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CASE REPORT

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Epidermal nevus superimposed by psoriatic plaque in a girl with proteous syndrome

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Abstract

Proteus syndrome (PS) is a rare syndrome characterized by asymmetric limb overgrowth, vascular malformation, and hamartomas. In this study we report a case of PS in a 13-year-old girl with chief complaint of a new cutaneous lesion that was diagnosed and treated as leishmaniasis.

KEYWORDS

epidermal nevus, leishmaniasis, proteus syndrome, psoriasis

1 | INTRODUCTION

Proteus syndrome (PS) is an extremely rare disorder characterized by postnatal disproportionate overgrowth of different parts of body, tumor predisposition, and diverse dermatological abnormalities.[1] This disorder has been originally introduced by Cohen and Hayden in 1979,[2] but later named as PS derived from the Greek sea-god Proteus, who has the ability to change his shape to avoid his capture.[3]

PS is estimated to occur in one per 1,000,000 cases and the symptoms usually initiate at early infancy. The severity of the disease varies in different cases and may affect any part of the body; however, the most common areas include the skin, connective tissue and bone, central nervous system, and eyes. The etiology of PS has not been well-elucidated, but genetic alterations such as AKT somatic mutations are assumed to be responsible.[4]

Several cutaneous manifestations including vascular malformations, dysregulated adipose tissue such as lipomas, epidermal nevus, and the characteristic cerebriform plantar connective tissue nevus in PS have been described.[5] This is a case presentation of an individual with PS who had a new skin lesion that has been misdiagnosed.

2 | CASE PRESENTATION

A 13-year-old girl referred to the skin outpatient clinic affiliated at Isfahan University of Medical Sciences with the chief complaint of a hyperkeratotic plaque with well-defined border and size of 5* 8 cm on the left upper limb.

The patient was a known case of PS whose disease has been notified from her infancy. The child appearance was normal at birth, while within her second month of life some reddish cutaneous alterations on her left upper limb were appeared. Afterward, the disproportionate growth in both upper and lower limbs and the scalp alarmed her mother. Further signs included linear verrucous epidermal nevi, and port-wine stain lesions on the trunk. The clinical manifestations including progressive and disproportionate manner of the extremities and the scalp growth as well as the nature of the cutaneous lesions led to PS diagnosis. Nevertheless, we had no amenity to perform genetic studies to confirm this diagnosis.

The patient referred to our clinic with the chief complaint of a new lesion on her left arm with mild pruritus, emerging 4 months before referral to the clinic.

The patient had referred to a primary health care center and as leishmaniasis was endemic to their habitat, a

smear was taken from the lesion that mistakenly was diagnosed as leishmaniasis. Given that, she received two sessions of intralesional Glucantime (Meglumine antimoniate) injections and because no improvement was seen, twice freezing was done. But due to irresponsiveness to the medications and the gradual lesion enlargement, the patient referred to our clinic.

In the physical examination, the lesion was a sharply demarcated well-defined erythematous and scaly hyperkeratotic plaque locating on a previous linear epidermal nevus (Figure 1). The patient had no complaint of ulcer, pain, or bleeding. The nails and oral mucosa were normal. A biopsy was taken from the lesion. The top list differential diagnoses included leishmaniasis, mycotic infection, and mycobacterial infections.

The primary lesion was a linear epidermal nevus that a plaque has been grown on. Histopathologic examination revealed papillomatosis, hyperkeratosis, and parakeratosis (Figure 2A). The epidermis was acanthotic with accumulation of neutrophils and lymphocytes (Figure 2B). The number of capillaries were increased in papillary dermis, and perivascular infiltration of lymphocytes and neutrophils were notified. These findings were mostly compatible with psoriasis manifestations. Accordingly, topical mometasone 0.1% (Iran Najo, Iran) with the order of twice daily for 2 weeks followed by twice weekly for 2 weeks was initiated. Further investigations within one and 3 months later revealed dramatic response without relapse.

About 2 months later, patient informed us that some new skin lesions similar to the previous lesion, were appeared on her left upper arm. We also prescribed topical mometasone for the new lesions and complete remission was happened.

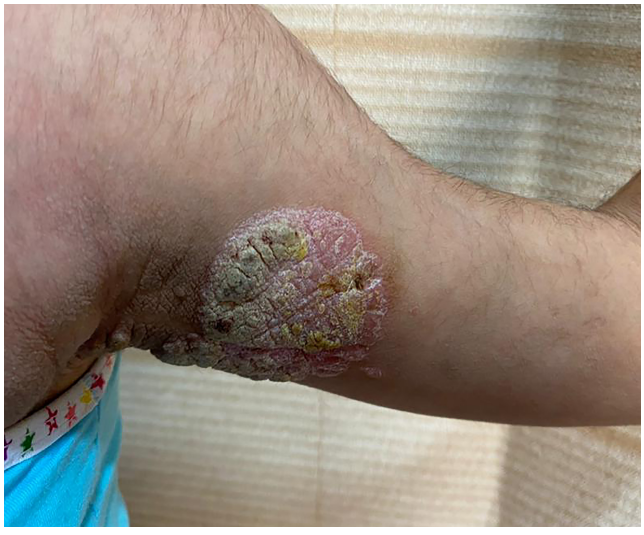

FIGURE 1 A demarcated well-defined erythematous and scaly hyperkeratotic plaque.

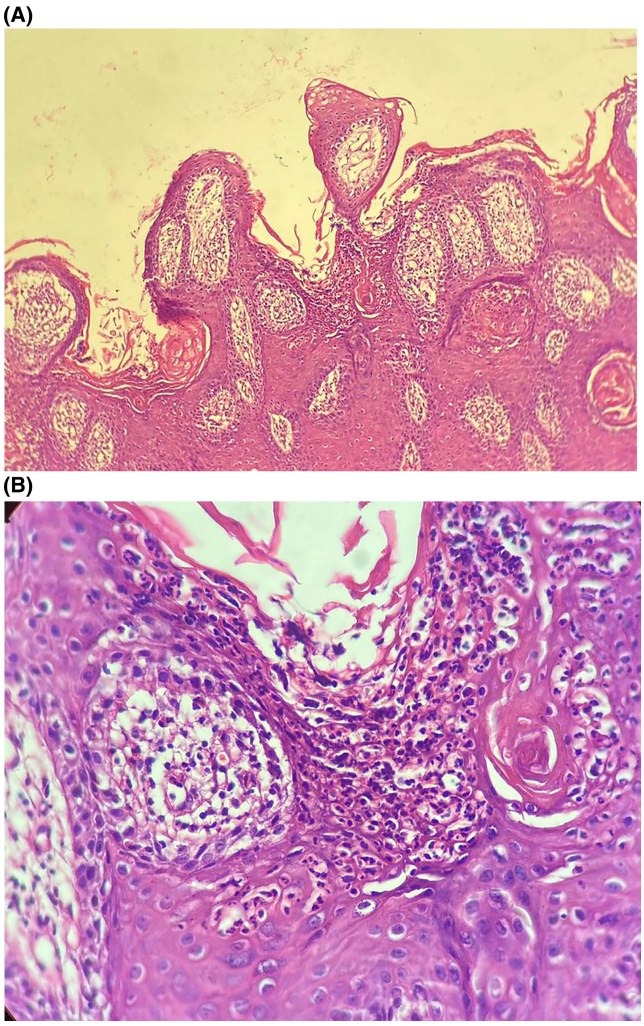

FIGURE 2 (A) papillomatosis, hyperkeratosis, and parakeratosis in histopathologic examination. (B) acanthotic epidermis with accumulation of neutrophils and lymphocytes.

3 | DISCUSSION

Although mutations in AKT1 have been identified as the probable etiology of PS, the exact cause of this uncommon syndrome remained uncommon yet. PS is a complex disorder particularly characterized with disproportionate gigantism of the limbs accompanying with other abnormalities such as lipomas, varicosities, and verrucous epidermal nevi.[6]

Although the most challenging part in the management of PS refers to the orthopedic abnormalities that might require multiple procedures, various cutaneous pathologies have been notified in PS and the patients with this syndrome may suffer severe cosmetic and functional consequences, even with aggressive treatments.[4]

The rarity of PS coupling with the remarkable cutaneous pleiotropy with over 100 different reported abnormalities have led to considerable misdiagnoses, leading to delayed

accurate understanding of skin lesions in this syndrome.[5] Given that, we described a known case of PS who presented a hyperkeratotic lesion on the upper extremity that is followed by the emergence of some other lesions, primarily diagnosed as leishmaniasis, but due to irresponsiveness to the treatment; biopsies were taken. The histopathological study of the biopsied tissue was compatible with psoriasis that well-managed with topical corticosteroids.

The cutaneous involvements in PS are generally categorized in two groups of non-progressive congenital or neonatal onset lesions including epidermal nevus and vascular malformations and postnatal ones that have progressive course, lipomas and cerebriform connective tissue nevi.[5]

The neonatal skin lesions in addition to the other mandatory general manifestations of PS helps early and correct diagnosis of this syndrome, while those late onset lesions such as cerebriform connective tissue nevi that has delayed onset can potentially lead to misdiagnosis.[7] However, in contrast to other studies that the correct diagnosis of PS syndrome in comparison with other disorders with similar manifestations such as Klippel-Trenaunay syndrome, epidermal nevus syndromes, Bannayan-Riley-Ruvalcaba syndrome, and hemihyperplasia multiple lipomatosis syndrome has been questioned,[5] in the current study a new hyperkeratotic psoriatic lesion formed on a PS-associated epidermal nevus led to misdiagnosis. Accordingly, we assume that the primary misdiagnosis has occurred due to the formation of the psoriatic lesion on a bed of a PS-related lesion, epidermal nevus. In confirmation, the histological study of the lesion revealed concurrent manifestations of an epidermal nevus such as papillomatosis plus the changes that were compatible with psoriasis.

Differences in the evolution of cutaneous lesions reflect differences in causation. Mosaicism is proposed as the underlying reason for PS incidence, where the early incidence of mutation in embryogenesis period results in two genetically different populations of cells that propagate throughout the body.[8] Cutaneous neoplasms should always be included in the differential diagnosis.[9] Mosaicism has been well-elucidated in type I lesions, epidermal nevi and vascular malformations not associated with PS, that are congenital and stable in regard to the involved area.[5] In contrast, group II lesions have inverse characteristics, including delayed onset and tendency to progress. The pathogenesis of late onset lesions requires further genetic or epigenetic events. It seems that additional somatic mutations are responsible for lipoma development in PS; as it has been seen in other sporadically lipomas. Another cutaneous lesion in PS, cerebriform connective tissue nevi requires other stimuli such as environmental, endocrine, or mechanical factors.[7]

Similarly, in addition to probable genetic etiology of psoriasis, other epigenetic factors including dysregulation of immunological cell function as well as keratinocyte proliferation/differentiation has substantial role in pathomechanism of psoriasis. T-helper 1 overactivation has been proposed as the trigger to psoriasis development. Besides, T-helper 17 has a key role in production of cytokines that induce keratocytes proliferation. Tumor necrosis factor alpha accelerates the infiltration of inflammatory cells from the peripheral blood into skin with dendritic cell activation. These processes in addition to genetic and environmental factors make a person prone to psoriatic lesions appearance.[10]

4 | CONCLUSION

We assume that the interactions between the genetic and epigenetic factors related to PS characterization as well as psoriasis led to the advent of a psoriatic lesion in a patient with PS. Therefore, it should be noted that other lesions than those common in PS may be notified in a patient with this disorder. Further evaluations should be considered to prevent misdiagnosis.

AUTHOR CONTRIBUTIONS

Fatemeh Mohaghegh: Conceptualization; project administration. **Marziehsadat Mousavi:** Investigation; writing – original draft.

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CONFLICT OF INTEREST STATEMENT

The authors declare that there is no conflict of interest.

DATA AVAILABILITY STATEMENT

The data is available upon request from corresponding author.

ETHICS STATEMENT

Written informed consent was obtained from the patient's mother for publication of this case report and any accompanying images.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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