Regression of Acanthosis Nigricans with the Addition of Sitagliptin and Pioglitazone

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ABSTRACT

Acanthosis nigricans (AN) is a cutaneous disorder associated with various diseases. There are few documented cases of regression of AN. We discuss a case of a 48-year old diabetic woman with resolution of AN after treatment with sitagliptin and pioglitazone.

Keywords: Acanthosis nigricans, DPP-4 inhibitor, thiazolidinedione

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RESUMEN

La acantosis nigricans (AN) es un trastorno cutáneo asociado con varias enfermedades. Hay pocos casos documentados de regresión de la AN. Discutimos el caso de una mujer diabética de 48 años con resolución del después del tratamiento con sitagliptina y pioglitazona.

Palabras claves: Acantosis nigricans, inhibidor de la DPP-4, tiazolidinediona

INTRODUCTION

Acanthosis nigricans (AN) is a cutaneous disorder characterized by hyperpigmentation and velvet-textured skin. There is an association between AN and various insulin-resistant states. There are few documented cases of regression of AN. We report the case of a 48-year old woman with AN that spontaneously resolved after the addition of sitagliptin, a DPP-4 inhibitor, and pioglitazone. These agents function to increase insulin secretion and sensitivity, respectively.

CASE REPORT

A 48-year old African-Bahamian woman presented with polyuria and polydipsia. She was diagnosed with diabetes mellitus and commenced on insulin. Ten months after diagnosis, she began to experience darkening of the skin and associated weight loss. She had amenorrhoea for approximately one year. Her medical history was positive for hypertension and there was a strong family history of diabetes mellitus. On examination, the patient was slim, body mass index (BMI) 21.5 kg/m², with acanthosis nigricans (AN) of the neck and a thyroid 1.5 times the normal size; the remainder of the examination was unremarkable.

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She was taking insulin lispro, pre-meals and insulin glargine, at bedtime. Despite high doses of insulin, glucose levels remained markedly elevated as evidenced by a glycated haemoglobin (HbA_{1c}) of 138 mmol/mol. Investigations revealed normal renal, liver, lipid, thyroid profiles and thyroid peroxidase antibody levels.

Excessive insulin requirements illustrated a state of insulin resistance. Therefore, sitagliptin and pioglitazone were added to increase insulin secretion and sensitivity. Twenty-four months after commencing combination therapy with oral agents and insulin, the patient had weight gain and, remarkably, began having improvement in her AN.

Home self-monitoring of serum glucose showed steadily decreased glucose levels, therefore, the patient significantly reduced insulin lispro doses and discontinued insulin detemir on her own. Also, she experienced a severe hypoglycaemic episode which required relatives to seek emergency care at a local hospital. Insulin was completely discontinued while continuing oral agents. Upon follow-up, the patient remained euglycaemic on sitagliptin and pioglitazone (HbA_{1c} 36 mmol/mol), had her first menses in two years, BMI increased to 26 kg/m², and notably, complete resolution of her AN was observed.

DISCUSSION

In 1976, Kahn *et al* made the association between AN and insulin-resistant states (1). Diabetes mellitus, obesity and Type

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A and B insulin resistance syndromes are examples of insulin-resistance states. The postulated mechanism for the pathogenesis of AN relates to hyperinsulinaemia that results from tissue resistance to insulin. High levels of insulin cause binding to insulin-like growth factor receptors which stimulate keratinocytes and dermal fibroblasts (2).

Fareau *et al* reported regression of AN with the use of a potent cytotoxic agent (3). Here, we presented the unique case of a middle-aged woman who had disappearance of AN after addition of sitagliptin and pioglitazone. To the best of our knowledge, there are no known documented cases of this phenomenon occurring.

Sitagliptin, a DPP-4 inhibitor, increases incretin levels which function to enhance synthesis and release of insulin from pancreatic β cells, and pioglitazone, a thiazolidinedione, is a selective ligand of peroxisome-proliferator-activated receptor γ which enhances insulin sensitivity in peripheral tissues.

The disappearance of AN after several months of sitagliptin and pioglitazone suggests improvement in insulin sensitivity and hyperinsulinaemia. Thus, these classes of oral agents may have a role in the reversal of this cutaneous disorder; the effectiveness of one drug over the other is uncertain.

AUTHORS' NOTE

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