THE **RETINA** PARTNERS

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Case of the Month – July 2019

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A 35 year-old female, with a history of type I diabetes and vitiligo diagnosed in childhood presented with 3 days of left eye pain and progressively decreased vision. Vision was 20/20 in the right eye and 20/800 in the left. There was no afferent pupillary defect. Intraocular pressures were normal. Examination of the right eye was unremarkable including the anterior chamber which was quiet. Examination of the left eye showed 2+ cells without keratic precipitates, posterior synechiae, iris nodules or other signs of prior inflammation. Imaging of the posterior segment of the left eye is shown below.

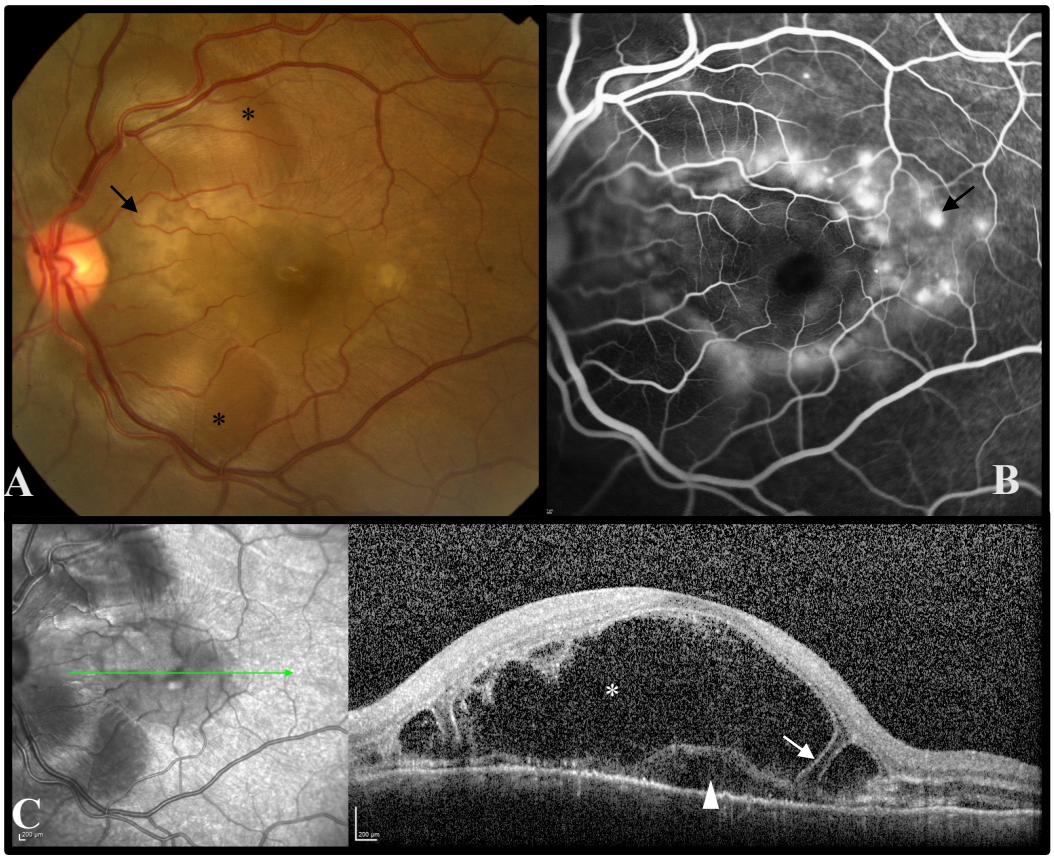


Figure 1: A. Color fundus photograph of the left eye shows clear media and mild optic nerve hyperemia. There are multiple well circumscribed areas of retinal elevation consistent with serous macular detachments (asterisks). There are also prominent yellowish intraretinal deposits, likely representing fibrin (arrow). **B.** Late phase fluorescein angiogram shows multiple focal hot spots which leak late into the angiogram (arrow). **C.** SD-OCT line scan through he fovea shows a large cavity of intraretinal fluid (asterisk), intraretinal septae (arrow) and subretinal fluid (arrowhead).

In contrast to the striking abnormalities in the left eye, ancillary testing of the right eye was normal.

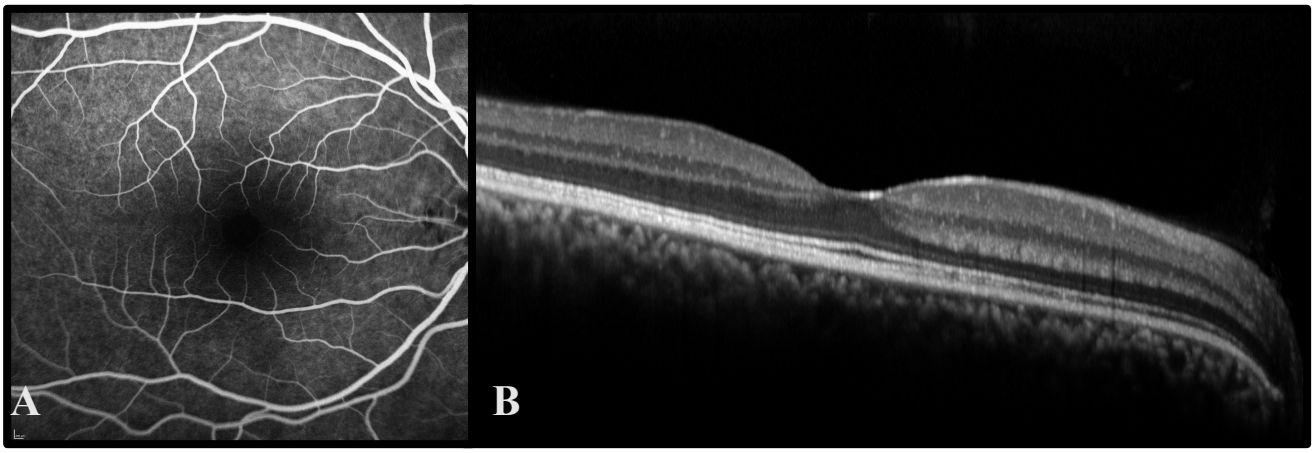


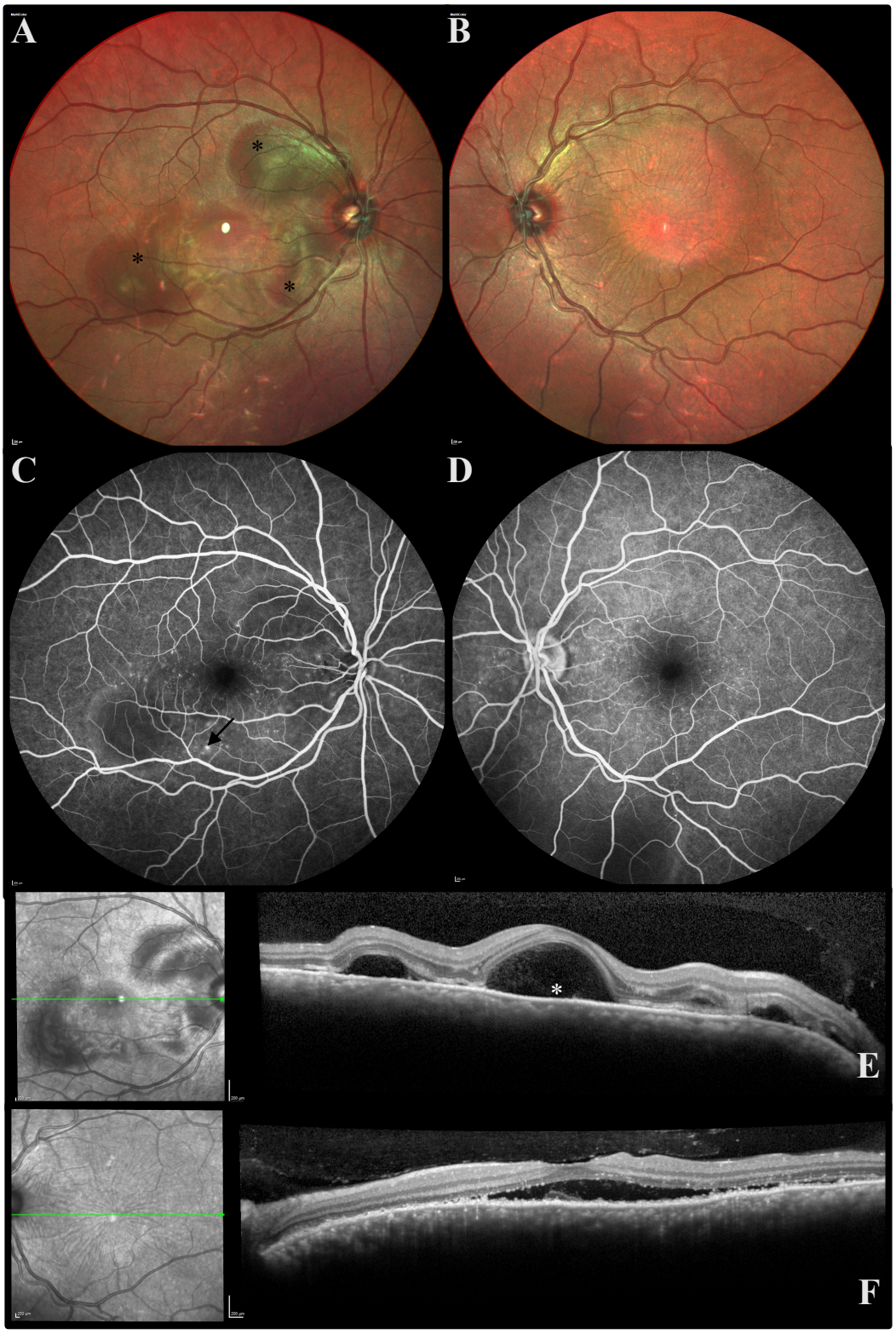
Figure 2: A. Fluorescein angiography of the right eye shows no hot spots, and no other abnormalities. **B.** SD-OCT of the right eye shows a normal foveal contour, retinal layers and choroid.

Differential Diagnosis: Posterior scleritis, Vogt-Koyanagi-Harada Disease, acute leukemia, central serous chorioretinopathy, uveal effusion syndrome, sympathetic ophthalmia, acute posterior multifocal placoid pigment epitheliopathy (APMPPE)

Clinical Course:

Further review of symptoms revealed neck stiffness and recent headaches prior to the onset of visual changes. B-scan ultrasound was performed in clinic (not shown) which showed a thickened choroid, but no t-sign. CBC, blood chemistries, RPR, quantiferon gold and chest X-ray were all within normal limits. Despite the unilateral presentation, there was strong clinical suspicion for early acute VKH. In coordination with the patient's endocrinologist, oral prednisone at a dose of 1 mg/kg was started along with topical prednisolone to the left eye.

The patient returned at 1 week follow up with improvement in vision and resolution of pain in the left eye, but worsening of vision in the right. Visual acuity had dropped to 20/25 in the right eye but improved to 20/70 in the left. Anterior segment examination of the right eye remained unremarkable, and the left showed improvement in anterior chamber cellular reaction. Color fundus photos, OCT and repeat fluorescein angiography are shown below.



F**igure 3: A.** Pseudocolor fundus photo of the right eye shows new multi-focal regions of retinal elevation consistent with serous retinal detachment (asterisks). **B.** Pseudocolor fundus photos of the left eye shows significant improvement in subretinal fluid pockets as compared to initial presentation (seen in Figure 1A). **C.** Fluorescein angiography of the right eye shows multiple new focal hot spots which leak late into the angiogram (arrow). **D.** Fluorescein angiography of the left eye shows significant improvement in focal leakage seen at the time of initial presentation (seen in Figure 1B). **E.** SD-OCT imaging of the right eye shows new pockets of subretinal fluid (asterisk). **F.** SD-OCT imaging of the left eye shows significant improvement in subretinal fluid as compared to initial presentation (seen in Figure 1C).

Given the drastic improvement in the left eye, the patient was continued on prednisone. Over the following week, subretinal and intraretinal fluid pockets resolved and visual acuity returned to 20/25 OU. Because of poorly controlled diabetes, and the need for prolonged immunosuppressive therapy, rheumatology was consulted and the patient was started on CellCept. Over the ensuing 3 month period, oral steroid was slowly tapered. At most recent follow up, the patient remained quiet in both eyes. Visual acuities returned to 20/20 OD and 20/25 OS. SD-OCT images are shown below.

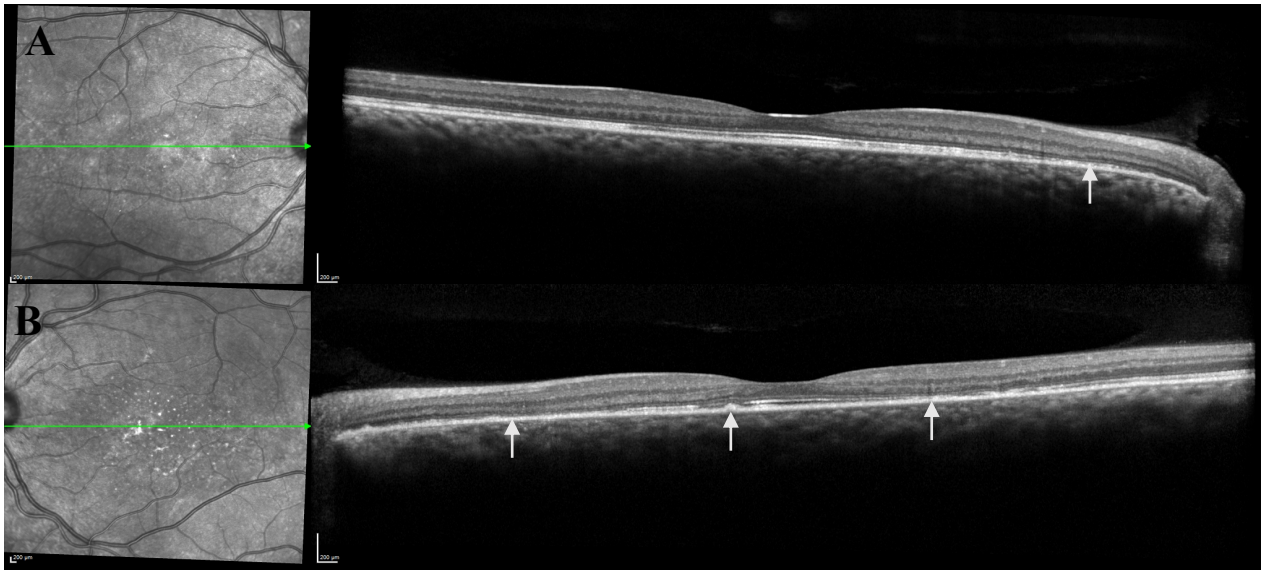


Figure 4: A. SD-OCT imaging of the right macula at 4 month follow up shows complete resolution. Minimal RPE abnormalities can be seen in the peripapillary area (arrow). **B.** Follow up SD-OCT imaging of the left macula shows resolution of subretinal fluid with residual RPE and ellipsoid zone changes (arrows)

Discussion:

Vogt-Koyanagi-Harada Disease (VKH) is a bilateral granulomatous panuveitis caused by an immune-mediated process directed at melanocyte-containing tissues. The disease most often effects individuals of pigmented races, specifically those of Asian, American Indian and Hispanic descent. It is relatively uncommon, representing less than 4% of all uveitis referrals in the United States. It is important to recognize, as early and aggressive therapy is essential to preserve vision.

The clinical presentation of VKH can be variable, depending upon the stage of the disease at presentation. Classically, VKH progresses through four well defined phases – the prodromal stage, acute uveitic stage, chronic uveitic stage and chronic recurrent stage.

The prodromal stage is defined by a viral-like syndrome which may include headache, nausea, fever and malaise. This typically precedes the onset of ocular symptoms by days to weeks. The acute uveitic phase occurs next. Patients present, as ours did, with pain and blurred vision. Usually both eyes are affected at the time of presentation, but as in our case, occasionally one eye may be affected first, followed days later by the contralateral eye. Examination will reveal varying degrees of anterior segment inflammation, optic nerve hyperemia, and thickening of the choroid with overlying serous macular detachments (Figure 1). Ancillary testing with OCT and fluorescein angiography can be very helpful in confirming the diagnosis at this stage (Figures 1 and 2). OCT imaging will show a thickened and infiltrated choroid, and characteristic subretinal and intraretinal fluid accumulations. Fluorescein angiography will show multiple pin point foci of hyper-fluorescence which leak late in a “starry sky” pattern. If not treated aggressively and early, the inflammation initially confined to the posterior segment will become increasingly diffuse with progressive involvement of the anterior segment structures.

VKH next progresses through the chronic uveitic stage, also called the convalescent stage. This usually begins several weeks after the onset of acute uveitic stage and is defined by progressive choroidal depigmentation, peripapillary atrophy, disc pallor and development of focal depigmented peripheral chorioretinal scars. Depigmentation of the choroid unmasks a deep red-orange hue, leading to what has been termed the “sunset glow” appearance. It is during this phase that some patients may also develop vitiligo.

The final stage of VKH is the chronic recurrent stage. This late stage is characterized by low levels of chronic anterior granulomatous uveitis which may be resistant to local and systemic corticosteroid therapy. Patients in this stage may therefore require other systemic immunomodulatory treatment. Vision loss can occur during this phase as a result of cataract, uveitic glaucoma, and occasionally the development of choroidal neovascular membranes. Fortunately, recurrent posterior uveitis and exudative detachments are rare. There is some evidence that early and prolonged aggressive immunosuppressive therapy during the acute phase of the disease may prevent progression to the chronic uveitic stage, therefore resulting in better outcomes.

The diagnosis of VKH disease remains clinical, and partially a diagnosis of exclusion. Sympathetic ophthalmia, which can present with nearly identical ocular findings, is easily ruled out by the absence of past penetrating ocular trauma or surgery. Although few diseases can mimic the complete presentation of VKH, it is nonetheless prudent to rule out infectious diseases (TB, syphilis, lyme disease), hematologic malignancy, and when the presentation is atypical, other inflammatory disorders of the choroid (lupus, sarcoidosis). While no laboratory test can confirm the diagnosis, lumbar puncture may reveal pleocytosis, and although this is typically not necessary to pursue, it can be helpful in atypical cases. Detailed specific diagnostic criteria have been set forth by an international panel of experts and are available at the link below.

Systemic corticosteroid therapy remains the mainstay of treatment. Early and aggressive management with high doses and prolonged treatment (typically greater than 6 months duration) can rapidly decrease intraocular inflammation and may prevent progression to the chronic recurrent stage of the disease. With early recognition and appropriate management visual outcomes can be very good, with 2/3 of patient retaining acuities better than the 20/40 level.

Our patient was atypical in several respects. First, she presented with sequential ocular involvement despite high doses of prednisone (80 mg daily). This illustrates the need for high doses of steroid, as even a dose of 80 mg daily was insufficient to completely suppress her exuberant inflammation. Second, the patient was a type I diabetic with marginal glucose control at baseline. Early co-management with endocrinology was important for diabetic control while on prednisone, and the patient was transitioned to a steroid sparing agent (CellCept) earlier than is typical in order to avoid prolonging this side effect. Fortunately, she has continued to do very well.

Take Home Points

- VKH is a bilateral granulomatous pan-uveitis with extraocular manifestations, most commonly effecting people of Asian, Hispanic and American Indian descent. It is characterized by four well defined clinical stages.
- The diagnosis of VKH is clinical. The detailed diagnostic criteria for VKH can be found at https://www.ajo.com/article/S0002-9394(01)00925-4/fulltext
- Ancillary testing with fluorescein angiography, optical coherence tomography and B-scan ultrasound can be helpful in making the diagnosis.
- Early diagnosis and management with high doses of corticosteroids is critical to ensure optimal visual outcomes.

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