

# Sitagliptin induced Stevens Johnson Syndrome in an Elderly Diabetic Patient

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**Abstract:** *Sitagliptin is being used as a monotherapy or combination therapy for management of type 2 diabetes mellitus. Very few cutaneous adverse events have been reported with the suspect drug and rarer is the occurrence of Steven Johnsons syndrome.*

**Keywords:** Sitagliptin, Stevens Johnson Syndrome, Diabetic patient

## 1. Introduction

Sitagliptin is a Dipeptidyl Peptidase - 4 inhibitor approved as a monotherapy or combination therapy for patients with type - 2 Diabetes Mellitus. It has shown to improve glycemic control in patients with type - 2 Diabetes which has been demonstrated various clinical trials. It has also shown to significantly decrease glycosylated hemoglobin (HbA1c) levels in monotherapy or in combination with metformin. Moreover, the major benefit of sitagliptin is that it has low chances of hypoglycemia and has shown to improve glycemic control. In a study conducted in Japan in 2020 to ascertain the adverse drug reactions (ADR) of sitagliptin, there were adverse reactions associated in 6.3% of the patients, thus exhibiting a good safety profile. The most common ADRs observed were metabolic disorders, followed by gastrointestinal disorders and hypoglycemia and no adverse event of severe skin problems was observed. Another study reported serious hypersensitivity reactions including Steven Johnson Syndrome with sitagliptin, although causality could not be definitely concluded. Steven Johnson Syndrome is manifested by skin and mucosal eruptions and is usually caused by antibacterial such as sulfonamides, anticonvulsants and non - steroidal inflammatory drugs. It is a serious condition and can also be fatal in severe cases. The dose of sitagliptin has been shown to range between 12.5 mg to 100 mg according to various clinical studies and the most common being 50 mg given once a day. In monkey model there were observed skin

related adverse effects, which were necrotic skin lesions. Hence, cutaneous adverse drug reactions associated with sitagliptin need to be studied more. Therefore, the case is worth reporting.

## 2. Case Report

This case involves an 88 years old patient with history of hypertension, Diabetes Mellitus type - 2 and syncopal attacks underwent stent for blockage of Right Coronary Artery on 18<sup>th</sup> March 2021. He was taking Metformin 1000 mg in the morning and 750 mg at night. However, during his stay in hospital, he was put on Sitagliptin 50 mg once a day. He started developing swelling of legs, feet with excoriation of skin. For this he was consulted skin specialist who prescribed him Clobetasol ointment and coconut oil. There was not much relief even after taking treatment for more than 2 weeks. Thereafter, another opinion was taken from skin specialist, who told that this is Stevens Johnson Syndrome. The patient was also started on oral corticosteroids and antihistamines. The skin lesions were extensive and present on arms, feet, hands as well as face. Accordingly, sitagliptin was immediately stopped and patient was put on metformin 500 mg BD, following which the patient recovered in a few days. The Naranjo's score was 5 (probable) and the World health Organization (WHO) - Uppsala monitoring Centre (UMC) causality assessment showed probable correlation with the current adverse event.



Photographs by Riya Y Mittal

### 3. Discussion

Sitagliptin is effective and well tolerated in patients with type 2 diabetes which is inadequately controlled with metformin monotherapy.<sup>8</sup>The adverse effect profile in drug - treated and placebo - treated patients has been similar. DPP - 4 is expressed on lymphocytes. There is some evidence of minor effects on in vitro lymphocyte function with DPP - 4 inhibitors. However, there has been no evidence from clinical studies of major adverse effects in humans.<sup>9</sup>Apart from systemic adverse effects like hypoglycemia, gastrointestinal effects, pancreatitis, respiratory side effects like nasopharyngitis and upper respiratory tract infections, sitagliptin has been known to cause a wide array of cutaneous adverse effects which include psoriasiform eruption, maculopapular rash, Stevens Johnson syndrome, toxic epidermal necrolysis, anaphylaxis, cutaneous vasculitis, bullous pemphigoid, photosensitivity and angioedema.<sup>10</sup> Sitagliptin has shown to cause approximately 4062 skin and subcutaneous tissue disorder, out of which 65 have been shown to be Stevens Johnsons Syndrome.<sup>11</sup>The patient was given 50 mg of Sitagliptin by the physician for type 2 diabetes mellitus following which he developed Stevens Johnson Syndrome. Although oral corticosteroids and anti - histamines were administered to the patient, treatment discontinuation formed the backbone of the treatment.<sup>10</sup>

### 4. Conclusion

Sitagliptin is being used as a monotherapy or combination therapy for management of type 2 diabetes mellitus. Very few cutaneous adverse events have been reported with the suspect drug and rarer is the occurrence of Steven Johnsons syndrome.

#### Financial Support and Sponsorship

Nil

#### Conflict of Interest

There is no conflict of interest.

#### Consent

Written informed consent was obtained from the patient for publication of this Case report.

### References

- [1] Plosker GL. Sitagliptin: a review of its use in patients with type 2 diabetes mellitus. *Drugs*.2014 Feb; 74 (2): 223 - 42.
- [2] Dhillon S. Sitagliptin. *Drugs*.2010 Mar; 70 (4): 489 - 512.
- [3] Yoshikawa K, Tsuchiya A, Kido T, Ota T, Ikeda K, Iwakura M et. al. Long - Term Safety and Efficacy of Sitagliptin for Type 2 Diabetes Mellitus in Japan: Results of a Multicentre, Open - Label, Observational Post - Marketing Surveillance Study. *Advances in therapy*.2020 May; 37 (5): 2442 - 59.
- [4] Williams - Herman D, Round E, Swern AS, Musser B, Davies MJ, Stein PP, Kaufman KD, Amatruda JM. Safety and tolerability of sitagliptin in patients with type 2 diabetes: a pooled analysis. *BMC Endocrine Disorders*.2008 Dec; 8 (1): 1 - 6.
- [5] Rajput R, Sagari S, Durgavanshi A, Kanwar A. Paracetamol induced Steven - Johnson syndrome: A rare case report. *Contemporary clinical dentistry*.2015 Sep; 6 (Suppl 1): S278.
- [6] Fukuda M, Doi K, Sugawara M, Mochizuki K. Efficacy and safety of sitagliptin in elderly patients with type 2 diabetes mellitus: a focus on hypoglycemia. *Journal of diabetes investigation*.2019 Mar; 10 (2): 383 - 91.
- [7] Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA et al. . A method for estimating the probability of adverse drug reactions. *Clin PharmacolTher* 1981; 30: 239 - 45.
- [8] Scott R, Loeys T, Davies MJ, Engel SS, Sitagliptin Study 801 Group. Efficacy and safety of sitagliptin when added to ongoing metformin therapy in patients with type 2 diabetes. *Diabetes, Obesity and metabolism*.2008 Oct; 10 (10): 959 - 69.
- [9] Brunton L. Laurence, Chabner B and Knollman B. *The Pharmacological Basis of Therapeutics*. Alvin C. Powers and David D'Alessio. *Endocrine Pancreas and Pharmacotherapy of Diabetes Mellitus and Hypoglycemia*. Mcgraw hills.2011 Ch43. Pg 1237 - 73.
- [10] Gupta M, Gupta A. Fixed drug eruption to sitagliptin. *Journal of Diabetes & Metabolic Disorders*.2015 Dec; 14 (1): 1 - 3.
- [11] Uppsala Monitoring Centre (UMC). WHO Collaborating Centre for International Drug Monitoring based. Available at [www.vigiaccess.org](http://www.vigiaccess.org) [Seen on 24/07/21]