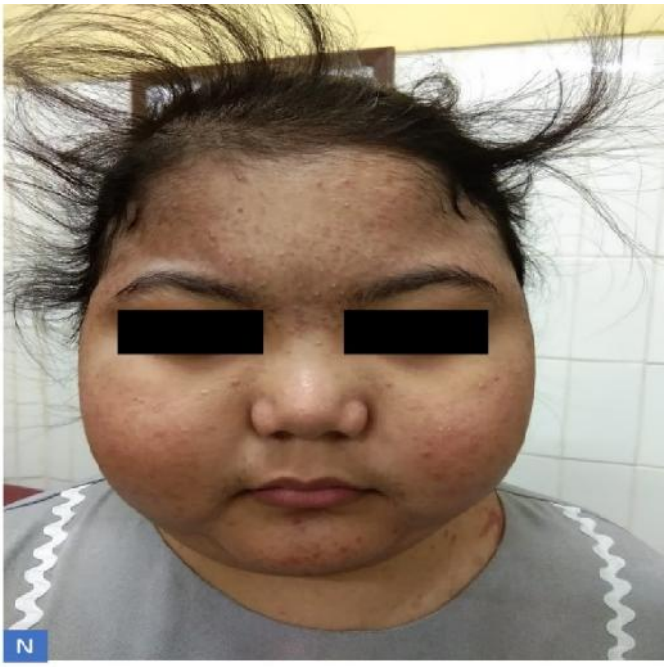

Fig.3.n.

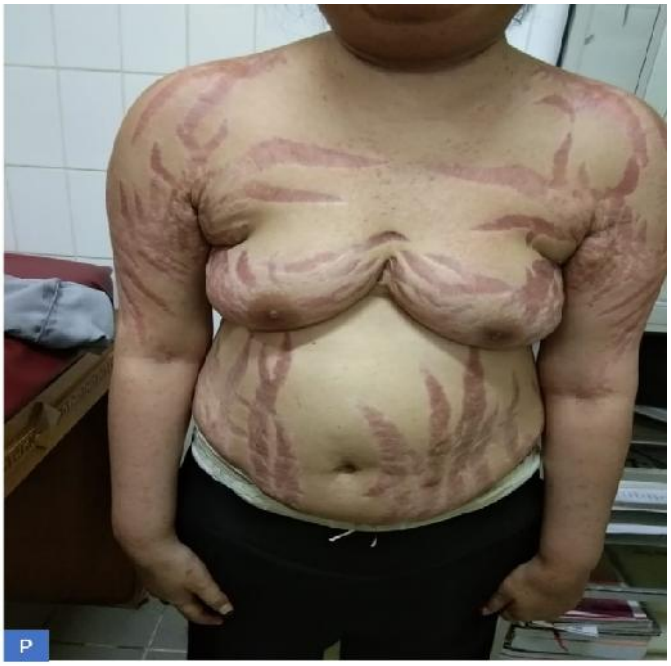

Fig.3.P.

Fig.3.Q.

were monomorphic skin-coloured and multiple erythematous papules and discretely scattered pustules on the face, trunk (especially on the chest and the back), as well as the superior and inferior extremities, with no evidence of blackheads. Also, history taking revealed oral methylprednisolone consumption within eight months.

We report a case of CD20-positive CTCL in a 90-year-old woman based on the history taking, physical examination, and laboratory findings. CTCL is twice as common in men as in women.[6] The incidence of CTCL increases significantly with age, with an average onset between 50 and 60 years old and a four-fold increased incidence in patients over 70 years.[9]

The results of the history and clinical features were consistent with the diagnosis of acneiform eruption due to prolonged systemic steroid consumption. The drug-induced acneform eruption, also known as acne medicamentosa, steroid acne or steroid folliculitis, is defined as monomorphic skin-coloured papules or pustules, mainly in the seborrheic areas on the face, chest, upper back, and shoulders.[7-9] In addition to corticosteroids, the acneform eruption can also be induced by other drugs such as antidepressants, hormonal contraceptives, retinoids, propranolol, isoniazid and rifampicin.[10] The absence of blackheads is an important feature that distinguishes acneform eruption from acne vulgaris [8, 11] However, some literature suggests that blackheads may also occur secondarily to the eruption and not primarily as in acne vulgaris.

As mentioned above, the term 'acne' is not appropriate for this condition since it is not a true acne but folliculitis with neutrophilic infiltration in or around the hair follicles.[3, 8] The pathogenesis of acneiform eruption is not fully understood, but it is estimated that corticosteroids are responsible to the increasing levels of free fatty acids in the skin surface which increases the number of colonies of Propionibacterium acnes (P.acnes) in the pilosebaceous unit. Free fatty acid breakdown by P.acne is thought to contribute to the formation of inflammatory papules.[7] Also, in-vitro studies showed that corticosteroid enhances the expression of Toll-like Receptor 2 (TLR2) by keratinocytes. It is known that TLR2 activation results in the increasing release of proinflammatory mediators such as interleukin (IL)- α.[12] Histologically, spongiosis followed by the rupture of follicular epithelial tissue to the dermis triggering inflammation can be observed.[13]

In this case, the eruption appeared four weeks after taking methylprednisolone. Before starting the treatment, the patient denied any history of similar complaints. Some factors could influence the onset of drug-induced acneiform eruptions such as the dose, duration of administration, and the susceptibility of the patient.[14] Depending on these factors, the eruption may occur within 2-4 weeks to several months.[7] The literature indicates that the most frequently involved locations are the abdomen, breast, femur, and gluteus.[15]

Striae distensae, or stretch marks, are lesions caused by stretching of the dermis that occurs due to rapid weight gain; such as the growth spurt in adolescence, pregnancy, or corticosteroids consumption.[16] There are two types of distensive striae, the rubra (acute) type and the alba (chronic). Stria distensae rubra appear erythematous until violaceus, can be symptomatic, and occur perpendicular to the direction of the skin tension.[15] The underlying mechanism is not clearly understood, but it is hypothesized as the result of mid-dermis elastolysis caused by mast cell degranulation and stimulation of macrophages. Also, compared to normal skin, the collagen tissue was thicker, dense, and arranged in parallel with a reduction of the elastin network.[17, 18]

Moon face and buffalo hump were observed in the facial and superoposterior trunk region. Both findings occurred due to an increase in the regional redistribution of triglycerides and fat as a result of an increase in lipolysis. Increased lipolysis itself occurs due to the effects of corticosteroids tend to produce glucose through a catabolic process involving the protein and fat reserves.[1]

This patient was given a combination of topical clindamycin 1.2% and tretinoin 0.025% gel. First-line treatment of acneiform eruption due to drug consumption is drug cessation which unfortunately could not be done in this case.[8, 19] Therefore, the topical supportive treatment was given. There are no well-established guidelines regarding the management of acneiform eruption due to corticosteroids. Present literature suggests that conventional acne vulgaris treatment may be attempted.[3] Clindamycin is the first-line topical antibiotic choice for acne vulgaris due to its antibacterial and anti-inflammatory properties.[20] Tretinoin is a class of retinoid (vitamin A derivatives) which function as comedolytic and anti-inflammation.[20] A double-blind, randomized study conducted on 2,010 patients showed that coadministration of both agents was synergistic and might enhance the therapeutic effectiveness.[21] Topical clindamycin has been shown to enhance the comedolytic activity of tretinoin in mitigating and preventing follicular impaction. Also, its properties can provide access for more effective penetration into the follicle which can reduce the risk of bacterial resistance.[22, 23]

Treatment for striae distensae, in this case, is 0.1% topical tretinoin cream and Centella Asiatica. Extract. The mechanism of tretinoin in the treatment of striae distensae is not known, but it suspected that tretinoin induces collagen production and improve skin elasticity.[15] A randomized controlled clinical trial showed that the use of tretinoin 0.1% for six months showed a reduction in the length and width of striae distensae. [24] Significant improvement was also shown after the use of tretinoin 0.05% for 16 weeks. [25] Centella Asiatica plant extract stimu-

lates fibroblasts and has an antagonistic effect on corticosteroids. [15, 26] A study showed that Centella Asiatica extracts improved appearance, texture, colour, and softness after 12 weeks. [27] Also, this extract was able to prevent striae progression. [26]

Conclusion

Long-term use of systemic corticosteroids may cause side effects in various organs, including the skin. As corticosteroids are frequently used, a proper comprehension of pathophysiology, clinical manifestations, and management of the potential side effects are of paramount importance. This case emphasizes the importance of a comprehensive understanding of cutaneous side effects due to long-term corticosteroid use and its evidence-based management.

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