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An unusual case of unilateral chorioretinitis and blind spot enlargement associated with asymptomatic West Nile virus infection

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ABSTRACT

Purpose: To report a case of unilateral chorioretinitis and acute blind spot enlargement occurring in a patient with asymptomatic West Nile virus (WNV) infection.

Observations: A 28-year-old Hispanic woman, residing in Puerto Rico, presented with an 18-month history of photopsia and a visual field disturbance of the left eye. She had no history of other neurologic symptoms or viral-like illness concurrent with the onset of her symptoms. Corrected visual acuity was 20/20 on both eyes. The left fundus revealed multifocal chorioretinitis, at different stages of evolution, several creamy orange lesions on the mid-periphery along with multiple small punched out lesions, some of which were following a curvilinear pattern distribution. Visual field testing revealed physiological blind spot enlargement on the left eye. Serum WNV antibody serology revealed negative IgM (< 0.90) and positive IgG (1.58, < 1.30 reference). The patient was treated with oral prednisone, 60mg for two weeks, followed by a 13-week taper of therapy, which resulted in normalization of the visual field defect.

Conclusion and Importance: Our case raises the possibility that ophthalmic manifestations may occur in some patients with asymptomatic WNV infection. It also suggests that acute blind spot enlargement may also be part of the myriad of ophthalmic manifestations present in WNV patients. In such instances where acute blind spot enlargement is present, oral prednisone may result in improvement and subsequent normalization of the visual field defect. Besides, our case provides evidence to suggest that primary WNV transmission is possible in Puerto Rico.

1. Introduction

West Nile virus (WNV) is an arthropod-borne arbovirus in the family Flaviviridae, genus Flavivirus.[1,2] It was first isolated in the West Nile district of Uganda in 1937 and finally recognized as a cause of severe human meningitis and encephalitis in 1957.[2] It has been documented in Africa, Europe, Asia, Australia, and, more recently, in the Americas.[1] In 1999 the first North American case of human WNV encephalitis was recorded in New York City. Subsequently, cases continued to spread westward through the United States in the following years. In 2005, WNV human infection was reported in the Caribbean islands of Cuba and La Hispaniola.[3,4] We believe that locally acquired WNV transmission and disease in humans is plausible in the island of Puerto Rico.

The life cycle of WNV involves a non-human primary vertebrate host, usually birds, and a primary arthropod vector.[2,5] Humans and other mammals can develop a clinical illness, but usually are incidental hosts and do not appear to contribute significantly to the spread of the virus.[5] Vectors for WNV include, but are not limited to, Aedes, Ochlerotatus, and Culex species.[1,5,6] The latter is highly abundant in Puerto Rico; specifically, *Culex quinquefasciatus*.[7] In 2002, Depuis and colleagues, described serological evidence of WNV infected birds (*Mniotilta varia*) in the island of Puerto Rico, granting plausibility to a local primary infection.[8]

Infection with WNV will most likely be asymptomatic.[2] Symptomatic patients will usually experience WNV fever, most commonly manifested by high-grade fever, weakness, myalgia, headaches, and gastrointestinal symptoms.[2,9] WNV may also present as a neuroinvasive disease in 1 in 150 patients.[10] These patients often present with a fever that develops into neurological abnormalities such as meningitis, encephalitis, respiratory failure, flaccid paralysis, and ocular disease.[2] WNV-specific IgM antibodies may be detected in the serum of affected individuals as early as three days following the onset of illness and

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usually persist for 30–90 days.[11] The presence of WNV serum or CSF IgM antibodies provides good evidence of WNV infection; however, cross-reaction with other flaviviruses is common.[11] Following a symptomatic or asymptomatic infection, and shortly after the onset of IgM antibodies, WNV IgG antibodies will emerge. These will persist for many years, serving as evidence of prior WNV infection.[11]

Ophthalmic manifestations of WNV infection include congenital scarring due to intrauterine transmission, uveitis without focal lesions, optic neuritis, occlusive retinal vasculitis, and chorioretinitis.[2] When presenting as a multifocal chorioretinitis, the lesions may be either scattered or arranged in typical curvilinear arrays.[2,9] To our knowledge, our case if the first description in the medical literature of acute blind spot enlargement in a patient with fundus findings and serology suggestive of WNV chorioretinitis. Our case also raises the possibility of primary WNV infection occurring within the island of Puerto Rico.

2. Case report

A 26-year-old Puerto Rican woman presented in December 2017, for a second opinion with regards to multiple retinal lesions on her left eye, whose etiology remained unestablished following an extensive work-up and evaluation by multiple, retina and uveitis specialists. For at least 18 months, she had complained of photopsia and a visual field disturbance on her left eye (OS).

Her examination revealed 20/20 corrected vision in both eyes (OU) wearing (−7.00 + 0.50 × 180) in her right eye (OD) and (−6.50 Sphere) OS. The intraocular pressure was in 15 mmHg OU. Pupils were round, reactive to light and accommodation, and without evidence of an afferent defect. The slit-lamp exam revealed 1+ nuclear sclerosis OU and was otherwise unremarkable. Dilated fundus exam revealed no vitritis OU. The right fundus exam was unremarkable. Both optic disks were of normal color and appearance, with well-demarcated margins. The left fundus revealed multifocal chorioretinitis at different stages of evolution. There were several creamy orange lesions present along the mid-periphery on the superior quadrants. Peripherally, there were multiple small punched out lesions, with some of those present in the superonasal periphery following a curvilinear pattern distribution (Fig. 1A).

Humphrey visual field (HVF) examination was normal OD and revealed physiological blind spot enlargement with superior extension OS (Fig. 2A and B). Fluorescein angiography revealed late disk hyperfluorescence and multiple transit defects that correlated with the multiple punched out lesions, some of which had developed a hypofluorescent center (Fig. 3A and B). Late indocyanine green angiography views revealed multiple hypocyanescent lesions OS nasal to the disk and temporal to the macula, most of which did not correlate with the lesions present clinically (Fig. 3C). Macula and optic nerve optical coherence tomography (OCT) were unremarkable.

A review of the work-up performed during the 18 months before presentation revealed abnormal complete blood count with leukocytosis (14.42 × 10^3/μl) with a neutrophilic and monocytic predominance: urinalysis and serum chemistry were normal. FTA-Abs, reactive plasma reagent, and HIV testing were negative. HSV I and HSV II IgG were negative. HSV I and II IgM were positive. Antinuclear antibodies (ANA) tested positive 1:160, homogenous pattern. SS-B, anti-Smith, and anti-RNP tests were negative. The angiotensin-converting-enzyme was elevated (92 units/L) while serum lysozyme was within normal limits (6.5 μg/ml). A chest CT scan without contrast performed to rule out sarcoidosis showed no hilar lymphadenopathy and unremarkable lungs. A review of Humphrey visual field testing performed 18 months before the presentation revealed left blind spot enlargement (Fig. 2A).

Past medical history was remarkable for bronchial asthma, controlled without medications, last exacerbation treated with IV methylprednisolone in 10 months before our initial exam. The review of systems was positive for photopsia and visual field disturbance; however, all other systems were negative. She had traveled to Haiti in the summer of 2015 and also to the continental United States in 2016, where she visited the states of Florida, North Carolina, Missouri, New York, and Massachusetts. Her brother, who lived in the same household as the patient, had been diagnosed with WNV meningitis in January 2016 and had no history of travel outside Puerto Rico. The patient reported that her brother's cerebrospinal fluid had been sent to the United States Centers for Disease Control and Prevention for analysis and that the results were positive for WNV infection. She also reports that there were no febrile family members or any other members suffering from other arboviral infections such as dengue fever while her brother was ill with WNV meningitis.

A working assessment of multifocal chorioretinitis with acute blind spot enlargement of the left eye was made. After a discussion of treatment alternatives, the patient was started on 60mg of oral prednisone daily; this dose was kept for two weeks and subsequently tapered over 13 weeks. She was monitored both clinically and with serial 30-2 Humphrey visual field testing. Serum WNV antibody serology was ordered yet obtained after the patient had concluded her oral corticosteroid therapy, it revealed negative IgM (< 0.90) and positive IgG (1.58, < 1.30 reference). As expected, WNV RNA was not detected in the patient's serum.

Immediately following the institution of therapy, the patient felt symptomatic relief. Clinical improvement of the choroidal lesions was noted on the 2-week follow-up visit post-initiation of therapy. The last fundus photographs taken two months after completion of therapy reveal further maturation of the choroidal lesions (Fig. 1B). The last Humphrey visual field exam, which was done three months after completion of therapy, revealed normalization of the visual field with the resolution of the left blind spot enlargement (Fig. 2C).

3. Discussion

To our knowledge, this case represents the first-ever report of ophthalmic manifestations of WNV occurring in a resident of Puerto Rico. Of particular importance is the fact that this patient had a family

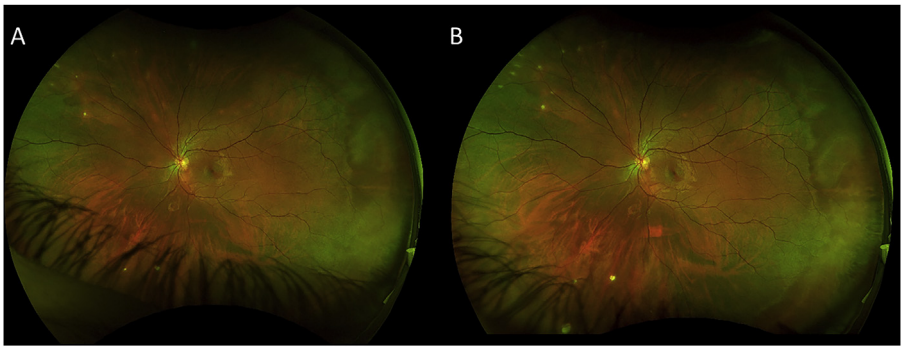

Fig. 1. Left fundus ultra-widefield color photography. A. Findings upon presentation reveal scattered creamy orange lesions on superior the mid-periphery and multiple small punched out lesions, some of which follow curvilinear pattern distribution. B. Two months following completion of therapy, there is further maturation of the chorioretinal lesions, with some of them becoming atrophic. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

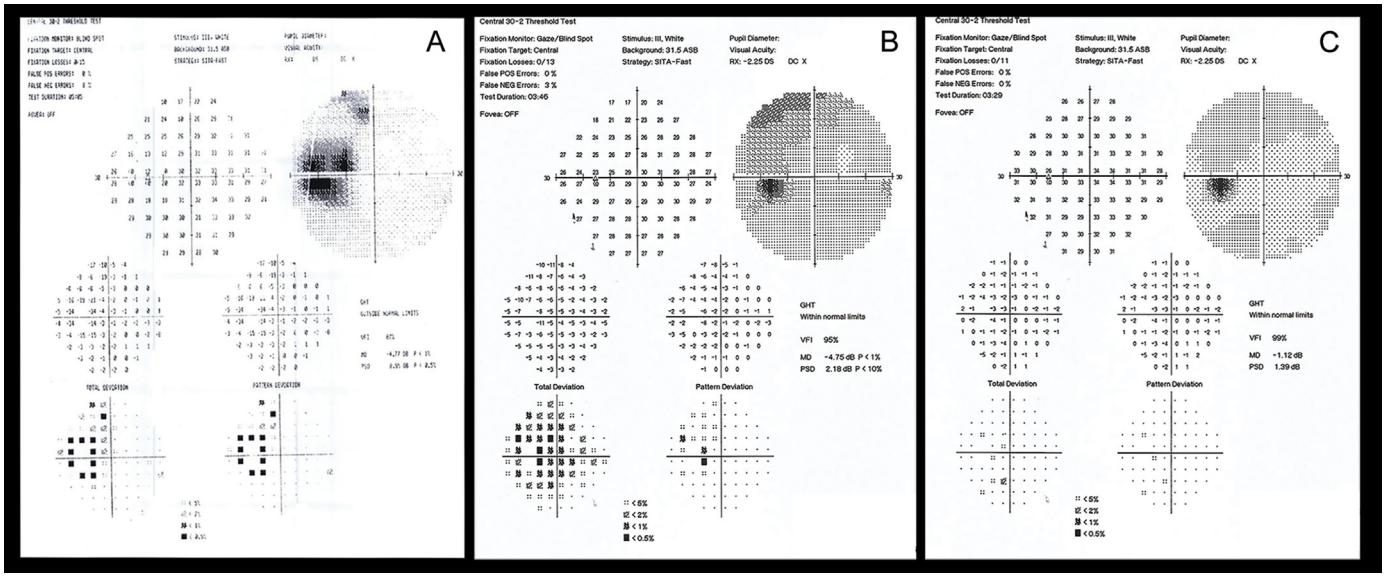

Fig. 2. Left eye visual field progression (Humphrey, Central 30-2 Threshold Test, stimulus III, white, SITA-FAST). A. Eighteen months before presentation, revealing enlargement of the physiologic blind spot with superior extension. B. Upon presentation, there is a persistence of the visual field defect. C. Seven months after the initiation of oral corticosteroids, and three months following the completion of therapy, resolution of the visual field defect is noted.

member of the same household, who had never traveled outside of Puerto Rico, diagnosed with WNV meningitis. The presence of both the primary end host and the disease vector, on the island of Puerto Rico, have been established in the scientific literature; therefore, the potential does exist for primary WNV infection of humans in the island.[7,8,12] Although our patient had traveled outside of Puerto Rico to zones where WNV human disease is prevalent, the potential exists for our patient, to have acquired the infection locally.

Our patient's examination revealed creamy choroidal lesions and punched out lesions in a curvilinear pattern, the latter, a feature typical of WNV chorioretinitis and not of infection by other flavivirus species know to be prevalent in the island of Puerto Rico such as dengue or chikungunya.[9,10] Although our patient had unilateral disease, which is atypical for WNV chorioretinitis, such unilateral cases have been described in the past.[2] Our patient also presented with an optic neuropathy a feature that also has been described in human WNV infection.[9] The fact that our patient had asymptomatic WNV disease makes this particular case unusual, as most previously reported cases had some degree of constitutional or neurological symptoms from WNV infection.[2,9] However, in most instances, WNV infection is asymptomatic or has self-limiting flu-like symptoms that last for approximately one week.

Since 1999, WNV has become an ever-present disease-causing agent in the Americas. As modern travel causes this virus to expand its geological borders, physicians must be aware of its presence and include it in the differential diagnosis of patients presenting with acute neurological symptoms or the typical findings on the fundus exam. We also believe WNV infection should be considered as part of the differential diagnosis of patients presenting with acute blind spot enlargement.

4. Conclusions

Our case raises the possibility of ocular manifestations being present in some patients with otherwise asymptomatic WNV infection. Our case also suggests acute blind spot enlargement may occur in patients with WNV chorioretinitis. According to our findings, the condition may persist for several months post-infection and may respond well to treatment with high dose oral corticosteroids. We also have provided evidence supporting the potential for primary WNV transmission to occur on the island of Puerto Rico.

Although our patient had extensive travel to areas where WNV transmission to humans has been well documented, the fact that she

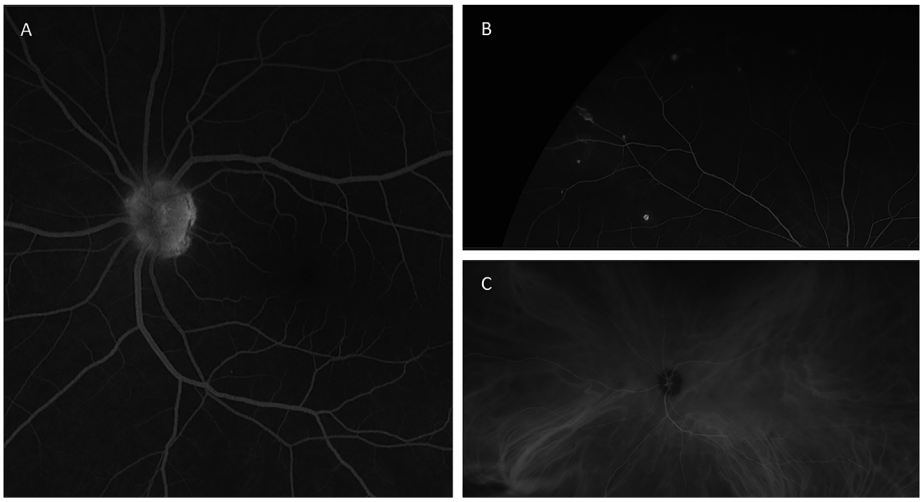

Fig. 3. Fluorescein angiography of the left fundus revealing late disk hyperfluorescence and multiple transit defects that correlated with the multiple punched out lesions, some of which have a hypofluorescent center, A and B respectively. C. Late phase indocyanine green angiography revealing multiple hypocyanescent lesions nasal to the disk and temporal to the macula, most of which do not correlate with the lesions noted clinically and on the color photographs.

had a household family member, who had never traveled outside of Puerto Rico, diagnosed with neuroinvasive WNV disease raises the probability of local transmission of the virus. This possibility is supported by the fact that both the vector for disease transmission and WNV infected birds have been observed in Puerto Rico.[7,8] We believe increased awareness should be raised among the medical community with regards to the fact that the island of Puerto Rico may very well be a source of human WNV infection.

Patient consent

This report does not contain any personal information that could lead to the identification of the patient. The patient provided written consent for the publication of this clinical case.

Disclosures

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