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Case of the Month – March 2021

Presented by Christian Sanfilippo, MD

A 63-year-old Female presented to the emergency department complaining of five days of severe headache, body aches, persistent fever, eye pain and floaters in both eyes. In the emergency department, her temperature was measured at 102.5 F. Rapid flu and COVID19 tests were negative. Complete blood count, blood chemistry and chest x-ray were also unremarkable. Urinalysis was positive for leukocyte esterase. The patient was started on antibiotics for presumed urinary tract infection and discharged home. Over the ensuing 2 days, she complained of worsening backpain, persistent headaches, floaters and visual decline in the left more than the right eye. She was seen by her primary care provider for follow up, by which time her fever had resolved, but headache, malaise and back pain persisted. Additional labs were unrevealing. Because of her worsening vision complaints, and unknown diagnosis she was referred for evaluation.

On presentation to our office, the patient's visual acuity was 20/30 in the right eye and 20/250 in the left eye. Intraocular pressures were normal. She had 1+ anterior chamber cells in the right eye and 2+ cells in the left. Posterior segment examination revealed 1+ vitritis in the right eye, 2+ vitritis in the left and bilateral scattered yellowish chorioretinal lesions with early pigmentation. Additional testing is shown below.

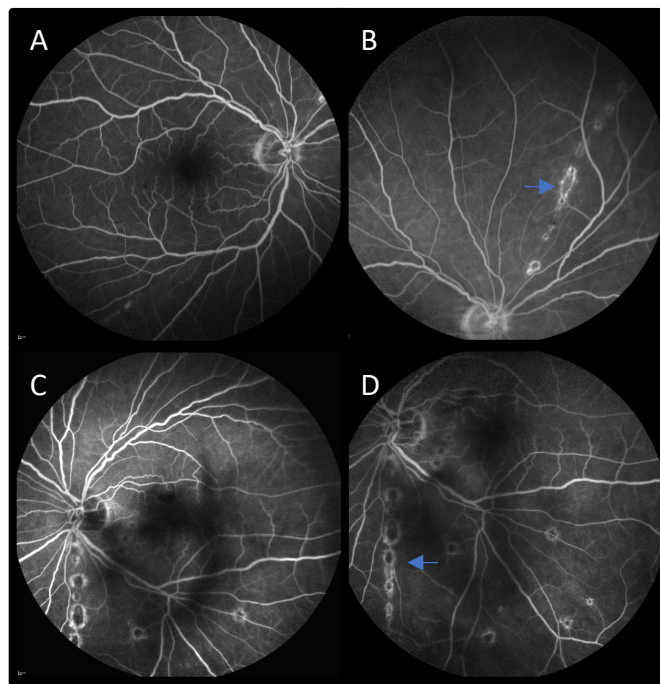


Figure 1: Fluorescein angiography of the right eye (A and B) and left eye (C and D) performed at time of presentation showed multiple chorioretinal lesions in both eyes and shadowing from vitritis in the left eye. Note the linear pattern of chorioretinal lesions in both eyes seemingly emanating from the optic nerve (arrows).

Differential Diagnosis: Multifocal choroiditis and panuveitis (MCP), Punctate Inner Choroiditis (PIC), Presumed Ocular Histoplasmosis Syndrome (POHS), fungal chorioretinitis, viral chorioretinitis

Additional History: Based on the linear pattern of chorioretinal lesions, and history of persistent fevers, severe headache, malaise and back pain, the patient was questioned about recent mosquito bites. This prompted her to reveal that a few days prior to symptom onset she had noticed several mosquito bites on her legs, and in fact, had taken a photograph of one of the mosquitos which had bitten her. She noted that she had recently noted this new type of mosquito in her neighborhood.

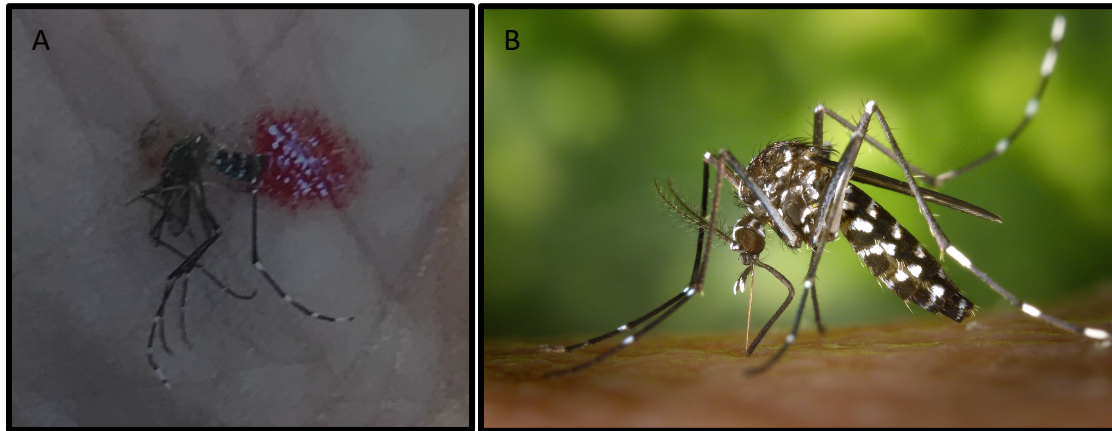


Figure 3: **A.** Image captured by our patient of one of the mosquitos which had bitten her. Note the white, striations on its legs and body, a characteristic of *Aedes albopictus*, also called the Asian Tiger Mosquito. **B.** Comparison to a higher quality, professional photograph of the same mosquito species.

Clinical Course: Based upon the entirety of information obtained, there was a high degree of suspicion for acute West Nile Virus infection. This was discussed with the patient's primary care provider and laboratory confirmation tests were sent. The patient was started on topical prednisolone every two hours to manage the anterior uveitis. IgM and IgG antibodies returned positive for West Nile Virus confirming the diagnosis. Because the patient's systemic condition was clinically improving, in consultation with an infectious disease specialist, close observation was recommended as an outpatient. Over the course of the ensuing month, the patient's systemic and visual symptoms improved. Her vision ultimately returned to 20/20 in both eyes. Color images were obtained at 2 month follow up and are shown below.

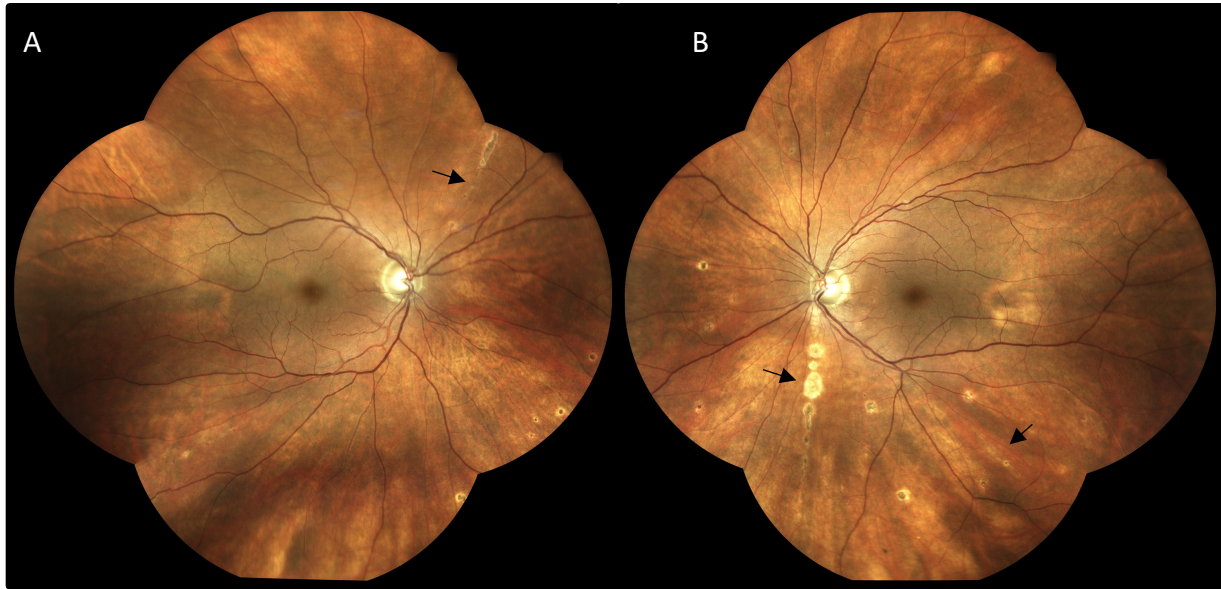


Figure 3: Color photographs of the right (A) and left (B) retinas show resolution of vitritis and pigmented, inactive chorioretinal scarring, some of which form linear patterns (arrows).

Discussion:

West Nile Virus (WNV) is a mosquito borne pathogen that causes acute febrile illness in humans which can progress to meningitis, encephalitis and even death. Cases of WNV were first documented in the United States in 1999 when an outbreak of encephalitis in Queens, New York was ultimately traced to the virus. Prior to this, cases of WNV were isolated to Africa, Asia, the Middle East and Europe. Since 1999, the virus has spread across the United States and is now endemic. Disease caused by WNV has been reported in all 50 states, Puerto Rico and the District of Columbia.

The WNV transmission cycle begins with a mosquito biting an infected bird. Several mosquito species can carry West Nile Virus including the common Culex mosquito as well as newer invasive species like the Asian Tiger Mosquito. Birds infected with WNV develop high levels of virus in their blood stream (much higher than humans and other mammals). If a mosquito bites a bird with a high viral load, the mosquito can later bite and transmit the virus to a human. Because humans do not develop high levels of virus in their blood stream, a mosquito cannot become an infected carrier by biting a human.

Fortunately, the majority of people exposed to WNV remain asymptomatic. In fact, serologic studies suggest that 70-80% of infections are subclinical or asymptomatic. The majority of those who do become symptomatic develop fever, headaches, fatigue, body/joint aches, gastrointestinal symptoms and in some cases a maculopapular rash. Fevers tend to last for about one week, but the fatigue and body aches can persist in some for months. It is estimated that 1% of those infected will develop the much more serious neuroinvasive form of the disease which consists of meningitis, encephalitis and in the worst cases, acute flaccid paralysis. The mortality rate of neuroinvasive disease is 10% without paralysis and may be as high as 30% in those who develop encephalitis with flaccid paralysis. In California, there were 197 reported cases of WNV in 2020, but 151 were reported to be neuroinvasive. If only 1% of infected individuals develop neuroinvasive disease, this would indicate that the true number of infections (symptomatic and asymptomatic) in California in 2020 is very under reported, and may have been as high as 15,000.

Ocular involvement is common among patients with the neuroinvasive form of the disease, occurring in up to 80% of these individuals. However, it is thought to be uncommon among those with the milder form of febrile illness. The most common ophthalmologic manifestation is multifocal chorioretinitis, which like in our patient,

presents with a unique linear pattern of lesions, often emanating from the optic nerve. Some have hypothesized that this pattern is due to migration of virus along the optic nerve with further extension along the nerve fiber layer of the retina. Alternatively, virus may be carried by the choroidal circulation with lesions falling along the choroidal vasculature. Recognition of this unique pattern was the clue which ultimately led to our patient's diagnosis.

Clinically, patients may also develop anterior uveitis, vitritis, optic neuritis and retinal vasculitis. As a result, affected individuals may complain of floaters, eye pain and decreased vision during the acute episode, but fortunately the ocular disease is typically self-limited. The vast majority of patients will regain their baseline visual acuity, with the exception of those with macular scarring, or other rare complications from optic neuritis or vasculitis.

Our case is unique in a few ways. First, West Nile Virus was suspected and diagnosed on the basis of the patient's eye examination, after trips to the emergency department and primary care setting proved unsuccessful in establishing a diagnosis. Second, ocular involvement is thought to be rare in the non-neuroinvasive form of the disease. Therefore, one might not expect to diagnose acute West Nile Virus in an individual who is not seriously ill. This suggests that our patient either had a mild form of neuroinvasive disease (mild meningitis), or perhaps ocular involvement is underrecognized in the more common, non-neuroinvasive forms of the illness.

Finally, and perhaps with the most public health implications, is the photograph of the *Aedes albopictus* mosquito (commonly called Asian Tiger Mosquito) that our patient took. This is an invasive species to Los Angeles, which has been traced to a shipment of bamboo from China in 2001. *Aedes albopictus* is worrisome since it is known to transmit a variety of mosquito borne diseases not transmissible by the predominant mosquito species in Los Angeles called *Culex*. These diseases include Dengue Fever, yellow fever, Zika, and Chikungunya. Furthermore, *Aedes* species can breed in tiny amounts of water (as small as a bottle cap full) making it very difficult to remove breeding areas. Whether these other diseases make their way to California remains to be seen, but certainly West Nile Virus has. As such, all physicians, including eye care providers, should be aware of the signs and symptoms of the disease.

Take Home Points

- West Nile Virus is endemic to Los Angeles
- West Nile Virus can cause chorioretinitis with a distinct linear pattern of lesions often emanating from the optic nerve head
- Ocular disease associated with West Nile Virus is typically self-limited, but proper identification can aid in the diagnosis of this sometimes deadly infection



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