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Case Report
A Rare Psoriasis Drug Eruption Induced by Levetiracetam: A Case Study from Saudi Arabia

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Abstract

Background and Objective: Drug-induced psoriasis, a rare adverse effect of certain medications, involves the onset or exacerbation of psoriatic symptoms triggered by pharmacological agents. The exact mechanisms underlying the development of psoriasis in response to these medications remain unclear, although hypotheses include drug-induced alterations in immune function and inflammatory pathways. **Materials and Methods:** A 40 years old Saudi female patient, with a history of bronchial asthma and newly diagnosed idiopathic epilepsy is under the treatment of levetiracetam 500 mg PO bid. The patient visited the dermatology clinic of the Armed Forces Hospital, Southern Region, Saudi Arabia, suffering from generalized body itching. Laboratory blood analysis and a hepatic investigation were performed. **Results:** The microscopic analysis showed focal parakeratosis with degenerated materials and neutrophilic aggregates, minimal epidermal hyperplasia, subtle exocytosis and basal vasculopathy. Also, mild perivascular lymphocytic infiltrates were noticed in the dermis layer. The presence of atypical features (basal vasculopathy and spongiosis) is a significant point towards possible drug-induced psoriasis. **Conclusion:** Psoriasis might be a comorbid symptom induced as a secondary side effect of the epilepsy drug's (levetiracetam) interaction with the immune system. Further investigations might be required to investigate the mechanism of levetiracetam-induced psoriasis.

Key words: Psoriasis, levetiracetam, epilepsy, drug inflammatory side effects, case report

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Psoriasis, a chronic autoimmune disorder characterized by the rapid proliferation of skin cells resulting in the formation of thick, red patches covered with silvery scales, has been extensively documented in medical literature[1,2]. Research exploring the potential association between psoriasis and epilepsy has garnered attention within the medical community. While individual studies have suggested a potential link, comprehensive investigations remain limited. For instance, a previous study proposed a positive association between psoriasis and epilepsy, citing shared inflammatory pathways as a possible mechanism[3].

Drug-induced psoriasis refers to the development or exacerbation of psoriatic symptoms triggered by certain medications. This phenomenon has been documented in medical literature, highlighting the importance of recognizing and managing this adverse drug reaction. Various medications, including but not limited to antihypertensives, antipsychotics and antiretrovirals, have been implicated in drug-induced psoriasis. For instance, lithium, a commonly used mood stabilizer, has been associated with psoriasis exacerbations in susceptible individuals[4].

Healthcare professionals need to be vigilant in monitoring patients for the onset or worsening of psoriatic symptoms following the initiation of potentially culprit medications.

Prompt recognition and withdrawal of the offending drug, in consultation with a dermatologist or relevant specialist, are crucial in managing drug-induced psoriasis and preventing further complications. Further research continues to contribute to our understanding of the mechanisms underlying drug-induced psoriasis and optimal management strategies.

The current research, reported a Saudi female case, who was treated with anti-seizure medication, levetiracetam, that induced a rare psoriasis drug eruption. To our knowledge, this is the first reported case of levetiracetam-induced psoriasis in Saudi Arabia.

Case presentation: A 40 years Saudi female was admitted to the hospital on October 15th, 2023, as postictal-epilepsy with a history of generalized tonic colonic convulsions for a minute. The patient had a past medical history of bronchial asthma. Her medical records reported previous attacks of loss of conciseness with prodromal symptoms aggravated by stress and reliving by sleep.

Table 1: Full blood analysis of the studied case

Variables	Results	Normal values
HbA1C	9.2%	<5.7%
Hemoglobin (Hb)	13 g/dL	12-16 g/dL
Platelet Count (PLT)	440×10^9/L	$150\text{-}400\times10^9$/L
Kidney function		
Serum Creatinine (Cr)	60 µmol/L	53-97.2 µmol/L
Creatine Kinase MB (CK-MB)	0.9 ng/mL	<4.4 ng/mL
Blood Urea Nitrogen (BUN)	3.34 mmol/L	2.1-8.5 mmol/L
Liver function		
Albumin (Alb)	37 g/dL	3.4-5.4 g/dL
Total Bilirubin (Tb)	7 µmol/L	0-17 µmol/L
Direct Bilirubin (Db)	21 mg/dL	0-7 µmol/L
Alanine Transaminase (ALT)	28 U/L	4-36 U/L
Aspartate Transaminase (AST)	20 U/L	10-36 U/L
Alkaline Phosphatase (ALP)	64 U/L	30-100 U/L
Gamma-Glutamyl Transpeptidase (GGT)	9 IU/L	0-30 IU/L
Prothrombin Time (PT)	14 sec	11-13 sec
Activated Partial Thromboplastin Time (APTT)	28 sec	21-35 sec
International Normalized Ratio (INR)	1.2	<1.1
Lactate Dehydrogenase (LDH)	200 U/L	140-280 U/L
Basic Metabolic Panel (Bmp)		
Sodium (Na)	137 mEq/L	135-145 mEq/L
Potassium (K)	3.4 mmol/L	3.6-5.2 mmol/L
Thyroid function test		
Thyroid Stimulating Hormone (TSH)	2.7 mIU/L	0.5-5 mIU/L
Thyroid Hormone (T4)	12 µg/dL	5.0-12 µg/dL

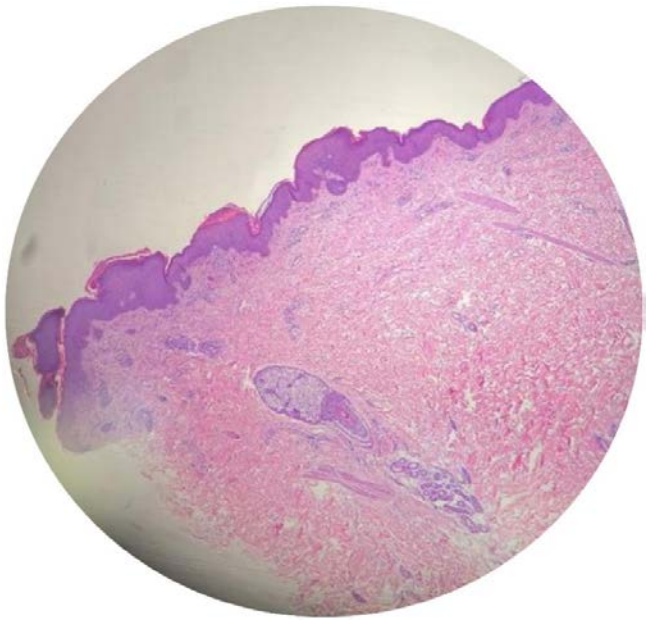

Fig. 1: Histopathological analysis of the skin biopsy of the studied case
A skin punch biopsy sized 6 mm was taken from the back, bisected and extended to the dermis. The slide was stained with Hematoxylin and Eosin (H&E) stains and visualized by Leica DM 2000 microscopy (Leica Microsystems-Danaher Corp., Washington, United States)

In the initial examination, the patient was alert and oriented with normal vital signs and her neurological examination was unremarkable. On admission, further laboratory tests were made to investigate any abnormal Complete Blood Count (CBC), liver functions, kidney functions or thyroid hormone levels. The results showed that the patient was diabetic with an HbA1C value of 9%. Abnormal liver function analysis was investigated with higher levels of serum albumin (Alb), direct bilirubin (Db) and increased Troponin I (TROP I) enzyme levels. Table 1 summarized the laboratory results.

Upon admission, the patient was started on levetiracetam 500 mg PO bid and vitamin B complex tab PO overdose. At that time, no more attacks of convulsions during her hospital stay were noticed. The Magnetic Resonance Imaging (MRI) was unremarkable. The Electroencephalogram (EEG) revealed a normal alpha rhythm background with intermittent generalized epileptiform discharges. The patient was discharged on October 17th, 2023, with a follow-up in the neurology clinic. On November 5th, 2023, the patient visited the dermatology clinic with a complaint of generalized body itching for 15 days. She suffered from a scattered generalized skin rash in the form of scaly erythematous patches involving the scalp, face, trunk and extremities. That might be due to a pityriasis rosea hat (PR)-like drug reactions, drug-induced psoriasis or psoriasis vulgaris.

Further histopathology analysis was performed to investigate any drug etiology. A 6 mm skin biopsy from the back was obtained. The microscopic analysis showed focal parakeratosis with degenerated materials and neutrophilic aggregates, minimal epidermal hyperplasia, subtle exocytosis and basal vasculopathy. Also, mild perivascular lymphocytic infiltrates were noticed in the dermis layer without any detection of fungal infection (Fig. 1). That indicated a drug-induced psoriasis.

DISCUSSION

While seizures themselves are not typically associated with psoriasis, medications used to manage seizure disorders have been implicated in drug-induced psoriasis. For instance, antiepileptic drugs (AEDs) such as phenytoin, carbamazepine and phenobarbital have been reported to induce or exacerbate psoriasis in susceptible individuals[5]. Levetiracetam is an antiepileptic medication that is widely used for the treatment of various types of seizures, including partial-onset seizures, myoclonic seizures and tonic-colonic seizures. It is considered a first-line treatment option for epilepsy due to its efficacy, tolerability and favorable side effect profile[6]. Levetiracetam is generally well-tolerated, with common side effects including dizziness, drowsiness and fatigue. It is available in various formulations, including tablets, extended-release tablets and oral solutions, allowing for flexible dosing regimens to suit individual patient needs[7].

Skin reactions are indeed recognized as potential side effects of AEDs, albeit they are not as common as other adverse reactions such as dizziness or drowsiness. These skin reactions can manifest in various forms, ranging from mild rashes to severe conditions like Stevens-Johnson syndrome or toxic epidermal necrolysis, although the latter are extremely rare[8]. The prevalence and severity of skin reactions associated with AEDs can vary depending on the specific medication, individual patient factors and the duration of treatment. Some AEDs have been more commonly implicated in skin reactions than others[9]. For instance, aromatic AEDs such as phenytoin, carbamazepine and phenobarbital are more frequently associated with cutaneous adverse effects, including hypersensitivity reactions and drug-induced skin eruptions[10]. Overall, while skin reactions are indeed recognized as potential side effects of AEDs, they are not as common as some other adverse effects. Nevertheless, healthcare providers should remain vigilant for signs of skin reactions and promptly address any concerns to ensure optimal patient care.

In the current case study, we reported a rare situation of levetiracetam-induced psoriasis. That was confirmed by the histopathological analysis of a skin biopsy of an epilepsy patient under the treatment of levetiracetam. The presence of atypical features (basal vasculopathy and spongiosis) are significant point toward possible drug-induced psoriasis.

There is limited evidence linking levetiracetam to the development or exacerbation of psoriasis or other skin diseases. In the case study conducted by Gencler *et al.*[11], they reported the case of psoriasiform drug eruption in a patient with newly diagnosed epilepsy who had been treated with levetiracetam. Other studies showed that levetiracetam induced maculopapular rash[12,13], morbilliform pruritic rash[14] and erythematous rash[15].

Overall, while the potential association between levetiracetam and psoriasis warrants consideration, it is important to weigh the risks and benefits of treatment on a case-by-case basis and to consult with healthcare professionals for personalized management strategies. Healthcare providers must be vigilant for signs of skin reactions in patients receiving AED therapy, especially during the initial stages of treatment or when medications are titrated upwards. Early recognition and appropriate management of these adverse reactions are essential to prevent complications and ensure patient safety. In cases of suspected drug-induced skin reactions, discontinuation of the offending medication and consultation with a dermatologist may be necessary.

CONCLUSION

Drug-induced psoriasis, though rare, can manifest as an adverse effect of certain medications, with unclear mechanisms speculated to involve alterations in immune function and inflammatory pathways. A case of a 40 years old Saudi female patient with bronchial asthma and newly diagnosed idiopathic epilepsy, treated with levetiracetam, presented with generalized body itching. Microscopic analysis revealed features consistent with possible drug-induced psoriasis, including focal parakeratosis, neutrophilic aggregates and basal vasculopathy. Considering the atypical presentation, it is suggested that psoriasis could be a comorbid symptom secondary to levetiracetam's interaction with the immune system. Further investigation into the mechanism of levetiracetam-induced psoriasis is warranted to guide clinical management and prevent potential complications. To our knowledge, that might be the first report of a rare side effect of levetiracetam in Saudi Arabia.

SIGNIFICANCE STATEMENT

Drug-induced psoriasis, a rare adverse effect of certain medications, involves the onset or exacerbation of psoriatic symptoms triggered by pharmacological agents, with unclear mechanisms possibly involving immune function and inflammatory pathways. The current report highlights a rare situation of psoriasis drug eruption induced by levetiracetam of a 40 years old Saudi female patient. This case highlights the need for further investigation into the mechanism of levetiracetam-induced psoriasis and the importance of recognizing and managing drug-induced adverse effects in clinical practice.

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