VILDAGLIPTIN INDUCED FIXED DRUG ERUPTION - A CASE STUDY

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ABSTRACT
Drug induced eruptions are reported to be the most common cause of cutaneous disorders encountered by the dermatologist. A Fixed drug eruption (FDE) is one among the cutaneous adverse reaction that is solely caused by the exogenous administration of drugs or chemicals and is usually characterized by recurrent site specific lesions whenever the offending drug is taken. In our study, FDE was first observed to appear on the patients left forearm after 7 weeks of initiation with stable dose of vildagliptin at 50mg/day and the site specific lesions healed gradually without the need of any pharmacological intervention upon its withdrawal. When causality assessment using Naranjo’s algorithm was made, vildagliptin was found as a probable causative agent in inducing FDE.

KEYWORDS: Cutaneous adverse reactions, Fixed drug eruptions, Vildagliptin.

INTRODUCTION
Drug induced eruptions are reported to be the most common cause of cutaneous disorders encountered by the dermatologist.[1] Several class of drugs have been identified to have a potential to induce cutaneous reaction. Among them antibiotics were reportedly the most commonly implicated drug, followed by anticonvulsants, non steroidal anti-inflammatory drugs (NSAIDs), and anti-gout agents.[2,3,4] A Fixed Drug Eruption (FDE) is a common type of cutaneous drug reaction with an unique cutaneous presentation in that the eruptions are usually characterized by the appearance of recurrent site specific lesions whenever the offending drug is taken.[5,6] Cotrimoxazole was identified to be the leading contributory agent...
for inducing FDE specifically on male genitals. Other drugs that were implicated to induce FDE include dipyrone that induced FDE on trunks and extremities, followed by naproxen and oxicam that induced FDE on lips.\cite{1,7,8,9} A FDE apart from these drugs are uncommon and even at times a significant relation between the drug and the clinical pattern couldn’t be made.\cite{7} Here, we present a case study wherein the patient received vildagliptin, a dipeptidyl peptidase-4 inhibitor for the treatment of his medical condition following which he developed FDE on his left forearm. Also, an assessment of whether withdrawing vildagliptin could contribute to reaction recovery was made.

**Case Study**

A 70- year- old male patient visited the outpatient department (OPD) of dermatology with the complaints of discolored lesions over his left forearm [Fig 1]. He was a known case of diabetes mellitus (type 2) since 15 years, hypertension since 10 years and had a history of cerebrovascular event 2 years back. He was receiving Tab Glimepiride/Metformin combination 3/850mg 1-0-1 since 15 years, Tab Voglibose 0.3mg 1-0-1 since 2 years, Tab Cilnidipine/Telmisartan 5/40mg 1-0-0 since 10 years, Tab Aspirin/Atorvastatin 75/10mg 1-0-0 since 2 years and Tab Vildagliptin 50mg 0-0-1 since 7 weeks. He did not have any other significant medical condition, and patient’s blood glucose level and blood pressure are under control. Previous history of allergy to the current medications was ruled out. Also, patient was not taking any over-the-counter medicines at the time of presentation. Based on the patient’s history, a diagnosis of drug induced fixed drug eruption was made suspecting Tab Vildagliptin as the offending agent. Based on the temporal time relationship with the reaction, the drug was withdrawn and the therapy was switched to Tab Dapagliflozin 10mg 1-0-0. After four days of stopping Tab Vildagliptin, the drug eruption on the patient’s left forearm gradually started to disappear, and he recovered from the suspected reaction.
DISCUSSION

Vildagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor is one among the several oral hypoglycaemic agents (OHA) that was approved in the recent years for the management of type 2 diabetes mellitus. Vildagliptin is considered to be similarly efficacious to sulfonylureas and pioglitazone in lowering HbA1c values. It is also thought to have the least adverse drug reaction profile than any of the older oral hypoglycaemics.\textsuperscript{[10,11]} A FDE induced by vildagliptin is not known and to the best of our knowledge there were no published studies that found an association between the vildagliptin and FDE.

In this case, FDE was first noted after 7 weeks of initiation with stable dose of vildagliptin at 50mg/day. And unlike Cotrimoxazole that induced FDE on male genitals, vildagliptin induced a site-specific lesion on forearm of the patient that appeared as a single huge lesion with a vertical diameter of roughly 7cm. However, the time of onset of reaction was fairly uncommon with other class of drugs that reportedly induced FDE within only days to few weeks (2 weeks) period from the initial drug exposure.\textsuperscript{[12,13]} But since the patient had developed FDE only after weeks of initiating vildagliptin, we suspected vildagliptin to be the offending drug to cause suspected reaction in this patient rather than Tab Voglibose and Tab Glimepiride/Metformin that he was receiving for the past 2 to 15 years, neither Tab Cilnidipine/Telmisartan nor Tab Aspirin/Atorvastatin that he was receiving for the past 10 years and 2 years respectively. Therefore, Tab vildagliptin was eventually stopped.

Fig 1: Figure showing a Fixed Drug Eruption on patient’s left forearm
Within 4 days of withdrawing vildagliptin, the drug eruption on the patient’s forearm started to gradually disappear. This period of healing of the lesion was in lieu with studies that observed healing to occur within 7 to 10 days after stopping the offending drug.\[12\] However, since there were limited/ no other studies available to compare the site specific reaction induced by vildagliptin, the specific number of lesions and the time required for its healing after withdrawing the vildagliptin may not be generated due to inter individual variability. However, in this case, the lesions started to heal gradually without the need of any pharmacological intervention as short as 4 days after its withdrawal. Reinitiating the suspected drug to establish vildagliptin as the offending agent to cause the FDE was discouraged due to ethical reasons, however, upon causality assessment using Naranjo’s algorithm, vildagliptin was found to be a ‘probable’ causative agent to induce FDE in this case.

**CONCLUSION**

Vildagliptin is having a potential to induce FDE on forearm which could appear within 7 weeks following its ingestion. However, the lesions formed usually recover within a week, once the offending drug is withdrawn. Therefore, although rare, an association of the reaction with the drug should be thought of as a probable cause prior to the initiation of therapy with vildagliptin.

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**BIBLIOGRAPHY**


