



Case report

Unilateral retinopathy post perilesional interferon α 2b injections for ocular surface squamous cell carcinoma

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ABSTRACT

Purpose: To describe the clinical course of a patient presenting with unilateral retinopathy after perilesional interferon alpha injections for treatment of ocular surface squamous cell carcinoma.

Observations: A patient, who was being treated with interferon alpha for ocular squamous cell carcinoma, presented with new onset decreased vision in her left eye. Upon examination, she was found to have cotton wool spots and retinal hemorrhages in the affected eye.

Conclusions and Importance: Retinopathy is a well-documented side effect of systemic usage of interferon alpha. However, retinopathy has not been well discussed in the scenario of perilesional injections of interferon. It is important for clinicians to monitor for such pathology when using interferon alpha not only systemically, but also locally.

1. Introduction

Interferon α 2b is a protein that resembles interferons that are secreted from human leukocytes and is most commonly used as an antiviral or antineoplastic agent. Specifically, IFN- α 2b has been used in the treatment in chronic hepatitis B and C as well as off-label treatment for T-cell leukemia, lymphoma and chronic myeloid leukemia.¹ Well documented adverse reactions to IFN- α 2b therapy includes flu-like symptoms (fatigue, headache, chills, nausea) as well as neutropenia and increased aspartate aminotransferase (AST) levels. Ophthalmic adverse reactions associated with systemic IFN- α 2b therapy, though less common, include periorbital edema, blurred vision, conjunctivitis, and retinopathy.^{2,3}

Administered topically, IFN- α 2b eye drops generally have minimal side effects. Subconjunctival and perilesional injections of IFN- α 2b can cause a flu-like syndrome.⁴ Interferon associated retinopathy has not been reported as an adverse effect of perilesional injections for ocular SCC.

2. Case report

A 57-year-old female was referred for decreased vision in her left eye and was diagnosed with left conjunctival SCC. Her past medical history

included controlled hypertension. After refusing surgical treatment for the SCC for personal reasons, she began a course of perilesional IFN- α 2b injections into the inferior fornix (3 million units/injection, 0.5mL) once a week. She reported some discomfort at the inferior fornix injection site and fatigue 8 hours post injections. After her 11th injection while in clinic for her 12th injection the following week, she presented with new complaints of decreased vision in the left eye. Her visual acuity in the left eye declined from 20/20 at the previous exam to 20/60. The right eye anterior and posterior segment exams were unremarkable. The left eye revealed significant ocular surface dryness and regressing ocular SCC. Fundoscopic exam showed multiple cotton wool spots and retinal hemorrhages in the posterior pole and peripapillary regions. The right eye exam was normal.

Fluorescein angiography confirmed an area of hypoperfusion consistent with the previously mentioned cotton wool spot.

The patient was diagnosed with interferon-associated retinopathy and advised to stop interferon injections. The left eye retinopathy resolved and patient was able to resume interferon injections after one month. She experienced no recurrences of the retinopathy.

Nine months later the patient presented with two cysts in the left inferior fornix and the injections were suspended. The patient underwent transconjunctival orbitotomy for the left inferior orbital and eyelid mass. A biopsy was taken and confirmed malignancy by pathology.

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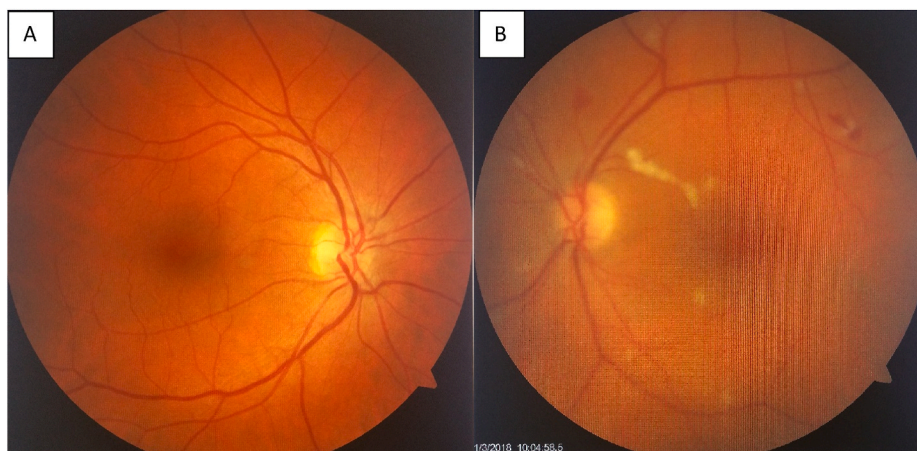


Fig. 1. Fundus photographs of the patient's right (A) and left (B) eye. The right eye (A) appears unaffected. The left eye (B) view is mildly blurred due to corneal dryness, and shows cotton wool spots and small hemorrhages.

Additional imaging was done and patient was referred to ENT and radiation oncology for either surgical or radiational intervention. Five months after injections had been suspended, patient underwent left eye exenteration.⁵

3. Discussion

Interferon α induced retinopathy is a well-documented adverse affect of systemic therapy for diseases such as hepatitis C.^{2,3,6} A systematic literature search of 21 studies showed that the overall incidence of interferon associated retinopathy in hepatitis C patients was 27.7%. This increased to 65.32% and 50.7% in patients with diabetes and hypertension, respectively. This suggests that diabetes and hypertension put patients at higher risk for retinopathy. The prognosis, however, for all patients was good as the resolution of retinopathy was 87%.³

Interferons are immunomodulatory glycoproteins that have both antitumor and antiviral properties. Our immune system releases a variety of interferons when it comes into contact with a virus. In turn, these interferons amplify many pathways and genes, called interferon stimulating genes (ISGs). Some of these pathways are thought to be anti-angiogenic leading to poor perfusion and ischemia in affected tissue.

Guyet et al. propose that an immune complex deposition with leukocyte recruitment causing retinal capillary occlusion and ischemia may be the source of these antiangiogenic effects.⁷

The most definitive evidence of the antiangiogenic comes from Nagaoka et al. Retinal blood velocity and wall shear were measured via doppler velocimetry before and then 2, 4, 8, 16, and 24 weeks after IFN Alpha administration. Both retinal blood velocity as well as wall shear significantly increased ($P < 0.0001$) in all patients at 2 weeks.⁸ This suggests vascular endothelial dysfunction possibly due to immune complex deposition.

Some evidence shows that high pressure injections of corticosteroids can overcome systemic blood pressure and lead to retrograde flow.⁹ A similar mechanism may be at play in the presented case.

As such, the exact etiology of the patient's retinopathy may be likely due to either immune complex deposition leading to ischemic changes or retrograde flow of the interferon injection. Especially due to the onset and cessation, it is most likely interferon associated. The anti-angiogenic affects are a likely cause of this retinopathy. However, given that this has not been documented before, further investigation is required on the mechanisms of this pathology. Physicians giving Perilesional Interferon $\alpha 2b$ Injections must consider regular dilated fundus examination to monitor for this adverse side effect.

Lastly, it is important to note that it is not typical for a patient to receive this many subsequent injections of Interferon $\alpha 2b$. Usually surgery is the first line treatment for ocular surface squamous neoplasias. However, extenuating circumstances of this patient's life lead to delaying of surgery and may be a driver for their outcome.

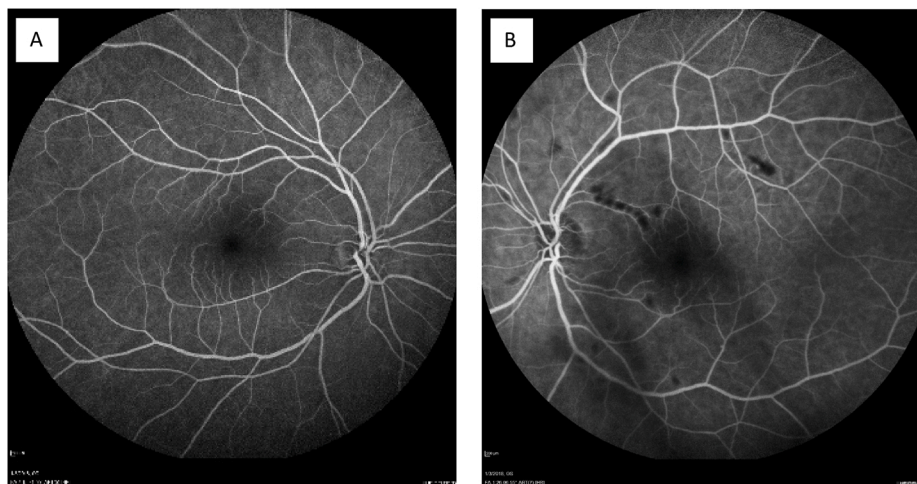


Fig. 2. Fluorescein angiography of the patient's right (A) and left (B) eye. The right eye (A) shows normal filling, however the left eye (B) shows hypofluorescence consistent with the cotton wool spots and hemorrhages seen in Fig. 1.

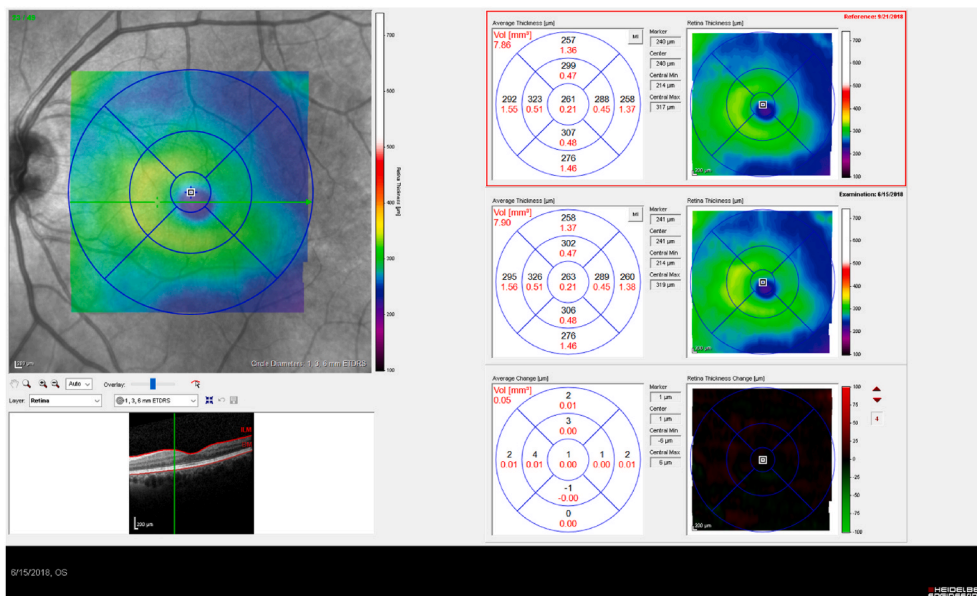


Fig. 3. Thickness map taken months after initial presentation of cotton wool spots shows thinning over time, corresponding with the location of the cotton wool spots.

4. Conclusions

Though Interferon associated retinopathy has been noted with systemic use, it has not been reported with perilesional injections for ocular squamous cell carcinoma.^{10,11} This newly recognized complication is important for clinicians to take note of when treating patients with such therapy, especially in the case of decreased visual acuity of the affected eye. Additionally, patients with diabetes or hypertension may be at higher risk.³ Physicians using Perilesional Interferon α2b injections may consider regular dilated fundus examinations to monitor for retinopathy. Angiography and other imaging modalities may also assist in monitoring for this possible adverse outcome.(see Figs. 2 and 3)

Patient consent

Consent was not needed as no identifying details have been presented in the report.

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