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Research Article

DERMATITIS MEDICAMENTOSA- A RARE CASE OF ADVERSE DRUG REACTION DUE TO SITAGLIPTIN

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A R T I C L E I N F O

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A B S T R A C T

Skin being the largest organ of the body accounts for two-three percent of all adverse drug reactions. Acute cutaneous drug induced reactions are caused by ingestion, inhalation or insertion of a drug and also due to allergic sensitization reactions to drugs applied to the cutaneous surface. We hereby report a case of *sitagliptin* (oral hypoglycemic drug) induced cutaneous adverse drug reaction in a 61 year old female who developed generalized hyper pigmentation worsening on exposed areas within two months of initiation of *sitagliptin*. The lesions started resolving on cessation of the drug. Dermatitis medicamentosa due to *sitagliptin* is very rare and first of such case is being reported in India at the time of diagnosis.

INTRODUCTION

It's indeed alarming to know the increasing diabetic population trend in India and simultaneously expanding various approaches of treatment from different health care workers existing in our society. The current diabetic age standardized death rate in India is 26.3 per 1,00,000 population.[1] *Sitagliptin* is the first selective antagonist of dipeptidylpeptidase-4 which improves the glycemic control in type 2 diabetes since FDA approved on 2006.[2] Acute cutaneous drug induced reactions are caused by ingestion, inhalation or insertion of a drug and also as a result of allergic sensitization reactions to drugs applied to the cutaneous surface. We are going to discuss a case of *sitagliptin* induced dermatitis medicamentosa or cutaneous adverse drug reaction which is very rare and first of such case is being reported in India at the time of diagnosis.

Case History

A 61 year old woman with primary level of education, home maker by occupation and a known case of type II diabetes mellitus since ten years came to our clinic with complaints of uncontrolled blood sugar levels, benign paroxysmal positional vertigo, dragging pain on both legs with burning and tingling sensation over the feet. On taking the detailed history, it was revealed that the patient was not compliant to bimodal treatment including allopathic (*sulfonylurea* and *metformin* 500mg twice daily) ayurvedic treatment for past five years. She was subjected to laboratory tests including complete blood count, glycemic profile, biochemistry profile which revealed hypochromic anemia, hyperglycemia, dyslipdemia, microalbuminuria and raised renal parameters [Table 1]. In view of her poor glycemic control she was started on with sulfonylurea (*glyclazide* XR 60mg twice daily) and with a combination dose of *sitagliptin* 50mg with *metformin* 500mg twice daily. She came for follow up after 15 days and complained of two episodes of low sugar for past few days. Physician then withheld *sulfonylurea* and continued her on combination dose of *sitagliptin* 50mg with *metformin* 500mg twice daily, dietary modification and self care management and advised her to come for follow up every month with blood sugar evaluation including fasting blood sugar (FBS) and post prandial blood sugar (PPBS) levels. She came for follow up after a period of three months with FBS- 161mg/dl and PPBS- 235mg/dl. Hence, Physician restarted her with mild dose of sulfonylurea (*glipizide* 2.5mg) twice daily and continued with combination dose of *sitagliptin* 50mg with *metformin* 500mg twice daily and further advised her to come for follow up every month. She returned again after a gap of four months with generalized hyper pigmentation of upper limbs, face and neck (mainly exposed areas) which she noticed lately progressing for past four months and neglected by not reporting to the physician early [Figure 1,2]. As per patient's words, she initially started noticing hyperpigmentation after two months of initiation of

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sitagliptin. There was no history of any other drug intake prior to the hyperpigmentation in the past.

Table 1 Investigation trends of the subject during the course of treatment

Test Name	Before starting Sitagliptine (10/12/13)	Continuing Sitagliptine 12/7/14	After stopping sitagliptine 28/01/15	Reference Range
Hemoglobin	10.0mg/dl	12.0mg/dl	12.0mg/dl	11.5 – 16.5
Blood sugar				
Fasting	261mg/dl	135mg/dl	118mg/dl	70-110
Post Prandial	293mg/dl	178mg/dl	160mg/dl	70-140
HBA1C	8.2%	6.6%	7.5%	4-6%
Lipid profile				
T.Cholesterol	324mg/dl	223mg/dl	181mg/dl	140-200mg/dl
TGL	197mg/dl	105mg/dl	159mg/dl	45-165mg/dl
HDL	40mg/dl	40mg/dl	34mg/dl	45-65mg/dl
LDL	245mg/dl	163mg/dl	108mg/dl	70-130mg/dl
VLDL	39mg/dl	20mg/dl	39mg/dl	10-40mg/dl
Urine Biochemistry Microalbumin Spot	214.1ug/mg of creatinine	340.0ug/mg of creatinine	123.8 ug/mg of creatinine	<20 ug/mg of creatinine
Blood Biochemistry				
Amyalse	67.0 U/L	83.1 U/L	78.1U/L	28-100U/L
Lipase	87.2 U/L	69.0 U/L	67.0 U/L	13-60 U/L
Urea	38mg/dl	30mg/dl	42mg/dl	10-40
Creatinine	1.3mg/dl	1.2mg/dl	1.0mg/dl	0.4-1.3

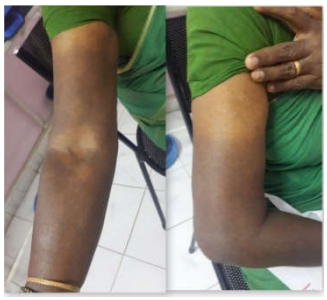

Figure 1 Picture showing hyperpigmentation of right arm during the course of Sitagliptin.

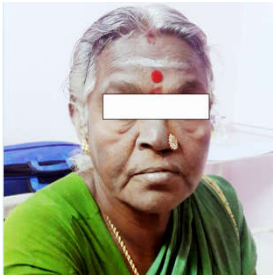

Figure 2 Picture showing hyperpigmentation of face during the course of Sitagliptin.

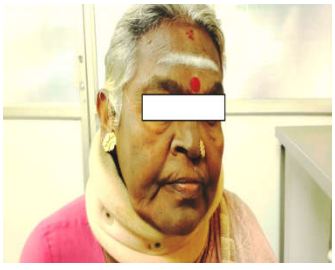

Figure 3 Picture showing the face post cessation of Sitagliptin.

She was referred to a dermatologist for expert opinion, he opined and diagnosed as fixed drug eruption at this juncture and he suggested it could be due to SULPHA group of antibiotics and NSAID group of drugs. She returned back to our clinic after a gap of two weeks, and for safety precaution we stopped her on DPP-4 inhibitor (*sitagliptin*) and continued her on mild dose of *sulfonylurea* and *metformin* twice daily, advised her to continue the topical medications as advised by dermatologist and further advised her to come for follow every month. She came back for follow up after a gap of six months and on examination revealed hyper pigmentation has remarkably reduced on both upper limbs and face [Figure 3]. As of now, the patient is having good glycemic control with alpha glucosidase inhibitor (*voglibose* 0.2mg) and *metformin* 500mg thrice daily with no further recurrence of such symptoms.

DISCUSSION

Sitagliptin is a modern drug developed for the management of type II diabetes mellitus approved by the US Food and Drug Administration in 2006 or the European Medicines Agency. Sitagliptin which is a DPP-4 dipeptidyl-peptidase inhibitor effective in lowering HBA1c, fasting as well as postprandial glucose whose action is mediated by increasing the levels of Incretin hormones Glucagon-like-peptide-1 (GLP-1) and Gastric inhibitory polypeptide (GIP).[3] *Sitagliptin* with *metformin* tablets in fixed-dose combinations is used for the treatment of type 2 diabetes when: HBA1C is > 7%, despite use of *metformin*, and when a combination of *metformin* and a *sulfonylurea* is contraindicated or not tolerated.[4] Twenty six serious skin reactions including two cases of Stevens-Johnson syndrome and two cases of toxic epidermal necrolysis, fifteen anaphylaxis, four angioedema, and three cutaneous vasculitis were confirmed.[5] Nakai *et al* had reported a case of a maculopapular eruption caused by *sitagliptin phosphate hydrate* in a 63 year old women.[6] Yet another study done by Nakatani *et al* reported generalized skin eruption with strong itching which was induced by *sitagliptin* in a patient almost six months after initiation of the drug.[7] Very few studies have reported fixed drug eruption due to *sitagliptin*. A study done by Gupta *et al* revealed *sitagliptin* induced fixed drug eruption in a 46 year old female who developed circumscribed, erythematous macules all over the body within one week of initiation of drug was the only Indian study found in the literature.[8] *Sitagliptin* improves serum triglycerides and high density lipoprotein levels in patients with type 2 diabetes mellitus.[9] In our case the diagnosis was made from medical history and clinical course. Generalized hyperpigmentation due to *sitagliptin* in our case was first of its kind in the literature and indeed there was good

improvement in lipid profiles during the course of treatment with this drug.

CONCLUSION

In this present case generalized hyperpigmentation would have been induced by cutaneous adverse drug reaction to *sitagliptin*. Diabetologist and physicians need to be cautious while introducing this drug in managing diabetic patients as various adverse drug events due to this drug have been reported in recent times.

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