VIGABATRIN TOXIC RETINOPATHY

RETINOPATÍA TÓXICA POR VIGABATRINA

SUÁREZ-BARAZA J¹, SUÁREZ-PARRA S¹

ABSTRACT

Case report: We report a case of a 63-year-old patient with epilepsy treated with vigabatrin, who was seen because of diminished visual acuity. Examination showed a toxic retinopathy with optic nerve pallor and severely constricted visual fields. One year after cessation of the vigabatrin, no change in the perimetric constriction had occurred.

Discussion: Ophthalmologists and neurologists need to be aware of the possibility of retinal toxicity due to the use of vigabatrin. It is still unclear as to which ophthalmologic assessment is of the most diagnostic value; however visual field examination covering the peripheral 60º and optical coherence tomography could be most useful for the screening of patients using this agent (Arch Soc Esp Oftalmol 2007; 82: 711-714).

Key words: Vigabatrin, Toxic retinopathy.

INTRODUCTION

Vigabatrin is a GABAergic agonist anticonvulsant used in the West syndrome and as adjuvant in partial crises. It acts by inhibiting the GABA transaminase, leading to an increase in presynaptic concentrations of gamma aminobutyric acid (GABA) (1).

CASE REPORT

A 63-year old patient reporting visual acuity (VA) deficit in right eye (RE) evolving over several months.

Of note in his personal history is posttraumatic epilepsy with a ten-year evolution, high blood pressure and diabetes mellitus type II.
He was being treated with 1.5 g of vigabatrin and 200 mg of carbamazepine daily since traumatism. His VA was 0.3 in RE and 0.8 in left eye with correction.

Anterior biomicroscopy and tonometry were normal.

The ophthalmoscopy highlighted the pallor of both papillae and macular epiretinal membrane in RE (figs. 1 and 2).

We conducted computerized Humphrey 30/2 white-white and blue-yellow perimetry which presented severe concentric campimetric reductions in both eyes (Humphrey instruments, model 745, Carl Zeiss Inc) (figs. 3 and 4).

He lacked a relevant family history, and accordingly hereditary optical neuropathy was ruled out.

Anamnesis and analytical determinations of average corpuscular volume, vitamins B1, B6, B12 and folic acid ruled out nutritional etiology.

We diagnosed retinotoxicity due to vigabatrin and referred him to the neurology unit.

After a year of follow-up, campimetric and VA loss persisted.

**DISCUSSION**

Since 1997 we know that patients treated with vigabatrin can develop campimetric constrictions, which are often asymptomatic.

Prevalence is unknown since it depends on the diagnosis strategy followed and the high rate of asymptomatic cases, but it is estimated to be about 30-40% in adults and 65% in children.

There are no data on the relation with dose, length of therapy and risk of toxicity (1,2).

The GABA inhibits neurotransmission of bipolar and amacrine cells and interacts in the phototransduction of photoreceptors to ganglionic cells. There is evidence of dysfunction both of the external and the internal retina although the pathophysiological mechanisms have not been established (1,2).

Vigabatrin accumulates in the retina leading to an increase in GABA concentrations, higher even than those in the brain. It is not known whether this toxicity is due to the direct toxic effect of the drug or an indirect action due to increased GABA concentrations. There is no evidence that GABA is retinotoxic, therefore it is necessary to study the effects of vigabatrin and other GABAergic agents on the retinal function (3).

The epiretinal membrane presented by our patient has been described by other authors together with pigmentary and retinal vascular alterations (4).

A greater loss of nerve fibers has been observed in the nasal and superior area which results in a characteristic nasal pallor of the optic disk. This has been termed inverse optic atrophy to differentiate it from the more common temporary atrophy of toxic and nutritional neuropathies. This is an important albeit late sign in the evolution of retinotoxicity especially in children, as it may entail significant campimetric loss without papillary pallor (4).
There is no consensus regarding the most reasonable diagnosis strategy to follow.

Although the blue-yellow perimetry has proven to be more sensitive to detect campimetric loss than the white-white one, it is more tiring and also requires patient collaboration, making it difficult to conduct in children.

It would seem reasonable to employ a 60/4 strategy before and after the start of treatment even when there is no standard database for comparison (2).

Electrophysiological anomalies have been reported which include reduction of the Arden ratio in the electrooculogram and drop of the b wave in the photopic, scotopic and flicker 30 Hz electroretinogram (ERG). These electrophysiological alterations could serve as indicators of campimetric loss in early stages, but there is a wide variation in the published rates of campimetric, electroretinographic and electrooculographic anomalies in the various studies (4).

Multifocal ERG is an objective test that covers various focal electric responses. Although sensitive, it is not specific enough to detect campimetric loss due to vigabatrin since the stimulation field is below 60º, which does not allow measuring peripheral retinal dysfunction. This is why a broad field multifocal ERG is being developed to evaluate the severity of vigabatrin toxicity and to act as a sensitive predictor of campimetric loss (5).

Fig. 3: Computerized perimetry 30/2 white-white (left) and blue-yellow (right) of RE. Severe concentric reduction of visual field.

Fig. 4: Conventional computerized perimetry 30/2 of LE. Severe campimetric constriction.
Optical coherence tomography (OCT) is an objective and reproducible test that documents the thickness of the nerve fiber layer and its loss earlier than with campimetry. A good correlation has been found between OCT and perimetry, so it may be the most sensitive test available to diagnose vigabatrin toxicity, especially in children and patients with difficulties for conducting campimetry (4).

The evolution of this case proves that neurologists and ophthalmologists should be aware of the potential toxic effect of this drug and the need to conduct regular campimetric controls as well as to evaluate the nerve fiber layer through OCT.

REFERENCES