Paraneoplastic retinopathy associated with occult bladder cancer

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The aim was to report the first case of cancer-associated retinopathy (CAR) presenting before bladder cancer diagnosis. A 71-year-old woman with a history of bilateral vision loss underwent subsequent complete ophthalmic examination include a fluorescein angiography, full-field electroretinogram (ERG), serology including serum antibodies for CAR, and positron emission tomography-computed tomography (PET-CT) scan. The patient was diagnosed with bladder carcinoma revealed by PET-CT. Timely recognition of this entity may be crucial for an increased patient survival thus adult onset progressive photoreceptor dysfunction, confirmed by ERG, should alert to a possible remote effect of known or occult malignancy. In the latter, PET-CT may be exploited as a powerful diagnostic tool.

Key words: Cancer-associated retinopathy, electroretinogram, melanoma-associated retinopathy, paraneoplastic retinopathy, positron emission tomography-computed tomography scan

Access this article online	
Quick Response Code:	**Website:** www.ijo.in
	DOI: 10.4103/0301-4738.181744

Cancer-associated retinopathy (CAR) is a paraneoplastic autoimmune retinopathy associated with a broad diversity of carcinomas, most commonly small-cell lung,[1,2] gynecologic,[1,3,4] and breast cancers.[1,5,6] Symptoms present bilaterally or sequentially over a period of weeks to months, either with transient monocular dimming, light flickering or with the loss of vision. Although retina may appear normal in early CAR, thinned, attenuated arterioles, mottled retinal pigment epithelium usually appears within several months. Histopathological and retinal optical coherence tomography (OCT) changes are a loss of the retinal outer nuclear and photoreceptor layers with preserved retinal nerve fiber layer (RNFL) and ganglion cell layers.[1,7] The irreversible photoreceptor (both cones and rods) degeneration

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Manuscript received: 12.07.15; Revision accepted: 12.01.16

Cite this article as: Nivean M, Muttuvelu DV, Afzelius P, Berman DC. Paraneoplastic retinopathy associated with occult bladder cancer. Indian J Ophthalmol 2016;64:248-50.

is initiated by an immune-mediated reaction due to the cross reaction between retinal and cancer proteins. Markers for these proteins, e.g., antirecoverin antibody, Anti-Enolase (anti-ENO), tubby-like protein-1, are widely reported in the literature.[7,8] The electroretinogram (ERG) usually reveals a markedly attenuated or absent photopic and scotopic response.[9]

To our knowledge, there is but one reported case of CAR in a patient with a known bladder, prostate, and laryngeal carcinoma.[10] We report the first case of CAR presenting before bladder cancer diagnosis.

Case Report

A 71-year-old Caucasian woman with Crohn's disease and colostomy, but no past ocular history, toxic exposures, or symptoms of malabsorption, was referred with a progressive painless asymmetric decrease in vision for 2 months. She noticed a significant dyschromatopsia along with visual field loss in both eyes but denied any positive visual phenomena. On examination, her corrected Snellen VA was the ability to see hand motions OD and 6/18 OS. She was not able to identify any Ishihara color plates in either eye. There was a severe diffuse visual field loss on automated perimetry (Humphrey Field Analyzer II [HFA II, Humphrey 750i Visual Field Analyzer]).

The anterior segment was quiet with early bilateral cataracts. There was mild vitritis in both eyes (OD > OS). Fundus examination showed normal optic discs, macular drusen, and no mid-periphery changes but somewhat attenuated arterioles (OD > OS). OCT revealed bilaterally thinned inner retinal layers [Fig. 1], RNFL was relatively well-preserved. Fluorescein angiography showed a delayed flow of fluorescein without definite retinal or choroidal filling defects or other abnormalities. As the patient was known to be prone to autoimmune diathesis, she was worked up with both autoimmune and inflammatory serologies, as well as specific serum antibody analysis for CAR (commercially available anti-ENO1 and antirecoverin). While awaiting the results, she was offered and accepted treatment with intravenous methylprednisolone 1 g daily for 5 days followed by oral steroid taper. Treatment response was only subjective and transient. All blood tests including vitamin status were normal. Full-field ERG was found extinguished both scotopic and photopic [Fig. 2]. Still considering a paraneoplastic autoimmune retinopathy a positron emission tomography-computed tomography (PET-CT) was performed and detected a transmural tumor in the bladder with lymph node extension [Fig. 3]. Biopsy revealed small-cell neuroendocrine carcinoma.

The patient was subsequently treated with chemo and radiation therapy, as surgical treatment was not possible due to previous intestinal surgery. Visual dysfunction progressed to hand movement in both eyes. The patient deceased a year after the first visual symptoms.

Discussion

CAR is a heterogeneous autoimmune response that is associated with several antibodies against the retinal proteins.

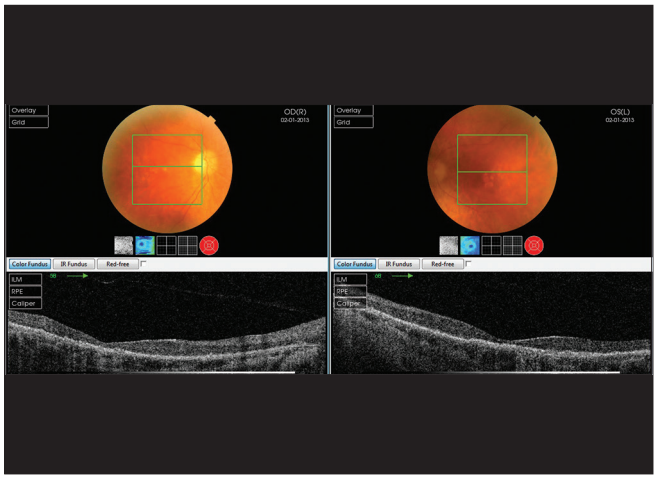

Figure 1: Fundus and optical coherence tomography scan bilaterally reveals thin retina (FT 165 um OD, 155 um OS), especially atrophy of the inner segments of retin

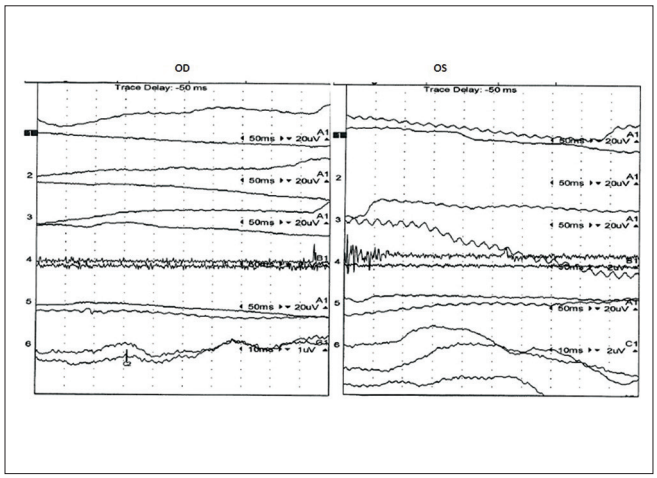

Figure 2: Full-field electroretinogram with bilateral extinguished scotopic and photopic response

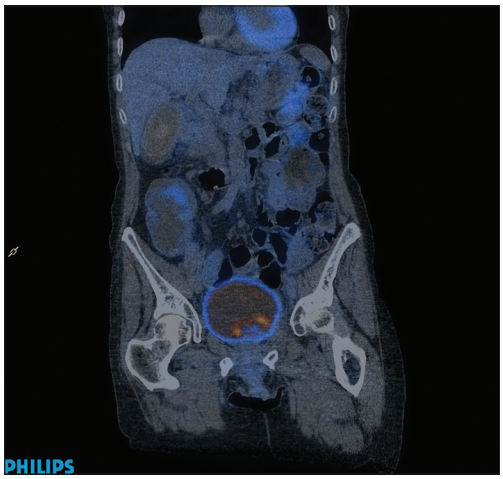

Figure 3: Co-registered 18F-fluorodeoxyglucose positron emission tomography and computed tomography image revealing a hypermetabolic mass in the wall of the urinary bladder

Especially in small-cell lung cancer, associated with CAR, there is a high predictive power with the sampled antirecoverin and anti-ENO1. Detection of paraneoplastic antibodies in blood samples directs the search of underlying neoplasm in about 60% of all paraneoplastic syndromes. All were negative in this case. A prompt lowering of these retinal antibodies is the key to stop the progression of vision. High dose steroid, gamma globulin treatment, and plasmapheresis are the treatment options, however, most still continue to progress to total visual loss within few months, as in this case.[11]

Since CAR was described in 1976, paraneoplastic autoimmune retinopathies have been increasingly recognized with varieties of carcinomas as well as melanomas.[1-7] In melanoma-associated retinopathy visual disturbances manifest at the time melanoma diagnosis is already established. Importantly, vision loss in CAR precedes the diagnosis of an underlying malignancy in half of the cases.[2] Thus, timely recognition of this entity may be crucial for increased patient survival. Hence, in any adult with unexplained visual loss, with adult onset of progressive photoreceptor dysfunction, confirmed by ERG, should alert to a possible remote effect of known or occult malignancy.

The diagnostic work-up of patients with occult cancer remains debatable and individual. Traditionally, CT of chest and pelvis for lung, breast, and gynecologic cancers have been advised though the superiority of full body PET-CT is indicated in newer studies.[12] In those cases, where there is no primary suspicion for the location of an occult tumor, PET-CT may be exploited as a powerful diagnostic tool.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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