Short communication

Ocular paraneoplastic syndrome: Cancer-associated retinopathy☆

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A B S T R A C T

Case report: We review a patient with ocular manifestations of a paraneoplastic syndrome. It was a cancer-associated retinopathy (CAR) in a woman with visual loss, and attenuated and sheathed retinal arterioles. The electroretinography (ERG) showed severe abnormalities of the a and b-waves. The tumor process was not discovered until 6 months later, when a squamous neoplasia that invaded the uterus and vagina was observed.

Discussion: Paraneoplastic syndromes are a group of manifestations produced as a remote effect of cancer cells. CAR syndrome is caused by autoimmune reactions to retinal antigens induced by aberrant expression of recoverin in cancer tissues. Ophthalmologists must be aware of ocular paraneoplastic signs as they can be the first manifestations of a malignant tumor.

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Síndrome paraneoplásico ocular: retinopatía asociada al cáncer

R E S U M E N

Caso clínico: Se presenta un síndrome paraneoplásico ocular con una retinopatía asociada al cáncer (RAC) que producía déficit visual, disminución de calibre y envainamiento de las arteriolas retinales. El ERG mostraba grandes alteraciones de las ondas a y b. El proceso tumoral no se descubrió hasta pasados 6 meses, en que apareció una neoplasia escamosa que invadió útero y vagina.

Discusión: Los síndromes paraneoplásicos son manifestaciones secundarias a la producción de sustancias, por las células neoplásicas, que actúan a distancia del foco tumoral. El síndrome RAC es una reacción autoinmune cruzada de antígenos de origen tumoral con la recoverina de la retina. El oftalmólogo debe conocer la existencia de estas manifestaciones paraneoplásicas oculares porque pueden constituir el primer signo de un tumor maligno no diagnosticado.

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Introduction

Paraneoplastic syndromes are secondary expressions to the production by neoplasia of biologically active substances which act at a distance from the tumor without direct dissemination.\textsuperscript{1,2}

The most frequent paraneoplastic expressions at the ocular level are cancer-associated retinopathy (CAR) and a retinopathy associated to skin melanoma (RAM), to which we must add bilateral diffuse uveal melanocytic proliferation, retinal disorders related to blood hyperviscosity and more exceptionally other inflammatory and optic nerve disorders.\textsuperscript{2}

The clinical importance of paraneoplastic syndromes is that they can constitute the first sign of an undiagnosed malign tumor or could indicate a relapse and, in some cases, can be used as tumor progression markers.\textsuperscript{1,2}

Clinic case

A female, aged 72 years, visited the practice due to loss of vision in the left eye (LE) with onset one week before. She had been treated 6 years ago of infiltrating ductal carcinoma by means of left mastectomy with armpit cleansing and chemotherapy. Subsequent checkups gave normal results. The ophthalmological exploration gave a visual acuity (VA) of 0.5 in the right eye (RE) and under 0.05 in LE, normal intraocular pressure and anterior pole biomicroscopy without other alteration than lens pseudoxefoliation. The RE fundus was apparently normal whereas the LE exhibited a vascular tree with thin arterial branches and segmented sheathings, without alterations in the veins. In the following days the patient partially recovered VA in the LE (up to 0.4) but 1 month later she exhibited visual loss in the RE, with a similar condition in the ocular fundus (Fig. 1).

The patient exhibited an attitude of blindness, with visual field diminished to the point that she did not perceive light stimuli. Fluorescein angiography (FA) exhibited rarefaction of the retinal vascular network without neovessels, and an ERG performed with full field stimuli revealed absent rods wave and cones wave with highly diminished amplitude and increased latency (Figs. 2 and 3).

Suspecting ocular paraneoplastic syndrome, the patient was referred to Internal Medicine without observing reactivation of the mammary carcinoma or other tumor process. The ophthalmological exploration remained stable with VA of 0.4–0.5 in each eye but 6 months later she was admitted due to abdominal pain, detecting a poorly differentiated squamous neoplasia that invaded the cervix, endometrium and vagina. The patient died a few days later.

Discussion

The CAR syndrome has been described in a few dozen cases since 1976, in over half of these due to lung tumors and mainly to small cell carcinoma. It can also appear in gynecological neoplasia (breast, ovary and uterus) and in isolated cases of colon, pancreas, prostate, bladder and lymphoma tumors.\textsuperscript{2} Visual loss symptoms usually precede the malign tumor which frequently remains undetectable for months.\textsuperscript{1,2}

The clinical expressions of CAR consist in photophobia, diminished VA, central scotoma due to involvement of the cones, peripheral scotoma due to the involvement of the rods, color vision deterioration and night blindness. The ocular fundus could be normal initially although it progresses toward the acceleration of the retinal arterioles, granular appearance of the retina pigmented epithelium and optic disk paleness. Vitreous or anterior chamber cellularity is usually not present.\textsuperscript{1} ERG exhibits extinguished waves a and b on the photopic and scotopic conditions.\textsuperscript{1,2}

In most cases, CAR pathogeny is based on a crossed self-immune reaction against recoverin, a calcium-linking protein of photoreceptors and bipolar cells.\textsuperscript{3,4} The recoverin gene is located in chromosome 17, close to gene p53, a tumor suppressing gene that produces a protein which is capable of...
halting the cellular cycle and repairing DNA. A mutation in this region of a chromosome could cause the deactivation of protein p53 thus facilitating tumor proliferation and at the same time giving rise to an aberrant recoverin expression with the appearance of anti-recoverin antibodies which unleash cellular apoptosis of photoreceptors and bipolar cells.  

In the CAR syndrome, the majority of cases evolve toward significant visual loss. Treating the neoplasia does not improve the condition whereas systemic corticoids could stabilize or improve vision in some patients although its possible negative effect on tumor growth must be considered.  

Ophthalmologists must be aware of the existence of CAR because it could be the first sign of an undiagnosed malign tumor. The diagnostic suspicion is based on ocular findings which are insignificant vis-à-vis the huge associated visual loss, which generally evolves to blindness, to which we must add flat ERG.  

Conflict of interests

No conflict of interests has been declared by the authors.

REFERENCES