CANCER ASSOCIATED RETINOPATHY WITH PERIPHLEBITIS AND BILATERAL VITREOUS HEMORRHAGE

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ABSTRACT

Introduction: Cancer associated retinopathy (CAR) is an uncommon paraneoplastic syndrome associated with epithelial neoplasm. Ocular symptoms of this syndrome are varied.

Case report: A 40-year-old man with an existing smoking history noticed a bilateral visual loss.Fundus examination showed a bilateral vitreous hemorrhage.In the left eye, there were narrowed retinal arterioles and peripapillary neovessels. An X-ray chest revealed a lung lesion which on biopsy proved to be a bronchial squamous cell carcinoma.
After conducting several explorations,we have diagnosed CAR.

Conclusion: Vitreous hemorrhage is one of the symptoms of CAR. Thus, systems review, searching for an extraocular cancer, X-ray chest and ERG are recommended in this case.

KEY WORDS

cancer, paraneoplastic syndrome, periphlebitis, retinopathy, vitreous hemorrhage.

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INTRODUCTION

Cancer associated retinopathy (CAR) is an uncommon paraneoplastic syndrome associated with epithelial neoplasm, mostly lung cancer. Many patients develop the retinopathy before the primary malignancy has been found. Ocular symptoms of this syndrome are varied and not specific. However several features should alert the clinician to the possibility of CAR.
We describe a first case of CAR revealed by bilateral vitreous hemorrhage in a patient presenting a lung cancer.

CASE REPORT

A 40-year-old man with an existing smoking history of 22 pack-years, had noticed a bilateral and progressive visual loss since 3 months, accompanied by an intermittent photophobia. His visual acuity was count fingers in the right eye (OD) and 1/10 in the left eye (OS). The anterior segments were normal in both eyes. Dilated fundus examination showed a bilateral vitreous hem orrhage that was more important in the right eye. In the left eye, narrowed retinal arterioles and peripapillary neovessels were visible (*Fig. 1*).

Fluorescein fundus angiography exhibited peripapillary neovessels, peripheral retinal ischemia and vascular sheathing consistent with retinal periphlebitis (*Fig. 2*).

Biological tests (glycemia, sedimentation rate, antiphospholipid antibodies, ...) were normal while ultrasonography of the supra-aortic trunks showed was in the normal limits.

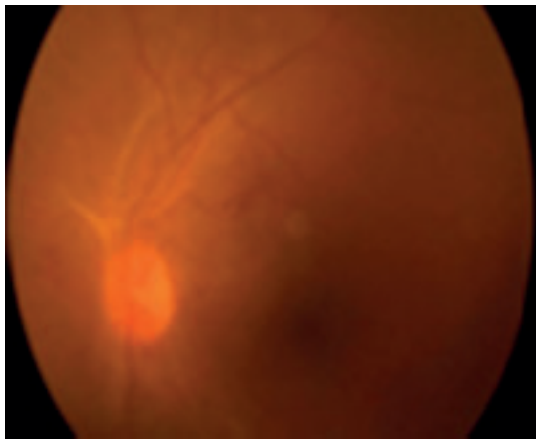

Fig. 1: Fundus photography of the left eye showing vitreous hemorrhage, narrowed retinal arterioles and peripapillary neovessels.

An X ray chest revealed a lesion in the left lung which on biopsy proved to be a bronchial squamous cell carcinoma (*Fig. 3*). The cerebral CT revealed metastasis in the occipital lobe.

Thus, a paraneoplastic ocular disease was considered. The Goldman visual field test highlighted a paracentral scotoma in the left eye. Multifocal electroretinogram (ERG) showed reduced scotopic and photopic a and b waves (*Fig. 4*). Western blot analysis of anti-recoverin antibody was not conducted.
We diagnosed CAR based on the exclusion of the others etiologies of vitreous hemorrhage, the results of the ERG and the clinical manifestations such as progressive loss of vision, photophobia, retinal phlebitis, attenuation of the retinal arterioles caliber and the presence of a lung cancer with brain metastasis.

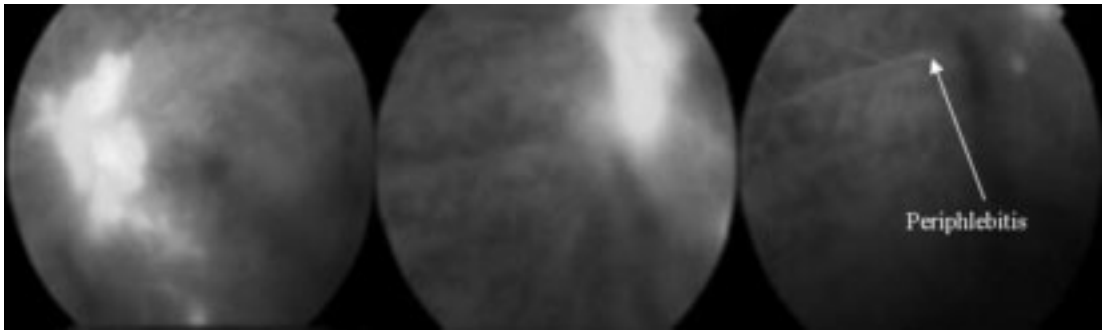

Fig. 2: Fluorescein fundus angiography showing peripapillary neovessels, peripheral retinal ischemia and vascular sheathing consistent with retinal periphlebitis.

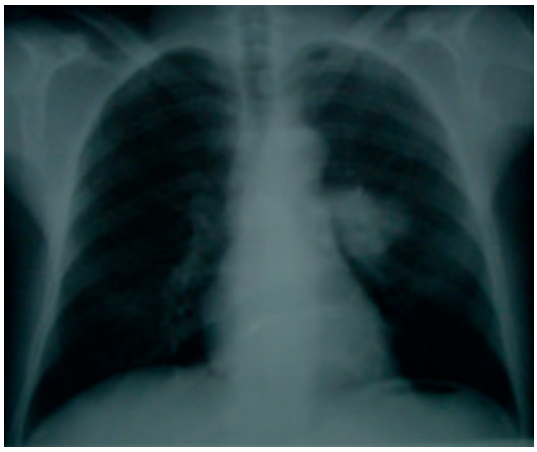

Fig. 3: X-ray chest revealing a lesion in the left lung.

DISCUSSION

Cancer associated retinopathy (CAR) belongs to a spectrum of uncommon ophthalmic disorders in which autoantibodies directed at various retinal components cause progressive vision loss. This retinopathy belongs to the category of paraneoplastic syndromes.

The exact prevalence of cancer associated retinopathy is unknown. It usually affects older adults, with no sex predilection. CAR is thought to be the most common form of paraneoplastic retinopathy. CAR is most commonly associated with carcinoma of the lung (bronchial small and squamous cell carcinomas) (2, 3), but it has also been less frequently reported in patients with breast, endometrial and other cancers.

In these patients, antibodies are directed at antigens of the retina and this reaction is associated with rod and cone dysfunction. The most common, but not the only antigen, is the 23-kDa recoverin (1, 3, 4, 5). The malignant cells were found to induce to express recoverin. It has been suggested that a mutational event inactivating the p53 tumor suppressor gene may turn on the synthesis of a recoverin protein.

Antibodies reactive to recoverin and may result in the blockage of ion channels and cellular depolarization. These events may lead to photoreceptor cell death (6, 7).

Postmortem examination of eyes with CAR demonstrated diffuse photoreceptor degeneration with or without inflammation whereas ganglion cells and retinal vasculature are spared.

In most cases of CAR, vision loss occurs before malignancy is diagnosed. Symptoms are usually bilateral, occasionally sequential, and progressive over weeks to months.

Individuals with cone dysfunction experience photosensitivity, prolonged glare after light exposure (hemeralopia), reduced visual acuity and loss of color vision.

Individuals with rod dysfunction have difficulty when they see in dim illumination (nyctalopia) and prolonged dark adaptation. In either case, some patients report flashing lights and smoky vision (8, 9).

Funduscopic findings can be normal at an early stage of the disease. However, characteristic changes occur over time and include attenuation of the arterioles, with thinning and mottling of the retinal pigment epithelium (RPE) (10). In occasional cases, vitreous cells, arteriolar sheathing and periphlebitis may be present, particularly late in the course of disease (9, 11).

Our patient presented a bilateral vitreous hemorrhage that was mild in the left eye and allowed, examine the fundus successfully. In the case of a severe bilateral vitreous hemorrhage, especially when the etiology is unknown, a vitrectomy is necessary.

In some cases, visual field testing shows paracentral scotomas that progress to classic ring scotomas. Goldmann perimetry is preferred because it tests the peripheral field; if automated perimetry is performed, the test should be adapted to include the peripheral field.

Fluorescein angiography is performed to exclude other entities as potential causes of vision loss. Findings can be normal, but, in occasional cases, fluorescein angiography may show mild peripheral vascular leakage consistent with vasculitis.

Optical coherence tomography (OCT) demonstrates thinning of the inner retinal layers.

Full-field ERG is crucial for localizing the disease process to the retina and for further defining the retinal layers involved (10). Multifocal ERG (MERG) may be useful in selected cases in which the visual field loss is localized. In addition, some authors have used MERG to quantify the loss of the electrical activity and to correlate this finding with the results of Goldmann perimetry. The findings given by the full-field ERG are almost always abnormal. Patients with CAR usually have abnormalities of the a

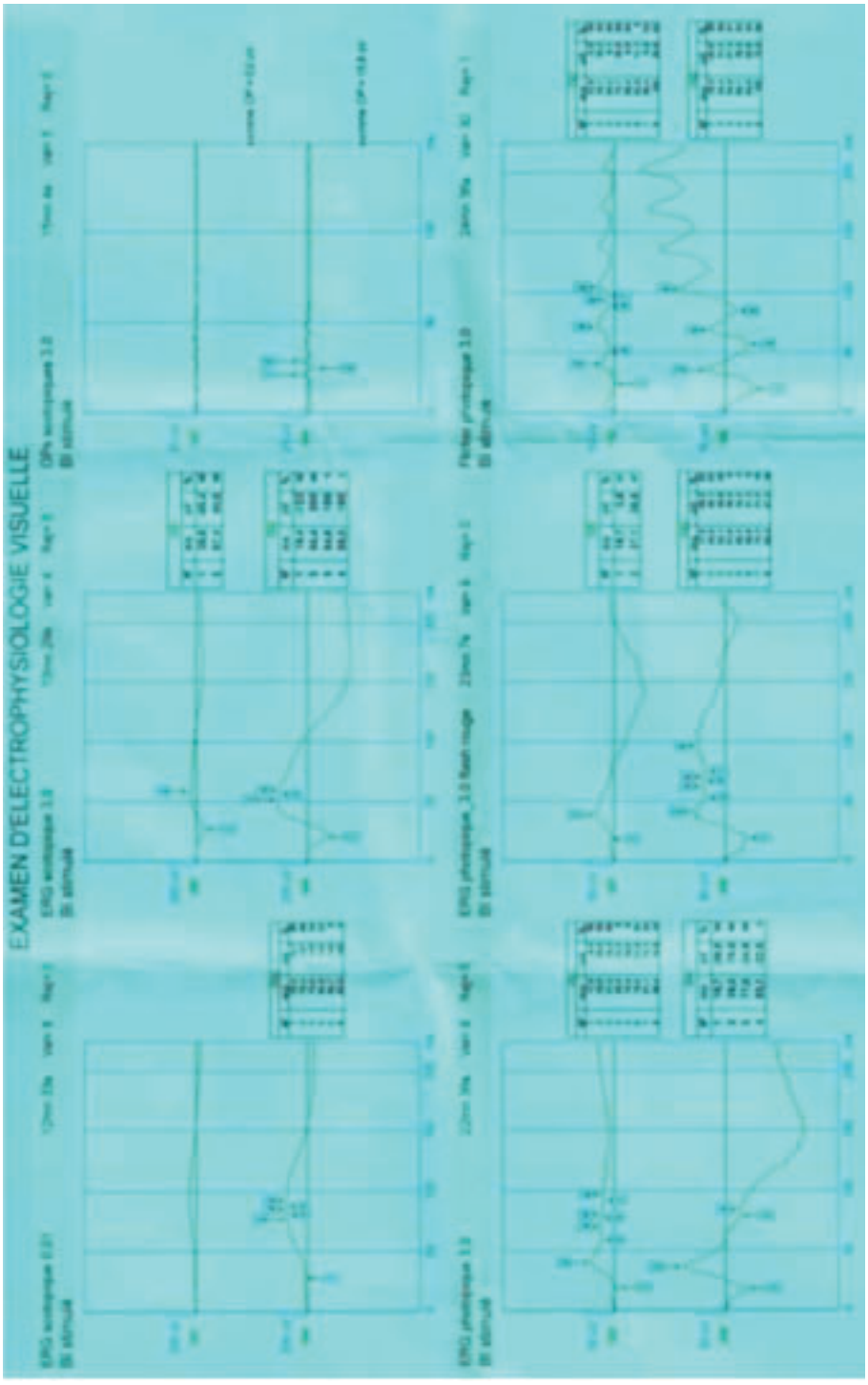

Fig. 4: ERG showing reduced scotopic and photopic a and b waves.

and b waves of the ERG. However, in the case of vitreous hemorrhage, full-field ERG is also abnormal. In our patient, we diagnosed CAR based on the results of the ERG but also on the exclusion of the others etiologies of retinopathy with vitreous hemorrhage.

A definitive diagnosis of CAR requires the demonstration of antiretinal antibodies. In many cases, individuals without clinical evidence of retinopathy have these antibodies, while in some cases of presumed CAR, the antibodies cannot be identified.

In a patient with suspected CAR and without a known malignancy, an X-ray imaging test of the chest should be obtained. If the result is normal, a CT-scan of the chest is appropriate.

Furthermore, complete physical examination including pelvic and breast examinations and mammography for women are also recommended.

Several differential diagnoses should be eliminated before a definitive diagnosis of CAR can be made. So a acute or subacute or bilateral vision loss with a normal-appearing fundus suggests the possibility of retrobulbar optic neuropathy. Patients with cancer associated cone dysfunction have bilateral central vision loss with poor color vision and central scotomas. These findings are also compatible with toxic, nutritional or hereditary optic neuropathy. Patients with these findings should be questioned about possible tobacco and alcohol use, dietary habits, a family history of similar problems and use of potentially toxic medications such as vincristine (12). In a patient with unexplained vision loss and a history of malignancy, the differential diagnosis may be complex. The vision loss can be due to metastatic disease with infiltration of cancerous cells around the optic nerve. Patients who have received cranial radiation are also at risk for vision loss. Hereditary photoreceptor degeneration (cone dystrophy, retinitis pigmentosa) and toxic retinopathy may also be differential diagnoses of CAR. Finally, in patients-presenting vasculitis like our patient, several systemic diseases should be excluded such as Behçet's disease, sarcoidosis, Wegener's granulomatosis, systemic lupus erythematosus, polyarteritis nodosa and other rheumatologic conditions. Primary ocular disease such as Eales disease, pars planitis, but also primary syphilitic vasculopathy birdshot retinochoroidopathy can also be causes of vasculitis with vitreous hemorrhage. All these etiologies could have been excluded in our patient.

The prognosis of patients with CAR is poor. Surgery, chemotherapy, and radiation therapy to treat the primary tumor do not appear to alter the visual prognosis. Various immunotherapies may result in modest visual recovery in some cases.

Corticosteroids (13, 14) have been shown to decrease the antibody titers in patients with CAR and may stabilize their vision (13, 14). Anecdotal reports described an improvement in CAR with high-dose intravenous methylprednisolone, plasmapheresis combined with steroids or intravenous immunoglobulin. However, the treatment results are largely disappointing. Espandar described a beneficial response in a patient with CAR treated with alemtuzumab, a monoclonal antibody that is used for the treatment of various B-cell mediated disorders (15).

Huynh N reported that intravitreal triamcinolone may be beneficial for maintenance of vision in patients with CAR (16).

CONCLUSION

Cancer associated retinopathy is a paraneoplastic syndrome. Vitreous hemorrhage is one of its symptoms. Thus, systems review, search for an extraocular cancer, X-ray chest and ERG are recommended in patients presenting vitreous hemorrhage, especially, those with a high risk of lung cancer. The treatments available for CAR can only stabilize the visual function. Further researchs are needed to improve its visual prognosis.

REFERENCES

(1) Thirkill CE – Cancer associated retinopathy. *Neuro-ophthalmology,* 1994; 14:297- 323.

(2) Sakamori Y, HakKim Y, Okuda C et al – Two Cases of Cancer-associated Retinopathy Combined with Small-cell Lung Cancer. Jpn. J. *Clin. Oncol,* 2011; 41 (5): 669-673.

(3) Bidegain C, Rigalt J, Ribot E, Dorca J, Vayreda J – Small Cell Lung Cancer and Cancer-Associated Retinopathy. *Arch Bronconeumol,* 2005; 41: 99-101.

(4) To KW, Thirkill CE, Jakobiee FA, Lessell S, Berson EL – Lymphoma- associated Retinopathy. *Ophthalmology,* 2002; 109: 2149-53.
(5) Ohguro H, Ogawa K, Maeda T, A Maeda, Maruyama I – Cancer-associated retinopathy induced by both anti-recoverin and anti-hsc70 antibodies in vivo. *Invest. Ophthalmol. Vis. Sci.* 1999; 40: 3160-3167.
(6) Adamus G, Machnicki M, Elerding H, Sugden B, Blocker YS, Fox DA – Antibodies to recoverin induce apoptosis of photoreceptor and bipolar cells in vivo. *J Autoimmun,* 1998; 11: 523-533.
(7) Matus G, Dicato M, Focan C – Cancer associated retinopathy (CAR): Présentation de deux cas cliniques et revue de la littérature. *Rev med Liege,* 2007; 62 no 3: 166-169.
(8) Sawyer RA, Sheihorst JB, Zimmerman LE, Hoyt WF – Blindness caused by photoreceptor degeneration as a remote effect of cancer. *Am J Ophthalmol*, 1976; 81: 606-13.
(9) Ohnishi Y, Ohara S, Sakamoto T, Kohno T, Nakao F – Cancer associated retinopathy with retinal phlebitis. *Br J Ophthalmol,* 1993; 77: 795-798.
(10) Jacobson DM, Thirkill CE, Tipping SJ – A clinical triad to diagnose paraneoplastic retinopathy. *Ann Neurol,* 1990; 28: 162-7.
(11) Sobottka B, Schlote T, Besch D, Djelebova T, Wilhelm H, Zrenner E – Carcinoma associated retinopathy: a review with clinical examples. *Klin Monatsbl Augenheilkd,* 2000; 216(1): 17-24.
(12) Weisfeld-Adams JD, Dutton GN, Murphy DM – Vincristine sulfate as a possible cause of optic neuropathy. *Pediatr Blood Cancer.* 2007; 48(2): 238-40.
(13) Keltner JL, Thirkill CE, Tyler NK, Roth AM – Management and monitoring of cancer-associated retinopathy. *Arch Ophthalmol,* 1992; 110: 48-53.
(14) Takahashi M, Hirami Y, Sakuma K et al – Case of cancer-associated retinopathy in which immediate treatment succeeded. *Nihon Ganka Gakkai Zasshi.* 2008; 112: 806-11.
(15) Espandar L, O'Brien S, Thirkill C, Lubecki LA, Esmaeli B – Successful treatment of cancer-associated retinopathy Lubecki with alemtuzumab. *J Neurooncol,* 2007; 83: 295-302
(16) Huynh N, Shildkrot Y, Lobo AM, Sobrin L – Intravitreal triamcinolone for cancer-associated retinopathy refractory to systemic therapy. *J Ophthalmic Inflamm Infect.* 2012, DOI: 10.1007/s12348-012-0067-9.

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