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Abstract

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Introduction

Pasireotide (Signifor®) is a new-generation, multi-receptor targeted somatostatin analogue approved for treatment of Cushing’s disease or acromegaly. It is indicated for patients who are non-surgical candidates or those inadequately treated with surgery [1,2]. Pasireotide decreases growth hormone (GH) secretion by binding to somatostatin receptor subtypes expressed by somatotroph tumors [3]. In a phase 3 study Colao et al. [4] evaluated 358 patients with medically naive acromegaly. One year of monthly injections were compared between pasireotide LAR vs. Octreotide LAR. Results favored pasireotide LAR with normalized IGF-1 levels (38.6% vs 23.6%) and attained GH <2.5 µg/L (48.3% vs 51.6%). Although most adverse events with pasireotide in this trial were similar to those experienced with other somatostatin receptor ligands (SRLs), the incidence of hyperglycemia-related adverse events was greater in those treated with pasireotide LAR (57.3% vs 21.7%) [5]. As a novel therapeutic agent for acromegaly, pasireotide’s potential for adverse events should be considered.

Case Presentation

A 38 year-old man with acromegaly underwent endoscopic transphenoidal hypophysectomy in February 2016. A two-month postoperative IGF-1 level remained elevated at 690 ng/ml (baseline 280 ng/ml). He was started on adjuvant therapy with pasireotide LAR 40 units IM every 4 weeks. After three doses, the patient presented with symptoms of nausea, polyuria, polydipsia, weakness, vomiting, and syncope. He also had an abrupt 20-pound weight loss. He was treated for DKA, and transitioned to Lantus for glucose control. Results favored pasireotide LAR with normalized FPG<100 mg/dL showed improvement in FPG if anti-diabetic medications were initiated within 2 weeks of the first dose of pasireotide LAR [3,10].

Discussion

Pasireotide has been associated more with hyperglycemia than any other SRLs in patients with acromegaly or Cushing’s disease [3-6]. The hyperglycemia is attributed to reducing insulin secretion and incretin response. On the other hand, glucagon secretion and insulin sensitivity appear to be minimally affected [7,8]. A phase 3 core study by Sheppard et al. [9] found that more patients with normal fasting plasma glucose (FPG)<100 mg/dL at baseline developed hyperglycemia at their final assessment on pasireotide compared with octreotide (69% vs 39%) [9]. Treatment options have been proposed. A phase 1 study by Breitschaft et al. [8] co-administered pasireotide along with an anti-hyperglycemic to healthy volunteers. GLP-1 agonists and DPP-4 inhibitors were most effective lowering plasma glucose AUC post-OGTT and attenuating decreases in serum insulin [8]. Furthermore, Gadelha et al. [10] found that patients with acromegaly and FPG>250 mg/dl showed improvement in FPG if anti-diabetic medications were initiated within 2 weeks of the first dose of pasireotide LAR [3,10].

Conclusion

Our case highlights the need for additional studies to better assess the long-term effects of pasireotide on glucose metabolism. Early initiation of anti-diabetic medications and close glucose monitoring will help improve glycemic control in acromegalic patients treated with pasireotide LAR.

References

