rotation and then a corrective movement before stabilizing. At present, he is still receiving carbamazepine.

Comment. Ocular neuromyotonia affects the extraocular muscles either individually or in combination, causing episodic diplopia that develops either spontaneously or after gaze in the direction of action of the affected muscle. Electromyography suggests a neurogenic basis for the movements.3,4 The tonic contractions are thought to result from the spontaneous discharge of unstable neurons, which are transmitted to adjacent neurons by ephaptic transmission. Consistent with the theory of axonal instability, membrane-stabilizing agents such as carbamazepine are effective.

To our knowledge, this is the first report of a patient whose ocular neuromyotonia was caused by a stroke, as well as the first in which the responsible lesion was intramedullary. Our patient’s lesions were predominantly contralateral to the side of his neuromyotonia, with only 1 small lesion at the ipsilateral mesodiencephalic junction. While we cannot determine which, if any, of his lesions caused the neuromyotonia of his right eye, we note that his lesions spared the nuclei and intramedullary fascicles of the right third nerve. We conclude that ocular neuromyotonia can result from purely intramedullary lesions, without the involvement of the lower motor neuron.

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Rosiglitazone-Induced Proptosis

Rosiglitazone maleate belongs to the class of thiazolidinedione drugs used to maintain glycemic control in patients with type 2 diabetes mellitus. The molecules in these drugs sensitize tissues to insulin activity through their ligation of the peroxisome proliferator-activated receptor-gamma (PPARγ) and by increasing expression of the glucose transporter 4 receptor. Peroxisome proliferator-activated receptor-gamma is a nuclear receptor that provokes adipocyte differentiation.1 The thiazolidinediones stimulate adipogenesis thus producing well-described weight gain by the generalized increase in subcutaneous fat volume.2

One case of reactivated thyroid associated ophthalmopathy (TAO) has been reported in a patient whose TAO had previously entered the stable phase of the disease within 3 months of instituting treatment with rosiglitazone.3 We now describe a patient without concurrent or historic thyroid disease who developed new-onset proptosis after treatment with this medication.

Report of a Case. A 53-year-old Hispanic woman had slowly progressive, painless, bilateral proptosis without periorbital inflammation, change in visual acuity, or diplopia over approximately 1 year. The patient also noticed a recent 9-kg weight gain, with a 4-in increase in abdominal girth. She denied changes in diet or exercise. The patient recalled a series of evaluations for globe prominence beginning at age 14 years. Despite her assurances to the treating physicians at that time that she manifested a familial trait.

Figure. Magnetic resonance images of the brain. A, Axial T2-weighted image showing high signal intensity (arrow) at the left mesodienecephalic junction. B, Axial T2-weighted image showing bilateral signal elevation (arrows) in the centromedial thalami and an incidentally noted left insular developmental venous anomaly (arrowhead). C, Axial gradient echo image showing focus of susceptibility (arrow) along the course of the left third nerve.
of “big eyes,” she underwent thyroid function testing, thyroid imaging, and computed tomography or magnetic resonance imaging of the orbit periodically over the next 40 years. She brought us a photograph of herself at age 25 years (Figure 1A). Her current complaints prompted a repeat of the thyroid function tests, a thyroid scan, and orbital computed tomography. Again the results of all of the laboratory investigations proved to be within normal limits.

Her medical history was significant for an 8-year history of type 2 diabetes mellitus treated with metformin hydrochloride and glipizide. In an attempt to improve glycemic control, she was started on a regimen of rosiglitazone 18 months prior to our seeing her. She was recently diagnosed as having an abdominal hernia, which may have contributed to the increased abdominal girth. She denied cigarette smoking and there was no family history of thyroid or eye disease.

On physical examination her visual acuity was 20/30 OU without spectacle correction. She identified all 6 Hardy-Rand-Rittler color plates with both eyes. Pupils reacted briskly without afferent pupillary defect. Her tel measurements were 28 mm in each eye. Applanation tension was 16 mm Hg in each eye. There was resistance to retropulsion in both eyes and both lacrimal glands were prolapsed. Ocular rotations were full. Vertical fissure heights were 12 mm in each eye with temporal flare of the upper eyelids. There was no evidence of cutaneous or conjunctival inflammation or chemosis (Figure 1B). Findings on fundoscopic evaluation were normal. The orbital computed tomographic scan, performed in January 2003, revealed bilateral proptosis with normal extraocular muscles and straightened optic nerves (Figure 2).

Correspondence was sent to the patient’s endocrinologist recommending discontinuation of treatment with rosiglitazone. The dosage was gradually decreased from 8 to 2 mg/d. At the 11-month follow-up visit the patient reported decreased pain and pressure in the orbits. Findings from physical examination showed no change in proptosis or eyelid retraction.

Figure 1. A, Patient at age 25 years. B, Patient at the time of this report, aged 53 years.

Figure 2. Computed tomographic (CT) scans of the patient. A, Current CT scan, axial view. The appearance of the orbital fat and extraocular muscles is normal. B, Current CT scan, coronal view. The appearance of the orbital fat and extraocular muscles is normal.
Comment. The most common cause of unilateral or bilateral proptosis in adults is TAO.4 The classic radiographic manifestation is a fusiform enlargement of the rectus muscles favoring the medial and inferior recti while sparing the tendinous insertions. Proptosis in the absence of enlarged extraocular muscles or some other mass lesion is usually attributable to increases in orbital fat volume. Preferential expansion of the orbital fat compartment is uniquely identified in patients with TAO who are younger than 40 years, and isolated fat hypertrophy is more common still among the pediatric population.

The presumptive diagnosis of euthyroid Graves’ disease is often made in patients who have signs of TAO but without evidence of thyroid disease or intraorbital abnormalities. Such individuals are usually expected to have serological manifestations of thyroid dysfunction develop some time in the future. Our patient was somewhat atypical. She was aware of her congenital globe prominence and was evaluated repeatedly over many years, effectively excluding autoimmune thyroid disease. No serological or radiographic evidence of thyroid or orbital disease was identified. Only after beginning therapy with rosiglitazone did she notice progressive bilateral proptosis and a coincidental increase in abdominal girth.

We speculate that the recent expansion of the orbital and abdominal fat compartments was provoked by the addition of rosiglitazone to her diabetes treatment regimen. It may be argued that she manifests euthyroid Graves’ disease and thus might be expected to ultimately have thyroid dysfunction develop. However, we are unaware of previously reported cases of euthyroid Graves’ disease in this age group that feature proptosis in the absence of either rectus muscle enlargement or cutaneous manifestations of inflammation.

A very recent report by Starkey et al3 described a 57-year-old patient with type 2 diabetes and Graves' disease and stable TAO manifesting proptosis and extraocular muscle enlargement who experienced reactivation of inflammatory orbitopathy after treatment with rosiglitazone. After discontinuing treatment with the drug, signs of cutaneous inflammation and chemosis resolved, but proptosis and eyelid fullness persisted. While our patient also developed proptosis after treatment with rosiglitazone, the absence of thyroid disease or inflammatory ocular involvement appears to make this case unique.

With regard to the cellular mechanism through which rosiglitazone might induce proptosis, Smith et al5 cultured orbital fibroblasts from patients with TAO and from individuals without inflammatory orbital disease. When the cultures were exposed to a medium containing rosiglitazone and cyclic adenosine monophosphate–enhancing agents, nearly 50% of the cells underwent differentiation into mature adipocytes. The lack of glycoprotein Thy-1 cell surface expression makes distinctive those orbital fibroblasts capable of in vitro adipogenic differentiation. Valyasevi and colleagues1 subsequently reported that treatment of orbital fibroblasts in culture with a PPARγ agonist could stimulate thyrotropin hormone receptor expression and in turn promote adipogenesis. This in vitro preadipocyte differentiation potential is shared with abdominal subcutaneous adipose tissue, as reported by Adams et al.2

We postulate that the proptosis and expanded abdominal girth in our patient resulted from analogous events occurring in vivo. It is possible that the congenitally prominent globes in our patient prompted relatively earlier identification of the new proptosis than would have occurred had her globes been more recessed. Although the evidence supporting this point of view is largely circumstantial, we cannot otherwise explain our patient’s new-onset proptosis. We believe she represents the first reported case of rosiglitazone-induced proptosis in a patient without apparent thyroid disease.

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