INTRODUCTION

The patient is a 56-year-old Caucasian woman with a medical history of Type II diabetes mellitus, hypertension, hyperlipidemia, and chronic kidney disease.

CASE PRESENTATION

Patient presented to primary care physician to establish care. Her home diabetes regimen included metformin 500mg BID and glimepiride 2mg BID, but she had run out of medication for the past four months. HgbA1C was 14%. She was restarted on metformin 500mg BID and glimepiride 2mg BID.

Patient declined initiating insulin therapy. Two months later, she started semaglutide 0.25 mg once weekly in addition to her metformin (switched to XR formulation) and glimepiride.

Seven months later, the A1C resulted at 5.7%. She reported hypoglycemic symptoms and morning home blood glucose checks occasionally in the 30s-40s. Glimepiride was discontinued.

Three months later, patient saw ophthalmology. She was diagnosed with severe non-proliferative diabetic retinopathy with bilaterally macular edema, as well as hypertensive retinopathy. Per ophthalmologist, rapid change in A1c values could have precipitated edema. Patient was started on bevacizumab eye injections.

Two weeks later patient received second eye injection. She voiced that her vision was significantly improved, and that the ophthalmologist did not have to do any more injections.

DISCUSSION

- Optic complications are a rare but serious effect seen with GLP-1 agonists.
- While early worsening of diabetic retinopathy has traditionally been associated with insulin, more evidence is showing that GLP-1 agonists also have early worsening of retinopathy.2
- Some hypotheses for the pathophysiology of early worsening diabetic retinopathy include:2
  - Osmotic force theory – changes in glucose changes osmotic pressures and water retention.
  - Synergistic hypothesis – there is a synergistic effect of insulin and VEGF on retinal vessels, causing proliferation and resulting retinopathy.
  - Blood-retinal barrier - breakdown of blood-brain barrier after insulin therapy.
  - VEGF hypothesis – VEGF may be upregulated when there is tight glycemic control in a hypoxic setting.
- This deterioration has been reported to occur anywhere from three months to three years after starting medication.4
- The Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes (LEADER) trial showed the retinopathy event incidence in the liraglutide group was non-significantly higher than placebo (0.6 vs. 0.5 events per 100 patient-years; HR, 1.15; P = 0.33).2
- However, the SUSTAIN-6 trial showed diabetic retinopathy complications were present in 3.0% of the semaglutide group compared to 1.8% of the placebo group (hazard ratio, 1.76; 95% CI, 1.11 to 2.78; P=0.02). A majority of those patients with retinopathologic complications had pre-existing retinopathy at baseline (42 of 50 in the semaglutide group and 24 of 29 in the placebo group).2
- Post-hoc analyses of the SUSTAIN trial by Vilsbøll et al. (2018) suggest that diabetic retinopathy complications were greatest in pre-existing retinopathy patients with HgbA1C reductions of > 1.5%, and those patients without baseline retinopathy had lower incidence of diabetic retinopathy complications. Additionally, the effect was most prominent during the first 15 weeks of the trial.2
- To our knowledge, this case is unique in that the over-correction of glycemia, as seen in reduction of HgbA1C over time, resulted in an increase in macular edema/non-proliferative diabetic retinopathy.
- Future studies should continue to examine the rate of reduction of HgbA1C and non-proliferative diabetic retinopathy.

REFERENCES