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Case Report

Proptosis secondary to rosiglitazone treatment

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Abstract
Objective: To report a case of new onset proptosis secondary to treatment with rosiglitazone. **Methods:** Case report **Results:** A patient developed symptomatic bilateral proptosis requiring surgical intervention, two years and a half after treatment with rosiglitazone. **Conclusion:** Asymptomatic eye protrussion is a frequent finding in patients treated with thiazolidinediones. In a few cases, the proptosis may be clinically significant and may present in patients with or without a previous history of thyroid disease.

Key Words: *proptosis, rosiglitazone, thiazolidinediones, ocular complication*

Introduction

Rosiglitazone and pioglitazone are two thiazolidinediones (TZDs) used to treat type 2 diabetes mellitus. TZDs act by sensitizing tissues to insulin action through binding to the peroxisome proliferator-activated receptor-gamma (PPARγ). This nuclear receptor is predominantly found in adipose tissues and has a key role in adipocyte differentiation, associated with well-described weight gain by the generalized increase in subcutaneous fat volume.[1] Proptosis in Type I thyroid orbitopathy has been found to correlate well with expansion of the orbital fat compartment, secondary to enhanced orbital adipogenesis.[2,3] Presentation of proptosis after thiazolidinedione use in type 2 diabetes patients associated with or without thyroid disease has been reported recently.[4-7] We report a case of proptosis with rosiglitazone use not associated with thyroid disease.

Case Report

A 67-year-old African-American male who was concerned about persistent and progressive edema of the upper and lower eyelids of both eyes for two and a half years presented to our office for consultation. The patient did not report symptoms of diplopia, ocular pain, or visual acuity changes. His general medical history included systemic hypertension and type 2 diabetes mellitus over the last 20 years. Hypertension was treated with amlodipine/benazepril. Diabetes was controlled with metformin hydrochloride and glipizide. Two and a half years prior to presentation, his internist added rosiglitazone to improve glycemic control. He denied any history of thyroid disease and cigarette smoking.

On clinical examination his visual acuity without correction was 20/20 in both eyes. Color vision and pupillary reaction were within normal ranges. We noted marked edema in the periocular region bilaterally (Figure 1) and proptosis with Hertel measurements of 23mm on the right and 25mm on the left. There was resistance to retropulsion in both eyes, and this was more pronounced on the left side. Subtle retraction of the left upper eyelid and mild lid lag on down-gaze were also documented. He presented with mild deficit in supraduction of the left eye and abduction of both eyes. Intraocular pressure of both eyes was within normal ranges. There were no signs of conjunctival inflammation or exposure keratopathy. Fundoscopy examination revealed a normal optic nerve.

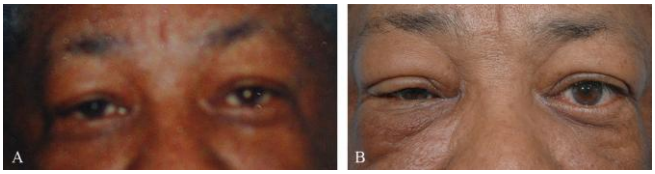

Figure 1: (A) Picture of patient 2 years prior to rosiglitazone treatment. (B) Picture of the patient with palpebral edema and proptosis at time of evaluation.

A complete thyroid panel and orbital CT scans were obtained. Thyroid hormone levels and TSH receptor antibodies were within normal ranges. Orbital CT scans demonstrated bilateral proptosis and an increase in the fat volume within the orbit but no enlargement of the extra-ocular muscles (Figure 2).

The patient's internist was contacted regarding these findings and discontinuation of rosiglitazone was recommended. The patient is scheduled for orbital decompression.

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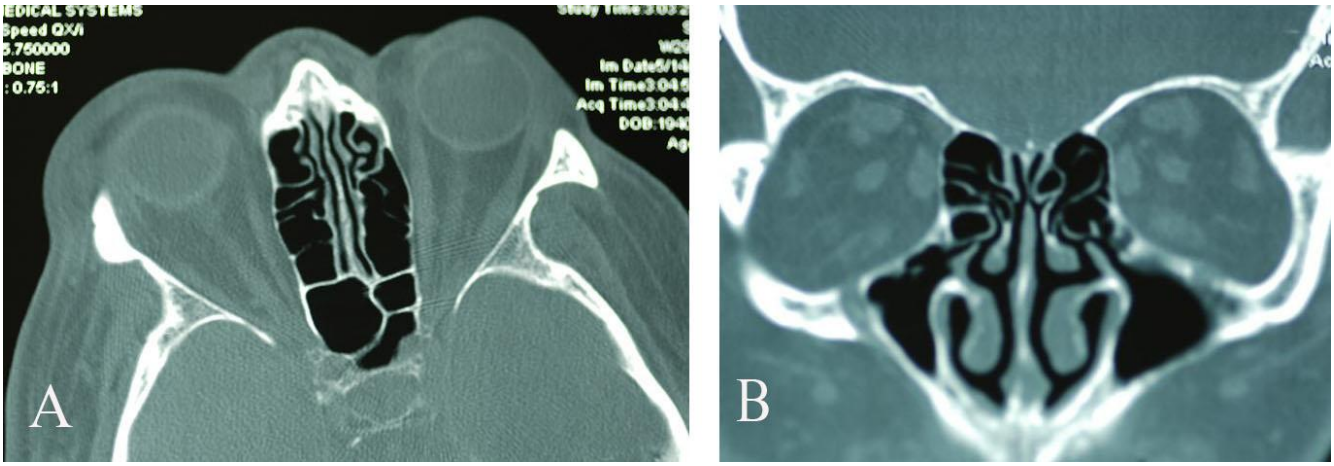

Figure 2: (A) Axial projection of CT scan of the patient showing bilateral proptosis, more pronounced on the left side. No evidence of extra-ocular muscles enlargement. (B) Coronal projection of CT scan demonstrating increase in orbital fat volume, but with normal size extra-ocular muscles

Comment

Over the last four years, proptosis as a complication secondary to thiazolidinedione treatment in type 2 diabetes patients associated with or without thyroid disease has been well described. [4-7] Although not a frequent presentation, physicians who utilize thiazolidinedine to treat diabetic patients have to be aware of this complication and ophthalmologists who manage proptosis cases of sudden onset have to keep this entity in mind as a differential diagnosis.

There are several mechanisms by which adipogenesis may increase proptosis. First of all, there is the mechanical effect by which a larger amount of adipose tissue will increase proptosis. Other mechanisms may include an up-regulation of TSH receptor antibodies (which is not in this case) and increase of pro-inflammatory adipokines. Starkey et al showed that by blocking the PPAR gamma receptor they could ameliorate thyroid eye disease by reducing adipogenesis.[4]

Dorkhan et al found that, even in patients without previous thyroid disease, pioglitazone increases eye protrusion on average by 1 mm although 36% of patients may increase more than 2 mm. None of the patients noted any changes in their eyes and had no symptoms. A history of previous thyroid disease and low adiponectin levels prior to and after pioglitazone use was a risk factor for a greater increase in eye protrusion.[5]

Levin et al also described a case of a patient without previous history of thyroid disease who developed proptosis after taking rosiglitazone. In this case, the proptosis did not show any change after stopping rosiglitazone.[6]

In patients with history of thyroid disease, rosiglitazone may cause a rapid progression of thyroid associated orbitopathy as described by Lee et al.[7] After stopping rosiglitazone, her ocular changes remained stable but later orbital decompression was required.

Although eye protrussion is a frequent finding in patients treated with thiazolidinediones, most of them will be asymptomatic. In a few cases, the proptosis may be clinically significant and may present in patients with or without a previous history of thyroid disease. Clinicians must be aware of this effect and consider thiazolidinediones in the differential diagnosis of proptosis.

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