OBSERVATIONS

Sitagliptin-Associated Angioedema

Postmarketing reports indicate that use of the dipeptidyl peptidase-IV (DPP-IV) inhibitor sitagliptin can be associated with the development of serious hypersensitivity reactions including angioedema (1). The clinical characteristics of individuals who are prone to develop DPP-IV inhibitor–associated angioedema are not completely understood. Here, we report a case of sitagliptin-associated angioedema and suggest a potential role of angiotensin II receptor blocker (ARB) losartan in the development of the sitagliptin side effect.

A 46-year-old African American female with a past medical history of uncomplicated hypertension treated with losartan 100-mg daily, obesity, and compensated vitamin D deficiency was referred to the endocrinology clinic by her internist for management of Riedel's thyroiditis. Physical examination was significant for BMI of 35 kg/m^2 and blood pressure of 125/78 mmHg. Thyroid function and glucose level were normal; prednisone 30 mg was begun for management of her thyroiditis. Three weeks later, the patient presented to the emergency room with polyuria and polydipsia and was found to have blood glucose of 350 mg/dL. The patient's internist subsequently started diabetes therapy and prescribed diet, exercise, and drug therapy consisting of sitagliptin/metformin 50/500-mg twice daily. Approximately 1 week after starting this combination, the patient developed pruritis centered along the left flank. This was followed by the appearance of hypopigmented, oval-shaped plaques first in the area of her pruritis, which soon spread to involve her abdomen, trunk, chest, and thighs, consistent with morbilliform rash. Her reaction then further progressed to parasthesias and edema of both the upper and lower lip. At this point she self-discontinued the sitagliptin/metformin but continued losartan. During the follow-up, we started metformin monotherapy, continued losartan, and initiated prednisone taper. Patient remains asymptomatic following these modifications.

This report describes patient characteristics and evolution of angioedema after initiation of sitagliptin. In addition to the degradation of glucagon-like peptide 1, DPP-IV can inactivate substance P (2) and bradykinin (3); both substances are known to produce angioedema. In a meta-analysis of phase III studies, a coadministration of angiotensin-converting enzyme (ACE) inhibitors with a DPP-IV inhibitor vildagliptin at the dose 100-mg daily emerged as a significant risk factor for the development of vildagliptin-induced angioedema (4). However, the incidence of angioedema was not different when 50-mg vildagliptin dose was used with ACE inhibitors versus comparator medications (4).

ARBs may increase bradykinin levels similar to ACE inhibitors (5). We speculate that in our patient the initiation of the DPP-IV inhibitor sitagliptin in the background of the concurrent administration of ARB losartan may have resulted in angioedema. Permanent discontinuation of sitagliptin has led to the resolution of angioedema. Recently, authors described angioedema that developed 14 days after sitagliptin initiation in a woman who was taking multiple other medications including the ARB irbesartan (3). Although the possibility of idiosyncratic reaction to sitagliptin in our patient cannot be ruled out, this and other reports (3,4) should raise awareness about potentially serious side effects of the combination of DPP-IV inhibitors and ACE inhibitors or ARB in patients with type 2 diabetes.

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