



Cancer-Associated Retinopathy Presenting as Panuveitis Secondary to Minimally Invasive Follicular Thyroid Carcinoma

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Abstract

Purpose: To describe a case of cancer-associated retinopathy (CAR) secondary to follicular thyroid carcinoma. **Methods:** A single retrospective case was evaluated. **Results:** A 68-year-old woman presented with floaters and decreased vision in the right eye and was found to have panuveitis. The left eye subsequently developed panuveitis 6 months later, ultimately resulting in retinal atrophy. Extensive investigations, including vitreous biopsies, imaging, and positron emission tomography, led to a diagnosis of CAR secondary to minimally invasive follicular thyroid carcinoma with serology positive for anti-enolase, anti-HSP60, and anti-glyceraldehyde-3-phosphate dehydrogenase. **Conclusions:** Cases of CAR secondary to minimally invasive follicular thyroid carcinoma are rare. Ensuring an early diagnosis and promptly initiating treatment, with a goal of preserving sight, are imperative.

Keywords

cancer-associated retinopathy, ocular oncology, retina

Introduction

Cancer-associated retinopathy (CAR) causes vision loss secondary to an underlying systemic malignancy.¹ Ocular findings can precede the diagnosis of underlying malignancy in up to 50% of cases.² Acute or subacute visual loss or symptoms such as positive visual phenomena with retinal degeneration seen on examination are commonly reported. Less common findings include vitreous cell and vascular sheathing. Treatment entails intensive immunosuppression with overall significant morbidity.

Thyroid cancers are the ninth most common carcinoma in the United States, comprising 3.8% of new cases.³ A higher incidence is seen in women than in men.⁴ The second most common variant of thyroid cancer is follicular thyroid cancer, comprising approximately 10% to 15% of cases.⁵ Although the overall mortality is low for thyroid carcinomas, the follicular subtype has a higher rate than the more common papillary variant.³ Paraneoplastic syndromes secondary to follicular thyroid cancer are very rare. Case reports exist of hypertrophic osteoarthropathy, leukocytosis, and cerebellar degeneration caused by paraneoplastic syndrome.^{6–8} Although there are reports of CAR secondary to papillary thyroid cancer, to our knowledge no cases stemming from follicular thyroid cancer have been reported.^{9–11}

In this report, we present a case of CAR secondary to follicular thyroid carcinoma in a patient who initially presented with panuveitis in the right eye. Progression of the disease resulted in retinal atrophy and development of panuveitis in the left eye.

Case Report

A 68-year-old woman presented to the retinal service with floaters and decreased visual acuity (VA) in the right eye. There was no previous ocular history, and she was systemically healthy. On examination, the VA was 20/70 OD and 20/60 OS, with pinhole VA improving to 20/25. In addition, the right eye was significant for mild anterior chamber and vitreous cells with central vitreous haze and subretinal deposits. The left eye was unremarkable. Fluorescein angiography (FA) of the right eye showed mild vasculitis, with the view partially obstructed by vitreous haze (Figure 1); FA of the left eye was normal.

After the diagnosis of panuveitis was made, treatment was started with prednisolone acetate 1% drops in the right eye, 4 times daily. A systemic workup, including magnetic resonance imaging of the brain and orbits, computed tomography of the chest, syphilis antibody serology, a tuberculosis purified protein derivative skin test, and inflammatory markers, was unremarkable. Likewise, no underlying systemic disorder was found in a

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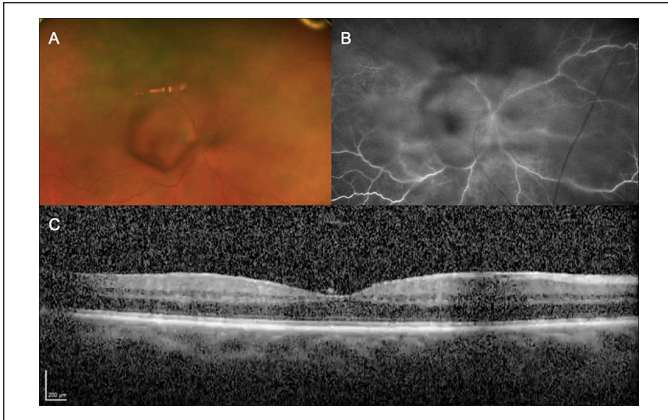


Figure 1. (A) Fundus autofluorescence reconstruction color fundus photograph of the right eye at the patient's initial presentation shows vitreous debris. (B) Fluorescein angiography of the right eye taken 38 seconds after dye injection shows mild vasculitis. (C) Optical coherence tomography of the right eye shows vitreous debris.

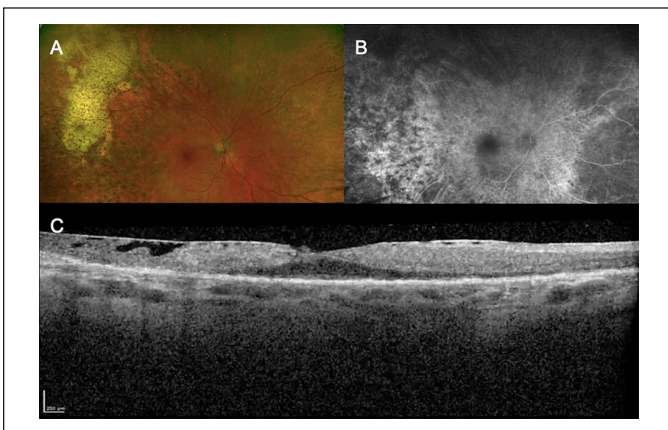


Figure 2. (A) Fundus autofluorescence reconstruction color fundus photograph of the right eye shows retinal atrophy. (B) Fluorescein angiography of the right eye taken 40 seconds after dye injection shows retinal atrophy. (C) Optical coherence tomography of the right eye shows photoreceptor loss.

rheumatology assessment. Out of concern for primary vitreoretinal lymphoma, a vitreous biopsy was performed. Flow cytometry analysis of the vitreous fluid was negative for lymphoproliferative disorders. Given the persistent inflammation, the patient was administered a sub-Tenon injection of 40 mg triamcinolone acetate. The inflammation gradually improved; however, the patient experienced subjective flashes of light in the right eye. No other visual phenomena, including nyctalopia or visual field changes, were reported.

At the patient's follow-up visit, optical coherence tomography (OCT) of the right eye showed retinal atrophy with loss of photoreceptors as well as loss of the outer retinal layers (Figure 2). In addition, mixed retinal pigment epithelium atrophy and clumps in a leopard-spot pattern were identified on fundus examination, again raising the concern for primary

vitreoretinal lymphoma. Full-field electroretinograms (ERGs) using skin electrodes were performed on both eyes with a RETeval system (LKC Technologies).¹² In the patient's right eye, the ERGs were almost undetectable for both rod and cone components; however, they were within normal range in the left eye (Figure 3). Given the patient's significant clinical response to steroids and the lack of diagnostic clarity at the time, no further immunosuppressive therapies were pursued.

Six months after initial presentation, the patient developed symptoms of blurred vision and floaters in the left eye. A workup showed ellipsoid loss in the macula of the left eye and corresponding staining on FA. Oral prednisone was started because of the advanced retinal findings. Given the bilateral retinal degeneration, oncology was consulted for a further systemic workup, and anti-retinal antibody serology was performed. Serology was positive for anti-enolase, anti-HSP60, and anti-glyceraldehyde-3-phosphate dehydrogenase. Immunohistochemistry was also positive, with staining of the photoreceptor layer and some bipolar cells and the ganglion cell layer, suggesting an autoimmune-associated retinopathy or CAR.

A positron emission tomography scan showed an excessively enlarging hypermetabolic left thyroid nodule (3.5 cm × 3.2 cm × 4.5 cm). A thyroid biopsy was performed, showing invasive follicular carcinoma (T2 NX MX). The patient was continued on high-dose oral steroids for presumed CAR secondary to follicular thyroid carcinoma, and a total thyroidectomy was subsequently performed.

At the patient's final follow-up visit, the best-corrected VA was 20/150 OD and 20/40 OS. The patient's right eye showed significant photoreceptor loss; the left eye had loss of the parafoveal ellipsoid layer, findings consistent with CAR (Figure 4). The inflammation responded well to oral steroids; therefore, no further immunosuppression was sought.

Conclusions

To our knowledge, this is the first reported case of paraneoplastic retinopathy secondary to follicular thyroid carcinoma. CAR is the most common intraocular paraneoplastic syndrome.¹ First identified in 1976, the majority of cases are secondary to small-cell lung cancer.¹³ The average age of onset is 65 years old, similar to our patient's age.

Because both the rod and cone responses are affected, symptoms can include photosensitivity, nyctalopia, and central and peripheral vision loss. Vasculitis, vitritis, and anterior uveitis, such as in our case, have been reported in the literature.¹ In a case series by Makiyama et al,¹⁴ 5 of the 8 cases presented with vasculitis and 2 with vitreous opacities. ERG responses typically show a severe reduction in both rod and cone responses, similar to what was seen in our patient. Unfortunately, because of a loss of follow-up, only 1 ERG was completed; therefore, we were unable to document bilateral ERG changes. In addition, OCT imaging showed atrophy and loss of outer retinal structures.

Few case reports have documented CAR in association with thyroid carcinoma; however, all previous cases have been papillary thyroid carcinoma. Two patients reported painless vision loss

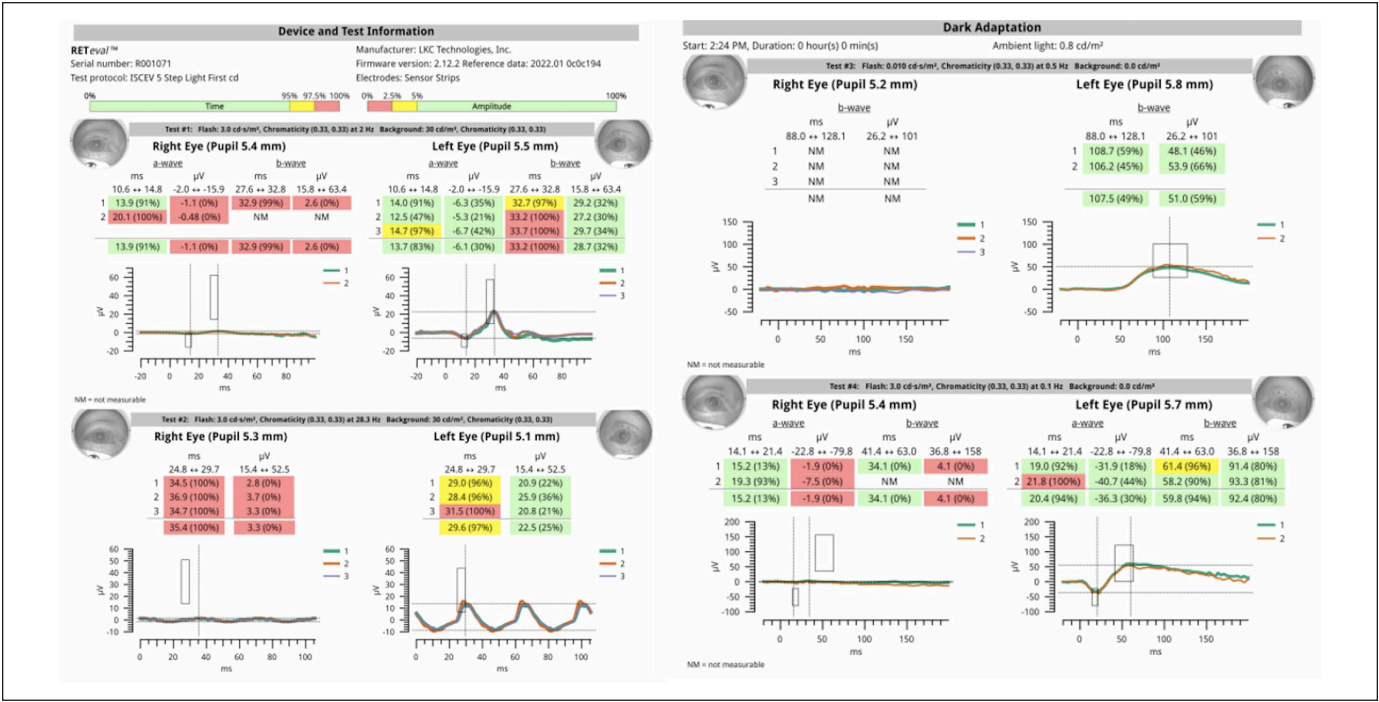


Figure 3. Electrophysiology of the right eye and left eye shows severe retinopathy seen in the right eye.

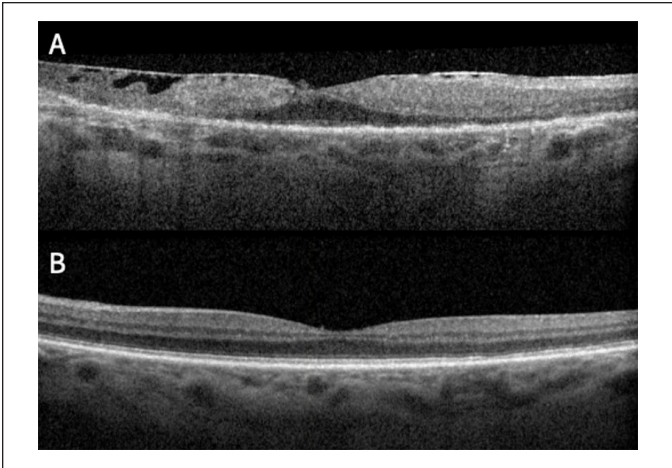


Figure 4. Optical coherence tomography of the (A) right eye and (B) left eye shows outer retina loss.

with an unremarkable fundus examination and subsequent diagnosis on electrophysiologic or immunohistochemical testing.^{9,10} Features of panuveitis, similar to our case, including vasculitis and vitreous opacities, were seen in another case.¹¹ An asymmetric presentation of findings is commonly seen, consistent with our patient's case.

The most important step in the management of CAR is identifying the underlying malignancy. In approximately 50% of cases, CAR precedes the diagnosis of the underlying malignancy, the treatment of which is vital.¹ In addition, treatment of

the ocular disease involves long-term immunosuppression. Despite aggressive treatment with corticosteroids, plasmapheresis, and intravenous immunoglobulins, the ocular prognosis tends to be poor, progressing to vision loss. Two known cases of CAR secondary to a thyroid malignancy resolved with a total thyroidectomy and a significant improvement in vision. One of the cases initially started with local and systemic immunosuppression, including glucocorticoids, and then trialed systemic rituximab, which resulted in an improvement in vision; however, a total thyroidectomy was ultimately needed to fully treat the condition.¹⁰ Our patient had a total thyroidectomy to resect the underlying malignancy; however, because of a loss to follow-up it is unknown whether this was sufficient to resolve the retinopathy.

Cases of CAR secondary to follicular thyroid carcinoma presenting with a uveitis-like clinical picture are rare. In cases like this, care should be taken to ensure an early diagnosis, with the goal of preserving the patient's sight.

Ethical Approval

This case report was conducted in accordance with the Declaration of Helsinki. The collection and evaluation of all protected patient health information were performed in a Health Insurance Portability and Accountability Act-compliant manner.

Statement of Informed Consent

Informed consent, including permission for publication of all photographs and images herein, was obtained before the procedure was performed.

Declaration of Conflicting Interests

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